

Examine.com

Supplement-Goals Reference Guide

Supplements - Health Goals

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The Supplement-Goals Reference Guide

"What supplements should I buy?" is an extremely common question. While it seems simple, the reality is that there is no one-size-fits-all answer. Depending on your situation (young, old, athletic, inactive), your health goals (general health, diabetic), and other attributes, each person's supplementation approach should be individualized to their needs.

This reference will be your guide to your individualized approach. It is a quick way for you to learn:

- Supplements, and what health goals they affect
- Health goals, and what supplements have an effect on them

Example 1 - Vitamin D (Supplement -> Health Goals)

This reference guide lets you quickly and easily scan supplements and what they can do for you.

So you've heard that Vitamin D is great for you. And you're wondering: what does it do? Looking at the reference table, you will see a whole host of positive effects that vitamin D has. It helps slightly decrease cardiovascular disease, it notably decreases the risk of colorectal cancer, it has a notable effect in decreasing risk of falls, and so forth.

Example 2 - Blood Glucose (Health Goal -> Supplements)

This is where the Supplement-Goals Reference Guide **really shines**. It lets you find which supplements you should consider taking, based on your goals.

Let's say you are diabetic - a big concern for you would be your blood glucose levels. Looking at the reference table for blood glucose, you can see that quite a few supplements (panax ginseng, psyllium, stevia, and more) can slightly decrease your blood glucose. You can also see that caffeine can slightly increase your blood glucose levels, and that berberine has a strong effect in decreasing your blood glucose level! Thus, it may be prudent for you to supplement with berberine.

With almost 200 different health goals listed, you can quickly see which supplements are effective (and which aren't) at achieving whatever your goals are.

How the Data is Accrued

Let's take a step back and see how scientific research progresses. Please note this will be a simplification of the actual process, meant to clarify important issues.

Studies are usually first conducted on research animals, often rats (although other rodents and sometimes fruit flies are used, depending on what is being researched). Research animals are cheap, easier than humans to control, have fewer ethical issues, and allow researchers to see the effect of any supplement over multiple generations very quickly.

Roughly around the same time, studies are performed in vitro. These are animal cells isolated from the living organism. The classical way of looking is to place specific human cells (e.g., muscle tissue) in a petri dish, and then applying supplements directly to those cells. While these studies have their complications if used by themselves, they allow research to fine-tune the knowledge of the supplement on a cellular level, and greatly help with completing the full picture.

After sufficient testing in animals and in vitro comes *human testing*. This is when supplements are ingested by humans, and we get to see how the supplement works in your body. It is not rare to find some supplement that is very promising in either rat or in vitro studies, but nearly useless in humans.

A great example of this problem is glutamine. In vitro testing showed glutamine to be amazing for building muscle. Yet when glutamine is ingested by a healthy adult, the small intestines basically keep all the glutamine for themselves. Very little of that glutamine gets to your muscles. So while glutamine was very promising in vitro, it was a failure in human testing.

All of the scientific research presented in our Supplement-Goals Reference Guide (over 2000 references) is human studies. While we factor in animal studies and in vitro studies while building up our knowledge on topics, we do not include them in our conclusions.

How to Read the Tables

The reference tables hold a vast amount of data, and we want to take a moment to explain how to read them.

Level of Evidence

This is very important. The reality is that the quality of evidence varies. Supplements like creatine and fish oil are heavily researched, while more esoteric supplements such as Pueraria mirifica and lavender do not have much information associated with them.

To help clarify how confident we are, we give a letter grade between A and D. To break it down:

- **A** - lots of evidence is present. You can rely on this to be true.
- **B** - there is ample evidence, but more research could be done.
- **C** - there is evidence, but not a lot of it.
- **D** - the evidence is very weak.

Overall, you can feel pretty safe that anything with confidence A or B works. Anything with C or D is an “iffy” proposition - it could work, or it could not. There simply is not enough evidence to make a call either way.

Supplement / Goals

For a supplement, we cover multiple health goals. For a health goal, we cover multiple supplements.

Change

This tells you if the result found was an increase, a decrease, or none. For example, if we look at blood pressure, we can see that supplements such as fish oil and grape seed extract decrease blood pressure, supplements such as creatine and alpha-lipoic acid have no effect on blood pressure, and supplements such as caffeine and ephedrine actually increase blood pressure.

Sometimes research will find that both an increase and a decrease occur. A good example of this is alcohol and its effect on testosterone. It turns out that for a short duration, alcohol increases your testosterone levels, but after a while it causes levels to drop!

Magnitude of Effect

This will tell you how potent the supplement is. There are four potential values:

- “-” - no observable changes were found.
- “**Minor**” - a change was noted, but it was small in magnitude. Technically the supplements work, but you won't be likely to notice a discernible change.
- “**Notable**” - the change is strong enough to be noticeable or measured.
- “**Strong**” - the change is quite strong. This level of classification is reserved for pharmaceutical-grade effects. It is rarely given.

Scientific Studies

Proper scientific research is always open about the data used to obtain supporting conclusions. We link to all the scientific studies we analyzed to reach our conclusions. The page we link to even gives demographic information (when available) such as age, body type, gender, and more. We also include comments specific to each study.

Comments

This is a very important section. The comments section clarifies any ambiguity and nuances that need to be stated. Observe our previous example about alcohol and its effect on testosterone. It is in the comments section that we clarify that the increase is in the short term, whereas long term usage decreases testosterone.

Get Started

The above information should make the Supplement-Goals Reference Guide a lot more usable and useful to you. It will help you unlock the best strategy for you to adopt with supplements.

See the [Supplement Reference](#) or the [Health Goals Reference](#).

So what Supplements Should I Buy?

Multivitamins

To be blunt, multivitamins tend to be useless (even though vitamin and mineral supplementation has a lot of potential). While the concept is quite novel (cover most dietary deficiencies in one pill), the execution tends to have quite a few glaring flaws:

- Getting the recommended daily allowance (RDA) does not mean you are getting the optimal dosage. The RDA has been set up to allow for a minimum level of health, not optimal. A great example is Vitamin D - while the RDA is 400-800 IU, the optimal levels tend to be > 2000 IU.
- There are usually many micronutrients that you get enough of (without even having to try), and adding even more can run the risk of overdosing (two easy examples are selenium and beta-carotene).
- The physical limitations inherent in one pill. People may prefer one pill a day, but there is only so much you can fit in one.
- Health is more than just the classically defined vitamins, and there are many compounds that are very healthy for the body but are not vitamins, and thus can be missing from multivitamins.

As a general rule, using a multivitamin is not a good idea. Tedious as it is, multivitamins have been analyzed on a per-vitamin basis in order figure out if they are any useful.

While multivitamins may appear to be an easy panacea, their execution tends to be poor. Focusing too heavily on the “multi” aspect, most tend to have below-optimal dosages of vitamins, tending to focus more on having a plethora of vitamins/minerals present. It is likely more prudent to get a few specific vitamins and minerals in isolation.

Vitamins You are Likely Underdosing

Your highest priority should be to supplement vitamins/minerals that are very difficult to get in optimal levels from your diet. These include:

- Vitamin D
- Vitamin K

A short list.

The RDA for vitamin D is roughly 400-800 IU, and the optimal level is roughly 2000 IU minimum. The only people who do not need to concern themselves with vitamin D are those that live within the tropics and have frequent sun exposure with bare skin (wearing a t-shirt and shorts is not enough).

The RDA for vitamin K is roughly 60-120 mcg, and the optimal level is roughly 1000 mcg. This optimal level is mostly the same for both vitamin K1 and K2. It should be noted that while many sources may claim to hit the RDA for vitamin K, they have poor bioavailability - your body is unable to extract the full amount from said foods.

The next priority goes to supplements that are difficult to get optimal levels via your diet. These include:

- Calcium
- Iron (mostly for people with low/no meat intake)
- Magnesium
- Zinc (mostly for people who sweat a lot)

Calcium deficiency is common in older persons and those with low dairy intake, and supplementation of calcium when dietary calcium is low (which is surprisingly common in the whole of society) would be prudent.

Alternatively, dietary protein supplements derived from dairy can help with calcium intake, as whey and casein protein have 20% and 60% of the RDA for calcium respectively (if desiring a calcium and protein supplement, two birds with one stone).

Iron tends to be handled by medical doctors since overdosing can be toxic, but it is also a mineral with surprisingly common deficiencies in society and its usage exemplified the “use only when needed and at no other times” idea of this category.

Zinc is not usually a concern for non-athletes, but it is excreted in higher amounts when a person sweats to a higher degree. In instances of high mineral excretion from sweating, then zinc supplementation would be useful. Alternatively, oysters provide it in the diet.

Magnesium does not have a really good single-food source aside from some nuts (the high calorie count of which limits how much can be consumed). If most of the foods in your diet contain appreciable levels of magnesium then you can avoid supplementation, but if too much of your diet is lacking magnesium then deficiency is likely.

Most other vitamins and minerals fall into one of two categories:

1. Even if you have a very poor diet, you are likely eating enough of the vitamin or mineral due to its low requirements and/or due to food fortification.
2. There is not enough information on select vitamin or mineral to determine if taking it daily above the RDA is better than just taking the RDA daily.

Vitamin D and Vitamin K should be taken by most persons regardless of diet or health goals, whereas select minerals (calcium, iron, magnesium, zinc) are to be looked at individually to see if your diet gives enough or not. In the cases where the diet is low in these minerals, only then would supplementation be prudent.

Things that aren't Vitamins, but are Similar in Concept

As mentioned in the final bullet point on why multivitamins are not a great option, there are many compounds that help the body and are vital for optimal performance. However, they are not classified as vitamins; not getting enough of them does not result in a diseased state.

Just because a lack of a compound does not cause disease does not mean it is unneeded. For example, a genetic fault that hinders creatine metabolism will cause mental retardation. Hindering the synthesis of CoQ10 causes muscular dystrophy.

We classify these important but not critical compounds as vitamin-like.

There are a collection of compounds that are not technically vitamins or minerals, but are important in optimal function of your body.

These vitamin-like compounds include:

- Creatine (particularly for vegetarians)
- Carnitine (particularly for vegetarians or the elderly)
- CoQ10 (assuming post-myocardial infarction or fibromyalgia)
- Cholinergics (assuming low egg and meat intake or cognitive decline)
- Uridine (assuming cognitive decline)

Of special note is fish oil, or specifically “omega-3 fatty acids.” Essential fatty acids (EFAs) can be divided into either omega-6 (n-6) or omega-3 (n-3) class. EFAs are required for survival, but it's a non-issue in developed countries (our intake far exceeds the minimums we require).

A dietary ratio of around 1:1 is optimal for n6:n3 ratio. As most people get ample n6 (due to meat consumption), fish oil supplementation can help bring the ratio back down. Supplementation is not needed if one eats sufficient fatty fish.

Macronutrient Supplementation

There are supplements that verge on the boundary between food and dietary supplement, belonging to both categories. These are supplements that confer appreciable calories to the diet, and the most relevant supplement in this category is the simple protein powder.

Similar to the above vitamins, if you get sufficient protein in the diet then a supplemental powder is not needed. Protein powders serve as a convenient way to get optimal protein levels on a daily basis, or perhaps to break the monotony of meat and egg products (with some chocolate shakes or pudding made from protein powder). Protein powders, usually casein, can also be used to cook with or prepare desserts (such as cheesecake) to enhance their protein content.

Rough protein targets can be read about [here](#), and tend to be based on bodyweight (assuming non-obese body composition, otherwise too much protein will be consumed daily).

Mass-gain powders tend to be nothing more than the cheapest filler carbohydrates available. They are, for better or worse, empty calories.

Protein powders are used as a part of the diet, to help round out protein requirements in the diet. Despite not being needed, they are very convenient.

Wrapping it Up

Supplementation is a very interesting field - some people over-rely on supplements, others quickly dismiss the entire concept. The truth is that done intelligently, supplementation can help shore up multiple deficiencies in your diet. Based on your health goals, it can be a great, targeted help.

See the [Supplement Reference](#) or the [Health Goals Reference](#).

This is a reference guide for supplementation provided by [Examine.com](https://www.examine.com). It allows one to quickly look up the effects of [supplements](#) or to look up which supplements affect various [health goals](#).

The **Human Effect Matrix** looks at human studies (excluding animal/petri-dish studies) to tell you which supplements have which effects.

GRADE	LEVEL OF EVIDENCE
A	Robust research conducted with repeated double blind clinical trials
B	Multiple studies where at least two are double-blind and placebo controlled
C	Single double blind study or multiple cohort studies
D	Uncontrolled or observational studies only

All Supplements

- [1,3-Dimethylamylamine](#)
- [5-HTP](#)
- [7-Keto DHEA](#)
- [Aframomum melegueta](#)
- [Agmatine](#)
- [Alcohol](#)
- [Alpha-GPC](#)
- [Alpha-Lipoic Acid](#)
- [Anatabine](#)
- [Andrographis paniculata](#)
- [Arginine](#)
- [Aronia melanocarpa](#)
- [Artichoke Extract](#)
- [Ascophyllum nodosum](#)
- [Ashwagandha](#)
- [Asteracantha longifolia](#)
- [Astragalus membranaceus](#)
- [Bacopa monnieri](#)
- [Banaba Leaf](#)
- [Benfotiamine](#)
- [Berberine](#)
- [Beta-Alanine](#)
- [Black Cohosh](#)
- [Bladderwrack](#)
- [Blueberry](#)
- [Boron](#)
- [Boswellia serrata](#)
- [Branched Chain Amino Acids](#)
- [Bromelain](#)
- [Butea superba](#)
- [Caffeine](#)
- [Caralluma fimbriata](#)
- [CDP-choline](#)
- [Centella asiatica](#)
- [Chlorella](#)
- [Chlorogenic Acid](#)
- [Chromium](#)
- [Chrysin](#)
- [Cissus quadrangularis](#)
- [Citrulline](#)
- [Citrullus colocynthis](#)
- [Coconut Oil](#)
- [Coenzyme Q10](#)
- [Coleus forskohlii](#)
- [Colostrum](#)
- [Conjugated Linoleic Acid](#)
- [Cordyceps](#)
- [Creatine](#)
- [Curcumin](#)
- [D-Aspartic Acid](#)
- [D-Serine](#)
- [Dehydroepiandrosterone](#)
- [Ecdysteroids](#)
- [Echinacea](#)
- [Ecklonia cava](#)
- [Eclipta alba](#)

- [Eleutherococcus senticosus](#)
- [Emblica officinalis](#)
- [Ephedrine](#)
- [Eurycoma Longifolia Jack](#)
- [Fenugreek](#)
- [Feverfew](#)
- [Fish Oil](#)
- [Fucoxanthin](#)
- [Gamma Oryzanol](#)
- [Ganoderma lucidum](#)
- [Garcinia cambogia](#)
- [Garlic](#)
- [Ginger](#)
- [Ginkgo biloba](#)
- [Glucosamine](#)
- [Glutamine](#)
- [Glycine](#)
- [Grape Seed Extract](#)
- [Grapefruit](#)
- [Green Coffee Extract](#)
- [Green Tea Catechins](#)
- [Guggul](#)
- [Gynostemma pentaphyllum](#)
- [Harpagophytum procumbens](#)
- [Hemp Protein](#)
- [Hesperidin](#)
- [Hibiscus sabdariffa](#)
- [HMB](#)
- [Holy Basil](#)
- [Hoodia gordonii](#)
- [Horny Goat Weed](#)
- [Horse Chestnut](#)
- [Inositol](#)
- [Iodine](#)
- [Irvingia gabonensis](#)
- [Japanese Knotweed](#)
- [Kaempferia parviflora](#)
- [Kava](#)
- [Krill Oil](#)
- [L-Carnitine](#)
- [L-Tyrosine](#)
- [Lavender](#)
- [Leucic Acid](#)
- [Licorice](#)
- [Maca](#)
- [Magnesium](#)
- [Magnolia officinalis](#)
- [Melatonin](#)
- [Melissa officinalis](#)
- [Methylsulfonylmethane](#)
- [Microlactin](#)
- [Minoxidil](#)
- [Modafinil](#)
- [Moringa oleifera](#)
- [Morus alba](#)
- [Mucuna pruriens](#)

- [N-Acetylcysteine](#)
- [Nattokinase](#)
- [Nicotine](#)
- [Nigella sativa](#)
- [Nitrate](#)
- [Noopept](#)
- [Olive leaf extract](#)
- [Origanum vulgare](#)
- [Ornithine](#)
- [Orthosiphon stamineus](#)
- [Oxiracetam](#)
- [Panax ginseng](#)
- [Patchouli](#)
- [Pelargonium sidoides](#)
- [Peppermint](#)
- [Phenylpiracetam](#)
- [Phosphatidylserine](#)
- [Picrorhiza kurroa](#)
- [Piracetam](#)
- [Policosanol](#)
- [Polypodium leucotomos](#)
- [Pramiracetam](#)
- [PRL-8-53](#)
- [Psyllium](#)
- [Pueraria lobata](#)
- [Pueraria mirifica](#)
- [Punicalagins](#)
- [Punicic Acid](#)
- [Pycnogenol](#)
- [Pygeum](#)
- [Pyrroloquinoline quinone](#)
- [Pyruvate](#)
- [Quercetin](#)
- [Raspberry Ketone](#)
- [Red Clover Extract](#)
- [Resveratrol](#)
- [Rhodiola Rosea](#)
- [Rooibos](#)
- [Rose Essential Oil](#)
- [Rose Hip](#)
- [Rosmarinic Acid](#)
- [Royal Jelly](#)
- [Rubus coreanus](#)
- [Rubus suavissimus](#)
- [Ruscus aculeatus](#)
- [S-Adenosyl Methionine](#)
- [Saffron](#)
- [Salacia reticulata](#)
- [Salvia hispanica](#)
- [Salvia sclarea](#)
- [Sarcosine](#)
- [Schisandra chinensis](#)
- [Sea Buckthorn](#)
- [Senna alexandrina](#)
- [Serrapeptase](#)
- [Sesamin](#)

- [Shilajit](#)
 - [Sodium Bicarbonate](#)
 - [Soy lecithin](#)
 - [Spirulina](#)
 - [Stephania tetrandra](#)
 - [Stevia](#)
 - [Stinging Nettle](#)
 - [Sulbutiamine](#)
 - [Taurine](#)
 - [Tauroursodeoxycholic Acid](#)
 - [Terminalia arjuna](#)
 - [Tetradecyl Thioacetic Acid](#)
 - [Theaflavins](#)
 - [Theanine](#)
 - [Tinospora cordifolia](#)
 - [Tribulus terrestris](#)
 - [Trimethylglycine](#)
 - [Uncaria tomentosa](#)
 - [Uridine](#)
 - [Valeriana officinalis](#)
 - [Vanadium](#)
 - [Velvet Antler](#)
 - [Vinpocetine](#)
 - [Vitamin B12](#)
 - [Vitamin C](#)
 - [Vitamin D](#)
 - [Vitamin E](#)
 - [Vitamin K](#)
 - [Vitex agnus castus](#)
 - [Watercress](#)
 - [Whey Protein](#)
 - [Yacon](#)
 - [Yamabushitake](#)
 - [Yerba mate](#)
 - [Yohimbine](#)
 - [Zinc](#)
 - [Ziziphus jujuba](#)
-

All Health Goals

- [8-isoPGF2a](#)
- [Acne](#)
- [ADHD in Children](#)
- [Adiponectin](#)
- [Adrenaline](#)
- [Aerobic Exercise](#)
- [Aggression](#)
- [Alertness](#)
- [All-Cause Mortality](#)
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- [Apolipoprotein A](#)
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- [Attention](#)
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- [Bleeding Time](#)
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- [Bone Mineral Density](#)
- [Breast Cancer Risk](#)
- [Breast Tenderness](#)
- [C-Reactive Protein](#)
- [Calmness](#)
- [Cancer Mortality](#)
- [Canker Sores](#)
- [Cardiovascular Disease Risk](#)
- [CD4 Lymphocytes](#)
- [CD8 Lymphocytes](#)
- [Cell Adhesion Factors](#)
- [Cerebral Blood Flow](#)
- [Chronic Venous Insufficiency](#)
- [Cocaine Addiction](#)
- [Cognition](#)
- [Cognitive Decline](#)
- [Colon cancer risk](#)
- [Colorectal Cancer Risk](#)
- [Constipation](#)
- [Cortisol](#)
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- [Creatinine](#)
- [Depression](#)
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- [Exercise-Induced Oxidation](#)
- [Fat Mass](#)
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- [Fatigue](#)
- [Fatigue Resistance](#)
- [Fecal Moisture](#)
- [Fecal Weight](#)
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- [General Oxidation](#)
- [Ghrelin](#)
- [Glycemic Control](#)
- [Glycogen Resynthesis](#)
- [Growth Hormone](#)
- [Hair Regrowth](#)
- [HbA1c](#)
- [HDL-C](#)
- [Heart Rate](#)
- [Hematocrit](#)
- [Hemoglobin](#)
- [Homocysteine](#)
- [Hydration](#)
- [IGF Binding Protein](#)
- [IGF-1](#)
- [Immunity](#)
- [Immunoglobulin A](#)
- [Immunoglobulin G](#)
- [Immunoglobulin M](#)
- [Inflammation](#)
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- [Insulin](#)
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-

1,3-Dimethylamylamine

Also known as: 4-methylhexan-2-amine, DMAA, Dimethylamylamine, 1,3-DMAA, Geranamine, Methylhexaneamine, 1,3-Dimethylpentylamine, Forthane

1,3-DMAA is a neural stimulant with a structure similar to Ephedrine and adrenaline that has been used as a pre-workout stimulant. Not much information is available on 1,3-DMAA supplementation, and is no longer commonly sold as a supplement.

See [1,3-Dimethylamylamine on Examine.com](#)

How to Take

A typical starting dose of 1,3-DMAA is in the 10-20mg range and eventually reaching up to 40-60mg a day, there is no actual evidence to support this dosage range but it seems to be the standard dosages range for supplemental 1,3-DMAA on the market. 1,3-DMAA is known to be banned by various sports organizations due to its amphetamine-like nature, and should not be used by tested athletes.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Blood Pressure	↑	★★☆ Notable	1 study	The increase in blood pressure with 1,3-DMAA was fairly notable and of concern, with 75mg paired with caffeine (common in preworkout supplements) increasing systolic by up to 20%.
C	Heart Rate	—	—	1 study	No significant effect on heart rate noted with DMAA supplementation despite the increase in blood pressure.

5-HTP

Also known as: 5-hydroxytryptophan, serotonin precursor

5-HTP is the precursor to serotonin, the neurotransmitter sometimes touted to be responsible for happiness. 5-HTP is a simple way to increase brain serotonin levels by bypassing the rate-limiting step, and users reap either the rewards or the hazards of increased brain serotonin.

See [5-HTP on Examine.com](#)

How to Take

A typical dose of 5-HTP is in the range of 300-500 mg, taken either once daily or in divided doses. Lower doses may also be effective, although usually when paired with other substances. For the purpose of reducing food intake, 5-HTP should be taken with a meal as it increases satiety from food intake (rather than reducing appetite/hunger). 5-HTP should not be taken with any neurological drug that has been prescribed for antidepressant or other cognitive purposes unless cleared by a medical doctor. This is most important for SSRI usage, wherein the combination with 5-HTP is potentially lethal.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Appetite	↓	★★★☆☆ Notable	3 studies	There does appear to be a fairly effective suppression in appetite noted with 5-HTP supplementation in the higher dosage range, which tends to reduce food intake.
B	Weight	↓	★★☆☆☆ Minor	3 studies	The reduction in weight appears to be mostly secondary to a reduction in food intake, and is not too remarkable in magnitude
C	Cortisol	↑	★★☆☆☆ Minor	1 study	At least one study has noted increased in salivary cortisol following acute ingestion of 5-HTP supplementation.
C	Sleep Terrors	↓	★★☆☆☆ Minor	1 study	At least one trial suggesting reductions in sleep terrors.

7-Keto DHEA

Also known as: 7-ketodehydroepiandrosterone, 7-oxodehydroepiandrosterone, 7-ketoDHEA, 7-oxoDHEA, 7-oxo, 7-keto

7-Keto DHEA is a metabolite of DHEA that is nonhormonal, and it appears to be fat loss agent as it may increase the metabolic rate. Studies in humans show promise for helping during a fat loss diet, but currently are of questionable quality due to potential conflicts of interest.

See [7-Keto DHEA on Examine.com](#)

How to Take

A typical supplemental dosage of 7-keto is 200-400mg daily in two divided doses (100-200mg), some limited evidence suggests that lower doses of 50-100mg may be effective for neural purposes. The optimal dosing schedule and overall dose of 7-keto is not yet known, and the above dosages are just based on what is known to have efficacy.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Fatigue	—	—	1 study	Insufficient evidence to support changes in fatigue and energy following 7-keto supplementation.
C	Blood Pressure	—	—	1 study	Insufficient evidence to support changes in blood pressure following 7-keto supplementation.
C	Testosterone	—	—	1 study	Insufficient evidence to support changes in testosterone following 7-keto supplementation.
C	Estrogen	—	—	1 study	Insufficient evidence to claim changes in estrogen following 7-keto supplementation.
C	Serum T3	↑	★☆☆ Minor	1 study	There appears to be an increase in circulating T3 hormone levels (active thyroid hormone) when 7-keto is paired with a caloric restriction

					and exercise (relative to placebo with the same regimen)
C	Parathyroid Hormone	—	—	1 study	Insufficient evidence to support changes in parathyroid hormone from 7-keto supplementation.
C	Fat Mass	↓	★☆☆ Minor	1 study	The amount of fat lost appears to be more with 7-keto than with placebo when either of them are paired with a low calories weight loss regiment.
C	Weight	↓	★☆☆ Minor	1 study	A weight loss of 2.88kg (1.8% body fat) was seen with 7-keto over placebo (0.97 kg loss with 0.28% bodyfat) which is significant but not overly notable, since the study used obese persons and exercise
C	Serum T4	—	—	1 study	Insufficient evidence to support alterations in T4, with no changes detected when it is measured
C	Blood Glucose	—	—	1 study	Insufficient evidence to support changes in blood glucose
C	Metabolic Rate	↑	★★★☆☆ Notable	1 study	Somewhat notable as the decrease seen with dieting was effectively abolished and reversed with 7-keto supplementation over 7 days of low caloric intake, but more evidence is required to establish the reliability of this and how strong it actually is.

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Aframomum melegueta

Also known as: Grains of Paradise, melegueta pepper, alligator pepper, Guinea pepper, Guinea grain

Aframomum melegueta (Grains of Paradise) is a spice with a similar composition as Ginger that belongs to the same Zingiberaceae family. It shows some promise in fat-mass control at doses possibly consumable via food products.

See [Aframomum melegueta on Examine.com](#)

How to Take

The only current human study used a 95%-ethanolic extract of Aframomum melegueta at 10 mg daily. There is no evidence to suggest whether this is the optimal dose, but it appears to be a low enough dose that the spice itself can be used on top of food.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Metabolic Rate	↑	★☆☆ Minor	1 study	Requires more evidence, and the increase in metabolic rate was wholly conditional on cold therapy also being used (where supplementation with aframomum melegueta increased cold therapy's efficacy rather than <i>per se</i> increasing metabolic rate)

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Agmatine

Also known as: Clonidine-displacing substance, 4-(aminobutyl)guanidine, Decarboxylated arginine

Agmatine is a metabolite of L-Arginine. It shows promise for alleviating neuropathic pain and drug addiction. Agmatine supplementation can also protect from strokes and benefit cognitive health.

See [Agmatine on Examine.com](#)

How to Take

There are no standard dosages for agmatine because of the lack of human evidence for its effects. However, a single human study used 1,300-2,670mg of agmatine, daily for the treatment of neuropathic pain. The estimated human dose for improving cognition is 1.6-6.4mg/kg of agmatine, taken orally. This is based off of the 10-40mg/kg dosage range for rats, and is equivalent to 217-435mg for a 150lb person. Supplementation should not exceed 6.4mg/kg of bodyweight. Studies on agmatine use a daily dosing protocol. Agmatine is not absorbed well when taken with dietary protein, because it uses the same transporters as Arginine. Further research is needed to determine if oral agmatine supplementation provides the same benefits as were observed in animal studies.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Pain	↓	★★★☆☆ Notable	1 study	In the trial on lumbar disc-associated radiculopathy, the degree of pain alleviation was fairly notable relative to placebo and persisted for two months after supplementation was ceased. No reference drug comparisons, unfortunately

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Alcohol

Also known as: Ethanol, Drinking alcohol, Beer, Gin, Vodka, Wine, Jager

Society's favorite anxiety-reducing agent and a common reason for social gatherings. Alcohol has some benefits, but a lot of drawbacks as well; it can exert toxic effects on the body quite potently when you get drunk. Many supplements interact with alcohol.

See [Alcohol on Examine.com](#)

How to Take

Abstinence from drinking is defined as having no ethanol intake whatsoever. "Moderate" drinking in the literature is dependent on gender and not ultimately defined, but an upper limit can be placed at 9 units per week for women and 12-14 units a week for men, with no single event exceeding 4 units. A unit is typically 12 oz (355 mL) of 5% beer, 5 oz (150 mL) 12.5% wine, or 1.5 oz (45 mL) of drinks with a higher (40%) alcohol content.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Testosterone	↓ ↑	★☆☆ Minor	9 studies	There appears to be a time-dependent influence on testosterone, with acute doses of alcohol increasing testosterone secondary to creating energy influx in the liver (small enough of an increase to be 'somewhat' effective but may contribute to libido) whereas abuse is known to reduce testosterone levels more notably. The acute increase in testosterone is thought to be related to spikes in libido
C	Estrogen	—	—	3 studies	No significant influence on fasting estrogen levels in males
C	Luteinizing Hormone	—	—	5 studies	No significant influence of alcohol on luteinizing hormone levels when consumed moderately
C	Cortisol	—	—	2 studies	

C					No significant alterations in cortisol levels seen with alcohol ingestion in moderate levels
C	Adrenaline	—	—	1 study	Serum adrenaline appears unaltered following alcohol ingestion
C	Power Output	↓	★☆☆ Minor	1 study	Acute ingestion of alcohol may be able to reduce subsequent power output
D	Follicle-Stimulating Hormone	↑	★☆☆ Minor	2 studies	Mixed effects on FSH, but although null effects have been reported an increase may be possible
D	Prolactin	↑	★☆☆ Minor	1 study	An increase in prolactin has been noted following acute ingestion of alcohol
D	Growth Hormone	↓	★☆☆ Minor	1 study	An acute suppression of growth hormone is noted with alcohol ingestion

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Alpha-GPC

Also known as: Alpha-glycerylphosphorylcholine, L-alpha-glycerophosphocholin, glycerophosphocholine, L-alpha-glyceryl-phosphorylcholine, Choline Alphoscerate

Alpha-glycerophosphocholine (Alpha-GPC or α -GPC) is a cholinergic compound that is used for its cognitive-promoting properties, and to enhance power output in athletes. It appears to also support cellular membranes, and may aid in preventing cognitive decline.

See [Alpha-GPC on Examine.com](#)

How to Take

Alpha-GPC is approximately 40% choline by weight, and as such 1,000 mg alpha-GPC confers about 400 mg of dietary choline. A standard dosage of alpha-GPC is 300-600 mg, according to the most common label doses. This dose is in accordance with the study using alpha-GPC to enhance power output (600 mg) and the two studies noting an increase in growth hormone secretion, and is likely a good dose to take for athletes. For the usage of alpha-GPC in attenuating symptoms of cognitive decline, almost all studies use a dosage of 1,200 mg daily, divided into three doses of 400 mg. It is unsure how lower doses would benefit cognition, but the 1,200 mg appears to be consistently associated with benefit. Rat studies suggest that the effects of alpha-GPC oral ingestion peak at 300-600 mg/kg, which is an estimated human dose of 48-96 mg/kg (and for a 150lb human, 3,272-6,545 mg daily).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Growth Hormone	↑	☆☆☆ Minor	2 studies	Has noted an increase in circulating growth hormone, but measurements were acute (whole-day measurements of growth hormone are more reliable due to hourly fluctuations)
C	Fat Oxidation	↑	☆☆☆ Minor	1 study	Some biomarkers of hepatic fat oxidation increased at rest, no indication as to the potency of this relative to reference drugs.
C	Cognitive Decline	↓	☆☆☆ Notable	1 study	The rate of cognitive decline of either degenerative or vascular origin appears to be significantly reduced with Alpha-GPC supplementation
C	Symptoms of	↓	☆☆☆	1 study	

	Alzheimers		Notable		At least among nutraceuticals, Alpha-GPC appears to significantly improve cognition in persons with Alzheimer's disease at the dose of 1,200mg when taken as a daily supplement over a prolonged period of time.
C	Power Output	↑	Minor	1 study	The lone pilot study noted a 14% increase in power output as assessed by bench throws, requires replication
D	Iron Absorption	↑	Minor	2 studies	It is possible that Alpha-GPC increases iron absorption from non-meat sources (nonheme iron), but the evidence is currently mixed and a very low dose of 46mg may be required (which would render supplementation irrelevant).

Alpha-Lipoic Acid

Also known as: ALA, thioctic acid, 1,2-dithiolane-3-pentanoic acid, ala, Tiolepta

ALA is a fatty acid that exists in the mitochondria and is involved in energy metabolism. Commonly taken with L-Carnitine supplements as they are related in mechanisms. ALA gives a short but potent reduction of oxidation by increasing anti-oxidant enzymes, and may decrease Blood Glucose acutely.

See [Alpha-Lipoic Acid on Examine.com](#)

How to Take

Standard dosages of Alpha-lipoic acid (ALA) tend to be in the range of 300-600mg; with little differentiation as to whether the racemic mixture of ALA (S- and R- isomers) or Na-R-ALA results in higher blood levels. Alpha-lipoic acid appears to be absorbed via transporter-related means, and despite being inherently fat-soluble it does not require dietary fatty acids to be absorbed from the gut. ALA supplementation can be taken in a fasted state.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	General Oxidation	↓	★☆☆ Minor	6 studies	Appears to reduce biomarkers of oxidation
B	Blood Pressure	—	—	6 studies	The majority of evidence using intravenous or oral supplements fail to find an influence, and the one study to suggest a reduction was also confounded with weight loss (known to reduce blood pressure). It can be assumed that ALA has no significant influence on blood pressure even in studies where blood flow is altered
B	Symptoms of Diabetic Neuropathy	↓	★★★☆☆ Notable	2 studies	Not yet compared to reference drugs, but it has been subject to a meta-analysis and appears to be more effective than other options for reducing nerve pain associated with diabetes. The lack of a reference comparison and some evidence suggesting no effect prevent a strong rating.

C	Weight	↓	★☆☆ Minor	4 studies	It is possible that high doses (1,800mg) may have a body weight reducing effect in obese persons, but this requires more evidence.
C	C-Reactive Protein	—	—	2 studies	Although there may be a reduction of C-Reactive protein in some populations, for the most part ALA does not seem significantly effective in reducing this inflammatory biomarker of cardiovascular disease
C	Treatment of Dementia	—	—	1 study	No significant rehabilitative effect of ALA on cognitive decline has been noted
C	Insulin Sensitivity	—	—	1 study	No significant influence on insulin sensitivity has been noted
C	Lipid Peroxidation	↓	★☆☆ Minor	2 studies	Appears to reduce biomarkers of lipid peroxidation (MDA mostly)
C	Inflammation	↓	★☆☆ Minor	2 studies	Mixed effects depending on what inflammatory biomarker or cytokine is measured; practical significance unknown
C	Symptoms of Rheumatoid Arthritis	—	—	1 study	No significant interaction between ALA supplementation and symptoms of rheumatoid arthritis
C	Motion Sickness	—	—	1 study	Insufficient evidence to support a reduction in motion sickness with ALA supplementation
C	Protein Carbonyl Content	↓	★☆☆ Minor	1 study	Appears to reduce protein carbonylation, which may be related to the antioxidative effects
C	Anti-Oxidant Enzyme	—	—	2 studies	

	Profile				Mixed effects on antioxidant enzymes, with decreases in glutathione peroxidase and increases in catalase with no effect on SOD
C	Symptoms of Intermittent Claudication	↓	★★★☆☆ Notable	1 study	The reduction of claudication symptoms appears to be fairly potent with ALA supplementation, although there is not a large body of evidence overall.
C	HbA1c	↓	★★☆☆☆ Minor	3 studies	There appears to be a slight reducing effect on HbA1c
C	Nerve Repair	↑	★★☆☆☆ Minor	1 study	May increase nerve regeneration rates and be of aid to nervous system injury
C	Blood Glucose	↓	—	1 study	A small decrease in blood glucose is noted with oral supplementation of ALA, related to the glucose disposal properties
C	Heart Rate	—	—	1 study	No significant interaction between ALA and heart rate has been noted
C	Blood Flow	↑	★★☆☆☆ Minor	2 studies	May increase blood flow, although not to a remarkable degree. Possibly secondary to antioxidative effects
D	Oxidation of LDL	↑	★★☆☆☆ Minor	1 study	Appeared to increase oxidation of LDL according to one study, which was abolished by exercise but noted to be a concern during rest.
D	Glycemic Control	—	—	1 study	No significant practical benefit on glycemic control noted
D	Skin Quality	↑	★★☆☆☆ Minor	1 study	May improve skin quality when topically applied

D	Muscle Creatine Content	↑	★☆☆ Minor	1 study	Has been associated with augmenting Creatine uptake into muscle cells acutely; long term influence unknown

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Anatabine

Also known as: Anatabloc (Brand Name)

Anatabine is a small alkaloid found in tobacco and plants in the solanaceae family (such as eggplant and peppers). It possesses antiinflammatory properties via inhibiting a protein known as STAT3, but this may occur at too high of an oral dose to matter with nutritional supplementation.

See [Anatabine on Examine.com](#)

How to Take

Animal research on anatabine have used oral intakes of 12.5-20mg/kg in mice for the purpose of reducing autoimmune diseases, which suggests a human preliminary dosage of: 70-110 mg for a 150lb person 90-150 mg for a 200lb person 110-180 mg for a 250lb person

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Muscle Damage	—	—	1 study	The progression of recovery after a novel workout (when measured over three days) was unaffected by 6-12mg anatabine
C	Power Output	—	—	1 study	Strength recovery over the course of three days recovery was not significantly improved by 6-12mg anatabine
C	Muscle Soreness	—	—	1 study	Perceived muscle soreness and pain from a workout was unaffected by anatabine supplementation.
C	Blood Pressure	—	—	1 study	6-12mg anatabine does not appear to significantly influence blood pressure in otherwise healthy persons.
C	Heart Rate	—	—	1 study	There is no significant influence on heart rate seen with 6-12mg anatabine in otherwise healthy persons

Andrographis paniculata

Also known as: Chiretta, King of Bitters, Kalmegh, Creat, Chuanxinlian, Yijianxi, Lanhelian

Andrographis paniculata is an herb derived from both Ayurveda and Traditional Chinese Medicine and appears to be a traditional remedy for the common cold. There is some evidence for this claim but it is currently limited. There are some anti-cancer properties with this herb as well.

See [Andrographis paniculata on Examine.com](#)

How to Take

When looking at the basic root extract (not concentrated in any way), the oral dose of Andrographis paniculata is in the range of 2,000-6,000 mg. The root extract tends to have an andrographolide content in the 1-2%, range with up to 4% having been reported. When looking at extracts, 200 mg appears to be effective if the andrographolide content is around 30% or so.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Symptoms of Pharyngotonsillitis	↓	★★★☆☆ Notable	1 study	Potency of andrographis in this regard was comparable to Tylenol, the reference drug.
C	Upper Respiratory Tract Infection Risk	↓	★★☆☆☆ Minor	1 study	Appears to be better than placebo, although it is difficult to assess potency.
C	Symptoms of Ulcerative Colitis	↓	★★★☆☆ Notable	2 studies	Appears to be quite effective based on preliminary evidence, with one study being comparable to sustained release mesalazine in potency.
C	Symptoms of Rheumatoid Arthritis	↓	★★☆☆☆ Minor	1 study	Reductions in joint pain and swelling were somewhat minimal in magnitude
C	Length of Sickness	↓	★★★☆☆ Notable	1 study	Seems to be one of the few compounds able to reduce the length of sickness when taken at the first signs of sickness. The lack of a reference drug to compare Andrographis limits the strength of the evidence

C	Severity of Sickness	↓	★★★ Notable	1 study	Seems to have more efficacy against nasal, ear, and throat symptoms of sickness. Lack of evidence and comparisons to reference drugs limits strong evidence
D	CD4 Lymphocytes	—	—	2 studies	Unclear effects on CD4+ lymphocytes at this moment in time
D	Liver Enzymes	↑	★☆☆ Minor	1 study	Study was in persons with HIV, although the magnitude was of concern it needs to be replicated.
D	Early Virologic Response	—	—	1 study	Insufficient evidence to support antiviral effects in HIV

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Arginine

Also known as: L-Arginine

A conditionally essential amino acid, L-arginine is important for regulation of blood flow and nitric oxide. Supplemental usage is limited by its absorption rates (bioavailability), and L-Citrulline is more commonly used due to better absorption and being the same molecule in the blood.

See [Arginine on Examine.com](#)

How to Take

For acute doses taken on a relatively empty stomach (such as a pre-workout supplement), oral doses of 3-6 g are used, and 5-6 g may be the ideal dose (similar serum increases in arginine as lower and higher doses with no intestinal side effects). Doses of 10 g have been noted to cause diarrhea when taken in this manner however, and thus are inadvisable. Arginine may be taken up to thrice a day in separated doses (as the intestinal side effects are from taking too much at once), reaching a total of 15-18 g daily. In this scenario though (wanting day-long increases in arginine concentrations), supplemental citrulline may be a more prudent option (since a single dose elevates serum arginine for longer).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Heart Rate	—	—	4 studies	No significant influence on heart rate seen with supplemental L-Arginine
B	Growth Hormone	↓↑	★☆☆ Minor	5 studies	Arginine has been implicated in increasing growth hormone (at rest) and suppressing an exercise-induced increase in growth hormone; both of these are short in duration, and it is unsure if there are any long lasting effects of such short a spike.
B	Plasma Arginine	↑	★☆☆ Minor	6 studies	Supplemental L-Arginine increases plasma L-Arginine. The spike in plasma L-arginine concentrations may be slightly more than that seen with L-citrulline, but the latter lasts longer and is thus more effective

B	Blood Pressure	↓	★☆☆ Minor	5 studies	Arginine has been implicated in reducing blood pressure, but the degree of reduction does not appear to be too remarkable and it is unreliable in doing so
B	Blood Flow	↑	★☆☆ Minor	6 studies	May increase blood flow secondary to activating nitric oxide, but due to the unreliability of increasing nitric oxide there is also unreliability in how arginine increases blood flow
B	Asymmetrical dimethylarginine	—	—	3 studies	Although there is some evidence for an increase in ADMA (a negative regulator of NOS that is derived from L-arginine), it does not appear to occur most of the time
B	Nitric Oxide	↑	★☆☆ Minor	7 studies	Has been implicated in increasing nitric oxide formation in the body, but this does not appear to be a reliably occurring phenomena (despite arginine being required to make nitric oxide, it is not a good inducer thereof)
C	Power Output	—	—	2 studies	No significant influence on power output
C	Symptoms of Intermittent Claudication	↓ ↑	★☆☆ Minor	2 studies	Both an improvement and an impairment have been noted on walking distance in persons with intermittend claudication, and it is not exactly known why this occurs (may be related to time, with prolonged usage being impairing)
C	Subjective Well-Being	—	—	1 study	In persons with peripheral artery disease (intermittent claudication), despite improving symptoms as assessed by a treadmill walking test there does not appear to be an improvement in self-reported well being

C	Oxygenation Cost of Exercise	↓	★☆☆ Minor	2 studies	When nitric oxide is increased, the oxygenation cost of exercise appears to be decreased. This is unreliable with supplemental L-arginine as arginine is unreliable in increasing nitric oxide
C	Anaerobic Running Capacity	↑	★☆☆ Minor	1 study	May be able to increase anaerobic physical performance, but this is unreliable due to arginine not reliably increasing nitric oxide concentrations.
C	Plasma Nitrate	—	—	1 study	There does not appear to be a reliable increase in plasma nitrate seen with arginine supplementation
C	Ammonia	—	—	1 study	Although it is plausible that arginine could decrease ammonia (secondary to ornithine), it does not appear to reliably occur
C	Cortisol	—	—	1 study	No significant influence on circulating cortisol concentrations
C	Testosterone	—	—	1 study	No significant influence on circulating testosterone concentrations
C	Glucagon	—	—	1 study	Does not appear to significantly influence circulating glucagon concentrations
C	Urea	—	—	1 study	Although it is theoretically plausible that arginine can increase urea concentrations (secondary to the actions of ornithine), it does not appear to reliably occur
C	Lactate Production	—	—	1 study	No significant influence on

					lactate production associated with L-arginine supplementation
C	Endothelial Function	↑	★☆☆ Minor	2 studies	Unreliable improvements in endothelial function, notably in persons with impaired glucose tolerance/type II diabetes, associated with the supposed increase in nitric oxide
C	Endothelin-1	↓	★☆☆ Minor	1 study	A decrease in concentrations of endothelin-1 has been noted with supplemental L-arginine
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	1 study	At least in persons with impaired glucose tolerance and/or type II diabetes, L-arginine appears to have an indirect antioxidant role and increase superoxide dismutase concentrations
C	Adiponectin	↑	★☆☆ Minor	1 study	At least in persons with impaired glucose tolerance, an increase in adiponectin (and the adiponectin:leptin ratio) has been noted with supplemental L-arginine
C	HbA1c	—	—	2 studies	No significant influence on HbA1c concentrations in persons with impaired glucose tolerance, even when endothelial function is improved
C	Blood Glucose	—	—	2 studies	No significant influence on fasting blood glucose concentrations even in persons with impaired glucose tolerance
C	General Oxidation	↓	★☆☆ Minor	1 study	A decrease in oxidation has been noted in persons with impaired glucose tolerance, thought to be associated with the increase in superoxide dismutase activity

C	Insulin Secretion	↑	★☆☆ Minor	1 study	An increase in insulin secretion has been noted with arginine supplementation. This is both due to arginine being a secretagogue (when used acutely), and prolonged usage in those with impaired glucose tolerance may regenerate pancreatic beta-cells
C	Insulin Sensitivity	↑	★☆☆ Minor	1 study	An increase in insulin sensitivity has been noted in persons with impaired glucose tolerance using arginine for long periods of time; this is thought to be secondary to increased pancreatic function
C	Fat Mass	↓	★☆☆ Minor	1 study	A slight reduction in fat mass has been noted with long-term usage in persons with impaired glucose tolerance. No evidence supports the usage of arginine as a fat burner in otherwise healthy persons
C	Lean Mass	↑	★☆☆ Minor	1 study	An increase in lean mass has been noted in persons with impaired glucose tolerance using L-arginine over a long period of time, where placebo experienced a decrease. It is unsure how this applies to otherwise healthy persons
D	Insulin	—	—	1 study	No significant influence on <i>fasting</i> insulin concentrations associated with arginine supplementation
D	Somatomedin A	—	—	1 study	No significant effect of arginine on somatomedin A concentrations

Aronia melanocarpa

Also known as: Chokeberry, Black Apple Berry, RowanBerry (hybrids with Aronia), Aronox (Brand Name)

Aronia melanocarpa (Black Chokeberry) is a berry with a sour/astringent taste and a very high anthocyanin and anti-oxidant content; greater than blueberries. It is being investigated for potential health-promoting properties.

See [Aronia melanocarpa on Examine.com](#)

How to Take

There is not a large body of evidence to suggest the best dose of Chokeberry, but 200 mL of unsweetened juice daily or 300 mg of an extract known as Aronox have both been associated with benefits in humans. The benefits of these dosages and this supplement should be comparable to the benefits associated with the recommended dosage of Blueberry supplementation.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	HbA1c	↓	★☆☆ Minor	1 study	Requires more studies before conclusions can be made, appears to simply be exerting anti-oxidant effects.
D	Blood Glucose	↓	★☆☆ Minor	1 study	Requires more studies before conclusions can be made, appears to simply be exerting anti-oxidant effects.
D	Triglycerides	↓	★☆☆ Minor	1 study	Requires more studies before conclusions can be made, appears to simply be exerting anti-oxidant effects.
D	Total Cholesterol	↓	★☆☆ Minor	2 studies	Requires more studies before conclusions can be made, appears to simply be exerting anti-oxidant effects.
D	Lipid Peroxidation	↓	★★★☆☆ Notable	1 study	Definitely requires more evidence, but appears to be fairly effective at reducing lipid peroxidation and other oxidative parameters (lone

					study noting a 40% reduction with aronia)
D	General Oxidation	↓	★★★☆☆ Notable	1 study	Requires more evidence, but it appears to reduce oxidative parameters more than other supplements.

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Artichoke Extract

Also known as: Artichoke

Artichoke Extract (*Cynara scolymus*) is an extract from the common bulb vegetable that appears to have the ability to stimulate bile secretion; this may underlie a weak reduction in cholesterol and improved fat digestion.

See [Artichoke Extract on Examine.com](#)

How to Take

A few doses have been used in human studies, including 6,000 mg of the basic extract (no concentrations) and also a 25-35:1 concentrated extract dosed at 1,800 mg. Both of these doses showed bioactivity, but there is no clear indication of which is the optimal dosage. It is unclear whether artichoke extract needs to be taken alongside a meal or not.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Triglycerides	—	—	4 studies	The two better controlled trials noted no change, whereas a decrease and increase has been noted otherwise. Unclear overall effects on triglycerides
C	LDL-C	↓	★☆☆ Minor	4 studies	Nothing remarkable about the reductions in LDL-C, seem to occur somewhat reliably and are minor in magnitude
C	Total Cholesterol	↓	★☆☆ Minor	4 studies	Despite its traditional usage, the decreases in cholesterol are not remarkable and are quite small in magnitude.
C	Blood Glucose	—	—	2 studies	There is still a possibility that artichoke extract is able to aid the blood glucose of diabetics, but currently the best evidence does not support this conclusion
C	HDL-C	—	—	3 studies	There does not appear to be an inherent effect of Artichoke

					on HDL-C, although the one study in diabetics suggest that HDL-C might increase when glucose is decreased.
C	Liver Enzymes	↓	★☆☆ Minor	1 study	More evidence is required to establish the potency of the hepatoprotective effects (with liver enzymes as a biomarker)
D	Blood Flow	↑	★☆☆ Minor	1 study	The increase in blood flow was relatively minor in magnitude, possibly related to antioxidant effects.
D	Cell Adhesion Factors	↓	★☆☆ Minor	1 study	ICAM-1 and VCAM-1 decreased, not to a remarkable degree that would be indicative of immunosuppression.

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Ascophyllum nodosum

Also known as: Kelp (one of many species), Egg Wrack, Rockweed

Ascophyllum nodosum is a particular species of seaweed that appears to be used for some supplemental purposes. It is one of many species referred to as kelp, and appears to have immunostimulatory properties, as well as possible inhibition of carbohydrate absorption.

See [Ascophyllum nodosum on Examine.com](#)

How to Take

Currently, the only human study using Ascophyllum nodosum has used the basic extract at 4,600 mg added to a food product. This is likely a bioactive dosage of the overall seaweed, although there is no indication if this is the optimal dose or not. It is unclear what concentrates are effective as they have not been tested.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Food Intake	↓	★☆☆ Minor	1 study	The reduction in voluntary food intake noted was 16.4% of a test meal (which was 80kcal in this study) and is not likely to make significant effects during weight loss.
D	Appetite	—	—	1 study	The noted reduction in food intake was not associated with decreased appetite.

Ashwagandha

Also known as: Withania Somnifera, Indian Ginseng, Smell of Horse, Winter Cherry, Dunal, Solanaceae

Ashwagandha is an herb and a popular supplement. It provides neuroprotection, anti-cancer effects, enhanced virility, and can even stave off anxiety.

See [Ashwagandha on Examine.com](#)

How to Take

The lowest effective dose for ashwagandha supplementation is 300-500mg. The optimal dose of ashwagandha is 2,000mg, taken three times a day. Low doses of ashwagandha (50-100mg) may be effective in very limited instances, and can be taken to reduce stress-related immunosuppression or to augment other anxiety-reducing agents. Ashwagandha root extract is the preferred form of ashwagandha, for the purposes of supplementation. Ashwagandha should be taken with meals. If taken once a day, it should be taken with breakfast.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Anxiety	↓	★★★☆☆ Notable	3 studies	Preliminary evidence suggests potent anxiolytic effects <i>in the context of</i> chronic stress, with lesser potency in standard forms of anxiety not related to stress. There may be more benefit to social anxiety as well with Ashwagandha relative to other anxiolytics
C	Sperm Quality	↑	★★☆☆☆ Minor	2 studies	Appears to enhance seminal quality (in a fairly general sense) but needs more studies against reference drugs to properly assess potency.
C	Testosterone	↑	★★☆☆☆ Minor	3 studies	Testosterone may be increased in infertile men (who have a reduction in testosterone), but there is currently no evidence to suggest an inherent testosterone boosting effect in otherwise normal men.

C	Follicle-Stimulating Hormone	↓	★☆☆ Minor	2 studies	Not overly notable, but a decrease has reached statistical significance
C	Luteinizing Hormone	↑	★☆☆ Minor	2 studies	An increase in luteinizing hormone has been detected with ashwagandha supplementation.
C	Total Cholesterol	↓	★★★☆☆ Notable	3 studies	There is a decrease in total cholesterol of around 10% when ashwagandha (water extract of the roots) is ingested. It is notable, however, since this appears to occur in all persons regardless of whether they have high cholesterol or not
C	Blood Glucose	↓	★☆☆ Minor	4 studies	A decrease in blood glucose has been noted with ashwagandha, although the magnitude is fairly small (4.7%)
C	LDL-C	↓	★☆☆ Minor	3 studies	A slight decrease in LDL-C has been noted following ashwagandha supplementation.
C	Triglycerides	↓	★☆☆ Minor	4 studies	The best evidence at this point in time suggests a slight decrease in triglycerides seen with Ashwagandha supplementation, although it does not appear to extend to persons with normal triglyceride levels but occurs in those with metabolic impairments.
C	Erections	—	—	1 study	Supplementation of 2,000mg of Ashwagandha thrice daily in men with psychogenic erectile dysfunction failed to exert any benefits more than placebo.
C	Stress	↓	★★★☆☆ Notable	1 study	Ashwagandha appears to significantly reduce the

					symptoms of stress and its comorbidities (fatigue, temporary cognitive impairment, etc.) as well as biomarkers such as cortisol.
C	Social functioning	↑	★☆☆ Minor	2 studies	Social dysfunction is reduced in anxious humans given ashwagandha, and animal studies suggest that this enhancement of socialization is a per se effect of supplementation.
C	Depression	↓	★☆☆ Minor	2 studies	Antidepressive effects have been found with ashwagandha, although they are less notable than the anti-anxiety effects. They may be mediated by similar mechanisms.
C	Cortisol	↓	★★★☆☆ Notable	3 studies	The decrease in cortisol noted in humans has reached 14.5-27.9% in otherwise healthy but stressed humans, which is significantly larger than many other supplements.
C	Seminal motility	↑	★☆☆ Minor	2 studies	Alongside improvements in all seminal parameters, ashwagandha is able to increase seminal motility as well; both are thought to underlie pro-fertility effects.
C	Weight	↓	★☆☆ Minor	2 studies	A decrease has been noted in one study where overweight persons with anxiety were being treated, and while the 1-2kg loss over 8 weeks was significant it is not sure if this applies to otherwise normal weight non-anxious persons.
C	Fatigue	↓	★☆☆ Minor	2 studies	Secondary to its adaptogenic effects, ashwagandha is able to reduce the perceptions of fatigue with prolonged daily usage.

C	Motivation	↑	★☆☆ Minor	1 study	An increase in motivation has been noted to occur in a study where anxiety was reduced; it is not sure if this is a per se effect of supplementation or due to reducing anxiety.
C	Subjective Well-Being	↑	★☆☆ Minor	1 study	An improvement in well being has been noted secondary to reducing anxiety symptoms.
C	HDL-C	↑	★☆☆ Minor	3 studies	A fairly notable increase in HDL-C has been reported with ashwagandha supplementation (17.3% over 60 days)
C	Blood Pressure	↓	★☆☆ Minor	2 studies	A small decrease in blood pressure (1.6% systolic and 5.6% diastolic) has been noted to occur alongside a reduction in pulse rate.
C	Heart Rate	↓	★☆☆ Minor	1 study	A slight reduction in pulse rate has been noted in otherwise healthy but anxious persons.
C	C-Reactive Protein	↓	★★★ Notable	1 study	The reduction seen in C-reactive protein over the course of 60 days has been noted to reach 31.6% with standard oral doses of ashwagandha supplementation.
C	Serum DHEA	↑	★☆☆ Minor	1 study	A slight increase has been detected in serum DHEA sulfate (13.2%) with 60 days of ashwagandha supplementation.
C	Hemoglobin	↑	★☆☆ Minor	1 study	A slight but significant 6.3% increase in hemoglobin has been detected in otherwise healthy persons given ashwagandha daily for a period of 60 days.
C	Anaerobic Running Capacity	↑	★☆☆ Minor	1 study	Supplementation of 500mg of

	Capacity		Minor		the water extract has been noted to improve intermittent sprint performance in otherwise untrained persons then subject to a training protocol.
C	VO2 max	↑	★☆☆ Minor	2 studies	A slight increase in VO2 max has been detected over the course of 8 weeks supplementation in otherwise untrained persons.
C	Power Output	↑	★☆☆ Minor	2 studies	Improvements in power output have been noted in trained persons subject to a sprint test and in sedentary persons who simply took the supplement for 30 days and assessed quadricep strength.
C	Aerobic exercise	↑	★☆☆ Minor	1 study	Appears to increase time to exhaustion on a treadmill test when given to athletes; the increase in endurance is mild but present
C	Fat Oxidation	—	—	1 study	Despite improvements seen in VO2 max and endurance capacities in this study, the respiratory exchange ratio (indicative of fat oxidation) was not significantly influenced.
D	Immunity	↑	★☆☆ Minor	1 study	Minor T-cell activation following ingestion of Ashwagandha tinctures, needs to be replicated.
D	Natural Killer Cell Activity	↑	★☆☆ Minor	1 study	A slight increase in natural killer cell activity has been noted with ashwagandha supplementation.
D	Diuresis	↑	★☆☆ Minor	1 study	May have diuretic effects, although not to a remarkable degree.
D	Red Blood Cell Count	—	—	1 study	Supplementation with the

					water extract of the roots for 30 days in otherwise healthy persons does not significantly influence red blood cell count.
D	Serum Platelets	—	—	1 study	There is no significant change in total platelet count seen with 30 days supplementation of the basic root extract in otherwise healthy persons
D	White Blood Cell Count	—	—	1 study	During toxicology testing in otherwise healthy persons, there is no significant alterations in white blood cell count seen with supplementation.
D	Liver Enzymes	—	—	1 study	In otherwise healthy persons, there is no significant influence on liver enzymes seen with supplementation.
D	Fat Mass	—	—	1 study	There was a trend to reduce fat mass over 30 days when supplemented to otherwise healthy persons, but this failed to reach statistical significance.
D	Lean Mass	—	—	1 study	There was a slight trend to increase lean mass in otherwise sedentary persons over 30 days, but it failed to reach statistical significance.
D	Rate of Perceived Exertion	—	—	1 study	Despite alterations in power output seen, the rate of perceived exertion in otherwise sedentary persons is not affected.
D	Subjective Well-being	↑	★☆☆ Minor	1 study	An improvement in well being has been noted secondary to reducing anxiety symptoms.
D	Pain	↓	★☆☆ Minor	1 study	A decrease in pain has been noted with supplementation of ashwagandha root during chemotherapy relative to

					control.
D	Insomnia	↓	★☆☆ Minor	1 study	Self-reports of insomnia have been reduced with supplementation of ashwagandha in women undergoing chemotherapy.
D	Sperm Count	↑	★☆☆ Minor	1 study	There appears to be an increase in sperm count in normozoospermic men with infertility consuming 5g ashwagandha daily, with more potency seen in men who self-identify as stressed.

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Asteracantha longifolia

Also known as: Hygrophila longifolia, Barleria auriculata, Barleria spinosa, Ikshura, Ikshugandha, Hygrophila spinosa, Hygrophila auriculata, Kokilaaksha, Talimakhana, gokulakanta, marsh barbel

Asteracantha longifolia (Kokilaaksha) is an ayurvedic aphrodisiac and liver protective agent. Currently, research on this plant is preliminary with limited information on both components of the plant and toxicology.

See [Asteracantha longifolia on Examine.com](#)

How to Take

There is currently not enough information available at this moment in time to recommend an oral dose of any medicinal component of this herb.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Blood Glucose	↓	★☆☆ Minor	1 study	Appears to reduce the spike and overall exposure to glucose following an oral glucose tolerance test in both healthy and diabetic adults

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Astragalus membranaceus

Also known as: Astragalus, huangqi, (A component of) Danggui buxue tang (DBT), membranous milk-vetch root, oqi, Huang Qi, TA-65, TAT2

Astragalus is a Traditional Chinese Medicine used for a wide variety of purposes and touted to increase lifespan. It has many human studies, but many cannot be applied to oral ingestion since they looked at injections. It is a moderate anti-inflammatory, especially beneficial to the kidneys.

See [Astragalus membranaceus on Examine.com](#)

How to Take

Traditional usage of Dang-Gui Buxue Tang involves 30 g Astragalus root paired with 6 g of Angelicae sinensis (a 5:1 ratio). Benefit has been associated with both this bulk amount as well as the specific ratio of the two plant extracts (the ratio appears to be the best for extracting the bioactives in the plants). If using a concentrated extract from the root, it should be dosed in accordance to the aforementioned 30 g of the root. This would mean that a 5:1 and a 10:1 concentrated extract would require 6 g and 3 g respectively to be bioequivalent. When sold in isolation, astragaloside IV appears to be effective in oral doses of 5-10 mg, and supplements that deliver this dosage of astragaloside IV are similarly effective (so this would be 500-1,000 mg of a 1-2% astragaloside extract, for example).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Diuresis	↑	★☆☆ Minor	1 study	Astragalus root appears to have diuretic properties with oral ingestion (0.3g/kg) in otherwise healthy persons.
C	Nasal Congestion	↓	★☆☆ Minor	1 study	Not an overly potent reduction of nasal congestion and other rhinitis symptoms, but more than placebo.
C	Immunity	↑	★★★☆☆ Notable	1 study	Appears to activate T-cells to a degree higher than the reference drug echinacea
C	Stroke Recovery Rate	↑	★☆☆ Minor	1 study	Not remarkably effective, but does confer some protective and cognitive promoting effects following acute stroke.
D	Kidney Function	↑	★☆☆ Minor	1 study	

			Notable		Despite statistically weak evidence, case studies suggest <i>curative</i> effects. Potential of astragalus for aiding kidney function.

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Bacopa monnieri

Also known as: Brahmi, Aindri, Lysimachia monnieri L. Cent., Graticola monnieri L., Herpestis monniera L. Kunth., Water hyssop, Thyme-leafed gratiola, Indian Pennywort, Jalabrahmi

Bacopa monnieri (simply Bacopa) is a Nootropic herb that has been used in traditional medicine for longevity and cognitive enhancement. Beyond a mild reduction in anxiety, there appears to be a reliable increase in memory formation seen after a month of supplementation.

See [Bacopa monnieri on Examine.com](#)

How to Take

Human evidence suggest that an oral dose of 300 mg Bacopa monnieri is effective when the total bacoside content (the active compounds) is 55% of the weight of the extract. If not using a concentrated extract, then the 10-20% naturally occurring bacoside content would require an oral dose of 750-1,500 mg of the leaf or a powder form the leaves. Bacopa has historically been consumed with ghee (animal fat), as aside from the supposed health properties of ghee itself bacopa is fat soluble and requires a lipid transporter to be best absorbed. Due to this, supplemental bacopa should be taken with meals.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Memory	↑	★★★☆☆ Notable	8 studies	Although general and requiring a long time to take effect (4-6 weeks), bacopa appears to reliably and effectively improve memory in both healthy persons and during cognitive decline
B	Attention	—	—	3 studies	There is unlikely to be an inherent effect of bacopa on attention, although at least one study noted improvements in attention in persons with attention deficit (ADD).
C	Depression	↓	★★☆☆☆ Minor	2 studies	An anti-depressive effect has been noted, but to a relatively small magnitude. Requires more context-based evidence
C	Anxiety	↓	★★☆☆☆ Minor	2 studies	Appears to prevent rises in anxiety, and does not appear to unilaterally reduce anxiety. May

					be more of a modulator than anything, but doesn't appear overly potent
C	Blood Pressure	—	—	1 study	No significant influence on blood pressure has been noted with chronic bacopa ingestion
C	Forgetting	↓	★☆☆ Minor	1 study	A small reduction of acute forgetting (just during a task, not outright amnesia) has been noted, which may contribute better to long term memory (ie. grasping concepts better)
C	Cognition	—	—	1 study	No significant influences noted on acute cognitive performance with bacopa monnieri ingestion

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Banaba Leaf

Also known as: Crape Myrtle, Crepe Myrtle, Lagerstroemia, Banaba

Lagerstroemia, also known as Banaba, is a plant whose leaves have been used for anti-diabetic purposes. It contains a variety of molecules such as corosolic acid which may confer benefit to glucose control.

See [Banaba Leaf on Examine.com](#)

How to Take

An oral supplement of 3,000mg of the leaf extract from Banaba appears to be used with efficacy. Other Banaba supplements may have concentrated supplements which increase the corosolic acid content, in which a 2:1 extract of 1,500mg would be equivalent to the 3,000mg leaf extract. Although the above dose is currently recommended, it is not known if this is the optimal dose or not. Furthermore, it is not known whether or not this supplement needs to be taken with meals (although it is recommended out of prudence for the purposes of helping glucose tolerance to take it with meals).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Blood Glucose	↓	★★★☆☆ Notable	1 study	The reduction in blood glucose appeared to range from 20-30%, which is more than usually seen with dietary supplements.

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Benfotiamine

Also known as: S-{(Z)-2-[(4-amino-2-methylpyrimidin-5-yl) methyl-formylamino]-5-phosphonooxypent-2-en-3-yl} benzenecarbothioate

Benfotiamine is a relative of the vitamin Thiamine (B1) that appears to have a therapeutic role in pain reduction and diabetic complications (neuropathies and nephropathies); confers bioavailable Vitamin B1 after oral ingestion.

See [Benfotiamine on Examine.com](#)

How to Take

Benfotiamine is commonly taken at the oral dose of 300-600mg over the course of the day, usually in two divided doses with meals (150mg or 300mg twice daily).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Protection from Smoking	↑	★☆☆ Minor	1 study	There appears to be an attenuation in how much a cigarette constricts peripheral blood flow by about half, with other biomarkers not changed overly to an overly potent degree.
C	Advanced Glycation End products	—	—	1 study	No significant changes in urinary or serum AGEs observed at the moment
C	Proteinuria	—	—	2 studies	No evidence to support a reduction in the amount of protein lost in the urine of persons with diabetic nephropathy (UAE between 15-300mg/24 hours). Whether there is a preventative effect or not, there does not appear to be a rehabilitative effect.
C	HDL-C	—	—	2 studies	No significant influences on HDL-C observed.
C	Inflammation	—	—	1 study	Insufficient evidence with the

					preliminary evidence failing to any influence on circulating cytokines.
C	HbA1c	—	—	2 studies	Two studies in diabetics have failed to find an influence of benfotiamine on HbA1c
C	Nerve Repair	—	—	1 study	Preliminary evidence has come back negative over 2 years in type 1 diabetics with diabetic neuropathy.
C	Total Cholesterol	—	—	1 study	No significant changes in total cholesterol
C	LDL-C	—	—	1 study	Although not a primary research end-point, no significant influence on LDL-C is seen.
C	Triglycerides	—	—	1 study	No significant influence on triglycerides.
C	Kidney Function	—	—	1 study	Insufficient evidence to support enhanced kidney function.
C	Blood Pressure	—	—	1 study	No significant evidence to support alterations in blood pressure.

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Berberine

Berberine is extracted from a variety of anti-diabetic herbs, which appears to have potent therapeutic effects in diabetes; it appears to have similar potency to some pharmaceuticals.

See [Berberine on Examine.com](#)

How to Take

The oral doses of berberine that are normally associated with positive effects range from 900mg (300mg taken three times a day) and can extend up to 2,000mg daily (in three or four divided doses). Berberine tends to be taken either with food or shortly after, not so much for absorption rates but due to the spike in blood glucose and lipids seen with meals. Higher doses do not appear to be adverse (no reported toxicity), but a large acute bolus of berberine may cause gastrointestinal upset and possible side effects such as cramping or diarrhea; this is the reason the dose is split, and is another reason for ingestion with meals (to reduce this side-effect).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Total Cholesterol	↓	★★★☆☆ Notable	2 studies	Total cholesterol appears to be decreased by around −0.58mmol/L (95% CI −1.02 to −0.14), which is not overly potent. The reduction is notable as if this mechanism is via PCSK9 inhibition then it would work very well with statin drugs.
B	Triglycerides	↓	★★☆☆☆ Minor	2 studies	Degree of reduction according to meta-analysis was −0.48mmol/L (95% CI −0.57 to −0.39) which was not overly remarkable.
B	Blood Glucose	↓	★★★★☆ Strong	2 studies	The usage of berberine in reducing blood glucose, according to the most recent meta-analysis, is comparable to the oral hypoglycemic drugs Metformin or Glibenclamide; this suggests berberine is one of the more effective supplements for blood glucose reductions.

B	Insulin	↓	★☆☆ Minor	2 studies	Degree of reduction of fasting insulin according to meta-analysis was SMD -0.50mU/L (95% CI -0.96 to -0.03) which is not overly remarkable.
B	HbA1c	↓	★★★ Strong	2 studies	The reduction of HbA1c associated with berberine, according to a meta-analysis of diabetics using 1,000-1,500mg berberine daily, was -0.72% (95% CI -0.97 to -0.47) more than placebo. This reduction appears to be one of the more significant reductions associated with dietary supplements.
B	LDL-C	↓	★☆☆ Minor	1 study	The reduction of LDL-C when berberine was paired with lifestyle changes was -0.58mmol/L (95% CI -0.78 to -0.39) in diabetics, suggesting a significant benefit but not remarkably potent.
B	HDL-C	↑	★☆☆ Minor	1 study	Degree of improvement was 0.07mmol/L (95% CI 0.04 to 0.10) according to the meta-analysis, not remarkably effective
C	Insulin Sensitivity	—	—	1 study	Currently no evidence to support efficacy, although it may increase insulin sensitivity (requires more research)
C	Exercise Capacity (with Heart Conditions)	↑	★☆☆ Minor	1 study	A positive effect, but the potency thereof was not overly remarkable
C	Quality of Life	↑	★☆☆ Minor	1 study	Minor effect in persons with cardiomyopathy, but it is unsure if berberine has a per se benefit on quality of life.
C	Canker Sores	↓	★☆☆ Minor	1 study	Was able to reduce canker sores when topically applied, but was not compared to a

					reference compound.

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Beta-Alanine

Also known as: Carnosine precursor, beta alanine

Beta-alanine is the building block of carnosine, a molecule that helps to buffer acid in muscles, increasing physical performance in the 60-240 second range. Beta-alanine can aid lean mass gain. Carnosine appears to be an anti-oxidant and anti-aging compound.

See [Beta-Alanine on Examine.com](#)

How to Take

Standard daily doses of beta-alanine are between 2,000 – 5,000mg. Beta-alanine supplementation is not timing-dependent, in relation to exercise. Using beta-alanine as part of a pre-workout stack is a popular option, however. Large doses of beta-alanine may result in a tingling feeling called paresthesia. It is a harmless side effect, but can be avoided by using a time release formulating or taking smaller doses, between 800-1000mg, several times a day.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Muscular Endurance	↑	★☆☆ Minor	8 studies	The data from the lone meta-analysis suggesting a 2.5% increase in muscular endurance during exercises between 60-240s (usually measured by time to exhaustion) seems to be a good summation. The benefit is present, but is pretty small in magnitude.
B	Power Output	—	—	5 studies	No significant effects on acute power output
B	VO2 Max	—	—	5 studies	Highly unreliable effects on VO2 max and currently is thought to have no significant effect.
B	Anaerobic Running Capacity	↑	★☆☆ Minor	4 studies	Somewhat effective, may simply be secondary to enhancing muscular endurance and reducing fatigue rather than any cardiopulmonary interaction

B	Fatigue	↓	★☆☆ Minor	7 studies	Seems somewhat effective in reducing fatigue and secondary to that, improving time to exhaustion.
C	Fat Mass	↓	★☆☆ Minor	2 studies	Mechanisms unknown, but some studies suggest a fat loss effect (possibly secondary to extra workout volume)
C	Lean Mass	↑	★☆☆ Minor	3 studies	Doesn't appear overly potent, but either inherently or through greater workload there appears to be a hypertrophic effect associated with beta-alanine.
C	Testosterone	—	—	1 study	
C	Cortisol	—	—	1 study	
C	Growth Hormone	—	—	1 study	

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Black Cohosh

Also known as: Cimicifuga racemosa, Bugbane, Bugroot, Snakeroot, Rattleroot, Blackroot, Black Snake Root

Black Cohosh is the most popular supplement for menopause in North America, but the human studies are mixed. Pretty down the middle, and placebo effect seems to play a great deal in these studies. It holds some benefit for controlling hot flashes and night sweats, but does not appear very potent.

See [Black Cohosh on Examine.com](#)

How to Take

If using an isopropanolic extract (usually sold under the brand name of Remifemin), 20-40mg daily is used in doses of 20mg; taking 20mg results in a once daily dosing, whereas taking 40mg is twice daily dosing of the 20mg. This dosage (20-40mg) confers 1-2mg of triterpenoid glycosides. If using an aqueous:ethanolic extract of black cohosh root (ie. not Remifemin) then doses range from 64-128mg daily which are usually taken in two divided doses. This contributed about the same amount of triterpenoid glycosides. It is not known whether or not black cohosh needs to be taken with food, although it is sometimes recommended to do so out of prudence.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Symptoms of Menopause	↓	★☆☆ Minor	13 studies	Although there appears to be some benefit over placebo, more recent studies note that the magnitude of benefit is much less than previously though (in the past, a false positive occurred when unblinded studies noted remarkable benefits with black cohosh; the placebo effect appears to be quite potent in regards to menopause)
C	Anxiety	—	—	1 study	The trial to measure anxiety related to menopausal symptoms failed to find a benefit associated with black cohosh
C	Estrogen	—	—	1 study	No significant influences on circulating estrogen levels or biomarkers of estrogenicity (vaginal cytology)

C	Memory	—	—	1 study	No significant effect on memory function
C	Cognition	—	—	1 study	No significant influences on cognition in menopausal women has been noted
C	LDL-C	—	—	1 study	No significant effects on LDL-C
C	HDL-C	—	—	1 study	No significant influence on HDL-C
C	Triglycerides	—	—	2 studies	No significant effect on triglyceride concentrations in serum
C	Blood Glucose	—	—	1 study	No significant influence on blood glucose levels
C	Insulin	—	—	1 study	No significant influence on fasting insulin
C	C-Reactive Protein	—	—	1 study	No significant alterations seen in C-RP with black cohosh
D	Breast Density	—	—	1 study	
D	Coronary Heart Disease Risk	↑	★☆☆ Minor	1 study	A slightly increased chance of heart disease was said to occur in one study pairing black cohosh with exercise, and an increased risk was also determined in control but not in black cohosh in isolation.
D	Bone Mineral Density	—	—	1 study	No significant influence on bone mineral density
D	Blood Pressure	—	—	1 study	No significant influence on blood pressure
D	Liver Enzymes	—	—	1 study	No significant influence on liver enzymes

D	Blood Flow	—	—	1 study	No significant influences on blood flow and vasodilation
D	Weight	—	—	1 study	No significant influences on body weight
D	Subjective Well-Being	↑	★☆☆ Minor	1 study	May increase well being in those with menopause if a reduction of symptoms occurs.

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Bladderwrack

Also known as: Fucus Vesiculosus

Bladderwrack is a species of seaweed known as Fucus vesiculosus that serves as a foodstuff and a source of Fucoxanthin, it is though to increase the metabolism via the thyroid but that is due to fixing iodine deficiencies historically.

See [Bladderwrack on Examine.com](#)

How to Take

Although there is not a large amount of evidence currently, the evidence in humans has noted that 500mg of bladderwrack (basic extract of the seaweed, not concentrated) appears to be bioactive. This is a lower dose than the 4,000mg used in studies on Ascophyllum nodosum, and due to their similar composition the ideal range may be somewhere in between these two doses (or above 4,000mg).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Skin Quality	↑	★☆☆ Minor	1 study	Limited evidence supports its efficacy, difficult to assess potency due to no reference drug.
C	Blood Glucose	↓	★☆☆ Minor	1 study	Appears somewhat potent at acutely reducing blood glucose following a meal (possibly by inhibiting absorption) but no long term studies.
C	Insulin	↓	★☆☆ Minor	1 study	Appears to reduce insulin AUC after a carbohydrate containing meal
C	Insulin Sensitivity	↑	★☆☆ Minor	1 study	Appears to be pretty effective at increasing insulin sensitivity acutely after a meal, which may be due to reduced insulin in serum.

Blueberry

Also known as: Blueberries, Blue berries

Blueberries (a part of the genus vaccinium) are fruits with a large content of molecules known as anthocyanins. These antioxidant compounds are sought after for their ability to improve cognition and as a general health promoting supplement. The fruits also confer benefits at 60-120g fresh weight.

See [Blueberry on Examine.com](#)

How to Take

If using a 'blueberry extract' (dehydrated blueberries, but not necessarily isolated anthocyanins) then the optimal dose tends to be in the 5.5-11g range with the higher dose being more effective. If using the isolated anthocyanins, then an oral dose of 500-1,000mg appears to be in the optimal range. Lower doses may still be effective. If using fresh or frozen blueberries with the water weight still in the equation, then the 5.5-11g of blueberry extract translates into about 60-120g of fresh berries daily. Blueberries and their extracts would be better stored in cold environments such as refrigeration, and while blanching berries is known to increase anthocyanin bioavailability excessive heat treatment or exposure degrades their anthocyanin content.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	DNA damage	↓	★★★☆☆ Notable	4 studies	DNA damage appears to be acutely decreased following consumption of blueberries or its extracts (375mg anthocyanins or more) and tends to be in the range of a 20% reduction.
B	Blood Glucose	—	—	5 studies	Although the leaf extract has once been associated with a reduction in blood glucose, the fruits do not appear to inhibit carbohydrate absorption nor reduce fasting glucose concentrations.
C	Heart Rate	—	—	1 study	No known interactions with heart rate and blueberry supplementation.
C	Nitric Oxide	—	—	1 study	Blueberries do not appear to significantly influence nitric

					oxide metabolism
C	Cognitive Decline	↓	★☆☆ Minor	1 study	Supplementation of blueberry extract does appear effective in elderly persons with general cognitive decline, able to improve cognition and memory.
C	Memory	↑	★☆☆ Minor	1 study	Memory formation in elderly subjects can be improved with daily supplementation of blueberries or their extract
C	Insulin	↓	★☆☆ Minor	1 study	Insulin has once been noted to be decreased in elderly persons with blueberry ingestion.
C	Subjective Well-Being	↑	★☆☆ Minor	1 study	A slight improvement in subjective well being and happiness has been noted in elderly persons given blueberries over a few weeks as a daily supplement.
C	General Oxidation	↓	★☆☆ Minor	3 studies	Oral ingestion of berries or their extracts tends to reduce oxidative biomarkers and improve antioxidant status either acutely or with daily supplementation
C	Oxidation of LDL	↓	★☆☆ Minor	2 studies	There appears to be a reduction in LDL oxidation, with the one chronic study suggesting a 27% reduction (the acute study noting less of a protective effect).
C	Appetite	—	—	1 study	No significant influence on appetite or satiety
C	Blood Pressure	↓	★☆☆ Minor	2 studies	A decrease in blood pressure has been noted in persons at risk for cardiovascular disease (6% systolic and 4% diastolic), but this may be limited to high risk individuals only.

C	Triglycerides	—	—	2 studies	No known interactions with serum triglycerides following supplementation of blueberries.
C	C-Reactive Protein	—	—	2 studies	C-reactive protein does not appear to be influenced with blueberry supplementation.
C	TNF-Alpha	—	—	1 study	No significant changes in TNF-alpha concentrations
C	Total Cholesterol	—	—	2 studies	No significant influence on total cholesterol concentrations in the blood.
C	LDL-C	—	—	2 studies	No significant changes in LDL-C concentrations in serum with blueberries.
C	HDL-C	—	—	2 studies	No significant influence on HDL-C
C	Insulin Sensitivity	↑	★☆☆ Minor	2 studies	An improvement of insulin sensitivity has been noted in persons with insulin resistance, but this may only affect high risk individuals.
C	Muscle Soreness	—	—	1 study	Despite the reduction in muscle damage and increased rate of recovery, there are no significant changes in subjective muscle soreness
C	Muscle Damage	↓	★☆☆ Minor	1 study	Appears to reduce biomarkers of muscle damage such as creatine kinase
C	Interleukin 6	—	—	2 studies	No significant influence on IL-6 concentrations in serum
D	Cortisol	—	—	1 study	Exercise-induced changes in cortisol are not influence by

					blueberry supplementation
D	nF-kB Activity	—	—	1 study	The study to measure nF-kB binding activity in muscle tissue after exercise failed to find an influence of blueberry supplementation.
D	Exercise-induced Oxidation	—	—	1 study	The lone study using a 2.5 hour running protocol at 72% VO2 max failed to find any significant differences between groups in oxidative status after exercise.
D	Interleukin 10	↑	★☆☆ Minor	1 study	An increase in IL-10 following exercise has been noted.
D	Natural Killer Cell Content	↑	★☆☆ Minor	1 study	An increase in natural killer cells has been noted in the range of 76-122% following physical exercise.
D	Exercise-Induced Immune Suppression	—	—	1 study	The alterations in most immune cells seen during exercise are wholly unaffected by blueberry supplementation.
D	Aerobic Exercise	—	—	1 study	Chronic loading of blueberries with an acute dose prior to prolonged exercise (2.5 hours) in trained men does not improve physical performance.
D	HbA1c	—	—	1 study	Currently no studies noting changes in HbA1c, as it appears to be unaffected by supplementation.
D	Weight	—	—	1 study	No significant influence on weight when taken as a daily supplement in obese individuals.
D	Lipid Peroxidation	↓	★☆☆ Minor	1 study	Alongside the reduction in serum oxidation comes a reduction in lipid peroxidation biomarkers such as MDA

D	Cell Adhesion Factors	—	—	1 study	No significant alterations in cell adhesion factors (sCAM-1 and vCAM-1)
D	Adiponectin	—	—	1 study	No significant influence on adiponectin concentrations in obese individuals

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Boron

Boron is a dietary mineral which is claimed to increase testosterone when supplemented at doses higher than from food.

See [Boron on Examine.com](#)

How to Take

The lowest active dose of Boron supplementation appears to be 3mg, which is effective in supporting hormonal parameters in postmenopausal women. Studies on osteoarthritis have used 6mg of Boron while studies in youth investigating hormonal changes have used 10mg. The optimal dose is currently not known, but the above doses appear to be active for their aforementioned goals.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Kidney Stones	↓	☆☆☆ Minor	1 study	Appears effective, but no comparison to a reference drug nor control group thus far
D	Testosterone	↑	☆☆☆ Minor	2 studies	There appears to be an interaction with Boron and testosterone in both genders, but it is seemingly unreliable
D	Estrogen	↓↑	☆☆☆ Minor	2 studies	Appears to influence estrogen, seems unreliable in its mechanisms and is likely context dependent. Both increases and decreases have been noted
D	Inflammation	↓	☆☆☆ Minor	1 study	Some influence on typically inflammatory cytokines, practical relevance of these changes unknown
D	DHT	—	—	1 study	No significant influences on serum DHT noted
D	Free Testosterone	↑	☆☆☆ Minor	1 study	Appears to be quite effective, but requires some more robust trials

D	Cortisol	—	—	1 study	No significant effect on cortisol has been noted with supplemental boron
D	C-Reactive Protein	—	—	1 study	No significant effect on this inflammatory biomarker

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Boswellia serrata

Also known as: Indian Frankincense, Salai, Salai Guggul, Gajabhakshya

An Ayurvedic herb also classified as a phytopharmaceutical (H15; Europe) which appears to be quite anti-inflammatory, helpful against osteoarthritis, and may help cerebral edema. Boswellia serrata appears to have preliminary evidence for anti-inflammatory joint disorders.

See [Boswellia serrata on Examine.com](#)

How to Take

The anti-inflammatory and anti-cancer benefits appear to be dose-dependent, with the minimal dose that has been seen as effective being 3 doses of 400mg Boswellia Serrata (basic extract) taken daily with meals. If using Boswellia Serrata itself, doses can increase up to 1800mg taken thrice a day, but are usually in the range of 800-1200mg taken thrice a day. If using the blends of 5-Loxin or Aflapin (concentrated sources of the main bioactive AKBA), oral doses of 100-250mg are taken once a day with a meal.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Symptoms of Osteoarthritis	↓	★★★☆☆ Notable	4 studies	The reduction observed with Boswellia serrata for pain and other symptoms of osteoarthritis are more profound than other supplements including that of glucosamine (reference), but study robustness is limited by industry influence.
C	Asthma	↓	★★★☆☆ Notable	1 study	Preliminary evidence, but boswellia appeared to benefit much more people than did placebo in symptoms of asthma.
D	Subjective Well-Being	↑	★★☆☆☆ Minor	1 study	Increase in well-being was likely secondary to reducing joint pain from osteoarthritis
D	Leg Swelling	↓	★★☆☆☆ Minor	1 study	Lack of reference drugs limits conclusions that can be made in regards to the potency

D	Skin Elasticity	↑	★☆☆ Minor	1 study	Not enough evidence to evaluate potency, but an increase in skin elasticity has been noted with topical boswellia
D	Skin Quality	↑	★☆☆ Minor	1 study	Somewhat effective, not enough evidence to fully evaluate potency.
D	Brain Tumor	↓	★★★☆☆ Notable	1 study	A lone case study of eliminating a brain tumor

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Branched Chain Amino Acids

Also known as: BCAAs, BCAA

Branched Chain Amino Acids (BCAAs) are three amino acids with similar structures that beneficially influence the muscles. They can be found in any food containing protein, such as eggs or meat. Supplementation is not necessary, but BCAAs may benefit the body if taken at specific times.

See [Branched Chain Amino Acids on Examine.com](#)

How to Take

BCAA dosages are based on goals. The standard dosage for isoleucine is 48-72mg/kg (assuming a non-obese person). The standard leucine dosage is between 2-10g. A combination dose is 20g of combined BCAAs, with a balanced ratio of leucine and isoleucine. Isoleucine is used for increasing glucose uptake into cells, while leucine is used to improve muscle protein synthesis. BCAA supplementation is not necessary if enough BCAAs are provided through the diet. Further research is needed to determine valine's optimal dosage and reason for supplementation.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Fatigue	↓	★☆☆ Minor	8 studies	A decrease in fatigue (mental fatigue when measured after the workout) results when BCAA supplementation is taken during exercise at a dose above 10g or so
B	Fat Oxidation	↑	★☆☆ Minor	3 studies	In prolonged exercise and somewhat related to the antifatigue effects, an increase in fat oxidation is noted with BCAA supplementation; this is thought to be related to the glycogen preserving effects of BCAAs.
B	Aerobic Exercise	↑	★☆☆ Minor	4 studies	An increase in time to exhaustion appears to exist in prolonged endurance exercise, but this benefit may only exist in untrained or lightly trained individuals. Several studies have noted that the anti-fatigue effects and increased time to exhaustion do not really occur

					in advanced athletes
B	Lactate Production	—	—	3 studies	There does not appear to be any reliable or significant changes in blood lactate concentrations following exercise with BCAA supplementation
C	Muscle Soreness	—	—	2 studies	No significant influence on muscle soreness when assessed 2-3 days after exercise that is preloaded with BCAA supplementation
C	Processing Accuracy	↑	★☆☆ Minor	1 study	The increased processing accuracy appears to be secondary to reducing exercise-related fatigue, and occurs when testing is after exercise.
C	Heart Rate	—	—	2 studies	No significant alterations in heart rate noted with BCAA supplementation at rest or during exercise
C	Cortisol	—	—	1 study	No significant interactions with BCAA supplementation and cortisol
C	Power Output	—	—	2 studies	Mixed effects on power output, but when it does occur it is not a <i>per se</i> increase in power output but secondary to reduced muscular soreness after repeated exercise. This may be more indicative of anti-fatigue effects than of genuine power output improvement
C	Rate of Perceived Exertion	↓	★☆☆ Minor	1 study	There is some evidence to support a reduction in the rate of perceived exertion during exercise under the influence of BCAA supplementation, but this appears to unreliably improve performance and is of low magnitude

C	Anaerobic Running Capacity	—	—	1 study	No significant performance enhancing effect on short-term cardiovascular exercise
C	Oxygen Uptake	—	—	1 study	Oxygen uptake during anaerobic cardiovascular exercise does not appear to be modified with BCAA supplementation
C	Weight Loss	↓	★☆☆ Minor	1 study	The weight loss that occurs during prolonged strenuous exercise (in these examples, skiing) are attenuated with BCAA supplementation relative to carbohydrate. This is likely indicative of lean mass and/or hydration, and is not necessarily an anti-fat loss effect
C	Ammonia	↓↑	★☆☆ Minor	1 study	Human studies suggest time-dependent influences on ammonia (increase after exercise up until 2 hours, a reduction the next day) while animal studies suggest that overdosing BCAAs can reverse a reduction into an increase
C	Insulin	—	—	1 study	No significant influence of BCAA supplementation on fasting insulin levels
C	Reaction Time	↓	★☆☆ Minor	1 study	A (beneficial) decrease in reaction time has been noted during a stimulated soccer test, which was thought to be secondary to the antifatigue effects. Hypothesized to be useful for prolonged sports
C	Adrenaline	—	—	1 study	No significant influence on adrenaline concentrations
C	Noradrenaline	—	—	1 study	BCAA supplementation does not appear to significantly influence noradrenaline concentrations in serum

C	Dopamine	—	—	1 study	Similar to the other catecholamines (adrenaline and noradrenaline), serum dopamine does not appear to be altered with supplemental BCAAs.
C	Blood Glucose	—	—	2 studies	There does not appear to be a likely alteration in blood glucose concentrations <i>per se</i> with BCAA supplementation, but the increased fat oxidation may attenuate the decline in glucose seen during prolonged exercise (which would appear to be a relative increase at later time points)
C	Ketone Bodies	—	—	1 study	No significant alterations in formation of ketone bodies, which may be due to the ketogenic BCAA (leucine) being offset by the other two glucogenic ones

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Bromelain

Also known as: Pineapple extract

A surprisingly potent anti-inflammatory molecule, Bromelain is a protein digestive enzyme that somehow makes it into the blood undigested and can transverse cell membranes. Reduces heart burn at meals, nasal decongestant, and flavors semen like pineapples.

See [Bromelain on Examine.com](#)

How to Take

For purposes that are not digestion related; benefits have been seen with doses ranging from 200-800mg, with the higher doses more effective than the lower ones within this range. It is anecdotally taken between meals to avoid potential degradation in the stomach if taken for a non-digestive reason. If taken as a digestive enzyme, doses between 200-2,000mg are common. This wide variance is due to variations in the enzymatic potential of Bromelain, which is standardized by either m.c.u (milk clotting units) or g.d.u (gelatin dissolving units). Dosages of 1,200 g.d.u or 2,000 m.c.u are used daily, with divided dosages at protein containing meals.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Incidence of Type 1 Diabetes	—	—	1 study	
C	Symptoms of Osteoarthritis	—	—	1 study	No significant influence on symptoms of osteoarthritis when tested
C	Muscle Soreness	↓	★☆☆ Minor	2 studies	It is possible bromelain might reduce muscle soreness, but currently the evidence does not support this claim (although the trial to note a failure of bromelain also noted a failure with Ibuprofen, a known active drug)
D	Nasal Congestion	↓	★☆☆ Minor	1 study	The potency at this moment in time does not appear remarkable.
D	Inflammation	↓	★☆☆ Minor	1 study	Requires more evidence, but at the moment appears somewhat effective

D	Subjective Well-Being	↑	★☆☆ Minor	1 study	Minor improvements in well being secondary to reducing joint pain

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Butea superba

Also known as: Red Kwao Krua

Butea Superba (Red Kwao Krua) is a herb from Thai medicine sometimes thought to be the male equivalent of Pueraria mirifica, a phytoestrogen known as White Kwao Krua; evidence for Butea Superba for these claims is lacking.

See [Butea superba on Examine.com](#)

How to Take

There is not enough information to recommend supplementation of butea superba, but it appears to be traditionally used in the range of 100-250mg. The exact bioactives that underlie its effects are not known

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Erections	—	—	2 studies	Currently assumed to be ineffective for erections or erectile dysfunction due to the poor quality of the evidence in existence.

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Caffeine

Also known as: Coffee extract, Tea extract, 1,3,7-Trimethylxanthine, Liquid crack

Caffeine is a stimulatory anti-sleep compound extracted from coffee beans. Habitual caffeine use leads to tolerance, which dulls several of caffeine’s effects.

See [Caffeine on Examine.com](#)

How to Take

Caffeine dosages should be tailored to individuals. If you are new to caffeine supplements, start with a 100mg dose. Typically, 200mg of caffeine is used for fat-burning supplementation, while acute strength increases occur at higher doses, 500mg and above. Researchers tend to use a dosage range of 4-6mg/kg bodyweight. Caffeine can be supplemented through popular beverages, like Coffee, Tea and Energy Drinks, but it can also be taken in a pill form. Many of caffeine’s effects, including fat burning, strength benefits, and euphoria, are subject to tolerance, and may not occur in people used to caffeine, no matter how large the dose is.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Lactate Production	↑	☆☆☆ Minor	6 studies	Seems to increase lactate production during exercise when caffeine is acutely preloaded
B	Heart Rate	↑	☆☆☆ Minor	6 studies	An increase in heart rate is noted, but not wholly consistent. It appears to affect those with lower caffeine tolerance or high overdoses of caffeine
B	Anaerobic Running Capacity	↑	☆☆☆ Notable	7 studies	Appears to benefit anaerobic cardiovascular exercise, perhaps due to combination antifatigue effects and increasing power output
B	Power Output	↑	☆☆☆ Notable	9 studies	There appears to be a reliable and significant increase in power output (both weight lifting as well as cycle ergometer measurements) in both trained and sedentary

					persons with doses of caffeine exceeding 5mg/kg, assuming the subject is not caffeine tolerant. Tolerance, or lower doses of caffeine, are not as effective.
B	Aerobic Exercise	↑	★☆☆ Minor	3 studies	An increase in aerobic exercise capacity is noted with caffeine, possibly secondary to increased free fatty acids and adrenaline
B	Blood Pressure	↑	★☆☆ Minor	6 studies	Tends to increase blood pressure more than it doesn't, which is in part due to caffeine tolerance (naive users experiencing increases in blood pressure at higher rates) or genetics; the increase in blood pressure tends to be transient and low in magnitude
B	Rate of Perceived Exertion	↓	★☆☆ Minor	5 studies	Although the effects are somewhat unreliable, there appears to be a reduction in the rate of perceived exertion associated with caffeine ingestion
B	Training Volume	↑	★☆☆ Minor	3 studies	There appears to be an increase in training volume (overall work performed during a workout) associated with caffeine ingestion relative to placebo, extending to both weightlifting and anaerobic cardiovascular exercise
B	Testosterone	↑	★☆☆ Minor	4 studies	A very small (usually 12%) increase is noted in trained athletes consuming caffeine above 250mg prior to exercise, this may be dependent on exercise as studies without exercise fail to find alterations in testosterone. This increase is unlikely to lead to significant testosterone-like effects
B	Cortisol	↑	★☆☆ Minor	4 studies	In general, cortisol appears to

			Minor		be increased at high doses of caffeine; lower doses may not have an effect.
B	Insulin Sensitivity	↓	★☆☆ Minor	4 studies	A decrease in insulin sensitivity is noted acutely when caffeine is taken alongside carbohydrates, thought to be secondary to reducing glucose deposition.
B	Blood Glucose	↑	★☆☆ Minor	3 studies	There may be an acute increase in blood glucose when caffeine is paired with a carbohydrate containing meal, but long term ingestion of caffeine does not appear to adversely influence glucose (only acutely)
B	Reaction Time	↑	★☆☆ Minor	5 studies	Although the overall effect is unreliable and context dependent, caffeine appears to increase reaction time and attention (possibly at the cost of accuracy)
B	Memory	—	—	5 studies	Overall, highly mixed effects effects of caffeine on memory. It appears to increase spatial/perceptual memory and reduce working memory (perhaps secondary to overstimulation)
B	Adrenaline	↑	★☆☆ Minor	3 studies	Serum catecholamines (adrenaline, noradrenaline) are increased in naive users of caffeine following acute ingestion
B	Fat Oxidation	↑	★☆☆ Minor	3 studies	An increase in fat oxidation appears to be apparent (assessed via increased serum glycerol and free fatty acids) which is thought to be secondary to increases in adrenaline
C	VO2 Max	—	—	1 study	No significant influence on VO2

					max ratings
C	Oxygen Uptake	↑	★☆☆ Minor	1 study	Appears to be an increase in oxygen uptake with caffeine consumption, may be related to the increase in metabolic rate
C	Subjective Well-Being	↑	★☆☆ Minor	2 studies	May increase subjective well being and mood state, possibly secondary to reducing fatigue or from catecholamines
C	Anxiety	↑	★☆☆ Minor	1 study	It is possible for caffeine to be anxiogenic, but requires genetic susceptibility to it
C	Fatigue	↓	★☆☆ Minor	2 studies	Decrease in fatigue have been noted during exercise and during low strenuous physical exercise
C	Visual Acuity	—	—	1 study	No significant influence on visual acuity has been noted with caffeine on hand-eye or target-based visual tasks
C	Metabolic Rate	↑	★☆☆ Minor	2 studies	Mixed effects on metabolic rate following acute doses of caffeine
C	HDL-C	—	—	1 study	No significant influences on HDL cholesterol noted
C	LDL-C	—	—	1 study	No significant influences on LDL cholesterol noted
C	Triglycerides	—	—	1 study	No significant influence on triglyceride levels
C	Insulin	—	—	2 studies	No significant influences on fasting insulin (not postprandial) are noted with caffeine
C	Thermogenesis	↑	★☆☆	1 study	Increases in heat production

			Minor		increases in heat production following caffeine consumption have been noted
C	Wakefulness	↑	★★★☆☆ Notable	2 studies	Caffeine is reliable and effective in increasing the state of wakefulness and suppressing sedation
C	Blood Flow	↑	★☆☆☆☆ Minor	1 study	An increase in blood flow (Flow mediated vasodilation) has been noted with caffeine.
C	Appetite	—	—	1 study	In elderly men, there does not appear to be a significant suppressive effect of caffeine on appetite.

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Caralluma fimbriata

Also known as: Slimaluma (Brand Name)

Caralluma Fimbriata is a certain species of the Caralluma genus that appears to have historical usage as a famine food, appetite suppressant, and thirst quencher when the vegetables are boiled and salted. Research is preliminary, but seems to validate these claims.

See [Caralluma fimbriata on Examine.com](#)

How to Take

Currently, the only human study used 1,000mg of a 14:1 concentrated extract (equivalent to 14g of the plant in dry weight). This dose appeared to be effective somewhat, and is currently the only lead for what oral dosage of supplementation is needed. Caralluma fimbriata appears to require up to a month or so to work for appetite suppression.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Appetite	↓	★☆☆ Minor	1 study	Might be more effective as the one study noted a time-dependent suppression of appetite (but was terminated at 2 months); requires more research and perhaps some comparators.
C	Weight	—	—	1 study	Study was too short for the appetite suppressing effects to manifest as weight loss, and thus no evidence exists for weight reducing effects.

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CDP-choline

Also known as: Citicholine, Cytidine Diphosphocholine

CDP-choline (citicholine) is a nootropic compound that converts to both Choline and cytidine upon ingestion, the latter of which converts into Uridine in the body. It appears to confer cognitive-promoting properties as a prodrug for these two compounds.

See [CDP-choline on Examine.com](#)

How to Take

Standard dosing of CDP-choline is to take 500-2,000 mg in two divided doses (of 250-1,000 mg) usually separated by 8-12 hours, although a single daily dose is also sometimes used. A single dose of 4,000 mg does not appear to affect the blood any differently than 2,000 mg, and so it is not necessary to take such a high dose. There are some properties, such as attention-promotion or improving bioenergetics, that seem to respond exclusively or more strongly to the lower dosage range. Other properties like appetite are the opposite, and thus the ideal dosage depends somewhat on the goal.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Cocaine Addiction	↓	★☆☆ Minor	3 studies	CDP-Choline appears to be weakly anti-addictive against cocaine addiction, although the one study undertaken in persons with no intention to minimize cocaine usage can back negative.
C	Symptoms of Bipolar Disorder	—	—	1 study	The lone study in persons with bipolar disorder was one investigating addiction, and when measuring symptoms of bipolar disorder they failed to find any influence of supplementation on symptoms.
C	Attention	↑	★☆☆ Minor	1 study	There appear to be attention promoting effects of CDP-Choline, with the one study in adult women noting that 250-500mg was effective but 250mg was more effective.
C	Coanitive Decline	↓	★☆☆	1 study	

			 Minor		The rate of memory decline seen in older persons during the aging process appears to be attenuated with supplementation of CDP-Choline
C	Memory	↑	 Minor	2 studies	Appears to promote cognition in otherwise healthy older adults. Although animal studies suggest this may apply to youthful subjects as well, no human currently exists for youth
C	Blood Pressure	↓	 Minor	1 study	One study in older adults noted, as a side-effect, that systolic blood pressure was slightly reduced
D	Appetite	↓	 Minor	1 study	There appear to be minor appetite suppressing effects at higher doses of oral CDP-choline ingestion (2,000mg daily), although on a 1-10 point Likert scale the reduction measured at 27% (6.8 to 5.92; 1 being the lowest possible ranking)
D	Weight	—	—	1 study	No significant effects of CDP-Choline on weight, despite the small appetite reducing effect
D	Visual Acuity	↑	 Minor	1 study	In persons with glaucoma, CDP-Choline ingestion appears to be somewhat protective of vision and has been noted to cause improvements in visual acuity
D	Intraocular Pressure	—	—	1 study	Despite the improvements seen in visual acuity and eye health with supplementation of CDP-Choline, intraocular pressure does not appear to be affected.

Centella asiatica

Also known as: Gotu kola, Indian Pennywort, Jal Brahmi and Mandookaparni, Brahmi, Tsubokusa

Centella asiatica (Gotu Kola) is a traditional medicine mainly renowned for its cognitive enhancing properties (usually alongside Bacopa monnieri) and its ability to regenerate wound healing. It appears effective on both parameters in preclinical evidence, and may also be anti-rheumatic.

See [Centella asiatica on Examine.com](#)

How to Take

Most of the human studies (on Chronic Venous Insufficiency) on this herb have used a centella asiatica supplement two to three times a day, and at each dose the total saponin dose (asiatic acid, madecassic acid, asiaticoside, and madecassoside) has totalled 30-60 mg given a total daily range of 60-180 mg total saponins. While there are currently no human studies on cognitive enhancement, rat studies have noted success with 200-300 mg per kilogram of the overall plant extract (since the saponins may not be the only active ingredient for cognition); this suggests a human dose of 32-48 mg/kg and thus: 2,100-3,300 mg for a 150lb person 2,900-4,400 mg for a 200lb person 3,600-5,500 mg for a 250lb person The above dosages ranges are but estimates for cognitive enhancement. Currently, 500mg of centella asiatica twice daily has shown anxiety reducing effects in humans and 750mg of a 5% asiaticoside extract has enhanced mood state; while these doses are active on the cognition, it is not yet demonstrated if they are the dose needed to boost learning.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Edema	↓	★☆☆ Minor	5 studies	There appears to be a decrease in edema associated with chronic venous insufficiency (CVI), associated with the treatment of CVI by <i>centella asiatica</i>
B	Leg Swelling	↓	★☆☆ Minor	5 studies	The leg swelling associated with chronic venous insufficiency appears to be significantly reduced secondary to treating the state of chronic venous insufficiency.
B	Blood Flow	↑	★☆☆ Minor	4 studies	Blood flow appears to be increased alongside improvements in microcirculation seen in persons with impaired venous

					insufficiency being treated with <i>centella asiatica</i>
B	Microcirculation	↑	★★★☆☆ Notable	8 studies	There appears to be a notable improvement in microcirculation associated with oral ingestion of <i>centella asiatica</i> in the treatment of chronic venous insufficiency; this may extend to otherwise healthy persons, albeit at a lesser magnitude
B	Chronic Venous Insufficiency	↓	★★★☆☆ Notable	8 studies	Symptoms of chronic venous insufficiency extending to poor circulation, venous reactivity, and adverse side-effects such as edema and leg pain are all reliably reduced with oral ingestion of <i>centella asiatica</i>
C	Wound Healing	↓ ↑	★★☆☆☆ Minor	2 studies	An increase in wound contraction rate has been noted with oral supplementation of <i>centella asiatica</i> yet an impairment in wound granulation (formation of connective tissue).
C	Stress	↓	★★☆☆☆ Minor	1 study	There appears to be stress reducing properties associated with supplementation of this herb at 1g daily, although they may be secondary to anxiety reduction.
C	Depression	↓	★★☆☆☆ Minor	1 study	A reduction in depressive effects may be secondary to the treatment of anxiety.
C	Anxiety	↓	★★☆☆☆ Minor	1 study	There appears to be a reduction in anxiety symptoms that build up over time (reaching a quarter reduction after two months) associated with twice daily ingestion of 500mg of the plant extract
C	Attention	↑	★★☆☆☆ Minor	1 study	An increase in attention has been noted which may be

					secondary to the treatment of anxiety (or the reductions in stress and depression that also occurred due to treating anxiety).
C	Calmness	↑	★☆☆ Minor	2 studies	A reduction in fear and anxiety responses to an acute startle response (indicative of less responsiveness to alerting stimuli and more calmness) has been noted with this plant extract
C	Subjective Well-being	—	—	1 study	Acute ingestion of this herb in otherwise healthy individuals does not appear to alter subjective mood parameters.
C	Heart Rate	—	—	1 study	No significant influence on heart rate with acute ingestion of the herb in healthy persons.
C	Blood Pressure	—	—	1 study	No significant influence on blood pressure in otherwise healthy persons given an acute dosage.
C	Reaction Time	↓	★☆☆ Minor	2 studies	There are decreased in reaction time when otherwise healthy older adults take this supplement (youth not tested) which span to choice recognition, and spatial memory reaction time but <i>not</i> digit vigilance and simple reaction time.
C	Processing Accuracy	—	—	1 study	No significant influence on processing accuracy is seen with <i>centella asiatica</i> supplementation
C	Alertness	↑	★☆☆ Minor	1 study	An increase in the self-rated sensation of alertness is noted in older healthy adults supplementing with <i>centella asiatica</i>
C	Contentment	↑	★☆☆	1 study	

			Minor		An increase in self-rated perceptions of contentment is seen in otherwise healthy adults given centella asiatica

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Chlorella

Also known as: Chlorella pyrenoidosa

Chlorella is a freshwater algae that is commonly supplemented by vegan populations (similar to Spirulina). Chlorella appears to be a bioavailable source of both Iron and Vitamin B12, and may have other benefits.

See [Chlorella on Examine.com](#)

How to Take

Supplementation of chlorella appears to be in the range of 6-10g daily. It is unsure why this dose is chosen, but it appears to be somewhat effective. Higher doses have not been sufficiently tested and the optimal dose of supplemental chlorella is not known.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Blood Pressure	↓	★☆☆ Minor	3 studies	Might reduce blood pressure in some instances but does not appear remarkably potent.
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	1 study	No remarkable effects following oral ingestion of chlorella, although some may be present
C	DNA Damage	—	—	1 study	Has once failed to modify the DNA damage observed in male smokers
C	Immunity	↑	★☆☆ Minor	1 study	Increase in salivary IgA suggests an immune enhancing effect; no comparison to an active control.
C	Fat Mass	—	—	1 study	No significant effects on fat mass
C	Heart Rate	—	—	1 study	No significant influence on heart rate has been detected
C	Weight	—	—	1 study	

					No significant effects on body weight
C	Vaccine Augmentation	—	—	1 study	Has once failed to act effectively as a vaccine adjuvant
D	Leg Swelling	↓	★☆☆ Minor	1 study	Study in pregnant women, it did have efficacy but more studies are required to assess chlorella overall.
D	Risk of Anemia	↓	★☆☆ Minor	1 study	May be secondary to the Iron content, somewhat effective in pregnant women. Requires more evidence, especially in anemics
D	Proteinuria	↓	★☆☆ Minor	1 study	Reduced proteinuria in pregnant women (possibly indicative of kidney protective effects); more studies would be prudent as to include comparators or use in other contexts.
D	Symptoms of Fibromyalgia	↓	★☆☆ Minor	1 study	May have efficacy in reducing pain associated with fibromyalgia, but requires more evidence

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Chlorogenic Acid

Also known as: Coffee bean extract, 5-O-caffeoylquinic acid, 3-O-caffeoylquinic acid Green coffee extract

Chlorogenic acid is found in Coffee mostly and a lot of plant compounds; it holds promise in many aspects of health and cognition similar to Bioflavonoids and shares some effects similar to Caffeine but less potent. May decrease the absorption of dietary carbohydrate.

See [Chlorogenic Acid on Examine.com](#)

How to Take

Supplemental chlorogenic acid appears to have benefit in the range of 120-300mg oral intake, with higher doses still possibly beneficial (not really tested sufficiently). These doses appear to benefit blood pressure and circulation mostly. This dose seems to be low enough that moderate to high doses of plants with a rich chlorogenic acid content may confer the benefits listed on this page, this most notably includes Green Coffee Extract.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Subjective Well-Being	↑	★☆☆ Minor	1 study	Chlorogenic acid may have a mood enhancing effect independent of caffeine
C	Glycemic Control	↓	★☆☆ Minor	1 study	Slight increase in glycemic control possibly secondary to reducing carbohydrate absorption
C	Weight	↓	★☆☆ Minor	2 studies	Although the reductions seen with chlorogenic acid seem remarkable, the studies conducted at this moment in time are somewhat industry influenced
C	Blood Pressure	↓	★★★☆☆ Notable	1 study	The decrease in systolic blood pressure with chlorogenic acid has reached 15 points systolic in hypertensives (150mmHg systolic initially) and appears to maintain at that level until supplement cessation.
C	Homocysteine	↑	★☆☆☆☆	1 study	

C			Minor		Somewhat high acute spike of homocysteine, which is normally a negative thing. Practical significance of this unknown
C	Insulin	↓	Minor	1 study	Spike in insulin was attenuated a bit, secondary to attenuating the rate of glucose absorption. Not overly remarkable
C	Blood Glucose	↓	Minor	1 study	Not overly remarkable reductions in blood glucose

Chromium

Chromium is an essential mineral. It regulates glucose metabolism and insulin sensitivity. Supplementing more chromium than the body needs does not produce reliable results, but it may be associated with minor benefits to diabetics.

See [Chromium on Examine.com](#)

How to Take

Chromium supplementation typically consists of 1,000 mcg of chromium picolinate, taken in at least two doses throughout the day. Chromium should be supplemented alongside a carbohydrate containing meal, due to its supposed interactions with glucose metabolism. Anyone wishing to supplement chromium should be aware that chromium supplementation is not associated with any reliable benefits on markers of glucose metabolism.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Weight	—	—	33 studies	There is no significant influence of chromium on weight in either healthy persons or those with diabetes, and although a possible interaction may occur in some instances of better glucose control or reduced appetite they are not frequent enough to establish a solid relationship to chromium.
A	LDL-C	—	—	13 studies	The best evidence to date does not support a role for chromium in the reduction of LDL cholesterol, even when assessing type II diabetic individuals.
A	HDL-C	—	—	16 studies	Although an increase in insulin sensitivity in diabetics should increase HDL cholesterol, the best evidence to date does not support a role for chromium supplementation in improving HDL cholesterol in diabetics.

A	Triglycerides	—	—	16 studies	Chromium does not appear to have a role in reducing triglyceride concentrations in the serum of subjects, including diabetic subjects given chromium supplementation.
A	Total Cholesterol	—	—	17 studies	Similar to its actions on LDL and HDL individually, chromium does not appear to have a significant role in improving total cholesterol levels in type II diabetic subjects.
A	HbA1c	—	—	17 studies	Although sporadic evidence suggest improvements in HbA1c in diabetics, the entirety of the evidence does not support a reliable and significant improvement in diabetic persons.
A	Blood Glucose	↓	★☆☆ Minor	28 studies	In looking at the entirety of the data on type II diabetic persons, there does appear to be a mild reduction in fasting blood glucose despite no apparent changes in insulin sensitivity or HbA1c. No significant or reliable effect in non-diabetic persons.
A	Insulin Sensitivity	—	—	16 studies	There appears to be highly unreliable evidence for this property for unknown reasons, but chromium <i>may</i> have a role in increasing insulin sensitivity in diabetic persons to a mild degree despite the majority of evidence showing no effects.
A	Insulin	—	—	18 studies	Somewhat similar to the influence on insulin sensitivity, the reductions in fasting insulin concentrations in diabetics appear to exist in some studies but are highly unreliable.

A	Fat Mass	—	—	11 studies	There doesn't appear to be a significant nor reliable reduction in fat mass even in diabetics given chromium supplementation according to the literature.
B	vLDL-C	—	—	3 studies	No significant influence on vLDL cholesterol seen in diabetics supplementing chromium.
B	Appetite	↓	★☆☆ Minor	3 studies	There may be a role in reducing appetite specifically in persons who self-report inappropriate eating patterns and carbohydrate cravings, with no known effect in persons who do not report such.
B	Food Intake	—	—	4 studies	No significant influence on food intake in standard diabetics, although limited evidence suggest a possible role specifically in persons who self-report elevated carbohydrate cravings and inappropriate eating patterns due to urges.
B	Blood Pressure	—	—	8 studies	The majority of evidence does not support a role for chromium in reducing blood pressure any more than placebo.
B	Liver Enzymes	—	—	3 studies	No known influence on liver enzymes or other markers of hepatic health.
B	Creatinine	—	—	3 studies	No known influence on creatinine, a biomarker for kidney health.
B	Lipid Peroxidation	↓ ↑	★☆☆ Minor	5 studies	While minor, increases in lipid peroxidation have been noted in nondiabetic controls while decreases have occurred in those with a high baseline

					HbA1c. A possible modulatory effect exists.
B	Anti-oxidant Enzyme Profile	—	—	4 studies	A lone study noted an increase in glutathione peroxidase, but the majority of the evidence finds no significant influence on antioxidant enzymes in the body (glutathione, SOD, or catalase).
B	Depression	↓	★☆☆ Minor	5 studies	There is limited preliminary evidence for chromium having an adjuvant role in aiding depressive symptoms (better overall outcomes when paired with a more effective 'reference' therapy), although the limited evidence for chromium in isolation is unconvincing.
B	Power Output	—	—	5 studies	No interaction between chromium and strength gain in naive nor trained athletes.
B	Lean Mass	—	—	8 studies	Studies in trained and untrained persons, with or without physical exercise, have failed to find an increase in the rate of lean mass accrual relative to placebo.
C	Hepatic Glucose Production	—	—	1 study	The lone study failed to find a significant influence on hepatic glucose production rates relative to placebo.
C	Adiponectin	—	—	2 studies	No significant influences on adiponectin concentrations in the blood relative to placebo.
C	Fat Oxidation	—	—	2 studies	Fat oxidation (percent of energy derived from fatty acids relative to glucose) does not appear to be influenced following supplementation of chromium.
C	Urea	—	—	1 study	The lone study assessing urea failed to find a significant

					interaction between it and supplementation of chromium.
C	Fructosamine	↓	★☆☆ Minor	2 studies	Both studies assessing fructosamine have found a mild decrease.
C	Apolipoprotein A	—	—	1 study	No known interactions with Apolipoprotein A.
C	Apolipoprotein B	—	—	1 study	No known interactions with Apolipoprotein B.
C	Memory	—	—	1 study	No evidence for chromium reducing memory decline seen with aging.
C	QTc Intervals	↓	★☆☆ Minor	1 study	One study in diabetic persons found shortened QTc intervals, suggestive of a cardioprotective effect.
C	Heart Rate	—	—	2 studies	No significant influence on heart rate is known with chromium supplementation.
C	Lymphocyte Count	—	—	1 study	No significant alterations in baseline lymphocyte count with chromium supplementation relative to placebo.
C	Eosinophil count	—	—	1 study	No significant influence on baseline eosinophil count with supplementation of chromium relative to placebo in otherwise healthy women.
C	Neutrophil count	—	—	1 study	No significant influence of chromium supplementation relative to placebo on neutrophil count.
C	Immunity	↑	★☆☆ Minor	1 study	At least one study has noted an increase rate of lymphocyte proliferation when they were stimulated with a mitogen (proliferation inducing factor)

					with chromium supplementation relative to placebo.
C	Luteinizing Hormone	—	—	1 study	No significant influence of chromium supplementation on luteinizing hormone (LH) in women with PCOS relative to placebo.
C	Follicle-Stimulating Hormone	—	—	1 study	No significant influence of chromium supplementation on follicle stimulating hormone (FSH) in women with PCOS relative to placebo.
C	Testosterone	—	—	1 study	Testosterone is not affected by chromium in women with PCOS. Currently no evidence in otherwise healthy men.
C	Free Testosterone	—	—	1 study	No significant influence of chromium supplementation on free testosterone concentrations in women with PCOS.
C	Sex Hormone Binding Globulin	—	—	1 study	In women with PCOS, chromium supplementation does not alter SHBG concentrations in serum.
C	Serum DHEA	—	—	1 study	Chromium supplementation does not appear to alter serum concentrations of DHEA or sulfated DHEA.
C	C-Peptide	—	—	1 study	No significant influence on C-peptide, a biomarker of insulin secretion status.
C	Glycogen content	—	—	1 study	Similar to the failure in increasing glycogen replenishment rate, the overall glycogen content increased by carbohydrate is not altered by supplementation of chromium.
C	Glycogen Resynthesis	—	—	1 study	

C					When testing the addition of chromium to a glycogen repletion protocol (after exercise), chromium failed to augment the replenishment from carbohydrates any more than placebo.
C	Lactate production	↑	★☆☆ Minor	2 studies	Mixed evidence, but at least one study has noted that lactate production during exercise was greater with 600mcg chromium than it was with placebo; no known mechanism for this observation.
C	Kidney function	—	—	1 study	No apparent influence on kidney function (negative nor positive) with chromium supplementation in older sedentary adults.
C	Anaerobic Running Capacity	—	—	1 study	No apparent influence of chromium supplementation on anaerobic cardiovascular exercise performance relative to placebo.
C	Symptoms of Schizophrenia	—	—	1 study	The addition of low dose chromium to antipsychotic therapy in schizophrenic persons failed to augment the efficacy of treatment.
C	Cell Adhesion Factors	—	—	1 study	Cell adhesion factors (ICAM-1 and VCAM-1) are unaffected with chromium supplementation in nondiabetic obese adults.
C	C-Reactive Protein	—	—	1 study	No significant influence on C-reactive protein, a biomarker for inflammation.
C	Bilirubin	—	—	1 study	No significant interactions with bilirubin concentrations in serum.
C	General Oxidation	↓ ↑	★☆☆	2 studies	

C			★☆☆ Minor		Mixed evidence leaning towards no effect, although a possible antioxidative effect remains possible in persons with high baseline HbA1c and a prooxidative effect in persons with normal HbA1c.
C	Libido	↑	★☆☆ Minor	1 study	Perhaps secondary to causing an antidepressive effect, supplementation of chromium was able to alleviate a suppressed libido resulting in an increase relative to control; no studies in nondepressed persons.
C	Binge-eating	↓	★☆☆ Minor	1 study	Although chromium showed an ability to reduce binge eating symptoms in persons with the disorder, this failed to reach statistical significance.
C	Blood Flow	—	—	1 study	In persons at risk for type II diabetics, chromium supplementation failed to improve blood flow relative to placebo.
C	Proteinuria	—	—	1 study	Chromium supplementation does not appear to cause proteinuria (protein losses in the urine) suggesting no kidney toxicity, as proteinuria is a biomarker of such damage.
C	Muscular Endurance	—	—	1 study	Low dose chromium supplementation failed to promote muscular endurance in trained athletes relative to placebo.
C	Insulin Secretion	↑	★☆☆ Minor	2 studies	Mixed evidence, but it is possible that chromium causes an increased insulin response to dietary glucose (leading to a greater release of insulin acutely, possibly preceding a reduction in blood glucose).

C	Resistin	—	—	1 study	The adipokine known as resistin is not affected by supplementation of chromium relative to placebo.
C	Oxidation of LDL	—	—	1 study	No significant influence on the rates of LDL oxidation when compared to placebo supplementation.
D	Metabolic Rate	—	—	1 study	Six months supplementation of chromium has failed to alter the metabolic rate relative to baseline.
D	Symptoms of Bipolar Disorder	↓	★☆☆ Minor	2 studies	In persons with bipolar disorder given supplementation of chromium, benefits were only noted against depressive symptoms and while significant (statistically) were mild; manic symptoms were not affected.
D	CD4+ Lymphocytes	—	—	1 study	No known immunomodulatory actions at the level of CD4+ lymphocytes
D	Viral Load	—	—	1 study	In persons with HIV, supplementation of chromium did not alter the levels of the virus in their body despite showing actions on glucose disposal rates.
D	DNA damage	—	—	1 study	One study assessing DNA damage following ingestion of chromium supplementation failed to find any harmful nor beneficial interactions.

Chrysin

Also known as: Propolis, Honey extract, Passiflora caerulea Linn

A flavonoid compound found in bee pollen and propolis. Can boost Testosterone when injected into testicles; otherwise isn't absorbed at all. Unless better absorption arises, chrysin remains a pretty interesting colon cancer preventative agent that does not boost testosterone.

See [Chrysin on Examine.com](#)

How to Take

Due to the poor bioavailability, the standard supplemental doses of chrysin (400-3,000mg) appear to be pretty much ineffective. Although enhancing absorption can theoretically aid in chryin's effects, this has not yet been demonstrated and thus supplementation of chrysin cannot be recommended for systemic purposes. A supplemental dose of 400mg chrysin should be sufficient for intestinal related issues.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Testosterone	—	—	1 study	Has failed to increase testosterone levels in one study.

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Cissus quadrangularis

Also known as: Harjor, Asthi Shrinkhala, Bone Setter

Cissus quadrangularis is a traditional medicine for joint and bone health (as well as various feminine disorders and menopause), and shows promise in promoting bone growth rates. It is popular as a joint aid for athletes, with preliminary evidence supporting this property of cissus.

See [Cissus quadrangularis on Examine.com](#)

How to Take

The one study to note benefit with oral supplementation in humans (for the purpose of reducing joint pain) has used 3,200mg of cissus quadrangularis as a daily supplement, which is also in the range for what animal studies suggest sedative and pain killing effects should occur with the water extract. Elsewhere, 300-600mg of a cissus quadrangularis extract standardized to 2.5% ketosteroids has shown biological activity in humans. Either of the two aforementioned doses should work (former probably more relevant for athletes), but the optimal dose is not known as this moment in time.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Hemorrhoids	—	—	1 study	Although some traditional usage of the herb suggests otherwise, limited (accessible) human data does not support a role for cissus in the treatment of hemhorroids
C	Weight	↓	★☆☆ Minor	1 study	There may be a small weight loss associated with 300mg cissus (2.5% ketosteroids) which was seen alongside a reduction in appetite in obese persons; no known direct fat burning properties.
C	Total Cholesterol	↓	★☆☆ Minor	1 study	Reductions in total cholesterol not overly remarkable relative to placebo and confounded with weight loss which occurred with cissus
C	Triglycerides	↓	★☆☆ Minor	1 study	Reduction in triglycerides is not overly potent and occurred alongside weight loss, which

					was likely a confounding factor.
C	Plasma Serotonin	↑	★★★☆☆ Notable	1 study	Increase in plasma serotonin was significant (30-39%) and fairly noteworthy, deserves more research.
C	Creatinine	↑	★☆☆☆☆ Minor	1 study	An increase in creatinine has been noted alongside weight loss; practical significance of this information is not known.
C	Lipid Peroxidation	↓	★☆☆☆☆ Minor	1 study	A minor reduction in lipid peroxidation has been seen in serum associated with weight loss; uncertain significance.
D	Bone Healing Rate	—	—	1 study	More evidence is required, as the one study noting that cissus was ineffective in isolation noted that combination therapy with cissus and calcium was quite effective. There may be a role of Cissus, but it currently is not demonstrated
D	Pain	↓	★★★☆☆ Notable	1 study	Joint pain appears to be reduced following supplementation of cissus, and while the magnitude is not remarkable (respectable, but comparable to other supplements) it seems to be one of the few validated in athletes with nonpathological joint pain.
D	Functionality in Elderly or Injured	↑	★★★☆☆ Notable	1 study	An increase in the function of the joint appears to occur alongside reductions in perceived pain and soreness when cissus treats athletic joint pain; one of the few options that sees to benefit athletes.
D	Heart Rate	—	—	1 study	No significant influence on heart rate when taken over the course of eight weeks.

D	Blood Pressure	-	-	1 study	In otherwise healthy athletic men, there is no significant influence of supplementation over eight weeks on blood pressure.

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Citrulline

Also known as: L-Citrulline, Stimol (Brand Name), Watermelon extract

L-Citrulline is one of the three amino acids in the Urea cycle alongside L-Arginine and L-Ornithine; it turns into L-Arginine after absorption and being sent to the kidneys, so it is actually a better method of getting supplemental L-Arginine into the blood rather than L-Arginine itself.

See [Citrulline on Examine.com](#)

How to Take

The lower end of dosing appears to be one gram (1,000mg) of citrulline taken thrice a day with meals, totalling 3,000mg at the end of the day. This appears to be somewhat effective for promoting circulatory health and alleviating erectile dysfunction (possible ED associated with high blood pressure). For ergogenic (performance enhancing) purposes, a dose in the range of 6,000-8,000mg is taken acutely about an hour before exercise.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Blood Glucose	—	—	3 studies	There do not appear to be any significant influences of supplemental citrulline on blood glucose concentrations
B	Insulin	—	—	4 studies	Most studies note that there is no significant change in insulin concentrations, although a lone study (not replicated) suggested that the exercise-induced increase in insulin was suppressed with citrulline. As this study also noted performance degradation, it may be a flaw
C	Urea	↑	★☆☆ Minor	1 study	An increase in urea is seen with citrulline supplementation (possibly due to increased serum Ornithine sequestering ammonia)
C	Nitric Oxide	↑	★★★☆☆ Notable	2 studies	Nitric oxide derivatives (nitrate and urinary cGMP, since nitric oxide itself is hard to measure

					these biomarkers are indicative of nitric oxide production) appear to be reliably increased following oral consumption of citrulline supplementation
C	Growth Hormone	↑	★☆☆ Minor	2 studies	An increase in growth hormone has been noted with exercise, but not at rest. Practical significance of this information is unknown, since Arginine supplementation has unreliable effects itself
C	Creatinine	↑	★☆☆ Minor	1 study	A slight increase in creatinine has been noted with citrulline supplementation, practical relevance unknown.
C	Plasma Glutamine	↓	★☆☆ Minor	2 studies	Although acute usage does not appear to influence plasma glutamine, a week of high dose supplementation (0.18g/kg) has been noted to reduce glutamine concentrations slightly.
C	Muscle Protein Synthesis	—	—	1 study	Currently no human evidence to support a practically significant increase in muscle protein synthesis at rest with citrulline supplementation
C	IGF-1	—	—	1 study	No demonstrated effects on IGF-1 concentrations following the usage of citrulline supplementation
C	Plasma Arginine	↑	★★★☆☆ Notable	2 studies	Citrulline can increase plasma arginine concentrations, and due to acting as a reservoir of arginine it is actually more effective overall at increasing plasma arginine than arginine itself (acute peaks are still observed to a higher level with arginine supplementation).
C	Fatigue	↓	★★★☆☆ Notable	3 studies	The decrease in fatigue during

					exercise is thought to underlie most of the benefit seen with training capacity (work volume), although in men who self-report fatigue issues supplemental citrulline appears to help with that as well (independent of exercise)
C	Training Volume	↑	★★★☆☆ Notable	1 study	The increase in work capacity seen with citrulline supplementation appears to be time dependent. While there are no inherent and immediate effect, the reduction of fatigue later in a weight lifting workout causes a relative increase that has at least one doubled reps conducted (on set 8 of exhaustive exercise)
C	Muscle Soreness	↓	★★★☆☆ Notable	1 study	The lone study using citrulline acutely pre-workout noted a 40% reduction in muscle soreness the following two days after the workout.
C	Blood Pressure	↓	★★☆☆☆ Minor	3 studies	A decrease in blood pressure is noted secondary to increasing plasma arginine (and thus increasing nitric oxide), but this blood pressure reduction may only occur in those with hypertension or prehypertension
C	Heart Rate	—	—	2 studies	No significant influence on heart rate seems likely, although at least one study noted a random but significant reduction post-exercise
C	Lactate Production	—	—	1 study	No significant influence on lactate production seen with citrulline supplementation before exercise
C	Aerobic Exercise	—	—	1 study	No significant influence on a treadmill test to exhaustion nor oxygen kinetics during this test

C	Immunity	↑	★☆☆ Minor	1 study	Neutrophil oxidative burst post-workout appears to be enhanced when the exercise is preloaded with citrulline supplementation
C	DNA Damage	—	—	1 study	No significant influence of citrulline on DNA damage
C	Lipid Peroxidation	—	—	1 study	No significant influence of citrulline on lipid peroxidation has been noted
C	Liver Enzymes	—	—	1 study	Plasma concentrations of LDH are unaffected following citrulline supplementation
C	Blood Flow	↑	★☆☆ Minor	1 study	An increase in blood flow is noted with citrulline supplementation in persons with impaired blood flow
C	Plasma Nitrate	↑	★☆☆ Minor	1 study	An increase in plasma nitrate has been noted with citrulline supplementation, but not to the degree of supplemental Nitrate itself
C	LDL-C	—	—	1 study	No significant influence on LDL-C concentrations in serum following citrulline supplementation
C	HDL-C	—	—	1 study	No significant influence on HDL-C concentrations
C	Total Cholesterol	—	—	1 study	No significant influence on total cholesterol concentrations
C	C-Reactive Protein	—	—	1 study	No significant influence on C-reactive protein concentrations
D	Muscle Oxygenation	↑	★☆☆ Minor	1 study	An increase in muscle ATP production via aerobic means was noted in men given 6g citrulline daily, but this

					appeared to be attenuated with time.
D	Erections	↑	★☆☆ Minor	1 study	Hardness of erections in persons with mild erectile dysfunction appears to be increased following supplementation of citrulline supplementation.
D	Exercise Capacity (with Heart Conditions)	↑	★☆☆ Minor	1 study	Citrulline has been noted to increase physical exercise capacity in persons with heart failure.
D	Right Ventricular Ejection Fraction	↑	★☆☆ Minor	1 study	In persons with heart failure with normal ejection fractions, right ventricular ejection fraction during exercise appears to be increased relative to control.

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Citrullus colocynthis

Also known as: Bitter apple, desert gourd, bitter cucumber

Citrullus colocynthis (Bitter cucumber) is a fruit bearing plant shows seeds and fruits are used in low doses to reduce blood glucose. Its evidence for this claim is promising but limited, and higher doses appear to cause reversible colonic inflammation and rectal bleeding.

See [Citrullus colocynthis on Examine.com](#)

How to Take

Limited human evidence suggests that 100mg of the seed or dry pulp extract taken thrice daily (300mg overall) may be effective for reducing blood glucose and improving the lipid profile in otherwise unhealthy persons. The traditional 'recommended dose' for this supplement is 300-800mg, but it would be highly prudent to stick to the lower end of the scale if supplementing due to reversible but severe intestinal inflammation with higher doses.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Blood Glucose	↓	★☆☆ Minor	1 study	May decrease blood glucose in diabetics at low doses, but the evidence at this moment in time is limited (due to differences between groups at the start of the study)
C	HbA1c	↓	★☆☆ Minor	1 study	May be able to mildly decrease HbA1c, although the research supporting this claim is very preliminary at this time.
C	Triglycerides	↓	★☆☆ Minor	2 studies	The decrease seen in triglycerides in one study was statistically significance, but the average reduction in hyperlipidemics (16%) has a very large range
C	Total Cholesterol	↓	★☆☆ Minor	2 studies	There may be a reduction in total cholesterol in those with high cholesterol, but it has a large degree of variability.
C	HDL-C	—	—	2 studies	

C	Urea	—	—	1 study	A possible benefit in hyperlipidemics only has failed to reach statistical significance.
C	LDL-C	—	—	2 studies	A possible reduction seen in persons with high blood triglycerides and cholesterol failed to reach statistical significance due to large variance.
C	Creatinine	—	—	1 study	No significant influence on creatinine concentrations with the lowest active dose of the supplement (300mg)
C	Urea	—	—	1 study	No significant alterations in serum urea, suggesting no renal toxicity with the low doses (300mg) of this supplement
C	Liver Enzymes	—	—	2 studies	Both studies using 300mg of either the fruit or seed extract have failed to find alterations in liver enzymes associated with supplementation.
C	Weight	—	—	1 study	In assessing the influence of the fruit extract on blood glucose, there was no significant influence on weight
C	Blood Pressure	—	—	1 study	No significant influence on blood pressure with up to 300mg of the fruit extract daily over two months

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Coconut Oil

Also known as: Cocos nucifera, Coconut, Medium Chain Triglycerides (partially synonymous but commonly touted as such)

Coconut oil is a highly saturated (90%) oil comprised of medium chain fatty acids (65%), mostly lauric and myristic acids (with a caprylic and capric acid content); it might exert minor anti-obesity effects and is an effective cosmetic.

See [Coconut Oil on Examine.com](#)

How to Take

Coconut oil tends to have efficacy when 5-10g of medium chain triglycerides are included in the diet (this is around 7.7-15g coconut oil overall) and when they replace other dietary fatty acids, as the extra calories coconut oil confers may inherently negate any fat loss effect if overall calories are not controlled. Coconut oil can be cooked with and should be fine to do so, as there do not appear to be a large amount of structural changes during single use cooking with coconut oil below the smoke point

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Metabolic Rate	↑	★☆☆ Minor	4 studies	Appears to be a short lived and of small magnitude increase in metabolic rate.
C	Processing Speed	↑	★☆☆ Minor	1 study	Study was unable to properly assess coconut oil as it was used as an active control; some benefit appears apparent relative to fish oil.
C	Working Memory	—	—	1 study	Insufficient evidence to support an increase in working memory
C	Skin dryness	↓	★★★☆☆ Notable	1 study	Appears to be comparable to mineral oil, which is usually the active control in these studies.
C	Skin moisture	↑	★★★☆☆ Notable	2 studies	Appears to be comparable to mineral oil, the active control
D	Blood Glucose	—	—	1 study	Insufficient evidence to support

					alterations in blood glucose.
D	Insulin Sensitivity	↑	★☆☆ Minor	1 study	May improve insulin sensitivity in diabetics, requires more evidence though as the one study was confounded with fat loss.
D	Triglycerides	—	—	1 study	Insufficient evidence to support changes in serum triglycerides.
D	Total Cholesterol	↓	★☆☆ Minor	1 study	A decrease in total cholesterol (both the LDL and HDL portions) has been noted with coconut oil to a minor degree relative to longer chain fatty acids
D	Weight	↓	★☆☆ Minor	1 study	Appears somewhat effective in reducing weight of obese persons to a greater degree than an isocaloric amount of longer chain fatty acids
D	LDL-C	↓	★☆☆ Minor	1 study	Not an overly significant reduction of LDL-C, but it does appear to be present relative to longer chain fatty acids
D	HDL-C	↓	★☆☆ Minor	1 study	Decrease in HDL-C is minor and likely not practically relevant.
D	Apolipoprotein B	—	—	1 study	No significant alterations in Apolipoprotein B levels
D	Insulin	—	—	1 study	No significant influence detected on fasting insulin levels following coconut oil consumption
D	Apolipoprotein A	—	—	1 study	No significant changes in apo-A levels with dietary inclusion of coconut oil
D	Thermic Effect of Food	—	—	1 study	Insufficient evidence to support

					alterations in the thermic effect of food compared to other oils
D	Ketone Bodies	↑	★☆☆ Minor	1 study	Has been implicated in increasing serum ketones more than other fatty acids.
D	Fat Mass	↓	★☆☆ Minor	1 study	May decrease fat mass to a greater degree than an isocaloric amount of long chain fatty acids.
D	Skeletal Muscle Atrophy	↓	★☆☆ Minor	1 study	Was able to attenuate the rate of skeletal muscle loss during a hypocaloric diet in obese persons; unknown if this applies to lean persons and may be related to ketone production.
D	Fat Oxidation	↑	★☆☆ Minor	1 study	Appears to increase the percentage of calories derived from lipids in obese persons; no comparator.
D	Infant Growth			1 study	

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Coenzyme Q10

Also known as: CoQ10, Ubiquinone, Ubiquinol, trans 2,3-dimethoxy-5-methyl-6-decaprenyl-1,4-benzoquinone

Coenzyme Q10 is a molecule found in mitochondria. It has a critical role in producing energy for the body.

See [Coenzyme Q10 on Examine.com](#)

How to Take

The standard dose for COQ10 is between 50-200mg. COQ10 supplements can be either the oxidized or reduced forms of ubiquinone or ubiquinol. Both forms increase circulating COQ10. COQ10 is usually taken once a day, with a meal. Higher doses do not appear to be significantly more effective than lower doses.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Endothelial Function	↑	★☆☆ Minor	5 studies	The effective size does not appear to be overly large, but CoQ10 is associated with a protective effect on blood flow and endothelial function in persons with otherwise impaired function.
B	Exercise-Induced Oxidation	↓	★☆☆ Minor	4 studies	Mixed effects on exercise-induced oxidation, but there appears to be some potential for CoQ10 supplementation to reduce oxidation.
B	Inflammation	—	—	3 studies	Classical inflammatory cytokines do not appear to be altered much following CoQ10 supplementation, although there may still be a minor antiinflammatory effect
B	General Oxidation	↓	★☆☆ Minor	6 studies	Appears to generally reduce pro-oxidative biomarkers in the body
B	Exercise Capacity (with Heart Conditions)	↑	★☆☆ Minor	4 studies	Appears to aid exercise capacity in persons after

					myocardial infarction
B	Blood Pressure	↓	★☆☆ Minor	6 studies	There appears to be an interaction between CoQ10 and blood pressure, but it is not wholly reliable and uncertain whether this is at the level of the cardiac tissue or at the level of the endothelium (both plausible). Magnitude of reductions don't appear too remarkable.
B	Fatigue	↓	★☆☆ Minor	3 studies	There may be an anti-fatigue effect of CoQ10 during exercise that may not extend to general fatigue.
B	Blood Flow	↑	★☆☆ Minor	3 studies	Appears to increase blood flow in metabolic conditions characterized by both insufficient blood flow and an excess of oxidative stress.
B	Lipid Peroxidation	↓	★★★☆☆ Notable	4 studies	Appears to reduce biomarkers of lipid peroxidation. CoQ10 tends to be a reference drug for lipid peroxidation, and although it is more potent than other nutraceuticals it is not astounding.
B	HbA1c	↓	★☆☆ Minor	3 studies	There may be an effect on HbA1c, but it appears unreliable and not overly potent.
C	Exercise Capacity	—	—	1 study	No significant detectable effect on exercise capacity when preloaded
C	Oxygen Uptake	—	—	1 study	No detectable influence on oxygen uptake during exercise
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	2 studies	May increase levels of antioxidant enzymes, does not appear to be reliable
C	Migraine	↓	★☆☆	1 study	

C		↑	★☆☆ Minor		Degree of improvement is not overly remarkable, with portions of the trial not outperforming placebo.
C	Total Cholesterol	—	—	2 studies	No significant or consistent effects on total cholesterol levels noted with CoQ10
C	Quality of Life	↑	★☆☆ Minor	3 studies	An increase in QOL has been noted in persons who either have heart ailments or are at risk for them, but this may not be a universal increase (perhaps dependent on reducing disease state symptoms)
C	C-Reactive Protein	—	—	2 studies	No significant influence on levels of C-reactive protein
C	Adiponectin	—	—	1 study	No detectable interaction of CoQ10 and adiponectin
C	Rate of Perceived Exertion	↓	★☆☆ Minor	1 study	A decrease in the rate of perceived exertion has been noted with CoQ10 supplementation
C	Symptoms of Fibromyalgia	↓	★★★★ Strong	5 studies	CoQ10 appears to be quite strongly effective for reducing symptoms of fibromyalgia (strong rating may be retracted at a later time when other reference drugs arise)
C	Sperm Quality	↑	★☆☆ Minor	4 studies	There may be some beneficial influences on the sperm quality, but they have not been reliably reported
C	Blood Glucose	—	—	2 studies	Insufficient evidence to support changes in blood glucose with CoQ10 supplementation
C	Symptoms of Peyronies disease	↓	★★★☆☆ Notable	1 study	Notable as CoQ10 is currently the only known oral therapy for Peyronie's disease, and may

					be a mechanism of increasing erectile properties.
C	Erections	↑	★☆☆ Minor	1 study	Increased erectile function has been noted with CoQ10, but this may be secondary to reductions in symptoms of Peyronie's Disease
C	Luteinizing Hormone	↓	★☆☆ Minor	1 study	A decrease in luteinizing hormone has been detected with CoQ10 supplementation
C	Follicle-Stimulating Hormone	↓	★☆☆ Minor	1 study	A decrease in follicle stimulating hormone has been detected
C	Testosterone	↑	★☆☆ Minor	1 study	Not the largest increase, and was in infertile men; may not apply to fertile men.
C	Seminal Motility	↑	★☆☆ Minor	2 studies	Requires more evidence to assess potency, but it does appear to reliably increase seminal motility
C	Pre-Eclampsia Risk	↓	★☆☆ Minor	1 study	A reduction in risk has been noted, but not to an overly amazing degree
C	Muscle Damage	↓	★☆☆ Minor	1 study	A slight decrease in biomarkers of muscle damage has been noted with CoQ10 supplementation.
C	Anaerobic Running Capacity	—	—	1 study	No significant influence on anaerobic cardiovascular exercise has been detected with CoQ10 (although an anti-fatigue effect has been noted)
C	VO2 Max	↑	★☆☆ Minor	2 studies	An increase in VO2 max of untrained persons has been noted following CoQ10 supplementation.
C	Symptoms of	↓	★☆☆	1 study	

	Parkinson's Disease		Minor		
C	Insulin	—	—	1 study	Insufficient evidence to support changes in insulin associated with CoQ10 supplementation.
D	UV Damage	↓	★☆☆ Minor	1 study	A decrease in UV damage has been detected with supplemental CoQ10
D	Symptoms of Prader Willi Syndrome	↓	★☆☆ Notable	1 study	Notable due to the aid to psychocognitive capabilities being comparable to the growth hormone active control (although not as effective in regards to physical development). Study in infants, not enough evidence in adults
D	Fertility	↑	★☆☆ Minor	1 study	Insufficient evidence to support whether the increase in fertility is large or not, but preliminary evidence suggests that it exists.
D	Left Ventricular Ejection Fraction	↑	★☆☆ Minor	1 study	Has been noted to increase LVEF in persons with myocardial impairment
D	Cardiac Mass	↓	★☆☆ Minor	1 study	A decrease in cardiac mass has been noted with CoQ10 supplementation

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Coleus forskohlii

Also known as: Forskolin, Coleonol, 7beta-acetoxy-1alpha,6beta,9alpha-trihydroxy-8,13-epoxy-labd-14-en-11-one

Coleus Forskohlii is a herb in Ayurveda, its component Forskolin is an activator of Adenyl Cyclase: it 'activates' cells and this activation differs depending on the cell. Can boost Testosterone and induce fat loss (more potent in men), under-researched given the possibilities.

See [Coleus forskohlii on Examine.com](#)

How to Take

Coleus forskohlii tends to be dosed at 500mg of a supplement that contains 10% forskolin by weight, taken in at least two divided doses throughout the day (250mg twice daily). The aerial parts tend to be used due to a higher forskolin content, but this is not a relevant point if it is standardized to 10%. It is currently not known if this is the optimal dosage or manner of which to spread the dose.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Blood Pressure	—	—	2 studies	No significant influence on blood pressure was noted with coleus supplementation
C	Weight	↓	★☆☆ Minor	4 studies	Mixed effects on overall weight, may be more effective in men rather than women. Overall, it requires more evidence to see if it has a role in weight loss regimens.
C	Asthma	↓	★★★☆☆ Notable	2 studies	Although more evidence is required, it appears to be more effective at suppressing asthmatic symptoms than other nutraceuticals. Mechanisms may be related to beta-adrenergic compounds (due to increasing cAMP and inducing bronchiol dilation)
C	Intraocular Pressure	↓	★☆☆ Minor	2 studies	Somewhat effective as ocular eyedrops in reducing ocular pressure.
C	Fatigue	↓	★☆☆	1 study	

C	Testosterone	↑	★☆☆ Minor	1 study	Less fatigue reported as a side-effect, no comparator or ability to assess potency.
C	Bone Mineral Density	↑	★★★☆☆ Notable	1 study	Increase of testosterone observed in men not overly potent and is highly variable.
C	Lean Mass	↑	★☆☆ Minor	1 study	Definitely requires more evidence, but a DXA confirmed increase in bone mass in men over 12 weeks makes this notable (rather than an increase in bone mass in osteoporotic women over 2 years)
C	Fat Mass	↓	★☆☆ Minor	1 study	Somewhat effective (2lbs over 12 weeks relative to placebo) although somewhat confounded with the increase in bone mass, as lean mass is inclusive of bone and skeletal muscle.
D	HDL-C	↑	★★★☆☆ Notable	1 study	Somewhat effective in reducing fat mass in obese and overweight persons.
					Needs to be replicated in larger trials, but the degree of increase was quite remarkable.

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Colostrum

Also known as: First Milk, Bovine colostrum

Colostrum, or first milk, is mammary secretions from bovine which contain higher concentrations of growth factors. Supplemental usage of colostrum seems comparable to whey protein for the most part, although it may have some unique immunity and intestinal properties.

See [Colostrum on Examine.com](#)

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Weight	—	—	13 studies	The majority of studies fail to find any significant influence of colostrum on body weight that is atypical of protein sources, although as it confers protein and calories it remains possible to gain weight from colostrum.
B	CD4 Lymphocytes	↑	★☆☆ Minor	4 studies	While there does not appear to be any influence in healthy controls or with low dose colostrum, higher doses of colostrum in persons with HIV (reduced CD4+ lymphocyte counts) may mildly increase CD4+ counts when compared to whey protein as control.
B	Diarrhea	↓	★★★☆☆ Notable	8 studies	Diarrhea can be potently reduced with colostrum under two conditions, either it is being used in persons with HIV-induced diarrhea from <i>cryptosporidium parvum</i> or when using colostrum (from cows immunized to E.coli) in response to food carrying E.coli (usually seen with traveler's diarrhea); despite being highly effective in those two scenarios it seems ineffective in other cases of diarrhea.
B	VO2 max	—	—	6 studies	

B					All studies assessing the effects of colostrum in athletes subject to cardiovascular training have failed to find any difference between colostrum and whey protein (control) for influencing VO ₂ max.
B	Intestinal Permeability	↓ ↑	★☆☆ Minor	3 studies	Evidence is preliminary, and there are studies suggesting both an increase in permeability and a decrease seen with endurance exercise (increase) or with high heat stress exercise or NSAID coingestion (decrease).
B	Fat Oxidation	—	—	3 studies	Colostrum does not influence fat oxidation rates or glucose expenditure during exercise any differently than other protein sources such as whey.
B	Heart Rate	—	—	4 studies	Heart rate during exercise, either submaximal or at lactate threshold, is not modified with dietary supplementation of colostrum.
B	Lactate production	—	—	4 studies	Lactate production during physical exercise does not appear to be any different with dietary colostrum when compared to whey protein.
B	Aerobic exercise	—	—	5 studies	For the most part colostrum influenced aerobic exercise similar to whey protein (ie. not much benefit) although in specific instances of high endurance stressors in elite cyclists there may be a small ergogenic benefit thought to be due to reducing the rate of immunosuppression.
B	IGF-1	—	—	5 studies	While any protein sources has the potential to increase IGF-1 when included in the diet, colostrum is no different than whey protein at doing so. The

					IGF-1 that is present in colostrum naturally appears to be fully digested in the intestinal tract and does not reach the blood.
B	Immunoglobulin G	—	—	4 studies	IgG has been noted to be increased once when colostrum was used as a vaccine adjuvant (relative to skim milk with whey as control), but in general there is no influence without coadministered vaccination.
B	Immunoglobulin A	—	—	8 studies	IgA concentrations in saliva and serum do not appear to be reliably increased although a few studies have noted spikes, which do not appear to be consistent in their magnitude nor incidence. The only incidence where IgA appears to be reliably increased is when it is taken as a vaccine adjuvant.
B	Power Output	—	—	9 studies	For the most part and aside from one pilot study, there is no consistent or remarkable increase in power output seen with colostrum that is not replicated by whey. Protein, inherently, may increase power output when combined in the diet over longer periods though.
B	Lean Mass	↑	★☆☆ Minor	5 studies	Colostrum, inherently due to being a dietary protein, appears to promote lean mass accrual. This is comparable to a similar dose of whey protein as the growth factors in colostrum do not appear to provide an additional benefit.
B	Fat Mass	—	—	3 studies	Supplementation of colostrum has failed to increase fat mass in subjects relative to baseline, similar to the same doses of whey protein which usually also fail to influence fat mass.

B	Anaerobic Running Capacity	—	—	5 studies	There does not appear to be any benefit of dietary colostrum, relative to whey protein, in improving cardiovascular performance in anaerobic instances such as Wingate testing, resisted treadmill tests, or rowing.
B	Length of Sickness	—	—	4 studies	Despite tenuous evidence suggesting a reduction in the frequency of sickness with colostrum, when sickness does occur there is no benefit of colostrum in reducing how long it occurs for.
B	Immunoglobulin M	—	—	3 studies	IgM does not appear to <i>per se</i> be modified in serum relative to control protein, and unlike the other immunoglobulins there is no augmentation of a vaccine-induced IgM spike.
C	Viral Load	—	—	1 study	Administration of colostrum to persons with HIV already on antiretroviral therapy does not further modify viral titres.
C	Abdominal Pain	↓	★☆☆ Minor	1 study	One study noted a reduction in abdominal pain associated with the successful treatment of diarrhea.
C	Intestinal Parasites	—	—	3 studies	Even in cases where traveler's diarrhea (from E.coli) is successfully treated, the overall amount of bacteria found in the stool is not modified suggesting no actual antibacterial properties.
C	Rate of Percieved Exertion	—	—	1 study	Colostrum does not appear to reduce (benefit) the rate of perceived exertion during physical exercise.
C	Body temperature	—	—	1 study	In assessing the effects of

					colostrum on gut permeability during exercise (secondary to an increase in body heat), colostrum benefited permeability without modifying body heat.
C	Glucagon-like Peptide 1	↓	★☆☆ Minor	1 study	An exercise increase in GLP-1 seen in placebo was attenuated with colostrum administration, thought to be related to the reduction in gut permeability seen with colostrum.
C	Ghrelin	—	—	1 study	Circulating ghrelin does not appear to be modified in response to colostrum supplementation.
C	Lactate Threshold	—	—	2 studies	Colostrum supplementation, relative to control proteins, does not appear to increase the lactate threshold (despite this being increased by training <i>per se</i> to a similar degree with or without colostrum).
C	Testosterone	—	—	3 studies	While one study noted a preservation of testosterone circadian rhythm during a five day cycling race (where testosterone tends to flatline), other studies have failed to find any influence on basal testosterone concentrations.
C	Cortisol	—	—	3 studies	While one study noted an increase in morning cortisol during multiple day training in elite cyclists (a beneficial response), basal cortisol concentrations and those immediately after standard exercise do not appear to be influenced with colostrum supplementation.
C	Vaccine Augmentation	↑	★☆☆ Minor	2 studies	Tenuous evidence for an increase in vaccine efficacy, as while the one study assessing

					antibody titres failed to find any influence (suggesting no benefit) there does appear to be a reliable increase in the secretion of IgA and IgG in response to the vaccine.
C	B cell count	—	—	1 study	The overall count of B cells in response to supplementation does not differ between colostrum and whey protein, both seeming to be without any effect.
C	T cell count	—	—	1 study	In otherwise healthy individuals, colostrum does not alter overall levels of T cells relative to baseline or control proteins.
C	CD8 Lymphocytes	↑	★☆☆ Minor	2 studies	At baseline CD8+ lymphocytes do not appear to be altered, although one study noted that the expected decrease in these lymphocytes during exercise was attenuated with colostrum (resulting in a relative increase to whey control).
C	Immunity	—	—	1 study	DTH responsiveness (indicative of T-cell mediated immunity) was not affected with colostrum in adults overall or in the elderly cohort which are normally more responsive to therapeutic interventions on DTH responsiveness.
C	Natural Killer Cell content	—	—	2 studies	There does not appear to be a sustained influence on NK cell content relative to controls, although one study noted very transient decreases (which were shortly normalized).
C	White Blood Cell Count	—	—	2 studies	White blood cell count does not appear to be chronically modified with colostrum supplementation, although a transient (one day) elevation was noted in one study.

C	Monocyte count	—	—	1 study	Monocytes do not appear to be influenced in their number with supplementation of colostrum.
C	Neutrophil count	—	—	2 studies	The overall amount of neutrophils in serum does not appear to be modified with supplementation of colostrum relative to placebo.
C	Cell Adhesion Factors	—	—	1 study	Cellular adhesion factors on immune cells do not appear to be modified with colostrum relative to whey protein.
C	Natural Killer Cell Activity	—	—	1 study	The phagocytic activity of natural killer cells does not appear to be modified with supplementation of colostrum relative to whey control.
C	Immunoglobulin E	—	—	2 studies	With exceptions to possible milk allergies (where an increase in IgE occurs with the allergic reaction), there is no influence of colostrum on baseline IgE concentrations.
C	Interleukin 10	—	—	2 studies	IL-10 does not appear to be significantly influenced with colostrum relative to baseline or other protein sources.
C	Interleukin 6	—	—	2 studies	IL-6 does not appear to be influenced with supplementation of colostrum.
C	TNF-Alpha	—	—	2 studies	TNF-a is not affected by supplementation of colostrum.
C	Exercise-Induced Immune Suppression	—	—	2 studies	The limited studies assessing sickness in athletes during exercise have not found a significant reduction in sickness rates relative to control protein sources (whey).

C	Ventilatory Threshold	—	—	1 study	Ventilatory threshold does not appear to be significantly influenced with supplementation of colostrum relative to control proteins.
C	Symptoms of Ulcerative Colitis	↓	★★★☆☆ Notable	1 study	One study using a solution of colostrum (as enema) in persons with distal colitis noted a large suppression of symptoms and inflammation relative to placebo. No studies available on oral supplementation of colostrum for inflammatory bowel diseases.
C	Macrophage Activity	↑	★☆☆☆☆ Minor	1 study	One study investigating acute usage of colostrum noted an increase in macrophage phagocytic activity, although as this study noted other immune variables were normalized after a day the long term implications of colostrum on this parameter are uncertain.
C	Severity of Sickness	—	—	2 studies	While in children with IgA deficiency colostrum appeared to reduce the severity of sickness when supplemented at the onset of sickness, this same effect was not observed in adults with suspected upper respiratory viral infections.
C	Upper Respiratory Tract Infection Risk	↓	★☆☆☆☆ Minor	3 studies	There may be a minor reduction in the incidence of upper respiratory tract infections (URTIs) seen with colostrum, although more evidence is needed to confirm this activity as current trials are usually underpowered.
C	C-Reactive Protein	—	—	2 studies	C-reactive protein does not appear to be significantly influenced with supplementation of colostrum relative to control or baseline values.

C	Lymphocyte Count	—	—	1 study	Overall lymphocyte count does not appear to be significantly influenced with supplementation of dietary colostrum.
C	Interferon Gamma	—	—	1 study	IFN-γ does not appear to be influenced with supplementation of colostrum relative to control proteins (whey).
C	Interleukin 8	—	—	1 study	IL-8 does not appear to be significantly influenced with supplementation of colostrum relative to placebo.
C	Interleukin 1-alpha	—	—	1 study	Supplemental colostrum does not appear to influence circulating concentrations of IL-1α when compared to whey control.
C	Blood Acidity	—	—	2 studies	While one study noted an increase in buffering capacity of the blood (reduction in acidity), this observation failed to be replicated in another study and both failed to find an ergogenic effect thought to occur after such an increase in buffer capacity.
C	Hemoglobin	—	—	2 studies	There does not appear to be an <i>inherent</i> increase in hemoglobin with colostrum, although when it successfully treated HIV-associated diarrhea an increase in hemoglobin was noted once (thought to partially underlie the reduction in fatigue).
C	Muscular Endurance	—	—	1 study	Supplementation of colostrum, relative to whey protein, does not appear to promote greater increases in muscular endurance (as assessed by bench press repetitions) when taken alongside a training

					regimen.
C	Fatigue	↓	★★★☆☆ Notable	2 studies	Both studies on fatigue assessed persons with HIV-related diarrhea, but when diarrhea was successfully (and greatly) benefited with colostrum containing porridge fatigue was reduced by over 80% of baseline values. It is uncertain if this anti-fatigue effect influences other persons.
C	Glucagon-like Peptide 2	—	—	1 study	Circulating levels of GLP2 do not appear to be significantly influenced relative to control protein.
C	Muscle Protein Synthesis	↑	★★★☆☆ Minor	1 study	There is an increase in protein synthesis with colostrum relative to maltodextrin due to colostrum being a dietary protein, but there is also an increase in protein breakdown seen; efficacy of colostrum relative to other protein sources in MPS is currently not well investigated.
D	Growth Hormone	—	—	1 study	There does not appear to be a significant influence of colostrum supplementation on circulating GH following oral supplementation relative to other protein sources.
D	Fecal weight	↓	★★★☆☆ Minor	1 study	A decrease in fecal weight has been noted in a trial assessing diarrhea, which was thought to be a consequence of successfully treating diarrhea.
D	Blood Glucose	↓	★★★☆☆ Minor	1 study	Preliminary trial in type II diabetics noted a reduction in fasting glucose concentrations to 10-14% with four weeks of colostrum supplementation; no control was used for reference.
D	Total Cholesterol	↓	★☆☆☆☆	1 study	

D			 Minor		A mild decrease in total cholesterol has been noted with supplementation of colostrum in type II diabetics.
D	Triglycerides	↓	 Minor	1 study	In type II diabetics, triglycerides in fasting conditions were noted to be reduced relative to baseline with colostrum ingestion.
D	Ketone bodies	↓	 Minor	1 study	A decrease in ketone bodies in type II diabetics was noted with supplementation of colostrum daily for four weeks; the decrease was mild, and there was no protein containing placebo for comparison.

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Conjugated Linoleic Acid

Also known as: CLA, Rumenic Acid

CLA are fatty acids that acts on a system known as PPAR to induce fat loss. At least, that is what the theory says. CLA too weakly affects PPAR receptors to really induce fat loss in an appreciable amount. TTA appears more promising.

See [Conjugated Linoleic Acid on Examine.com](#)

How to Take

Supplementation of conjugated linoleic acid (CLA) tends to be in the range of 3,200-6,400mg daily, taken with meals. This dosage assumes that approximately 70% of the product by weight is comprised of one of the two main active isomers, cis-9 trans-11 (c9t11) and trans-10 cis-12 (t10c12). Limited studies using higher doses than the aforementioned have failed to find additional benefit, and while this could simply be due to the unreliability of CLA supplements it also means that there is no evidence that doses higher than the above are more effective.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	HDL-C	—	—	15 studies	Insufficient evidence to support significant influences on HDL-C
A	Weight	—	—	21 studies	CLA is considered ineffective for weight loss to the high degree of unreliability in the results, with most evidence suggesting no effects and some sparse evidence to suggest both increases and decreases.
A	Fat Mass	—	—	19 studies	Evidence is too unreliable to conclude an inhernent effect of CLA on fat mass. There may be a context-dependent reduction in body fat and explanation for the observed variability, but at this moment in time too much evidence concludes no effect
A	Lean Mass	↑	★☆☆ Minor	13 studies	Some evidence that CLA can

					preserve lean mass during fat loss in an obese cohort of patients, but even in this subgroup the results are highly unreliable.
A	Insulin Sensitivity	—	—	12 studies	For the most part, ineffective; too unreliable to reach any conclusions in regards to the efficacy of CLA. There appears to be some manner of interaction, but both sensitization and resistance has been noted
B	Triglycerides	↑	★☆☆ Minor	7 studies	May possible increase triglycerides, but is unreliable in doing so and not overly potent.
B	Liver Enzymes	—	—	8 studies	Inconsistent and unreliable effects on liver enzymes, no significant influence is thought to exist.
B	LDL-C	—	—	11 studies	Insufficient evidence to support decreases of LDL-C and evidence to support no influence whatsoever.
B	Inflammation	—	—	4 studies	Insufficient evidence to support significant changes in inflammatory status.
B	C-Reactive Protein	—	—	8 studies	For the most part, CLA is seen as ineffective.
B	TNF-Alpha	—	—	4 studies	Insufficient evidence to support changes in TNFa, a biomarker of inflammation.
B	Adiponectin	—	—	3 studies	No alterations in adiponectin has been noted with CLA supplementation
B	Blood Glucose	—	—	9 studies	Insufficient evidence to support reliable increases in blood glucose

B	Insulin	—	—	5 studies	No significant influence on fasting insulin levels
B	HbA1c	—	—	3 studies	No significant reduction (or increase) in HbA1c levels following CLA supplementation
B	Metabolic Rate	—	—	5 studies	Currently thought to be somewhat ineffective as the evidence supporting an increase are confounded with food intake whereas the evidence supporting no increase is more statistically robust.
C	Blood Pressure	—	—	4 studies	No significant interaction between CLA and blood pressure
C	Oxidation of LDL	—	—	1 study	No significant protective or augmenting effects on the oxidation rates of LDL-C.
C	Antioxidant Potential	—	—	1 study	Does not appear to influence oxidative status in the body.
C	DNA Damage	—	—	2 studies	Insufficient evidence to suggest alterations in the rate of DNA damage with CLA ingestion.
C	Blood Flow	—	—	1 study	Insufficient evidence to support changes in blood flow.
C	8-isoPGF2a	↑	★☆☆ Minor	3 studies	8-isoPGF(2)a is normally a biomarker of lipid peroxidation, but CLA may be causing a false positive (as fatty acids are known to interact with the enzymes in question and other markers of lipid peroxidation are unchanged).
C	Fat Oxidation	↑	★☆☆ Minor	1 study	May influence fat oxidation, but more evidence is required.

C	Leptin	—	—	2 studies	Not enough evidence to support alterations in circulating leptin due to CLA ingestion.
C	Appetite	—	—	2 studies	Mixed evidence, and even the promising evidence noted that the degree of appetite suppression was insufficient to suppress food intake.
C	Subjective Well-Being	—	—	2 studies	Insufficient evidence to support an inherent contentment boosting effect, as the lone study was confounded with weight loss.
C	Cell Adhesion Factors (Youth)	—	—	1 study	No significant influence on cell adhesion factors
C	Bone Mineral Density	—	—	1 study	No evidence to support a link between CLA and alterations in bone mineral density
D	Heart Rate	—	—	1 study	No significant interaction between heart rate and CLA supplementation
D	Asthma	—	—	1 study	No significant interaction between CLA supplementation and asthmatic symptoms
D	Kidney Function	—	—	1 study	No significant influence of CLA supplementation on renal functioning
D	Cell Adhesion Factors (Elderly)	—	—	1 study	No significant alterations in cellular adhesion factors (linked to atherosclerosis via the immune system)
D	Symptoms of Crohns Disease			1 study	
D	Interleukin 2			1 study	
D	Interleukin 6			1 study	

Cordyceps

Also known as: Cordyceps Sinensis, Cordyceps Militaris, Caterpillar Fungus, Cetepiller Mushroom, Summer grass-winter worm, Totsu kasu, Yarchakunbu, Aweto

Cordyceps is a mushroom used in Traditional Chinese Medicine that is touted to be anti-aging and pro-vitality; these quite vague claims have not yet been looked at in human interventions. It can regulate testicular testosterone production, but has complex mechanisms.

See [Cordyceps on Examine.com](#)

How to Take

Cordyceps has been used in human trials in the dosage range of 1,000-3,000mg daily, either in one single dose or multiple doses with meals. There is no indication if this is the optimal dose or not, and it is uncertain if this dosage is even effective as some of the research has come back null.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	VO2 Max	—	—	2 studies	No significant influence on VO2 max in otherwise healthy persons.
C	Aerobic Exercise	—	—	1 study	No significant improvements in prolonged aerobic exercise have been noted with cordyceps supplementation
C	Lactate Threshold	↑	★☆☆ Minor	1 study	Might increase lactate threshold, but requires more evidence.

Creatine

Also known as: a-methylguanidinoacetic acid, creatine monohydrate, creatine 2-oxopropanoate

Creatine is a molecule in an energy system (creatine phosphate) that can rapidly produce energy (ATP) to support cellular function. This underlies the performance enhancing and neuroprotective properties of creatine. Creatine is remarkably safe for most people and is a well-researched supplement.

See [Creatine on Examine.com](#)

How to Take

Creatine monohydrate can be supplemented through a loading protocol. To start loading, take 0.3g/kg bodyweight for 5-7 days, then follow with a daily 5g dose. Using 2g daily is another option, as that is enough to maintain average creatine stores. There are many different forms of creatine available on the market, but creatine monohydrate is the cheapest and most effective form of creatine. Micronized creatine is easier to dissolve in water, which may make it easier to supplement. Creatine is usually taken daily. Too much creatine at once may cause diarrhea. Not drinking enough water while taking creatine may also cause stomach cramping.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Power Output	↑	★★★ Strong	65 studies	Creatine is the reference compound for power improvement, with numbers from one meta-analysis to assess potency being "Able to increase a 12% improvement in strength to 20% and able to increase a 12% increase in power to 26% following a training regiment using creatine monohydrate". There does appear to be a high degree of variability, which is correlated with the amount of creatine reaching muscle tissue. There does not appear to be much difference between trained and untrained persons. An acute study noted an increase in peak torque by 33.4% and reduction in the time to reach peak torque by 54.7%; perhaps useful as comparator.

A	Muscle Creatine Content	↑	★★★ Strong	18 studies	Creatine supplementation is the reference compound for increasing muscular creatine levels; there is variability in this increase, however, with some nonresponders.
A	Lean Mass	↑	★☆☆ Minor	19 studies	Does appear to have inherent lean mass building properties, but a large amount of research is confounded with water weight gains (difficult to assess potency).
A	Weight	↑	★★★ Strong	28 studies	Appears to have a large effect on increasing overall weight due to water retention in persons who respond to creatine supplementation. Degree of increase is variable.
A	Hydration	↑	★★★☆☆ Notable	9 studies	Appears to be quite notable due to the increase in water weight in skeletal muscle tissue following creatine supplementation.
A	Anaerobic Running Capacity	↑	★☆☆ Minor	19 studies	Appears to increase anaerobic cardiovascular capacity, not to a remarkable degree however.
A	Swimming Performance	—	—	17 studies	On the whole, there is no reliable improvement in swimming performance with creatine supplementation. In the instances where it could be beneficial, a loading period (no maintenance) is used prior to short sprint tests (50-100m for 1-3 sprints) in order to reduce time by around 2%, or prolonged swimming (400m) may have benefits in the last stretch only.
A	Creatinine	↑	★★★☆☆ Notable	12 studies	Creatine supplementation usually increases serum creatinine levels during the loading phase (usually not maintenance) since creatinine

					is the breakdown product of creatine; this is <i>not</i> indicative of kidney damage.
B	Lipid Peroxidation	↓	★☆☆ Minor	3 studies	A minor reduction, nothing to a remarkable degree.
B	Fat Mass	—	—	9 studies	While creatine is reliable at increasing lean mass (acutely water, more prolonged supplementation is muscle), it does not appear to significantly modify fat mass at all.
B	Kidney Function	—	—	10 studies	In otherwise healthy persons given creatine supplementation, there is no significant beneficial nor negative influence on kidney function.
B	Testosterone	↑	★☆☆ Minor	6 studies	Degree of testosterone spike is not overly notable, although it appears to be present
B	Subjective Well-Being	↑	★☆☆ Minor	10 studies	The influence of creatine on well being and general happiness is usually dependent on it treating a disease state; there does not appear to be a <i>per se</i> benefit to well being.
B	Cognition (Omnivores)	—	—	3 studies	No inherent benefit to omnivore cognition appears apparent, but it may benefit cognition in the sleep deprived.
B	VO2 Max	↑	★☆☆ Minor	3 studies	Improvements in VO2 max are not wholly reliable, and appear to be low in magnitude.
B	Fatigue Resistance	↑	★☆☆ Minor	8 studies	Small degree of fatigue reduction during exercise, but appears unreliable.
B	Exercise Capacity (with Heart Conditions)	—	—	3 studies	Although there may be a small reduction of power output

					(typical of creatine), the main parameter of interest (cardiorespiratory output) is mostly unaffected by creatine supplementation.
B	Muscle Damage	↓	★☆☆ Minor	6 studies	Not overly protective, but there appears to be a degree of protection.
B	Total Cholesterol	—	—	4 studies	In otherwise healthy males given creatine supplementation, overall levels of cholesterol are unaffected.
B	IGF-1	—	—	5 studies	Insufficient evidence to support a role of creatine in increasing IGF-1
B	Treatment of COPD	—	—	3 studies	The main parameters of concern when treating COPD (lung and heart function, cardiovascular exercise performance) are not affected with creatine supplementation.
B	Exercise Capacity in COPD	—	—	3 studies	The main parameter of interest with exercise in COPD (cardiovascular capacity and aerobic exercise) is wholly unaffected with supplementation, although power output still can be increased.
B	Lung Function	—	—	7 studies	Either in healthy persons or in disease states characterized by impaired lung function, creatine supplementation does not modify the strength of exhalations or lung power.
B	Muscular Endurance	↑	★☆☆ Minor	3 studies	Somewhat effective.
B	Blood Pressure	—	—	4 studies	Does not appear to significantly influence blood pressure.
B	Blood Glucose	↓	★☆☆	4 studies	

B			★ ★ ★ Minor		The spike in blood glucose following a meal may be reduced in the range of 11-22% following creatine supplementation, with no apparent influence on fasting blood glucose.
B	Insulin	—	—	3 studies	Fasting insulin concentrations are not affected with creatine supplementation.
B	Cortisol	—	—	4 studies	Cortisol changes associated with sleep deprivation are not affected with supplementation of creatine.
B	Aerobic Exercise	—	—	4 studies	Does not appear to confer any apparent benefit to prolonged cardiovascular exercise.
B	Fatigue	↓	★ ★ ☆ Notable	7 studies	In the fatigue experienced by children subject to traumatic brain injury, frequency of fatigue is reduced from 90% down to 10% with 400mg/kg oral ingestion daily. Fatigue is also reduced to a lesser degree in sleep deprivation
B	Aerobic exercise	—	—	3 studies	Does not appear to confer any apparent benefit to prolonged cardiovascular exercise.
B	Bone Mineral Density	↑	★ ☆ ☆ Minor	3 studies	Limited evidence in favor of improvements in bone mineral density with creatine supplementation
B	Liver Enzymes	—	—	7 studies	No known influence on circulating liver enzymes, suggesting no liver toxicity in humans.
B	Treatment of Amyotrophic lateral sclerosis (ALS)	—	—	6 studies	Short term usage may increase power output like usual, but prolonged supplementation of creatine has failed to alter the

					deterioration of muscle and lung function. While no reduction in mortality has been noted statistically, two studies have noted a trend towards reductions in mortality suggesting an unknown protective effect.
B	Kidney function	—	—	3 studies	In otherwise healthy persons given creatine supplementation, there is no significant beneficial nor negative influence on kidney function.
B	Lactate production	—	—	6 studies	On studies in swimmers, there is no apparent reduction or increase in lactate after sprinting exercises.
B	Heart Rate	—	—	3 studies	There is no known influence of creatine supplementation on heart rate.
B	Treatment of Myotonic Dystrophy	↑	★☆☆ Minor	3 studies	It seems that preliminary evidence supports a beneficial role for Myotonic Dystrophy type II (DM2) to a minor to moderate degree, and there is either a mild or no benefit to DM1.
B	VO2 max	↑	★☆☆ Minor	3 studies	Improvements in VO2 max are not wholly reliable, and appear to be low in magnitude.
C	DNA Damage	↓	★☆☆ Minor	1 study	Appears to reduce exercise-induced DNA damage; practical relevance unknown but potentially promising for cancer prevention.
C	DNA methylation	↑	★☆☆ Minor	1 study	Lack of comparator prevents proper assessment of potency; practical relevance unknown
C	Proteinuria	—	—	1 study	No significant influence on protein losses in the urine (proteinuria)

C	Symptoms of Osteoarthritis	↓	★☆☆ Minor	1 study	Appeared to increase functionality, although not to a remarkable degree.
C	Food Intake	—	—	2 studies	Creatine supplementation does not appear to significantly alter food intake (unconsciously).
C	Cognition (Vegetarians)	↑	★☆☆ Minor	2 studies	Appears to be reliable in increasing cognition in vegetarians, but is based on limited evidence and not yet compared to a reference drug.
C	Glycemic Control	↑	★☆☆ Minor	2 studies	Appears to be somewhat effective in diabetics for improving glycemic control.
C	DHT	↑	★☆☆ Minor	1 study	An increase in DHT has been noted in one study independent of an increase in testosterone, requires replication due to some potential issues (location of study, lack of biological plausibility, etc.)
C	Symptoms of Duchenne Muscular Dystrophy	↓	★☆☆ Minor	2 studies	There appears to be a mild therapeutic effect of creatine supplementation (2-5g) to boys with DMD, mostly related to an improvement in handgrip strength and body composition with some parent-rated improvements.
C	Skeletal Muscle Atrophy	—	—	2 studies	One study noted a prevention of lean mass loss (did not distinguish between water and muscle), while the study measuring muscle mass specifically failed to find a protective effect during limb immobilization.
C	Uric Acid	↓	★☆☆ Minor	2 studies	Minor reductions in uric acid.

C	Depression	↓	★★★☆☆ Notable	3 studies	Notable due to seeming to be related to serotonin and augmenting SSRI therapy, and appears to have a gender difference (efficacy in females) which needs to be explored more.
C	Schizophrenia	—	—	1 study	Insufficient evidence to support a role in schizophrenia
C	Insulin Sensitivity	—	—	1 study	There do not appear to be any alterations in insulin sensitivity associated with creatine supplementation.
C	Symptoms of Sleep Deprivation	↓	★★☆☆☆ Minor	2 studies	The cognitive dysfunction associated with prolonged sleep deprivation can be attenuated with creatine loading prior to said sleep deprivation, but this is to a small degree.
C	Memory	—	—	2 studies	Supplementation of creatine does not influence short term recall during sleep deprivation
C	Treatment of Parkinsons	—	—	1 study	Insufficient evidence to support an improvement in cognitive symptoms of Parkinson's (may aid physical capacities)
C	Body Cell Mass	↑	★★☆☆☆ Minor	1 study	Limited evidence measuring cell volume, but creatine may increase the cell mass.
C	Satellite Cell Recruitment	↑	★★☆☆☆ Minor	1 study	Unable to assess potency of this change based on comparisons to reference drugs.
C	Myonuclei proliferation	↑	★★☆☆☆ Minor	1 study	Appears to induce myonuclei proliferation, unknown potency relative to other agents.
C	Functionality in Elderly or Injured	↑	★★☆☆☆ Minor	2 studies	Possibly an effect, but the less

	Or Injured				reliable effects of creatine in the older population (which seem to respond less) seems to manifest here.
C	Attention	—	—	1 study	Attention during sleep deprivation is not affected with creatine supplementation
C	Adrenaline	—	—	1 study	No significant alterations in plasma adrenaline are seen with creatine supplementation during sleep deprivation.
C	Noradrenaline	—	—	1 study	No significant alterations in plasma noradrenaline are seen with creatine supplementation during sleep deprivation.
C	Dopamine	—	—	1 study	No significant alterations in plasma dopamine are seen with creatine supplementation during sleep deprivation.
C	Growth Hormone	↓ ↑	★★★☆☆ Notable	4 studies	Creatine is able to suppress growth hormone secretion during exercise when loaded (up to 35%) and to a lesser degree during maintenance (5% or less) while creatine at rest can spike growth hormone up to 83+/-45%. This bidirectional effect is similar to Arginine supplementation.
C	Training Volume	—	—	2 studies	Swimming training volume is unaffected by creatine supplementation.
C	Bilirubin			3 studies	
C	Treatment of Huntington's Disease	—	—	2 studies	Insufficient evidence to support a rehabilitative role of creatine.
C	Homocysteine	↓	★★☆☆☆ Minor	1 study	Decrease in homocysteine (biomarker of inflammatory cardiovascular disease) was present, but not to a

					remarkable magnitude
C	DNA damage	↓	★☆☆ Minor	1 study	Appears to reduce exercise-induced DNA damage; practical relevance unknown but potentially promising for cancer prevention.
C	Glycogen Resynthesis	↑	★★★☆☆ Notable	1 study	Degree of improvement is somewhat more potent than other supplemental options, and may be related to the improvements in glycemic control seen with creatine.
C	Myostatin	↓	★★★☆☆ Notable	1 study	Notable as it may be a reference compound (17% reduction in circulating Myostatin) although it is uncertain what practical relevance this holds.
C	Insulin Secretion	—	—	1 study	The insulin secretion in response to a test meal does not appear to be altered with creatine supplementation.
C	Injury Rehabilitation Rate			1 study	
C	Symptoms of McArdles Disease	↓ ↑	★☆☆ Minor	2 studies	The two trials conducted at this moment in time have shown differing effects, and the reason for these differing effects are currently not known.
C	Symptoms of Mitochondrial Cytopathies			3 studies	
C	Glycogen content			2 studies	
C	Urea			4 studies	
C	Triglycerides			3 studies	
C	LDL-C			2 studies	
C	HDL-C			2 studies	
C	General Oxidation			1 study	
C	Anti-Oxidant Enzyme			1 study	

	Profile				
C	C-Reactive Protein			1 study	
C	TNF-Alpha			1 study	
C	Fat Oxidation			2 studies	
C	Muscle Oxygenation			1 study	
C	vLDL-C			1 study	
C	Cerebral Oxygenation			1 study	
C	Aldosterone			2 studies	
C	Sprint performance			1 study	
D	Alertness	↑	★☆☆ Minor	2 studies	Increases in alertness tend to be during sleep deprivation or stress, rather than outright increases in alertness. Not overly potent
D	Blood Flow	↑	★☆☆ Minor	1 study	Lack of comparator prevents assessment of potency.
D	Range of Motion	↓	★☆☆ Minor	1 study	One study noting a reduction in range of motion with creatine supplementation, needs to be replicated.
D	Symptoms of Cystic Fibrosis	—	—	1 study	Although there is an increase in well being and muscular strength in youth given creatine supplementation, the main parameters under investigation (lung and chest symptoms) are wholly unaffected.
D	Dizziness	↓	★★★☆☆ Notable	1 study	Dizziness as a side-effect of traumatic brain injury is halved in frequency with daily supplementation of 400mg/kg creatine intake.
D	Treatment of Headaches	↑	★★★☆☆ Notable	1 study	In children and adolescents subject to traumatic brain injury who then received 400mg/kg creatine supplementation, headache frequency as a side effect is reduced from around 90% down to 10%.

D	Subjective Well-being	↑	★☆☆ Minor	1 study	The influence of creatine on well being and general happiness is usually dependent on it treating a disease state; there does not appear to be a <i>per se</i> benefit to well being.

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Curcumin

Also known as: Turmeric extract, Curry Extract, Curcuma, Diferuloylmethane, JiangHuang, Curcuma Longa, 1,7-bis-{3-methoxy-4-hydroxyphenyl}-1,6-heptadiene-3,5-dione

Curcumin is the active ingredient of turmeric, and is also found in limited amounts in Ginger. It is a potent anti-inflammatory and cancer preventative molecule, and similar to Fish Oil it seems to be an effective metabolic syndrome band-aid. Black Pepper greatly enhances absorption.

See [Curcumin on Examine.com](#)

How to Take

For any systemic purpose (requiring absorption from the intestines), then an oral supplementation of curcumin in the range of 80-500mg would be required assuming an enhancement. Curcumin is poorly absorbed inherently, and one of the following is mandatory: Pairing curcumin with Black Pepper (piperidine) Curcumin phytosomes complexed with Phosphatidylcholine (Meriva or BCM-95) Curcumin nanoparticles (THERACURCUMIN) Water-soluble curcumin (polyvinyl pyrrolidone) If one of the above enhancements are not used, then too little curcumin will be absorbed and even doses of up to 4,000mg may be wholly inactive (8-16g would only be slightly active). If using curcumin for intestinal purposes, then absorption from the intestines into the blood is not necessarily required. Due to this, one can simply use Turmeric at the dose of 2-4g daily or take curcumin supplementation without any of the aforementioned enhancements.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	LDL-C	—	—	3 studies	Possible reducing effects that need to be further demonstrated
B	HDL-C	↑	★☆☆ Minor	3 studies	Possible increases in HDL-C
B	Total Cholesterol	—	—	5 studies	More robust evidence suggests no significant influence of curcumin on total cholesterol, although there may be a potential role
B	Inflammation	↓	★★★☆☆ Notable	5 studies	There appears to be a decrease in disease states or conditions characterized by inflammation associated with curcumin ingestion, does not appear to be too discriminatory

					in which inflammatory states it benefits
B	C-Reactive Protein	↓	★☆☆ Minor	3 studies	May decrease C-reactive protein if elevated
B	General Oxidation	↓	★☆☆ Minor	5 studies	Prooxidative biomarkers appear to be reduced following long term supplementation of curcumin
B	Triglycerides	↓	★☆☆ Minor	5 studies	Some reducing effects have been noted, but they seem to be unreliable and not overly potent
B	Pain	↓	★★★☆☆ Notable	4 studies	There appear to be decreases in pain associated with curcumin at higher doses (400-500mg) which extend to post-operative, arthritic, and general pain symptoms. This does seem comparable to 2g acetaminophen in potency.
B	Lipid Peroxidation	↓	★☆☆ Minor	3 studies	A decrease in lipid peroxidation results following curcumin ingestion chronically
B	Anti-Oxidant Enzyme Profile	↑	★★★☆☆ Notable	4 studies	Although the exact enzyme that increases is not overly reliable (SOD, glutathione, and catalase), all three enzymes have individually been noted to be increased and they tend to do so to a large degree.
B	Blood Pressure	↓	★☆☆ Minor	3 studies	May decrease blood pressure, but more contextual evidence is required
C	Symptoms of Osteoarthritis	↓	★★★☆☆ Notable	3 studies	There appears to be significant reductions in symptoms of osteoarthritis, with the largest decrease noted occurring after eight months of supplementation and reaching 41% of baseline (more than a halving of symptoms).

C	Blood Glucose	—	—	2 studies	No significant influence on blood glucose
C	Edema	↓	★☆☆ Minor	1 study	A decrease in edema has been noted with curcumin supplementation
C	Blood Flow	↑	★☆☆ Minor	2 studies	An increase in blood flow has been noted with curcumin supplementation
C	Mucositis	↓	★☆☆ Minor	1 study	Symptoms of mucositis have been noted to be decreased with curcumin supplementation
C	Liver Enzymes	—	—	2 studies	No significant influence on liver enzymes associated with curcumin supplementation
C	Fatigue	↓	★☆☆ Minor	1 study	A decrease in postoperative fatigue has been noted with curcumin supplementation
C	Functionality in Elderly or Injured	↑	★★★☆☆ Notable	2 studies	In persons with osteoarthritis, the performance on a treadmill test after eight months was significantly increased (more than twice the distance covered with curcumin relative to control).
C	Interleukin 6	↓	★☆☆ Minor	1 study	A slight decrease in IL-6 concentrations has been noted, practical relevance unknown.
C	Interleukin 1-beta	↓	★☆☆ Minor	1 study	A reduction in IL-1b has been noted in osteoarthritic patients, which is thought to underlie the benefits to joint health seen with curcumin.
C	Cell Adhesion Factors	↓	★☆☆ Minor	2 studies	Decreases in cell adhesion factors have been noted, which may underlie therapeutic

					benefits towards atherosclerosis of curcumin supplementation.
C	Prostate Cancer Risk	↓	★☆☆ Minor	1 study	Appears to be associated with a reduced risk of prostate cancer
C	Prostate Specific Antigen	↓	★☆☆ Minor	1 study	Has been noted to decrease prostate specific antigen levels following supplementation
C	Stomach Ulcers	—	—	1 study	No significant influence on stomach ulceration detected
C	Cognitive Decline	↓	★☆☆ Minor	1 study	Rate of cognitive decline may be lesser with dietary inclusion of curcumin, but requires more evidence
C	DNA Damage	↓	★☆☆ Minor	1 study	A decrease in DNA damage has been noted to be secondary to reducing arsenic toxicity
C	Arsenic Poisoning	↓	★☆☆ Minor	1 study	Appears to reduce the DNA damage induced by arsenic in persons with high arsenic exposure; uncertain if this applies to other toxic minerals
C	Protein Carbonyl Content	—	—	1 study	No significant influence on protein carbonylation has been noted with curcumin ingestion
C	Symptoms of Pancreatitis	—	—	1 study	No significant influence on pain associated with pancreatitis
C	Symptoms of Ulcerative Colitis	↓	★☆☆ Minor	2 studies	Symptoms of ulcerative colitis reduced with supplementation of curcumin
C	Kidney Function	↑	★☆☆ Minor	2 studies	Appears to promote kidney function in instances where function is normally hindered

C	Proteinuria	↓	★☆☆ Minor	1 study	A reduction in proteinuria has been noted in persons with kidney impairment given curcumin
C	Colorectal Cancer Risk	↓	★☆☆ Minor	2 studies	Appears to be associated with a reduced risk for colon cancer
C	Intestinal Motility	↑	★☆☆ Minor	1 study	May increase intestinal motility
C	Vascular Function	↑	★☆☆ Minor	1 study	An increase in vascular function has been noted with curcumin supplementation
C	Heart Rate	—	—	1 study	No significant influence on heart rate seen with curcumin supplementation
C	VO2 max	—	—	1 study	In postmenopausal women, curcumin supplementation does not improve VO2 max.
C	Weight	—	—	1 study	Currently no demonstrable anti-obese effect of isolated curcumin supplementation.
C	Nitric Oxide	↑	★★★☆☆ Notable	1 study	80mg of a bioavailability enhanced curcumin supplement has been reported to increase nitric oxide in serum by 40% or so, which is significantly larger than many other dietary supplements.
C	Myeloperoxidase	↑	★☆☆ Minor	1 study	A slight increase in MPO concentrations has been detected.
C	Insulin Sensitivity	↑	★☆☆ Minor	1 study	In insulin resistant persons, curcumin can increase insulin sensitivity.
C	Insulin Secretion	↑	★☆☆ Minor	1 study	Curcumin has been found to increase insulin secretion in insulin resistant persons, suggesting benefits to

					pancreatic tissue.
C	Adiponectin	↑	★☆☆ Minor	1 study	Curcumin has been implicated in increasing adiponectin concentrations.
D	Insulin	↑	★☆☆ Minor	1 study	May increase postprandial insulin concentrations
D	Symptoms of Crohn's Disease	↓	★☆☆ Minor	1 study	Possible reductions of symptoms associated with Crohns Disease
D	Iron Absorption	—	—	1 study	No significant influence on iron absorption
D	Depression	↓	★★★☆☆ Notable	1 study	One study has noted improvements in major depressive disorder (1g curcumin) which were comparable to fluoxetine (20mg) as a reference, but no placebo group was available for comparison.

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D-Aspartic Acid

Also known as: D-AA, D-Aspartate, DAA

D-aspartic acid (D-AA) is an amino acid regulator of testosterone synthesis. It also makes a stimulatory neurotransmitter (NMDA). D-AA shows promise in aiding male fertility. Healthy men supplementing D-AA experience only temporary increases in testosterone, which limits its use.

See [D-Aspartic Acid on Examine.com](#)

How to Take

The standard dose for D-aspartic acid is between 2,000 – 3,000mg. D-AA is taken daily. Different studies have used different supplementation protocols. One study used 3,000mg for 12 days, taken daily, followed by a week with no supplementation. A different study did not cycle D-AA, and used 2,000mg of continual daily supplementation with no harm. Further study is needed to determine whether D-AA should be cycled.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Testosterone	↑	☆☆☆ Minor	3 studies	There appears to be an increase in testosterone in most subjects acutely (6-12 days), and while this may persist to the tune of 30-60% in infertile men it is reduced to baseline within a month in otherwise healthy men with normal testosterone at baseline.
C	Lean Mass	—	—	1 study	No significant influence on lean mass in otherwise healthy trained men.
C	Fat Mass	—	—	1 study	Fat mass does not appear to be altered with D-aspartic acid supplementation alongside exercise.
C	Estrogen	—	—	1 study	Despite a possible induction of aromatase seen in some species, D-aspartic acid supplementation does not appear to increase serum estrogen.

C	Power Output	—	—	1 study	Otherwise healthy trained men do not experience a further increase in power output relative to placebo when D-aspartic acid is taken alongside resistance training.
C	Weight	—	—	1 study	No significant alterations in body weight when D-aspartic acid is taken alongside resistance training.
D	Fertility	↑	★★★☆☆ Notable	2 studies	Limited evidence for D-aspartic acid suggest an increase in fertility of men, with one study noting that a group went from no conceptions to 26.6% of subjects reporting conception over 90 days.
D	Sperm Quality	↑	★☆☆☆☆ Minor	1 study	Appears effective, needs to be compared against a comparator.
D	Sperm Count	↑	★☆☆☆☆ Minor	1 study	Improvements of sperm count in infertile men have been noted to vary between 50-100% increases over baseline.
D	Seminal motility	↑	★☆☆☆☆ Minor	1 study	Seminal motility is increased 50-100% in infertile men supplementing with D-aspartic acid
D	Luteinizing Hormone	↑	★☆☆☆☆ Minor	1 study	An increase in LH concentrations has been noted to 30-60% in infertile men, correlating well with the testosterone increases seen in this study.

D-Serine

D-Serine is an amino acid that acts similar to Glycine although may be more effective at augmenting stimulation. It is released from glial cells rather than neurons, but still has a role in cognitive enhancement and schizophrenia treatment.

See [D-Serine on Examine.com](#)

How to Take

D-Serine has been used in studies at an oral dose of 30mg/kg (assuming nonobese human), which correlates to an estimated dosage range of 2,045-2,727mg for 150-200lb persons. This is the dose that appears minimally effective for promoting cognition in a variety of disease states. Preliminary evidence for schizophrenia suggests that a doubling or quadrupling of the dosage (60mg/kg and 120mg/kg, respectively) causes additional benefits due to increasing bodily exposure to D-serine.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Symptoms of Schizophrenia	↓	★☆☆ Minor	6 studies	D-Serine supplementation is able to reduce symptoms of schizophrenia (more efficacy on negative and cognitive symptoms rather than positive) in a dose-dependent manner between 30-120mg/kg, but possibly due to the unreliable increases in blood D-serine its benefits are also unreliable
B	Cognition	↑	★☆☆ Minor	3 studies	There may be an improvement in cognitive performance secondary to reducing symptoms of schizophrenia, and while there is mechanistic plausibility that this can also work in normal controls it has not yet been demonstrated
C	Symptoms of Parkinsons Disease	↓	★☆☆ Minor	1 study	Preliminary evidence suggests that the standard dosage of D-Serine can alleviate some symptoms of Parkinson's disease
C	Symptoms of Post			1 study	

	Traumatic Stress Disorder				

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Dehydroepiandrosterone

Also known as: DHEA, Pradesterone, Hydroxyandrosterone, 3β-Hydroxy-5-Androstene-17-one

DHEA is a naturally occurring hormone and either exerts benefits on its own, or can convert into both Testosterone or Estrogen depending on the body's need. DHEA supplementation is potent for reducing the 'effects of aging', but appears quite unreliable in its benefits.

See [Dehydroepiandrosterone on Examine.com](#)

How to Take

Supplementation of DHEA appears to be effective in persons over 40 in the dosage range of 25-50mg, while prolonged usage of 100mg appears to be safe in this demographic. While the usage of DHEA in young persons for the purpose of testosterone enhancement is not clear, it tends to be used at 200mg for this purpose.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Testosterone	↑	★★★☆☆ Notable	18 studies	There appears to be an increase in testosterone following DHEA supplementation, but the vast majority of literature is in menopausal women (where testosterone contributes to libido). There is variability in the results, and DHEA is unreliable in increasing testosterone, but this unreliability extends to all demographics and subjects (with limited evidence of DHEA increasing testosterone in all studies including youthful athletes, which are less studied).
A	Estrogen	↑	★★★☆☆ Notable	14 studies	There appears to be a notable and unreliable increase in estrogen following DHEA supplementation, with most research being conducted in menopausal women. This increase in estrogen has been noted in men as well, although similarly unreliable.

A	Serum DHEA	↑	★★★ Strong	13 studies	Supplemental DHEA results in a reliable and significant increase in DHEA concentrations in the blood (both sulfated DHEAS and unsulfated DHEA)
B	Bone Mineral Density	—	—	7 studies	Most evidence suggests no increase in bone mineral density, but this may be due to short trials (6 months). Longer trials note a small but unreliable increase in bone mineral density, so there may be a role of DHEA in bone health
B	Functionality in Elderly or Injured	—	—	3 studies	Most evidence measuring functionality in elderly persons have not found any improvement with DHEA supplementation, although it is possible that DHEA may play a role
B	Sex Hormone Binding Globulin	↓	★☆☆ Minor	4 studies	There appears to be a decrease in SHBG concentrations in older individuals who also experience an increase in androgen/estrogen concentrations, but this is similarly unreliable
B	Libido	—	—	3 studies	Insufficient evidence to support an increase in libido despite increases in androgen status
B	Fat Mass	—	—	8 studies	No significant influence on fat mass appears to exist with DHEA supplementation in youth or in elderly persons
B	Lean Mass	—	—	8 studies	Perhaps due to a lack of studies pairing DHEA with a prolonged resistance training program, there is no evidence to support DHEA supplementation to increase muscular or lean mass

B	IGF-1	↑	★☆☆ Minor	6 studies	An increase in IGF-1 hormone levels may exist following DHEA supplementation, although this has only been investigated in older persons.
B	Subjective Well-Being	—	—	4 studies	No significant influence on well being is noted with DHEA per se, although it may come secondary to other changes occurring during DHEA supplementation (such as improved functionality in elderly persons)
B	LDL-C	—	—	4 studies	Although there is some counter evidence, usually DHEA supplementation does not alter LDL-C concentrations
B	HDL-C	—	—	5 studies	Most of the evidence leans towards no significant influence of DHEA on HDL-C levels
B	Triglycerides	—	—	3 studies	Mixed evidence, but it seems that DHEA doesn't have a significant influence on triglycerides
B	Cortisol	↓	★☆☆ Minor	5 studies	Highly unreliable influences on cortisol, with decreases seen in studies where androgens and estrogens are also increased (with no significant influence or possibly an increase in other studies)
B	Blood Glucose	—	—	3 studies	Most evidence suggests no alterations to fasting blood glucose levels
B	Power Output	—	—	3 studies	No significant improvement in power output has been noted with DHEA supplementation (studies mostly in older individuals)

C	Stress	—	—	1 study	No significant influence on parameters of stress
C	Fertility	↑	★☆☆ Minor	2 studies	An increase in fertility has been noted with DHEA supplementation
C	Cognitive Decline	↓	★☆☆ Minor	2 studies	May attenuate the rate of cognitive decline in persons at higher risk, but this protective effect does not seem to be overly remarkable
C	Prostate Specific Antigen	—	—	2 studies	No significant influence on PSA levels
C	Erections	—	—	1 study	No significant influence on erectile properties in persons with sexual dysfunction
C	Weight	—	—	1 study	No significant influence on weight noted with DHEA supplementation
C	Free Testosterone	↑	★☆☆ Minor	2 studies	Increases in free testosterone have been noted to coincide with testosterone increases (which are unreliable)
C	Cognition	—	—	1 study	Overall cognition not affected by DHEA supplementation
C	Depression	—	—	1 study	No significant interactions with depression noted
C	Insulin Sensitivity	—	—	3 studies	No significant influences on insulin sensitivity seem apparent with DHEA supplementation
C	Oxidation of LDL	↓	★☆☆ Minor	1 study	One study has noted less small particles of LDL, indicative of less LDL oxidation; possibly protective effects

C	IGF Binding Protein	—	—	1 study	There may be an influence (study noted both increases and decreases with high variability) but this does not appear to be a clinical concern
C	Nitric Oxide	↑	★☆☆ Minor	1 study	Has been detected to increase nitric oxide concentrations in serum, needs to be replicated to investigate mechanisms
C	Insulin	—	—	1 study	No significant alterations in fasting glucose levels
C	Sleep Quality	—	—	1 study	No significant influence on sleep quality in menopausal women
C	Total Cholesterol	↓	★☆☆ Minor	3 studies	There may be a decrease in cholesterol seen with DHEA in hypercholesterolemics, but it is not overly reliable
C	Luteinizing Hormone	—	—	2 studies	No significant alterations detected in luteinizing hormone levels
C	Follicle-Stimulating Hormone	—	—	2 studies	No significant alterations in follicle-stimulating hormone levels
C	DHT	↑	★☆☆ Minor	2 studies	May increase DHT levels alongside testosterone levels, but this has only been observed in postmenopausal women
C	Progesterone	—	—	2 studies	Mixed effects on progesterone (and 17-hydroxyprogesterone) leaning towards no significant influence (although increases have been noted)
C	Blood Flow	↑	★☆☆ Minor	1 study	Possible increases in blood flow associated with DHEA supplementation

C	Liver Enzymes	—	—	1 study	No detectable alteration in serum liver enzymes (biomarker of liver damage) seen with DHEA supplementation
D	Symptoms of Menopause	↓	★☆☆ Minor	2 studies	Decreases in menopausal symptoms have been noted with DHEA supplementation
D	Serum T3	—	—	1 study	No significant influence on serum T3 has been noted
D	Growth Hormone	↑	★☆☆ Minor	2 studies	May increase growth hormone concentrations, but this appears to be unreliable
D	Plasma Endorphins	↑	★☆☆ Minor	1 study	An increase in plasma endorphins has been noted with DHEA supplementation

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Ecdysteroids

Also known as: Suma extract, pfaffia extract, Brazilian ginseng extract, beta-ecdysterone, turkesterone, ecdysterone

Ecdysteroids are a class of hormones that are the androgens of insects; they are involved with reproduction and molting, but human ingestion might be healthy or increase muscle mass. Human interventions are lacking and problems with ecdysteroid ingestion exist.

See [Ecdysteroids on Examine.com](#)

How to Take

Hypoglycemic effects of edcdysterone and its plant sources seems to be dose-dependent, although a good dose that is used safely is typically 200mg a day. An oral dose of 5mg/kg bodyweight in rats seems to possess anabolic properties, and would be a good place to start for increasing muscle mass.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Testosterone	—	—	1 study	No alterations noted in serum testosterone associated with ecdysterone consumption
C	Lean Mass	—	—	1 study	No differences between ecdysteroids and placebo in improving lean mass accrual during a weight lifting program
C	Total Cholesterol	—	—	1 study	In resistance trained males, no significant influence of ecdysterone supplementation on cholesterol
C	Liver Enzymes	—	—	1 study	No significant alterations in any measured liver enzymes (ALT, AST, GGT)
C	Power Output	—	—	1 study	No difference between improvements in power output between ecdysteroids and placebo
C	Triglycerides	—	—	1 study	No significant influence on

					triglycerides
C	Cortisol	—	—	1 study	No demonstrated changes in cortisol levels with ecdysterone consumption

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Echinacea

Also known as: Brauneria purpurea, Echinacea intermedia, Rudbeckia purpurea, Purple coneflower herb, Coneflower, red sunflower

Echinacea purpurea is a herb commonly used either in response to or daily for prevention of the common cold. It may hold benefit in doing so, although it outperforms placebo unreliably and the amount of benefit derived is similarly unreliable.

See [Echinacea on Examine.com](#)

How to Take

For dehydrated powders (including encapsulated echinacea) the species of purpuera tends to be used and oral doses are taken upwards of 300mg thrice a day (900mg daily) and 500mg thrice daily (1,500mg daily). Tinctures of an ethanolic extract of the aerial parts (leaves and stems) appears to be used in the concentration of 2.5mL thrice a day or up to 10mL daily. There is no much evidence as to whether these are the optimal doses, and studies seem to be very hetereogeneous in their benefits due to lack of standardization.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Upper Respiratory Tract Infection Risk	↓	★★★☆☆ Notable	11 studies	The reduction in rate of sickness seen with echinacea as a daily supplement is highly effective in some instances, but subject to a high degree of variability. It is notable due to it being a comparator.
A	Length of Sickness	↓	★★★☆☆ Notable	6 studies	Although a high variability exists, the meta-analysis has concluded a 1.4-day reduction in sickness when it occurs relative to placebo. As echinacea is also a comparator for sickness, this reduction in notable
B	Symptoms of the Common Cold	—	—	4 studies	Insufficient evidence to support modification of symptoms of sickness
C	Erythropoietin	↑	★☆☆☆☆ Minor	1 study	Lone trial noted an increase in EPO production without an

					accompanying increase in red blood cell count; practical significance of these results uncertain
C	Oxygenation Cost of Exercise	↓	★☆☆ Minor	1 study	Effective, but to a small degree based on one trial.
C	VO2 Max	↑	★☆☆ Minor	1 study	Not an astounding increase in VO2 max, requires replication.
C	Red Blood Cell Count	—	—	1 study	Oddly ineffective despite an increase in erythropoietin seen
C	Exercise-Induced Immune Suppression	↓	★☆☆ Minor	1 study	Possible effects, but study assessed salivary IgA (biomarker of immunity) and not sickness rates; hard to assess potency.
C	Sleep Quality	—	—	1 study	Likely related to the inefficacy in treating symptoms, but no significant ability to aid in sleep quality during or without sickness
C	Blood Pressure	—	—	1 study	No significant known effects on blood pressure

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Ecklonia cava

Ecklonia Cava is a brown seaweed with a rich polyphenolic content (this particular subset being known as eckols or phlorotannins) that confers anti-oxidant properties, it is being investigated for health properties.

See [Ecklonia cava on Examine.com](#)

How to Take

Ecklonia Cava products appear to benefit the body in relatively low doses, with weak health benefits on blood pressure and glucose in the range of 100mg; higher doses (which would be expected when consuming the seaweed itself as a food product) confer dose-dependent responses.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Blood Pressure	↓	★☆☆ Minor	2 studies	A possible reduction in blood pressure in overweight persons with supplementation of ecklonia cava
C	Triglycerides	—	—	1 study	No significant influence on triglycerides noted with ecklonia cava
C	Total Cholesterol	↓	★☆☆ Minor	2 studies	A possible reduction in total cholesterol concentrations
C	LDL-C	↓	★☆☆ Minor	2 studies	Possible reductions in LDL-C
C	Blood Glucose	↓	★☆☆ Minor	1 study	May reduce blood glucose levels, not overly potent in doing so
D	C-Reactive Protein	↓	★★★☆☆ Notable	1 study	Appears to reduce C-reactive protein, with the degree of reduction being noted almost a halving
D	HDL-C	—	—	1 study	No significant influence on HDL-C detected

Eclipta alba

Also known as: False Daisy, Yerba de tago, Kehraj, Karisalankanni

Eclipta Alba (False Daisy) is a herb that has traditional usage as a liver tonic in Ayurveda. It appears to have preliminary evidence to suggest hair growth promotion as potent as Minoxidil and some anti-diabetic effects as well as liver protection.

See [Eclipta alba on Examine.com](#)

How to Take

Currently, the only human study using Eclipta Alba merely consumed 3,000mg of the leaves. This study did not use a particular extract, but crushed and encapsulated the leaves themselves. Benefits are seen with the petroleum ether extract on hair growth (up to 5% of solution when applied topically) and the ethanolic extract for pain reduction (dose dependent up to 500mg/kg in rats, which is 80mg/kg in human equivalence).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Diuresis	↑	★★★☆☆ Notable	1 study	Urine volume has been noted to be increased by 34%, which is fairly notable as it outperforms other nutraceuticals
D	Blood Pressure	↓	★★★☆☆ Notable	1 study	Decreases of blood pressure in unhealthy persons using eclipta alba have occurred by 15% (mean arterial pressure)
D	HDL-C	—	—	1 study	No detectable influence on HDL-C cholesterol
D	vLDL-C	↓	★★☆☆☆ Minor	1 study	Decreases in fasting vLDL have been noted
D	LDL-C	↓	★★★☆☆ Notable	1 study	Decreases in LDL-C have been noted with eclipta alba in hypertensive persons to 24%, which is quite a significant reduction.

D	Total Cholesterol	↓	★☆☆ Minor	1 study	A decrease in total cholesterol has been noted with supplementation of eclipta alba
D	Triglycerides	↓	★☆☆ Minor	1 study	Decreases in triglycerides have been noted, but not to a remarkable degree
D	Lipid Peroxidation	↓	★☆☆ Minor	1 study	A decrease in biomarkers of lipid peroxidation has been noted, possible related to an increase in serum Vitamin E concentrations

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Eleutherococcus senticosus

Also known as: Siberian ginseng, Ciwujia, Acanthopanax senticosus, Eleuthero

Eleutherococcus senticosus (Siberian Ginseng or simply Eleuthero) is an adaptogenic herb that may be able to increase work capacity during strenuous aerobic activity alongside other anti-stress and possible immunity boosting effects. Preliminary evidence supports traditional uses and animal models.

See [Eleutherococcus senticosus on Examine.com](#)

How to Take

The lowest dose where benefit has been seen with eleuthero has been 300mg, with the recommended dosage range being around 300-1,200mg (Western supplement) while doses in the 2-4g range or higher have traditionally been recommended. The root and stem extracts are more commonly used with benefit.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	LDL-C	↓	★☆☆ Minor	1 study	A decrease in LDL-C has once been noted
C	HDL-C	—	—	1 study	No significant influences yet known for HDL cholesterol
C	Total Cholesterol	—	—	1 study	No significant influences yet known for total cholesterol
C	Triglycerides	—	—	1 study	No significant influences yet known for triglycerides
C	Liver Enzymes	—	—	2 studies	No significant influence on liver enzymes when measured as a part of a safety test battery
C	Protein Carbonyl Content	↓	★☆☆ Minor	1 study	A decrease in protein carbonylation has been noted, which is thought to be secondary to antioxidative effects
C	Lipid Peroxidation	—	—	1 study	Insufficient evidence to evaluate lipid peroxidation

					reducing effects
C	DNA Damage	↓	★☆☆ Minor	1 study	A decrease in DNA damage biomarker has been noted, thought to be secondary to antioxidative effects
C	Rate of Perceived Exertion	—	—	1 study	Despite possible influences on fatigue production, there is currently no demonstrated reduction in the rate of perceived exertion during exercise
C	Fat Oxidation	↑	★☆☆ Minor	2 studies	Some studies have noted an increase in fat oxidation during exercise; no current studies conducted at rest
C	Blood Glucose	↓	★☆☆ Minor	1 study	A decrease in glucose consumption during exercise (without affecting metabolic rate and due to an increase in fat oxidation) has once caused an acute lowering of glucose. The magnitude is quite minor, and there is no evidence to assess the effects of eleuthero on fasting blood glucose or in diabetes management
C	Fatigue Resistance	↑	★☆☆ Minor	2 studies	May increase physical performance, but is unreliable in doing so
C	Immunity	↑	★☆☆ Minor	2 studies	Appears to have a stimulating effect on T-cell proliferation and NK cell activity, but requires more evidence.
C	Natural Killer Cell Content	↑	★☆☆ Minor	1 study	An increase has been noted, but there is insufficient evidence to assess the magnitude of increase or the reliability
C	Oxygen Uptake	↑	★☆☆ Minor	1 study	Limited evidence, but it is in support of an increase in oxygen consumption

C	Anaerobic Running Capacity	↑	★☆☆ Minor	1 study	Possibly effective at increasing cardiovascular exercise performance, likely secondary to fatigue reduction (although similarly unreliable)
C	Social functioning in Elderly	↑	★☆☆ Minor	1 study	Appears to increase social functioning in elderly persons, which is a measurement of cognition (and eleuthero is thought to, via this, possible attenuate the rate of cognitive aging)
C	Cognitive Decline	↓	★☆☆ Minor	1 study	A positive influence on the cognitive state of elderly persons (reduction of cognitive decline) has once been noted
D	VO2 Max	↑	★☆☆ Minor	1 study	Possible increases in VO2 max, but requires more evidence to ascertain potency and reliability
D	Heart Rate	—	—	1 study	No significant influences on heart rate are yet known

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Emblica officinalis

Also known as: Phyllanthus emblica, Amla, Anwala, Indian gooseberry

Emblica officinalis (Amla) is an ayurvedic herb which has all parts, including the fruits, used for preventative and therapeutic purposes. It appears to be most used for regulating glucose metabolism and cardiac health, and may also be neuroprotective.

See [Emblica officinalis on Examine.com](#)

How to Take

Unless otherwise specified, most benefits associated with emblica officinalis are from the fruits of the plant. The fruits themselves (dry weight) or their powder are taken in the dosage range of 1-3g daily with the higher part of this range being seen as more effective.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Blood Glucose	↓	★★★☆☆ Notable	1 study	Preliminary evidence suggested that 3g of the fruits (a fairly reasonable dosage) was as effective as 5mg glibenclamide twice daily
D	Total Cholesterol	↓	★☆☆☆☆ Minor	1 study	A decrease in cholesterol has been noted and appears to affect both healthy controls as well as diabetics
D	Triglycerides	↓	★☆☆☆☆ Minor	1 study	Appears to have triglyceride reducing properties
D	HDL-C	↑	★☆☆☆☆ Minor	1 study	Higher doses of the fruits (3g) appear to be able to increase circulating HDL cholesterol in otherwise healthy persons and diabetics
D	LDL-C	↓	★☆☆☆☆ Minor	1 study	A decrease in LDL-C has been noted with consumption of the fruits over 21 days, affecting both healthy controls and diabetics

Ephedrine

Also known as: Ephedra Vulgaris, Ephedraceae, ma huang

Ephedrine is one of the four active components of the herb Ephedra. It is able to induce fat loss via increasing the amount of fat available for fuel as well as by increasing heat expenditure. It has been implicated in increasing the metabolic rate by up to 5% in humans.

See [Ephedrine on Examine.com](#)

How to Take

All Doses Standardized to Ephedrine HCl In an ECA stack, ephedrine is dosed at 20-24mg for three doses taken throughout the day. Human studies have found success with ephedrine in isolation on fat metabolism with doses of 20-50mg thrice a day. The higher range (150mg) may be too stimulatory for some, and can induce headaches or light hand tremors. Ephedrine tends to be consumed with xanthine compounds like Caffeine and sometimes with Aspirin. The combination of Ephedrine and caffeine is shown repeatedly to be highly synergistic.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Fat Mass	↓	★★★☆☆ Notable	4 studies	It is thought that most weight lost with ephedrine administration is due to fat mass, due to a slight muscle preserving effect; studies that note reductions in fat mass support this hypothesis
B	Weight	↓	★★★☆☆ Notable	10 studies	Ephedrine tends to result in reliable weight loss over time relative to control (assuming calories are held equal), which is mostly due to a loss of body fat
B	Blood Pressure	↑	★★☆☆☆ Minor	5 studies	There may be an acute increase in blood pressure seen with ephedrine intake, although this does not appear to be overly reliable; long-term usage of ephedrine does not seem to alter blood pressure, and may reduce it secondary to weight loss

B	Heart Rate	↑	★☆☆ Minor	5 studies	An increase in heart rate is present following ephedrine administration which correlates well with its psychostimulatory properties; this is not 100% reliable, and heart rate increases may not occur
B	Metabolic Rate	↑	★★★☆☆ Notable	6 studies	Ephedrine, secondary to the stimulatory properties, appears to reliably increase metabolic rate
C	Triglycerides	↓	★☆☆ Minor	2 studies	There appears to be a decrease in triglycerides over time with ephedrine ingestion, which may be due to either the fat burning effects of ephedrine or the weight loss that tends to ensue
C	HDL-C	↑	★☆☆ Minor	2 studies	An increase in HDL-C has been noted with ingestion of ephedrine, may be confounded with weight loss also seen in the trials
C	LDL-C	↓	★☆☆ Minor	1 study	A decrease in LDL-C has been noted to be associated with ephedrine, although this may be confounded with weight loss (also seen in the trials)
C	Nasal Congestion	↓	★★★☆☆ Notable	2 studies	Ephedrine appears to result in notable nasal decongestion
C	Power Output	—	—	1 study	No significant influence on power output with standard oral doses of ephedrine (higher doses may influence power output, but this is not well researched)
C	Subjective Well-Being	↑	★☆☆ Minor	1 study	Appears to increase well being acutely following the first doses of ephedrine, secondary to the psychostimulatory effects

C	Skeletal Muscle Atrophy	↓	★☆☆ Minor	1 study	May decrease the rate of skeletal muscle breakdown over time
D	Nausea	↑	—	1 study	Ephedrine has been noted to reduce postoperative nausea, but is also linked to inducing nausea secondary to its psychostimulatory and appetite suppressing effects. The latter is more practical for supplementation
D	Appetite	↓	★☆☆ Minor	1 study	A decrease in appetite following ephedrine intake is noted and thought to be secondary to its psychostimulatory effects

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Eurycoma Longifolia Jack

Also known as: Longjack, Tongkat Ali, Malaysian Ginseng, longjax, Cay Ba Binh, Pasak Bumi, Langir Siam, Tung Sawa

Eurycoma (Tongkat Ali, LongJack) is a pro-fertility agent and aphrodisiac that appears to have a large body of evidence supporting this role and some evidence suggesting it may be an anti-estrogen and pro-erectile agent. Lack of evidence for testosterone boosting.

See [Eurycoma Longifolia Jack on Examine.com](#)

How to Take

The standard dosage of eurycoma longifolia jack is 200-300mg of a 100:1 extract (the concentration is based on the eurycomamone content), which at least in regards to eurycomamone is as effective as 20-30g of the dry root of the plant. This dose tends to be taken in 1-2 doses throughout the day, and it is unsure if this is the optimal dose.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Testosterone	—	—	3 studies	Although the protective effects of tongkat ali on the testicles and the profertility effects may result in a slight increase in testosterone in infertile men and the adaptogenic effects may cause a preservation of testosterone in stressed men, there is no evidence in otherwise healthy and unanxious men.
C	Libido	↑	★☆☆ Minor	1 study	An increase in libido is seen with prolonged daily ingestion of eurycoma supplements in the range of 8.4-10.8%
C	Subjective Well-Being	↑	★☆☆ Minor	1 study	In otherwise normal men supplementing eurycoma, an increase in overall quality of life and happiness is seen (alongside increases in libido)
C	Erections	↑	★☆☆ Minor	1 study	There appears to be a slight proerectile effect of eurycoma

					supplements as assessed by self-report survey
C	Serum DHEA	—	—	1 study	No significant changes in the sulfate form of DHEA (DHEA-S) is noted after twelve continual weeks of supplementation
C	IGF-1	—	—	1 study	No detectable alterations in IGF-1 for eurycoma extract
C	Sex Hormone Binding Globulin	—	—	1 study	No significant influence on circulating SHBG over the course of 12 weeks in otherwise healthy men.
C	Seminal motility	↑	★☆☆ Minor	1 study	Sperm motility appears to be increased, with more efficacy in those with lower baseline motility and improvements averaging 44.4%
C	Sperm Quality	↑	★☆☆ Minor	1 study	May increase parameters of sperm quality and volume.
C	Weight	↓	★☆☆ Minor	1 study	A decrease in weight has been noted in overweight and obese men, but did not extend to men of normal weight. Mechanisms unknown.
C	Stress	↓	★☆☆ Minor	1 study	Supplementation of eurycoma in stressed persons appears to reduce subjective perceptions of stress.
C	Cortisol	↓	★☆☆ Minor	1 study	In stressed persons, daily supplementation of eurycoma is associated with a 16% reduction in cortisol concentrations.
D	Lean Mass	↑	★☆☆ Minor	1 study	One pilot study has noted an increase more than control when both eurycoma and control were paired with exercise

D	Fat Mass	—	—	1 study	No significant known influences on fat mass
D	Power Output	↑	★☆☆ Minor	1 study	A slight increase in power output has been noted, which may be secondary to increased training adaptations

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Fenugreek

Also known as: Trigonella foecum-graecum, fenugreek seeds

Fenugreek is a product sometimes processed into breads, and sometimes supplemented. It can make urine and sweat smell of maple syrup. It also appears to be a libido enhancer, anti-diabetic and is pretty healthy; many people like the maple syrup urine aspect of it, conversation starter.

See [Fenugreek on Examine.com](#)

How to Take

For the purposes of increasing milk production in women, there isn't much evidence to go on for 'best' dosage although somewhere in the range of 500-1000mg would be advisable. For men increasing testosterone concentrations or libido, 500-600mg of a fenugreek product known as 'Testofen' (50% fenusides by weight) is used. The seeds of fenugreek themselves (not an extract) may be used at an oral dose of 2-5g daily, and this dose shows efficacy in helping blood glucose in diabetics.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Testosterone	—	—	3 studies	Although there is limited evidence to support an increase in testosterone, more evidence than not denies such an increase
B	Appetite	—	—	4 studies	Variable effects on appetite, but it seems the fenugreek fibers (not commonly in supplements) may reduce appetite similar to most dietary fibers while the saponins (commonly supplemented) have no significant effect or a possible increase
B	Insulin	—	—	3 studies	No consensus as to the influence of fenugreek on insulin levels
C	Fat Mass	↓	★☆☆ Minor	1 study	A lone study measuring fat mass in athletes given fenugreek noted a reduction in fat mass, which was not to a remarkable degree

C	DHT	↓	★☆☆ Minor	2 studies	A decrease in DHT has been noted following consumption of fenugreek seeds in otherwise healthy men, but appears to be unreliable
C	Estrogen	—	—	2 studies	No significant influences detected on estrogen levels
C	Lean Mass	—	—	1 study	No demonstrated benefit to lean mass accrual in otherwise healthy trained men given a workout program
C	Glycogen Resynthesis	↑	★☆☆ Minor	2 studies	Mixed influence on glycogen resynthesis rates, but may have a possible benefit
C	Blood Glucose	↓	★☆☆ Minor	3 studies	Appears to result in a decrease of blood glucose following ingestion of fenugreek
C	Libido	↑	★★★☆☆ Notable	1 study	Increases in libido have been noted before, which is notable due to the lack of significant influence on testosterone and possible suppression of DHT (theoretically should reduce libido, yet a large increase is seen with fenugreek)
C	Prolactin	—	—	1 study	No detectable interactions with fenugreek and prolactin levels
C	Prostate Specific Antigen	—	—	1 study	No significant influence on prostate specific antigen levels
C	Milk Production	↑	★★★★ Strong	1 study	Increases in milk production have been noted in lactating women given fenugreek, and appears to be a fairly significant degree of improvement with the best trial conducted noting a doubling of milk production
C	Insulin Sensitivity	↑	★★★★☆	1 study	

C	Insulin Sensitivity	↑	★☆☆ Minor	1 study	An increase in insulin sensitivity has been noted with fenugreek ingestion
C	HDL-C	↑	★☆☆ Minor	1 study	An increase in HDL-C has been associated with fenugreek ingestion
C	Triglycerides	↓	★☆☆ Minor	1 study	May reduce triglyceride levels
C	Glycemic Control	↑	★☆☆ Minor	1 study	May improve glycemic control secondary to reduction in blood glucose, although this may be more indicative of fenugreek fibers than the saponin content
C	Cortisol	—	—	1 study	No significant influence on cortisol levels following fenugreek ingestion
C	Leptin	—	—	1 study	No significant influences detected on circulating leptin levels with fenugreek

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Feverfew

Also known as: Tanacetum parthenium, Wild Chamomile, Featherfew, Chrysanthemum parthenium, Matricaria parthenium, Pyrenthrum parthenium, Leucanthemum parthenium, Mutterroot, midsummer daisy, nosebleed, Medieval Aspirin, 18th century Aspirin

Feverfew, also known as Wild Chamomile or Medieval Aspirin, is a herb with anti-inflammatory properties that appears to be effective as an anti-migraine preventative and therapeutic medication, although its traditional claims of anti-arthritis need to be validated.

See [Feverfew on Examine.com](#)

How to Take

Adult usage of Fever is to take 100-300mg (of 0.2-0.4% Parthenolide) of Feverfew 1-4 times a day, although if the supplement is a carbon-dioxide (CO2) extraction, which increases Parthenolide content, three doses of 6.25mg can be used. Child doses are contradicted (to not use) for children under 2 years of age, but aside from that use the dosage based on a ratio of adult weight (assuming 150lbs as a standard). If a child weights 50lbs, the oral dose is one third that of an adult. Liquids are sometimes used against arthritis, in which the commonly suggested dose is 60-120 drops of a 1:1 (fluid) or 1:5 (tincture) taken twice a day.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Migraine	↓	★★★ Strong	5 studies	Feverfew appears to be strongly effective in reducing migraines when the population in question are people with high frequency migraines possibly accompanied by auras. Feverfew is not as effective, although still somewhat effective, in persons with less frequent migraines.
C	Erythema	↓	★★★ Notable	1 study	The reduction in erythema with topical parthenolide-depleted feverfew was greater than that of the active control, Ibuprofen.
C	Symptoms of Osteoarthritis	—	—	1 study	No significant interaction between supplemental Feverfew and osteoarthritic symptoms

C	C-Reactive Protein	—	—	1 study	No significant effect on C-Reactive Protein
C	Symptoms of Rheumatoid Arthritis	—	—	1 study	Preliminary evidence has failed to find an effect of Feverfew on reducing symptoms of Rheumatoid arthritis
C	Immunity	—	—	1 study	No significant influence detected on immunity

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Fish Oil

Also known as: Eicosapentaenoic Acid, EPA, Docosahexaenoic Acid, DHA, Omega-3 fatty acids, Omega-3, Omega 3, N-3 Fatty Acids

Fish oil is a general health supplement, and is taken as a source of omega-3 fats. It is not needed if one eats enough fatty fish.

See [Fish Oil on Examine.com](#)

How to Take

Fish oil doses vary depending on the goal of supplementation. For general health, 250mg is the minimum dose. The American Heart Association recommends 1g daily. If the goal of supplementation is to reduce soreness, a 6g dose, spread over the course of a day, will be effective. Since fish oil is a combination of two different fatty acids, these numbers reflect a combined total. Total eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) consumption should come from a mix of real food and supplements. The more EPA and DHA is provided by the diet, the less supplementation is required. Fish oil can be taken throughout the day. To minimize the "fish burp" taste, take fish oil with meals. Pregnant women should increase their intake of DHA by at least 200mg a day, as long as there is no risk of elevated mercury levels.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	C-Reactive Protein	—	—	16 studies	Although some decreases have been noted, the vast majority of the evidence suggests that there is no significant influence
A	Blood Pressure	↓	★☆☆ Minor	8 studies	May decrease blood pressure in persons with high blood pressure, but does not appear to have efficacy in persons with normal blood pressure
A	Inflammation	↓	★☆☆ Minor	17 studies	Highly mixed and unreliable influences on circulating inflammatory cytokines (although, due to immunosuppression on cellular adhesion factors, the overall effect may still be antiinflammatory)
A	LDL-C	↓↑	★☆☆	30 studies	A decrease has been noted in

			Minor		Also has been noted in persons without high cholesterol in the first place, and the decreasing effect of statins appears to be augmented with fish oil. However, in persons at higher risk for cardiovascular disease due to high triglycerides and cholesterol (who more frequently use fish oil as therapy) it is possible LDL-C may actually be increased. The magnitude tends to be in the 5-10% range.
A	HDL-C	↑	★☆☆ Minor	27 studies	Mixed evidence, but a possible increase in HDL-C is seen with fish oil supplementation in unhealthy persons
A	Total Cholesterol	—	—	18 studies	Although some decreases have been noted, overall there does not appear to be a significant clinical reduction in total cholesterol like there is with triglycerides
A	Triglycerides	↓	★★★ Strong	44 studies	Fish oil, both EPA and DHA, are reference drugs for the purpose of reducing triglycerides with highly reliable reductions in the range of 15-30% (higher reductions seen in persons with higher baseline triglycerides)
A	ADHD in Children	↓	★☆☆ Minor	7 studies	Supplemental DHA above 300mg appears to be effective in reducing ADHD symptoms in children when supplemented
A	Depression	↓	★★★ Notable	22 studies	Fish oil supplementation has been noted to be comparable to pharmaceutical drugs (fluoxetine) in majorly depressed persons, but this may be the only cohort that experiences a reduction of depression. There is insufficient evidence to support a reduction of depressive

					symptoms in persons with minor depression (ie. not diagnosed major depressive disorder)
A	Weight	—	—	14 studies	For the most part, no significant influence on body weight over time
A	Blood Glucose	—	—	19 studies	No significant alterations in fasting glucose are seen over time with fish oil supplementation
A	HbA1c	—	—	10 studies	Although the majority of evidence suggests absolutely no influence on HbA1c, reductions have been reported and a lone case has noted a clinically irrelevant increase of HbA1c (secondary to the increase in glucose). Practically, there is unlikely to be any large changes
A	Insulin Sensitivity	—	—	12 studies	No significant influence on insulin sensitivity seems to be the consensus, although there are isolated reports of both an increase and decrease (in response to a glucose tolerance test and fasting, respectively)
B	Muscle Soreness	—	—	3 studies	Although one study suggests a decrease, most evidence suggest no significant influence
B	TNF-Alpha	↓	★☆☆ Minor	6 studies	May decrease TNF-a
B	VO2 Max	—	—	3 studies	There is no evidence to support an improvement of VO2 max when fish oil is consumed alongside an exercise routine
B	Cell Adhesion Factors	↓ ↑	★☆☆ Minor	8 studies	Appears to be able to reduce cellular adhesion factors (that

					draw immune cells into tissue to aid in inflammatory processes, reducing these is immunosuppressive) in elderly persons, while slightly increasing expression in youth
B	Cortisol	↓	★☆☆ Minor	4 studies	A possible reducing effect of fish oil supplementation on cortisol
B	Endothelial Function	↑	★☆☆ Minor	4 studies	There appears to be a slight increase in vascular reactivity and blood vessel responsiveness that may be independent of both blood flow alterations and blood pressure
B	Platelet Aggregation	↓	★☆☆ Minor	4 studies	Possible decreases in platelet aggregation
B	Insulin	—	—	10 studies	No significant influence on fasting insulin levels
B	vLDL-C	↓	★☆☆ Minor	6 studies	May decrease vLDL cholesterol
B	Apolipoprotein B	—	—	6 studies	Although at least one study has noted a decrease, usually there is no significant changes
B	Blood Flow	—	—	5 studies	Although there is some counter evidence to suggest an improvement of small magnitude, most evidence suggest no significant changes in blood flow
B	Lipid Peroxidation	↓ ↑	★☆☆ Minor	5 studies	Both increases and decreases in lipid peroxidation have been noted with fish oil supplementation, with the increases in peroxidation usually seen with high doses of fish oil paired with other oxidative stressors (such as marathon running)
B	Natural Killer Cell Content	—	—	3 studies	Although one increase in NK

	Content				cell content has been noted after exercise, the two studies using similar doses at rest have failed to find a significant influence on NK cell content
B	T Cell Count	—	—	4 studies	Although there is some evidence to suggest an immunosuppressive effect on T cells, most evidence suggest no significant effect. When the immunosuppression does occur, it is due to the EPA content
B	B cell count	—	—	3 studies	The overall quantity of B lymphocytes does not appear to be altered with fish oil supplementation
B	Natural Killer Cell Activity	↓	★☆☆ Minor	3 studies	Although there do not appear to be changes in the amounts of NK cells in the body following fish oil, their activity appears to be a tad reduced
B	Pre-Eclampsia Risk	—	—	2 studies	There does not appear to be a significant protective effect against pre-eclampsia in women who supplement fish oil during pregnancy
B	Infant Birth Weight	↑	★☆☆ Minor	1 study	There appears to be an increased infant birth weight in mothers that consume fish oil (or fish weekly) relative to no fish oil intake, which may be due to prolonging pregnancy by a few days and reducing the risk of premature birth (thus giving more time to grow in utero)
B	Postpartum Depression	—	—	5 studies	There does not appear to be any unique effect of supplemental fish oil on postpartum depression. Fish oil in postpartum and perinatal periods follows the same motifs as other depressive states, with EPA being the

					active molecule but likely only of benefit in major depressive disorder
B	Photoprotection	↑	★☆☆ Minor	3 studies	There appears to be reduced risk of DNA damage, immunosuppression, and erythema in response to sunlight associated with fish oil consumption. Studies have only investigated higher doses (1,800mg EPA minimum) and it is unsure if these protective effects apply to lower doses
B	Symptoms of Bipolar Disorder	↓	★☆☆ Minor	5 studies	There appears to be reduced depressive symptoms in bipolar disorder when the depression is of a large magnitude (similar to the anti-depressant effects of fish oil in general). There may not be a reduction in depressive symptoms with lower severity depression (a trend to increase has been noted) and manic symptoms do not appear to be significantly influenced.
B	Insulin Secretion	—	—	5 studies	There does not appear to be an augmented insulin release from dietary carbohydrate nor an inherent insulin release from the pancreas associated with fish oil supplementation
B	Symptoms of Systemic Lupus Erythematosus	↓	★★★☆☆ Notable	7 studies	The decrease in symptoms of lupus as assessed by SLAM-R and BILAG at times reaches up to 50% symptom reduction and tends to exceed 30%, and the first pilot studies noted remission in all subjects (although they have not been replicated since). Oddly, benefit may come from lower doses (160mg EPA and 140mg DHA) with higher doses conferring less benefit
C	Muscle Damage	—	—	1 study	No significant influence on biomarkers of muscle damage

					seen with fish oil supplementation
C	Heart Rate	—	—	1 study	No significant acute effect on heart rate seen with fish oil supplementation
C	Interleukin 2	↑	★☆☆ Minor	2 studies	Mixed effects on IL-2 concentrations, with an increase noted when supplemented around exercise and no change noted at rest.
C	Interleukin 5	—	—	1 study	No significant influence on circulating IL-5 concentrations
C	Interleukin 1-beta	—	—	1 study	No significant influence on circulating IL-1β concentrations
C	Leptin	—	—	2 studies	No significant influence on Leptin in serum
C	Adiponectin	—	—	2 studies	No significant influence on Adiponectin concentrations
C	Testosterone	—	—	1 study	No detectable influence on testosterone levels in serum
C	Sex Hormone Binding Globulin	—	—	1 study	No significant influence on SHBG levels
C	DHEA	—	—	1 study	No significant influence on DHEA sulfate in serum
C	Liver Fat	↓	★☆☆ Minor	1 study	A possible decreasing effect of liver fat seen in persons with NAFLD
C	Liver Enzymes	—	—	1 study	No significant influence on liver enzymes noted
C	Apolipoprotein A	—	—	2 studies	No significant influence on Apolipoprotein A concentrations

C	General Oxidation	↑	★☆☆ Minor	2 studies	May increase general oxidation in the body, but seems unreliable in doing so
C	Nitric Oxide	↑	★☆☆ Minor	1 study	An increase in exercise-induced nitric oxide production has been noted
C	Exercise-Induced Oxidation	↑	★☆☆ Minor	1 study	Exercise induced oxidation has been noted to be increased in elite athletes with fish oil supplementation
C	DNA Damage	—	—	2 studies	Does not appear to influence DNA damage
C	Oxidation of LDL	—	—	2 studies	No significant influence detected
C	Homocysteine	↓	★☆☆ Minor	2 studies	May decrease homocysteine content
C	Lymphocyte Count	↓	★☆☆ Minor	1 study	A decrease in lymphocytic count has been noted in obese persons
C	Anxiety	↓	★☆☆ Minor	2 studies	A decrease in anxiety has been noted in medical students
C	Memory	↑	★☆☆ Minor	2 studies	Possible improvements in memory
C	Exercise-Induced Immune Suppression	—	—	1 study	Does not appear to augment nor alleviate the immunosuppression that occurs during exercise in otherwise healthy persons
C	Food Intake	—	—	2 studies	There does not appear to be a significant influence of fish oil supplementation on food intake
C	Fat Mass	—	—	3 studies	No significant influence on fat

					mass with routine supplemental fish oil
C	Lean Mass	—	—	3 studies	No significant influence on lean mass associated with fish oil supplementation
C	Ketone Bodies	↑	★☆☆ Minor	1 study	An increase in ketone bodies has been noted when fish oil is paired with a weight loss diet (relative to placebo)
C	Subjective Well-Being	↑	★☆☆ Minor	3 studies	An improvement in well being has been noted in nondepressed and nonelderly obese persons given fish oil supplementation to a small magnitude.
C	Interleukin 6	↓	★☆☆ Minor	1 study	A decrease in circulating IL-6 has been noted with fish oil supplementation
C	Infant Death Risk	↓	★☆☆ Minor	1 study	A reduced risk of death of infants after pregnancy has been noted with maternal consumption of fish oil, but this information is preliminary and needs replication (noted offhand in one study)
C	Cognition of Offspring	—	—	1 study	Despite the importance of DHA in cognition of offspring (and absolute deprivation likely to reduce cognitive development), additional supplemental fish oil does not appear to be supported for further enhancing the cognition of offspring although it is plausible
C	Leukotriene B4	—	—	2 studies	No significant influence on LKB4 concentrations
C	Leukotriene B5	↑	★☆☆ Minor	2 studies	An increase in LKB5 has been noted following fish oil supplementation

C	5-HETE	—	—	1 study	5-HETE is a catabolite of arachidonic acid (omega-6 fatty acids), and its serum levels do not appear to be significantly influenced by ingestion of fish oil supplementation despite an increase in EPA and DHA
C	5-HEPE	↑	★★★☆☆ Notable	1 study	5-HEPE is a catabolite of EPA, and its blood levels are increased following consumption of EPA in a dose-dependent manner
C	Erythema	↓	★★☆☆☆ Minor	2 studies	Ingestion of fish oil appears to prolong the time required for sunlight to induce reddening of the skin, and secondary to this fish oil ingestion above 1,800mg EPA is able to reduce the risk of sunburn.
C	Cognitive Decline	↓	★★☆☆☆ Minor	1 study	High dose (900mg) DHA appears to be somewhat beneficial in reducing the rate of cognitive decline in elderly but otherwise healthy persons
C	Symptoms of Alzheimers	—	—	1 study	Despite the benefit seen with high dose DHA in cognitive decline, there does not appear to be a proven significant protective effect in persons already with Alzheimer's
C	Stress	↓	★★☆☆☆ Minor	1 study	Self-reported stress in distressed women given fish oil supplementation appears to be reduced
C	Fatigue	—	—	2 studies	No demonstrable benefit to fatigue
C	Fructosamine	—	—	1 study	No evidence to support an increase in fructosamine, which alongside HbA1c is thought to indicate pathology from elevated blood glucose (fish oil appears to elevate

					glucose, but does not appear to be associated with higher diabetes risk)
C	Plasminogen Inhibitor 1	↑	★☆☆ Minor	1 study	An increase in PAI-1 is noted with fish oil supplementation
C	Glucagon	—	—	1 study	No significant influence on plasma glucagon concentrations
C	Factor VII	↑	★☆☆ Minor	1 study	An increase in serum Factor VII has been noted with fish oil supplementation
C	Prostaglandin J2a	↑	★☆☆ Minor	1 study	An increase in prostaglandin J2A is noted with fish oil supplementation, which is thought to mediate a variety of fish oil's effects
C	Thromboxane B2	↑	★☆☆ Minor	1 study	An increase in thromboxane B2 is noted with fish oil supplementation
C	Proteinuria	—	—	1 study	Although a trend to reduce protein losses in the urine was noted (which would be kidney protective), this was a statistically insignificant and secondary to lupus treatment
C	Attention	—	—	1 study	Fish oil supplementation in otherwise healthy adults has failed to significantly influence attention processing
C	Aggression	↓	★☆☆ Minor	1 study	A decrease in aggression has been noted, which is thought to be secondary to improvements in mood state and general well being
C	Processing Accuracy	↑	★☆☆ Minor	1 study	An improvement in processing accuracy (assessed by amount of errors in a cognitive test) has been noted with fish oil in otherwise healthy adults that

					do not frequently consume fish products
C	Reaction Time	↓	★☆☆ Minor	1 study	A reduction in reaction time has been noted with fish oil supplementation in persons who consume low levels of fish in the diet
C	Cerebral Blood Flow	↑	★☆☆ Minor	1 study	Appears to improve cerebral blood flow and volume in persons with low dietary fish intake
C	Cerebral Oxygenation	↑	★☆☆ Minor	1 study	The increase in cerebral oxygenation appears to exist in otherwise healthy persons with low dietary fish intake, and appears to be secondary to improvements in blood flow in general
D	Metabolic Rate	—	—	1 study	No significant influence on metabolic rate seen with fish oil supplementation
D	Fat Oxidation	↑	★☆☆ Minor	1 study	An increase in fat oxidation (percentage of energy being taken from fat tissue) has been noted with fish oil supplementation
D	Bone Mineral Density	—	—	1 study	No significant influence on bone mineral density noted with fish oil supplementation

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Fucoxanthin

Also known as: Seaweed Extract, Undaria Pinnatifida, fuco, fucothin

Fucoxanthin is a carotenoid found in brown seaweed that is being investigated for its fat burning abilities. It reduces fat mass, but has a time delay due to build up in fat tissue and does not stimulate the brain. Also appears healthy, but needs more corroborating evidence.

See [Fucoxanthin on Examine.com](#)

How to Take

A daily dosage of 2.4-8mg fucoxanthin has shown benefit in some human studies over a prolonged period of time, and while within this range the benefits are dose-dependent higher doses have not been tested sufficiently. If buying a seaweed standardized for fucoxanthin, look for the extract percentage and then backtrack. Buying an undaria pinnatifida supplement that is 1% fucoxanthin by weight would require 240-800mg of the supplement to get 2.4-8mg fucoxanthin. Assuming this page is read and understood, then daily consumption of dietary seaweed may be sufficient to get enough fucoxanthin for optimal antioxidative and fat burning effects.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Weight	↓	★★★☆☆ Notable	1 study	The lone study in obese menopausal women noted a large degree of weight loss over time relative to control, which was thought to be due to increasing the metabolic rate (secondary to alleviating fatty liver). Needs to be replicated in other demographics
C	Liver Enzymes	↓	★★★☆☆ Notable	1 study	In a model of liver fat in obese premenopausal women, fucoxanthin was fairly effective at reducing liver enzymes after prolonged usage
C	Liver Fat	↓	★★★☆☆ Notable	1 study	The decrease in liver fat seen with fucoxanthin tends to be greater than that seen with other supplements, although insufficient evidence exists to suggest reliability of results

C	C-Reactive Protein	↓	★☆☆ Minor	1 study	A decrease in C-reactive protein is noted with fucoxanthin ingestion
C	Triglycerides	↓	★☆☆ Minor	1 study	A decrease in circulating triglycerides is noted with fucoxanthine
C	Blood Pressure	↓	★☆☆ Minor	1 study	In obese menopausal women, fucoxanthin may lower blood pressure; this is confounded with overall weight loss, however
C	Metabolic Rate	↑	★★☆ Notable	1 study	The lone study in obese premenopausal women noted a fairly remarkable increase in metabolic rate (the highest estimate being around 450kcal daily); this study requires replication to see if the effect size persists

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Gamma Oryzanol

Also known as: γ -Oryzanol

Gamma Oryzanol (γ -Oryzanol) is a mixture of compounds in Rice Bran Oil and other sources that share a common structure. Promising but unproven cholesterol lowering agent with some skin health properties, does not increase Testosterone.

See [Gamma Oryzanol on Examine.com](#)

How to Take

The dosages of Gamma-oryzanol used are highly variable, with some studies using a lower dose (50mg once daily or 20mg thrice daily) and other studies using a markedly higher dosage (300-800mg daily). As there are no reliable benefits associated with Gamma-oryzanol supplementation in the first place, it is unsure what dosage should be recommended (if this supplement is to be recommended at all).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	LDL-C	—	—	1 study	Although rice bran oil may reduce LDL cholesterol, there is insufficient evidence to support the role of gamma-oryzanol in this role
C	Total Cholesterol	—	—	2 studies	No significant alterations seen in total cholesterol levels with supplementation
C	HDL-C	—	—	2 studies	No detectable influences on HDL cholesterol, although rice bran oil (a source of gamma oryzanol) may have a slight positive effect
C	Testosterone	—	—	1 study	No detectable influence on testosterone levels in otherwise healthy men
C	Cortisol	—	—	1 study	No significant influence on cortisol levels with prolonged supplementation

C	Estrogen	—	—	1 study	No significant influence on circulating estrogen levels in healthy men given gamma-oryzanol over a few weeks
C	Growth Hormone	—	—	1 study	No significant alterations in growth hormone following ingestion of gamma-oryzanol
C	Insulin	—	—	1 study	No significant alterations noted in fasting insulin levels following prolonged ingestion of gamma-oryzanol in healthy persons
C	Plasma Endorphins	—	—	1 study	Plasma beta-endorphin is unaltered following ingestion of standard doses of gamma-oryzanol
C	Power Output	—	—	1 study	No interactions with power output have been noted with gamma-oryzanol ingestion
C	Triglycerides	—	—	1 study	No significant alterations in plasma triglycerides seen with supplementation

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Ganoderma lucidum

Also known as: Reishi, Lingzhi, Yeongji, Mannamtake, 10,000 years mushroom, Mushroom of Immortality, Antlered Reishi, Rokkaku-Reishi, Ganoderma spores

If Ashwagandha is the top of Ayurveda, Ling Zhi is the top of Traditional Chinese Medicine. As a potent immunomodulator (regulator of the immune system) and promising anti-cancer agent, Ling Zhi can also reduce stress; its potency fighting sickness should not be underestimated.

See [Ganoderma lucidum on Examine.com](#)

How to Take

If using the ethanolic extract, 6mg appears to be the dosage used to get the most out of the triterpenoids. If using the water-soluble fragment, doses between 1.44g to 5.2g are commonly used; many benefits appear to be dose dependent, and 5.2g (divided into three daily doses of 1,800mg at morning, afternoon, and night) appear to be most commonly used. A general 'Ganoderma Lucidum extract' that does not separate the triterpenoids (ethanolic extract) and the polysaccharides (water-soluble) is dosed similar to the water-soluble fragment, since the ethanolic portion weighs about 1% of it and makes little to no difference. This basic 'extract' is basically dehydrated mushroom powder, and its bioactivity on a weight basis is roughly 10x as potent as the actual mushroom (due to losing 90% of the water content); 5g extract is similar to 50g whole mushroom, but the mushroom is hard to eat and pills simpler.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Subjective Well-Being	↑	★☆☆ Minor	3 studies	Subjective well being increases in disease states where other symptoms (seen as adverse) are decreased; an inherent increase of well being is uncertain.
C	Colorectal Cancer	↓	★☆☆ Minor	1 study	There appears to be a suppressive effect of reishi ingestion of colorectal adenocarcinomas with prolonged ingestion
C	Weight	—	—	1 study	No significant alterations in body weight seen with ganoderma ingestion
C	Blood Pressure	—	—	1 study	No significant influence on blood pressure noted with

					reishi
C	Adrenaline	—	—	1 study	No significant influence on serum adrenaline
C	Dopamine	—	—	1 study	No significant influence on serum dopamine
C	HDL-C	↑	★★★☆☆ Notable	2 studies	There may be an increase in HDL-C in persons with hyperlipidemia that doesn't occur in otherwise healthy adults, but this is not certain due to lack of evidence. The degree of increase was fairly strong (24%).
C	Triglycerides	↓	★★☆☆☆ Minor	2 studies	There may be a small decrease in triglycerides (8% or so) in unhealthy persons, but this has not been observed in otherwise healthy individuals
C	General Oxidation	—	—	2 studies	No significant alterations in whole-body oxidation are apparent
C	Lipid Peroxidation	—	—	2 studies	No significant changes in lipid peroxidation biomarkers (such as MDA) are present following ingestion of Reishi
C	Anti-Oxidant Enzyme Profile	—	—	2 studies	No significant influences on superoxide dismutase or glutathione peroxidase are noted with ganoderma polysaccharide ingestion
C	Testosterone	—	—	1 study	No significant influence on testosterone levels following ingestion of Reishi
C	Prostate Hypertrophy	—	—	2 studies	At an oral dose that can reduce symptoms of prostatic hyperplasia, there is no apparent effect on prostatic hypertrophy

C	Prostate Specific Antigen	—	—	2 studies	The ethanolic extract has failed to alter serum levels of PSA
C	Symptoms of the Lower Urinary Tract	↓	★☆☆ Minor	2 studies	Total symptoms scores (IPSS) appear to be decreased following ingestion of the ethanolic extract of reishi, although not to a remarkable degree (peak urine flow and residual urine seem unaffected)
C	Immunity	↑	★☆☆ Minor	4 studies	There appears to be proliferative effects on T-lymphocytes and natural killer cells and no significant alteration in a CD4:CD8 lymphocytic ratio following ingestion of Ganoderma polysaccharides.
C	CD3 Lymphocytes	↑	★☆☆ Minor	1 study	Reishi appears to directly stimulate production of CD3+ T-cells at a dosage of 5,000mg of the water soluble polysaccharides in otherwise healthy athletes
C	CD4 Lymphocytes	↑	★☆☆ Minor	1 study	The decrease in the CD4:CD8 ratio seen with altitude training is attenuated with 2,500-5,000mg of the water soluble polysaccharides
C	Symptoms of Neurasthenia	↓	★☆☆ Minor	1 study	Appears to slightly reduce the symptoms of neurasthenia, although this needs to be replicated
C	Fatigue	↓	★☆☆ Minor	2 studies	A decrease in fatigue has been noted, but secondary to disease states characterized by fatigue. Usage of Reishi to reduce fatigue outright or to aid exercise is unexplored
C	TNF-Alpha	↓	★☆☆ Minor	2 studies	A reduction in TNF-alpha levels have been noted in persons with elevated baseline TNF-

					alpha levels
C	LDL-C	—	—	1 study	No significant reducing effects on LDL cholesterol have been noted with ganoderma supplementation
C	C-Reactive Protein	—	—	1 study	No significant interactions with C-reactive protein have been detected
C	Total Cholesterol	—	—	1 study	No significant alterations in total cholesterol observed with reishi ingestion
C	DNA Damage	—	—	1 study	DNA damage in lymphocytes of volunteers given the polysaccharides appear unchanged
C	Uric Acid	—	—	1 study	No changes in serum uric acid seem apparent
C	Liver Enzymes	—	—	1 study	No significant influence on liver enzymes has been noted in toxicological testing with ganoderma
C	Blood Flow	—	—	1 study	No significant influence on blood flow noted with reishi ingestion
C	Depression	↓	★☆☆ Minor	1 study	Depression as a symptom of cancer-related fatigue was reduced, may not hold inherent antidepressive effects
C	Anxiety	↓	★☆☆ Minor	1 study	Some possible anti-anxiety effects secondary to reducing symptoms of cancer related fatigue
D	Natural Killer Cell Activity	↑	★★★☆☆ Notable	1 study	Up to a 50% increase in NK cell activity relative to control has been noted with reishi, and this may be independent of a basic stimulatory action

					(which would lead into possible supplement combinations)
D	Proteinuria	↓	★☆☆ Minor	1 study	A decrease in urinary protein has been noted, indicative of kidney protective effects

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Garcinia cambogia

Also known as: Gambooge, Pazham Puzhi, Bitter Kola, Malabar tamarind, (-)-Hydroxycitric acid, HCA, Hydroxycitric acid

Garcinia Cambogia (Malabar Tamarind) is a fruit that is known to enhance the culinary experience of food, and enhances satiety from a meal (possibly by enhancing the flavor experience). Its usage as a fat burner does not appear to extend to humans.

See [Garcinia cambogia](#) on [Examine.com](#)

How to Take

Standard dosing of Garcinia Cambogia and its bioactive, (-)-Hydroxycitric acid, is 500mg of (-)-Hydroxycitric acid taken 30-60 minutes prior to a meal and usually taken at up to three different meals daily. It is unsure if this is the ideal dose since human studies usually fail to find a benefit with any dosage.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Weight	—	—	3 studies	Although there is some counter evidence, it tends to be less robust and for the most part there is no significant weight reducing effect of garcinia cambogia supplementation
C	Apolipoprotein B	—	—	1 study	No significant influence on apolipoprotein B detected
C	HDL-C	—	—	1 study	No significant influence on HDL-C levels
C	Triglycerides	—	—	1 study	No detectable influence on triglyceride levels
C	LDL-C	—	—	1 study	Garcinia appears unable to influence LDL-C levels based on preliminary evidence
C	Total Cholesterol	—	—	1 study	No significant alterations seen in total cholesterol levels

C	Food Intake	—	—	1 study	Food intake appears to be unaltered following ingestion of garcinia supplements, which is different than results seen in rats
C	Appetite	—	—	1 study	No significant influence of acute HCA supplementation on appetite when taken before a meal
C	Testosterone	—	—	1 study	Testosterone appears to be unaltered following ingestion of garcinia cambogia
C	Estrogen	—	—	1 study	No significant influence on circulating estrogen levels associated with garcinia

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Garlic

Also known as: Allium sativum, Vegetable Viagra, Da suan, Camphor of the poor, Lasun, Stinking Rose, Ail, Ajo

Garlic (*Allium sativum*) is a food product that can improve immunity and cardiovascular health.

See [Garlic on Examine.com](#)

How to Take

Most studies on garlic use a dosage range of 600-1,200mg a day, usually divided into multiple doses. The minimum effective dose for raw garlic is a single segment of a garlic bulb (called a clove), eaten with meals two or three times a day. Aged garlic is a popular form of garlic to use for supplementation, since it does not have a fresh garlic scent. Garlic supplementation can also be done through food alone, though side-effects will include strong garlic-scented breath. Microwaving garlic will partially destroy the beneficial components of the vegetable, but grilling and roasting will not damage the bioactives, provided the garlic is sliced or crushed beforehand. Garlic can be toxic if consumed in very high doses, so supplementation should never go beyond 5% of the diet. This results in the following maximum dosages: 17.0 grams for a 150lb person 22.7 grams for a 200lb person 28.4 grams for a 250lb person

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	HDL-C	↑	★★★☆☆ Notable	14 studies	Garlic supplementation tends to increase HDL cholesterol in persons with cardiovascular disease risk reliably and in the range of 10-15% when looking at individual trials and by 1.49mg/dL (95% CI of 0.19-2.79mg/dL) as assessed by meta-analysis.
A	LDL-C	↓	★★★☆☆ Notable	14 studies	There appears to be a reliable and significant reduction in circulating LDL cholesterol in hypercholesterolemic persons with garlic supplementation, and the magnitude of this change tends to be in the range of 10-20% (more potency in those with worse profiles at baseline)
A	Total Cholesterol	↓	★★★☆☆ Notable	17 studies	Garlic supplementation or the raw garlic bulb appears to reduce cholesterol (total

					cholesterol, mostly due to LDL reductions) reliably and in the range of 10-15%
A	Triglycerides	↓	☆☆☆ Minor	15 studies	There appears to be quite an unreliable decrease in triglycerides following garlic supplementation. When looking at meta-analyses, there is either a significant but small decrease or a reduction that fails to reach statistical significance.
B	Blood Pressure	↓	☆☆☆ Notable	12 studies	Garlic supplementation appears to reduce blood pressure, and the magnitude is quite respectable in persons with hypertension (around 10 points systolic or 8-10%) whereas there is a smaller but present reduction in persons with normal blood pressure.
B	White Blood Cell Count	—	—	3 studies	While there are significant modifications in the subpopulations of white blood cells (ie. <i>which</i> immune cells you have) the overall quantity does not appear significantly affected.
B	Symptoms of Peripheral Vascular Disease	—	—	2 studies	Although there may theoretically be some benefit with higher doses, currently the available evidence has not found a protective effect with 900mg of raw garlic extract.
C	Weight	—	—	2 studies	Although there are theoretical benefits of garlic to weight loss, prolonged supplementation of garlic in other studies (where weight is measured as a secondary parameter of interest) is not altered. The weight loss effects are either small or nonexistent in otherwise normal conditions
C	Interleukin 6	—	—	2 studies	Supplementation of garlic to

					persons in chronic pro-inflammatory states does not seem to significantly influence circulating IL-6 concentrations
C	C-Reactive Protein	—	—	2 studies	No significant influence on C-reactive protein is noted with supplementation of garlic.
C	Leptin	—	—	1 study	In a study that noted an increase in adiponectin in persons with metabolic syndrome, there was no influence on circulating leptin concentrations.
C	Adiponectin	↑	★☆☆ Minor	1 study	There appears to be an increase in adiponectin associated with 1,200mg of aged garlic supplementation despite no other influence on the body of persons with metabolic syndrome.
C	Insulin	—	—	1 study	In persons with metabolic syndrome, there is no significant influence on fasting insulin concentrations relative to placebo after supplementation of garlic.
C	Insulin Sensitivity	—	—	1 study	There is no significant influence on insulin sensitivity when garlic is given to persons with metabolic syndrome.
C	Blood Flow	—	—	2 studies	Minimal studies have directly measured blood flow associated with garlic, and the best evidence currently suggests that basal flow mediated vasodilation is unaffected; there is likely an effect, although most studies indirectly measure blood pressure.
C	Blood Glucose	—	—	1 study	Supplementation of garlic does not appear to significantly reduce fasting blood glucose

					in persons with metabolic syndrome.
C	Lipid Peroxidation	↓	★☆☆ Minor	3 studies	A reduction in lipid peroxidation in the blood and in red blood cells has been noted in some states of metabolic ailment (aging and hypertension). Not 100% reliable as it wasn't seen in one study on hypercholesterolemia, and no studies in healthy controls.
C	Gastric Cancer Risk	—	—	2 studies	800mg aged garlic extract has failed to reduce the risk of developing gastric cancer when taken daily for 7.3 years
C	Red Blood Cell Count	—	—	1 study	There are no alterations in red blood cell count with normal doses of garlic (although there does appear to be a decrease when a <i>toxic</i> dose of garlic oil is ingested)
C	Liver Enzymes	↓	★☆☆ Minor	2 studies	One study has noted a 20% decrease in the ALT enzyme following garlic supplementation to otherwise healthy controls.
C	Platelet Aggregation	↓	★☆☆ Minor	4 studies	Garlic appears to reduce platelet aggregation at the supplemental dose, but not a moderate dietary dose of garlic cloves. The potency is less than Ginkgo biloba as a reference.
C	Food Intake	—	—	1 study	No significant alterations in food intake are seen with garlic ingestion (assuming no taste aversion).
C	TNF-Alpha	↓ ↑	★☆☆ Minor	2 studies	Decreases have been noted in inflammatory states (indicative of antiinflammatory effects) and increases seen in healthy persons; suggesting an immunomodulatory effect

C	Interleukin 1	—	—	1 study	No significant influence on circulating IL-1 concentrations seen with garlic supplementation (alongside no influence on IL-6 yet a decrease in TNF-α)
C	Arterial Stiffness	↓	★☆☆ Minor	2 studies	There appears to be a reduction in arterial stiffness seen with daily supplementation of garlic when measured over the course of a few years, relative to no garlic ingestion.
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	3 studies	There appears to be an increase in glutathione related enzymes in red and white blood cells following ingestion of garlic supplements.
C	Serum Platelets	—	—	1 study	Despite any possible interactions with the platelets (in regards to preventing their clotting), there are no alterations in the overall amount of platelets.
C	Homocysteine	—	—	2 studies	No significant alterations in homocysteine concentrations are seen with garlic supplementation.
C	Creatinine	—	—	1 study	No significant influence of garlic supplement on creatinine concentrations in serum are present.
C	Atherosclerosis	↓	★☆☆ Minor	1 study	Stasis has been reported in the growth of arterial plaque over 48 months when people consume 900mg of garlic, but this effect may only be statistically significant for women.
C	Length of Sickness	↓	★☆☆ Minor	1 study	The length that one is sick for is only modestly reduced with garlic supplementation even at

					higher doses.
C	Symptoms of the Common Cold	↓	★☆☆ Minor	2 studies	Similar to symptoms of sickness in general and the length of sickness, the therapeutic efficacy of garlic appears to be modest at best.
C	Rate of Sickness	↓	★★★ Strong	2 studies	The rate (frequency of occurring) of the common cold has twice been found to be reduced by 60-70% in persons who take garlic supplementation daily; this is associated with both allicin and the aged garlic extract, and requires higher doses (2.5g aged extract or 180mg allicin).
C	Upper Respiratory Tract Infection Risk	↓	★☆☆ Minor	1 study	There appears to be a reduction in the lung infection risks with garlic supplementation.
C	Quality of Life	—	—	1 study	Quality of life in cancer patients is unaffected despite an increase in NK cell activity, thought to be indicative of a therapeutic effect of supplementation.
C	Natural Killer Cell content	↑	★☆☆ Minor	2 studies	There is an increase in NK cell levels seen in both healthy controls as well as cancer patients, and this is thought to be due in part to both immunostimulatory and anti-immunosuppressive effects.
C	Natural Killer Cell Activity	↑	★☆☆ Minor	2 studies	There is an increase in NK cell activity alongside the increase in NK cell content, although it is not sure if there is an inherent increase in NK cell activity if you control for the increase in cell content.
C	CD4 Lymphocytes	—	—	1 study	CD4+ Lymphocytes do not appear to be influenced with supplementation of garlic

C	CD8 Lymphocytes	—	—	1 study	CD8+ Lymphocytes do not appear to be influenced with supplementation of garlic.
C	Cortisol	—	—	1 study	No significant influence of garlic supplementation has been found on cortisol in cancer patients.
C	γδ-T Cell Count	↑	★★★☆☆ Notable	1 study	The lone human study using a rather high dose of Aged Garlic extract (2.56g) noted an 8-fold increase of this T-cell subpopulation relative to control; thought to be related to the cold fighting properties of garlic
C	Interferon Gamma	↑	★★☆☆☆ Minor	1 study	Alongside the increase in immune cell activity in otherwise healthy persons is an increase in IFN-γ concentrations
C	Severity of Sickness	↓	★★☆☆☆ Minor	1 study	Despite the potent efficacy in reducing the occurrence of sickness, the actual severity of symptoms is only modestly reduced with garlic.
C	Blood Viscosity	—	—	1 study	The long study to assess basal viscosity of the blood has failed to find an interaction with garlic supplementation.
C	Oxidation of LDL	↓	★★☆☆☆ Minor	2 studies	A possible decrease in LDL oxidation rates, although this does not appear to be overly reliable.
C	Treatment of Hepatopulmonary Syndrome	↑	★★★☆☆ Notable	1 study	Following 250mg of garlic oil ingestion for a variable 9-18 months, two thirds of the group given supplementation reversed their status of having hepatopulmonary symptoms (1 person in placebo) and the mortality rate during followup

					was greatly reduced.
D	General Oxidation	↓	★☆☆ Minor	1 study	Oxidative biomarkers in the blood appear to be modestly reduced following supplementation of garlic in persons with high levels of oxidative damage indicative in serum.
D	DNA damage	↓	★☆☆ Minor	1 study	Urinary biomarkers of DNA damage are reduced in hypertensive persons following supplementation of garlic.
D	Esophageal Cancer Risk	—	—	1 study	The protective effect of 800mg aged garlic extract daily for 7.3 years does not appear to be statistically significant
D	Cancer Mortality	—	—	1 study	The overall mortality rate from stomach cancer is not influence with garlic supplementation during 15 years of followup
D	Thromboxane B2	—	—	1 study	No significant interactions with Thromboxane A2 are currently known.
D	Prostate Specific Antigen	↓	★★★☆☆ Notable	1 study	The lone study (no placebo control) noted a 60% reduction in both total and free PSA in a small group of men with prostate cancer; requires more evidence to evaluate the therapeutic potential
D	Prostate Hypertrophy	↓	★★★☆☆ Notable	1 study	The lone pilot study has noted a 32% reduction in prostatic size after a month of eating 200mg/kg garlic (as a water soluble liquid extract)
D	Symptoms of Benign Prostatic Hyperplasia	↓	★☆☆☆☆ Minor	1 study	A decrease was noted alongside improvements in prostatic size, but a magnitude of reduction was not given for evaluation.

D	Exercise performance during hypoxia	—	—	1 study	Large doses of garlic (4.5g of the bulb) to athletes undergoing hypoxic training does not appear to increase performance.
D	Heart Rate	—	—	4 studies	There is no inherent influence of garlic on heart rate, although when garlic aids cardiovascular performance in persons with heart problems it is associated with a reduced heart rate relative to control (due to less stress on the tissue).
D	Oxygen Uptake	—	—	1 study	In otherwise healthy athletes given 4.5g of garlic cloves daily before a performance test, the lack of increased performance is met by a lack of changes in oxygen uptake.
D	Exercise Capacity (with Heart Conditions)	↑	★☆☆ Minor	1 study	In persons with coronary heart disease, supplementation of garlic appears to increase physical performance when ingested at a food dose (1g) daily over six weeks; the increase in performance is moderate.
D	Nitric Oxide	↑	★★★☆☆ Notable	1 study	The lone study assessing nitric oxide and garlic noted that a raw garlic clove (2g) could increase nitric oxide by 224% in otherwise healthy persons within 2-4 hours of ingestion; potency did not decrease after seven days
D	Interferon Alpha	↑	★★★☆☆ Notable	1 study	The lone study noted that interferon alpha concentrations in serum increased 384% when measured 2-4 hours after 2g of raw garlic clove.
D	Uric Acid	—	—	1 study	No significant interactions with uric acid concentrations in serum.

D	Helicobacter Pylori Infection	—	—	2 studies	Despite potent antibacterial properties of garlic oil when tested outside of the body, it appears to be ineffective when given to human volunteers.
D	Basal Cell Carcinoma	↓	★★★☆☆ Notable	1 study	Topical application of a solution containing the sulfur bearing molecule Ajoene was able to half the tumor size and Bcl-2 expression after half a year of once daily application.
D	Mineral Bioaccumulation	↓	★★★☆☆ Notable	1 study	Mineral bioaccumulation from garlic ingestion (allicin in particular) is reduced in persons working in a car battery factory with excessive lead levels to a level similar to the reference drug D-penicillamine

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Ginger

Also known as: Zingiber officinale Roscoe, Zingiberaceae

Ginger is a spice that has traditionally been treated as medicine in both Traditional Chinese Medicine and Ayurveda, doses of 1-2g can reduce nausea and ease digestion quite effectively; superloading the powdered rhizome (vertical root) at 10-15g daily might increase Testosterone.

See [Ginger on Examine.com](#)

How to Take

Typically, dosages of 1-3g are used as a preventative treatment for nausea. This applies to morning sickness in pregnancy, motion sickness, and sometimes chemotherapy or operation-induced nausea. For other usages of ginger, 1g is typically used. This seems to be effective for increasing intestinal motility, but was insufficient in reducing blood glucose in the one study attempting it. For testosterone boosting, a supplement is probably advised. The dosage used in rats, after conversion to humans based on Body Surface Area, equates to about 14g from natural sources (usually less of an extract percentage than is possible with supplements). Ginger can be ingested via several ways, and the following is an approximate standardization table for 1g of Ginger Extract:[1] A capsule that has 1g ginger extract in it A teaspoon of fresh, grated, rhizome (the vertical aspect of ginger root) 2 droppers (2mL) of liquid extract 2 teaspoons (10mL) of syrup 4 cups (8 oz each) ginger tea, steeping 1/2 teaspoon grated ginger for 5–10 min 8-oz cup ginger ale, made with real ginger 2 pieces crystallized ginger, each 1 inch square, 1/4 inch thick

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Nausea	↓	★★★☆☆ Notable	11 studies	There appears to be a reliable and fairly notable decrease in nausea symptoms with 1-3g of ginger related to pregnancy and seasickness (not as much consensus for post-operative nausea)
B	Rate of Gastric Emptying	↑	★☆☆☆☆ Minor	4 studies	Ginger appears to increase the rate of gastric digestion, although the potency thereof is not too reliable
B	Symptoms of Osteoarthritis	↓	★☆☆☆☆ Minor	3 studies	There may be a small reducing effect, but it does not appear to be greater than the active control of Ibuprofen
B	Inflammation	↓	★☆☆☆☆	4 studies	

			Minor		Inflammatory parameters seem to be reduced following ginger consumption
C	Colon cancer risk	↓	☆☆☆ Minor	1 study	May reduce colon cancer risk as assessed by a beneficial influence in eicosanoids in the colon; requires more evidence
C	Lower Esophageal Pressure	↓	☆☆☆ Minor	1 study	A decrease in LES pressure (not necessarily a good thing, especially for acid reflux) has been noted with ginger ingestion
C	Muscle Soreness	↓	☆☆☆ Minor	2 studies	A possible reduction of delayed onset muscle soreness, but this topic is a bit contested
C	Total Cholesterol	↓	☆☆☆ Minor	1 study	Possible cholesterol reducing effects associated with ginger consumption
C	HDL-C	↑	☆☆☆ Minor	1 study	May increase HDL-C levels
C	LDL-C	↓	☆☆☆ Minor	1 study	May decrease LDL-C
C	Triglycerides	↓	☆☆☆ Minor	1 study	May decrease triglycerides
C	Dysmenorrhea	↓	☆☆☆ Minor	1 study	Ginger was capable of reducing menstrual pain at 1g daily
C	Rate of Perceived Exertion	—	—	1 study	No significant influence on the rate of perceived exertion
C	Motion Sickness	—	—	1 study	Despite the reduction in nausea associated with ginger consumption, it does not appear to be associated with reduced symptoms of motion sickness
C	Vertigo	↓	☆☆☆ Minor	1 study	May reduce symptoms of vertigo related to the anti-nausea effects, but this

					research is highly preliminary
C	Nystagmus	—	—	1 study	No significant influence on pathological involuntary eye movements
C	Memory	↑	★☆☆ Minor	1 study	An increase in memory has been noted in older women, no current studies in youth
C	Reaction Time	↓	★☆☆ Minor	1 study	A decrease in reaction time has been noted to be secondary to improvements in cognition in older women; no studies in youth at this moment in time.
D	Appetite	↓	★☆☆ Minor	1 study	A decrease in appetite has been noted with ginger intake
D	Blood Glucose	—	—	1 study	No significant alterations in blood glucose seen with ginger ingestion
D	Insulin	—	—	1 study	No significant alterations in insulin levels (fasting) seen with ginger
D	Thermic Effect of Food	↑	★☆☆ Minor	1 study	Ginger has been found to increase the thermic effect of coingested food products
D	Metabolic Rate	—	—	1 study	Despite an increase in the thermic effect of food, overall metabolic rate does not appear affected
D	Ejaculate Volume	↑	★☆☆ Minor	1 study	In infertile men, an undisclosed amount of ginger for three months is able to increase ejaculate volume by an average of 36.1%
D	Testosterone	↑	★☆☆ Minor	1 study	An increase in testosterone has been noted to reach 17.7% in infertile men given an undisclosed amount of ginger

					over three months.
D	Follicle-Stimulating Hormone	↑	★☆☆ Minor	1 study	A 17.6% increase in follicle stimulating hormone has been noted in infertile men given ginger, which is thought to underlie the observed pro-seminal effects of supplementation.
D	Luteinizing Hormone	↑	★★★☆☆ Notable	1 study	Although the study is limited by lack of placebo control and disclosure of dosage, ginger is associated with a 43.2% increase in serum luteinizing hormone over three months in infertile men.
D	Sperm Count	↑	★☆☆ Minor	1 study	A somewhat minor increase in sperm count (16.2%) is seen with supplementation of ginger (amount undisclosed) to infertile men over three months.
D	Sperm Quality	↑	★☆☆ Minor	1 study	Seminal viability (40.7%) and normal morphology () is increased in infertile men given ginger.
D	Seminal motility	↑	★★★☆☆ Notable	1 study	Preliminary evidence suggests a 47.3% increase in seminal motility seen with three months supplementation of ginger to infertile men.
D	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	1 study	An increase in seminal glutathione has been noted to reach 26.7% in otherwise infertile men.
D	Lipid Peroxidation	↓	★★★☆☆ Notable	1 study	In the semen of infertile men, the reduction in lipid peroxidation has reached 53.7% with supplementation of ginger over three months.

Ginkgo biloba

Also known as: Tanakan, Tebonin, Rökan, Maidenhair

Ginkgo biloba is the most commonly ingested herb for brain health. While it can boost cognition, this effect is not very reliable.

See [Ginkgo biloba on Examine.com](#)

How to Take

Ginkgo biloba can be supplemented for cognitive enhancement, or to alleviate cognitive decline. For cognitive enhancement, take 120-240mg, one to four hours before performance. To alleviate cognitive decline in older adults, take 40-120mg, three times a day. The supplement form of Ginkgo biloba is called Bikbo Biloba EGb-761 extract. It should be a 50:1 concentrated extract. Ginkgo biloba should be taken with meals.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Memory	↑	☆☆☆ Minor	12 studies	There appears to be a fairly reliable increase in short term memory and free recall associated with ginkgo supplementation in older individuals (55yrs or above) either with or without diagnosed neurodegenerative disease states.
A	Cognitive Decline	↓	☆☆☆ Notable	11 studies	For usage of EGb-761 at 240-360mg daily as a therapeutic option in people who already are experiencing cognitive decline, then it appears to be reliably effective and comparable to 10mg Donezepil. Usage of Ginkgo biloba for the purpose of reducing the risk of cognitive decline (as a preventative supplement) is currently not supported.
A	Symptoms of Intermittent Claudication	↓	☆☆☆ Minor	6 studies	There appears to be reduced symptoms of intermittent

	Circulation				claudication with ginkgo supplementation, although it seems to vary significantly from one individual to another and despite some persons experiencing large benefit the overall 'net' benefit is relatively minor.
B	Libido	—	—	4 studies	Although a potential benefit cannot be ruled out at this moment in time (the first pilot study showed promise and there are some responders), overall ginkgo does not appear to influence SSRI-induced sexual dysfunction in more well conducted trials.
B	Attention	—	—	5 studies	Attentional focus and similar parameters (task switching) do not appear to be significantly influenced by ginkgo supplementation.
B	Blood Flow	↓ ↑	★☆☆ Minor	7 studies	Ginkgo biloba has shown both vasodilatory effects (via nitric oxide metabolism) and some possible constrictive effects, depending on the context of supplementation.
B	Blood Pressure	—	—	7 studies	Despite the influence on blood flow and circulation, there does not appear to be a significant influence on blood pressure
B	Symptoms of Alzheimers	↓	★☆☆ Minor	5 studies	Cognitive impairment that is associated with Alzheimer's appears to be significantly reduced with ginkgo supplementation.
B	Working Memory	—	—	3 studies	Despite the improvement in short term memory and recall, there does not appear to be a significant improvement in working memory.
B	Cognition	↑	★☆☆ Minor	7 studies	Other parameters of cognition

			Minor		are differentially influenced by ginkgo, as facial recognition in those with dementia has noted improvement yet trip planning in middle-aged persons is unaffected.
B	Subjective Well-being	↑	★☆☆ Minor	3 studies	An improvement in mood has been noted in persons with cerebral injury, but not in otherwise healthy middle aged persons.
B	Stroke Recovery Rate	—	—	1 study	Although there is some scattered evidence to support the role of ginkgo in stroke recovery rates, the best evidence currently available does not find a significant therapeutic benefit.
B	Symptoms of Tinnitus	—	—	4 studies	There does not appear to be a significant and reliable therapeutic effect of ginkgo on tinnitus symptoms, although limited evidence suggests that if tinnitus is a side-effect of cognitive decline that it may be attenuated.
B	Ocular Blood Flow	↑	★☆☆ Minor	3 studies	An increase in ocular blood flow has been noted in instances of normal tension glaucoma as well as healthy controls, although a one-time oral dose is ineffective (at least two days supplementation is required)
B	Heart Rate	—	—	6 studies	No significant influence of ginkgo biloba supplementation on heart rate.
B	Symptoms of Acute Mountain Sickness	↓	★★★☆☆ Notable	7 studies	There appears to be a quite potent yet quite unreliable reduction in symptoms of AMS when ginkgo is taken at 240mg daily for 1-5 days prior to a trip up a mountain. The reason for this variability is not known.

B	Intraocular Pressure	—	—	3 studies	Despite the increase in ocular blood flow associated with repeated dosing of ginkgo biloba, there does not appear to be a significant modification of intraocular blood pressure in persons with normal IOP.
B	Sleep Quality	↑	★☆☆ Minor	3 studies	There may be an increase in sleep efficiency (reduced waking during the night) without any apparent enhancement of REM sleep, this seems to be related to the flavonoid portion
C	Depression	—	—	1 study	Supplementation of ginkgo does not appear to significantly influence depressive symptoms in older individuals
C	Risk of Alzheimers Disease	—	—	2 studies	Although ginkgo may have an acute therapeutic benefit, supplementation of ginkgo daily over the course of years in persons at risk for Alzheimer's does not appear to be too effective as a preventative supplement
C	Reaction Time	↑	★☆☆ Minor	2 studies	Alongside improvements in general cognition in older individuals, an increase in reaction time has been noted.
C	Processing Speed	↑	★☆☆ Minor	2 studies	In older individuals, there appears to be an increase in processing speed without a sacrifice in accuracy
C	Symptoms of Multiple Sclerosis	—	—	1 study	Supplementation of ginkgo has failed to significantly benefit the cognition of persons with multiple sclerosis
C	Cerebral Blood Flow	↑	★☆☆ Minor	1 study	There appears to be a significant improvement in blood flow to the middle and anterior cerebral arteries, although other arteries are

					unaffected.
C	Verbal Fluency	—	—	2 studies	No significant influence of supplemental ginkgo on verbal fluency even in persons with cognitive injuries.
C	Risk of Dementia	—	—	1 study	Similar to the inability of ginkgo biloba to influence Alzheimer's disease occurrence, ginkgo does not appear to reduce the risk of developing dementia.
C	Symptoms of Tardive Dyskinesia	↓	★☆☆ Minor	1 study	Symptoms of tardive dyskinesia appear to be slightly reduced with supplementation of ginkgo biloba
C	Serum BDNF	↑	★☆☆ Minor	1 study	An increase in serum BDNF has been confirmed in persons with schizophrenia and tardive dyskinesia only
C	Microcirculation	↑	★☆☆ Minor	1 study	There is a small increase in microcirculation seen in elderly persons given ginkgo biloba, extending to both periphery and the liver. Benefits seem to be time dependent and greater at day 30 relative to day 10
C	General Oxidation	↓	★☆☆ Minor	1 study	There appears to be a reduction in general oxidation as assessed by biomarkers (reduced glutathione, etc.) associated with supplementation of ginkgo biloba
C	Symptoms of Raynauds Phenomena	—	—	2 studies	No significant influence of ginkgo biloba supplementation on the symptomology of Raynaud's Phenomenon
C	Cancer Risk	—	—	1 study	No significant influence on overall cancer risk associated with prolonged usage of EGb-761 in elderly individuals

C	Breast Cancer Risk	↑	★☆☆ Minor	1 study	An increase in breast cancer risk has been noted to barely pass statistical significance in an analysis of cancer development in elderly persons (75 years or older) given EGb-761 daily for a median 6.1 years.
C	Apolipoprotein A	↓	★☆☆ Minor	1 study	In high risk individuals, the reduction has been noted to be 23.4+/-7.9%
C	Oxidation of LDL	↓	★★★☆☆ Notable	2 studies	In high risk individuals, the reduction has been noted to be 17.0+/-5.5%
C	Anti-Oxidant Enzyme Profile	↓ ↑	★☆☆ Minor	2 studies	Superoxide dismutase and glutathione have been noted to be increased with supplementation of ginkgo (240mg EGb-761) in persons with metabolic syndrome, while the abnormal elevation of these enzymes in schizophrenia is attenuated; essentially, a beneficial modulation appears to exist
C	Atherosclerosis	↓	★☆☆ Minor	1 study	In high risk subjects, supplementation of ginkgo biloba appeared to reduce atherosclerotic buildup relative to control at the standard supplemental dose.
C	Nitric Oxide	↑	★☆☆ Minor	2 studies	An increase in cGMP (downstream mediator of nitric oxide signalling) has been noted in high risk individuals alongside an increase in superoxide dismutase, to the degree of 27.7+/-8.3% and nitric oxide itself has been increased by up to 40% in persons with poor circulation.
C	Myeloperoxidase	↓	★★★☆☆ Notable	1 study	The 29.6% reduction in MPO concentrations following

					supplementation of 240mg EGb-761 in persons with metabolic syndrome was fairly notable.
C	Interleukin 6	↓	★☆☆ Minor	1 study	A slight reduction in IL-6 has been reported in persons who are diagnosed with metabolic syndrome
C	C-Reactive Protein	↓	★☆☆ Minor	1 study	A decrease in C-reactive protein is noted with supplementation of Ginkgo biloba
C	Symptoms of Vitiligo	↓	★☆☆ Minor	2 studies	EGb-761 appears to be associated with skin repigmentation in persons suffering from vitiligo, although the degree of this effect is fairly modest
C	Risk of Peripheral Vascular Disease	↓	★☆☆ Minor	1 study	There appears to be a significantly reduced risk of developing peripheral vascular diseases when using ginkgo biloba supplementation relative to placebo in older individuals
C	Risk of Myocardial Infarction	—	—	1 study	The risk of myocardial infarction (as well as other heart conditions such as angina) does not appear to be significantly affected by ginkgo supplementation.
C	Risk of Stroke	—	—	1 study	The risk of stroke does not appear to be reduced with supplementation of 240mg EGb-761 in older individuals.
C	ADHD in Children	↓	★☆☆ Minor	1 study	Ginkgo appears to reduce symptoms of ADHD, but 80-120mg of the EGb-761 extract has been confirmed to be less potent than 20-30mg Ritalin
C	Symptoms of Schizophrenia	↓	★☆☆ Minor	4 studies	Symptoms of schizophrenia

	Schizophrenia				appear to be reduced with supplementation of ginkgo biloba (EGb-761 at 240-360mg daily), although all studies currently use ginkgo alongside standard antipsychotic therapy. It appears effective as an add-on
C	Symptoms of PMS	↓	★☆☆ Minor	2 studies	There appear to be reductions in the symptoms of PMS associated with ginkgo supplementation, the degree of reduction being reported at up to 23.68%
C	Pink Eye	↓	★☆☆ Minor	1 study	Eye drops containing ginkgo biloba appear to be more effective than control in reducing symptoms of conjunctivitis (pink eye) after a month of treatment
C	Oxygen Uptake	↑	★☆☆ Minor	1 study	In persons undergoing high altitude climbing, the reduced risk of AMD is associated with increased functional capacity of blood to carry oxygen.
C	Creatinine	↓	★☆☆ Minor	1 study	A slight decrease in urinary creatinine has been noted with ginkgo supplementation in diabetics with nephropathy
C	Proteinuria	↓	★★★☆☆ Notable	1 study	The study in diabetics noting a reduction in urinary albumin noted a near halving over 8 weeks with a low dose of ginkgo.
C	Blood Glucose	—	—	1 study	In diabetics, ginkgo does not appear to significantly reduce blood glucose
C	Symptoms of Autism	—	—	2 studies	The better conducted trial and parts of the preliminary evidence suggest no therapeutic benefit of ginkgo biloba in the treatment of autism

C	Apolipoprotein B	—	—	1 study	No significant alterations are observed in apolipoprotein B concentrations
C	Anxiety	↓	★☆☆ Minor	1 study	Prolonged supplementation of ginkgo biloba appears to confer anxiolytic effects in persons with generalized anxiety disorder. Anxiety in dementia may also be reduced secondary to treating the symptoms of dementia
C	Stress	↓	★☆☆ Minor	1 study	There may be some anti-stress properties of ginkgo biloba supplementation when a single dose is taken prior to a stress test
C	Cortisol	↓	★☆☆ Minor	1 study	The increase in cortisol seen before a stress test is attenuated with supplementation of ginkgo, secondary to its anti-stress effects
C	Cerebral Blood flow	↑	★☆☆ Minor	2 studies	There appears to be a significant improvement in blood flow to the middle and anterior cerebral arteries, although other arteries are unaffected.
C	Visual Acuity	↑	★☆☆ Minor	1 study	Improvements have been noted in the visual field in persons with normal tension glaucoma, which is characterized by damage to this parameter. It is uncertain whether ginkgo increases visual acuity in otherwise healthy persons.
C	Processing Accuracy	↑	★☆☆ Minor	2 studies	The number of errors seen in serial threes and serial sevens tasks appears to be reduced with acute supplementation of EGb-761

C	Numerical Memory	↓	★☆☆ Minor	1 study	The study that investigated numerical working memory has noted an impairment associated with ginkgo relative to placebo
C	Calmness	↑	★☆☆ Minor	1 study	One study to assess the effects of ginkgo biloba in cognition, which failed to improve alertness, noted an increase in self-reported calmness with 120mg (EGb-761)
D	Wrinkles	↓	★☆☆ Minor	1 study	There appears to be a slight decrease in skin wrinkling following topical application of 0.3% ginkgo for 28 days
D	Skin Moisture	↑	★★★☆☆ Notable	1 study	The lone study assessing the effects of topical application of 0.3% ginkgo flavonoids in a cream noted a 28% increase in skin moisture content over 28 days, a highly relevant increase.
D	Skin Quality	↑	★☆☆ Minor	1 study	Skin smoothness/roughness is beneficially influenced with topical application of ginkgo flavonoids at 0.3%

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Glucosamine

Glucosamine, derived from shellfish, is a supplement (in sulfate form) that slightly delays the progression of knee osteoarthritis and provides minor pain relief. Benefits seem limited to osteoarthritis and the effect appears small.

See [Glucosamine on Examine.com](#)

How to Take

Glucosamine supplementation tends to be taken in three divided doses with food throughout the day, with the most commonly used doses being 900-1500mg daily (300x3 and 500x3, respectively). The benefits are dose dependent, and studies assessing higher doses (2,000mg or 3,000mg in two or three daily doses) tend to report more benefit in regards to joint health. Currently, 3,000mg in three divided doses of 1,000mg is the highest dose tested in repeated trials reporting efficacy and safety. Glucosamine Sulfate (as salts) are likely the best option, followed by Glucosamine Sulfate whereas Glucosamine hydrochloride is likely ineffective; N-Acetylglucosamine is unlikely to confer the same effects as Glucosamine supplementation (and should be considered an independent supplement) At the bare minimum, 1,500mg of Glucosamine Sulfate taken in three doses of 500mg for the purpose of attenuating the rate of knee osteoarthritis disease progression

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Symptoms of Osteoarthritis	↓	★☆☆ Minor	19 studies	There appears to be a small decrease in osteoarthritis symptoms associated with glucosamine (as sulfate, not hydrochloride) which is somewhat unreliable but consistently outperforms placebo on meta-analyses. The magnitude of reduction, however, is somewhat minor but still comparable to acetaminophen
A	Pain	↓	★☆☆ Minor	8 studies	There appears to be a decrease in pain, with one meta-analysis noting that over the long term it account for "a 13 point reduction on a scale of 0-100". Although present, it is not as effective as most painkillers and may be exclusive to osteoarthritis

C	Range of Motion	↑	★☆☆ Minor	1 study	An increase in range of motion has been noted alongside general osteoarthritis symptom reduction
C	Injury Rehabilitation Rate	↑	★☆☆ Minor	1 study	May be able to accelerate the rate of tissue injuries, limited evidence however
C	CTX-II	↓	★☆☆ Minor	2 studies	This biomarker of collagen degradation has been twice noted to be suppressed in athletes given 3g glucosamine sulfate daily, suggesting that prevention of collagen degradation applies (without measuring collagen per se)
C	Lower Back Pain	—	—	1 study	No significant benefits seen on lower back pain; all benefits associated with glucosamine are related to the knee
C	Symptoms of Kashin-Beck Disease	↓	★☆☆ Minor	2 studies	Can decrease the rate of collagen degradation in this disease state; lack of reference drugs prevents gauging potency
C	Symptoms of Temporomandibular osteoarthritis	—	—	2 studies	Limited evidence suggests that glucosamine's benefits do not extend to the jaw

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Glutamine

Also known as: L-Glutamine

A conditionally essential amino acid which only appears to benefit the body as supplementation when otherwise deficient (vegans, vegetarians with low dairy intake) or during prolonged endurance exercise. Anecdotal reported to reduce sugar cravings.

See [Glutamine on Examine.com](#)

How to Take

Supplementation of L-glutamine tends to be dosed at 5g or above, with a recommended 'upper limit' of 14g or 0.75g/kg (the upper limit based on increasing ammonia levels in the blood, which is seen as an adverse effect of supplementation). Due to the relative inefficacy of glutamine supplementation for increasing muscle mass, the optimal dosage is not known. The above recommended doses are sufficient for intestinal health reasons and for attenuating a possible relative glutamine deficiency (seen in instances of low protein intake or veganism).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Ammonia	↓↑	★☆☆ Minor	3 studies	Differential effects on ammonia, with decreases being present when glutamine is taken as part of a daily supplement routine and measured during prolonged exercise with a possible increase with high acute doses (which fades with time)
C	Inflammation	—	—	1 study	No significant influence on inflammatory cytokines except perhaps IL-6 seen with glutamine supplementation
C	Testosterone	—	—	1 study	No significant alterations in testosterone noted
C	Cortisol	—	—	1 study	No significant alterations in cortisol noted
C	Insulin	↑	★☆☆ Minor	2 studies	An increase in insulin occurs following ingestion of

					glutamine supplementation, which is thought to be secondary to the increase in blood glucose seen with glutamine ingestion
C	C-Reactive Protein	—	—	1 study	No significant alterations in C-Reactive Protein levels
C	Blood Glucose	↑	★☆☆ Minor	2 studies	An increase in blood glucose may occur from direct conversion of glutamine into glucose following oral ingestion
C	Exercise Capacity (with Heart Conditions)	↑	★☆☆ Minor	2 studies	Although a failure has been noted in persons with COPD, one study has noted acute benefits in chronic stable angina with 80mg/kg oral glutamine supplementation.
C	Immunity	—	—	1 study	No significant influence on immunity per se
C	Creatinine	↑	★☆☆ Minor	1 study	An increase in serum creatinine has been noted, but thought to be due to a reduction in glomerular filtration rate acutely rather than due to alterations in muscle damage
C	Urea	↑	★☆☆ Minor	1 study	An increase in urea has been noted with glutamine supplementation
C	Glomerular Filtration Rate	↓	★☆☆ Minor	1 study	A decrease has been noted in elderly persons given 0.5g/kg glutamine to a level where although the authors were not concerned but some serum biomarkers were adversely affected; long-term significance of this unknown
C	White Blood Cell Count	—	—	1 study	In safety testing, no significant alterations in white blood cell count is noted.

C	Liver Enzymes	—	—	1 study	In safety testing, there does not appear to be an adverse effect of glutamine supplementation on liver enzymes in serum
C	Hematocrit	—	—	1 study	No significant alterations in hematocrit noted
C	Symptoms of Duchenne Muscular Dystrophy	—	—	1 study	Glutamine has failed to be of benefit to symptoms associated with Duchenne muscle dystrophy
C	Uric Acid	↑	★☆☆ Minor	1 study	An increase in serum urate has been noted in the range of 10-20% acutely, but attenuates with time and is likely not a concern within a week. Practical significance of this increase unknown.
C	Muscle Damage	—	—	1 study	Serum creatinine (increased during exercise and thought to be indicative of muscle damage) does not appear to be significantly altered with glutamine supplementation
C	Fat Mass	—	—	1 study	The addition of glutamine supplementation to an exercise regiment has failed to outperform placebo in reducing fat mass.
C	Lean Mass	—	—	1 study	Supplemental glutamine does not appear capable of increasing lean mass when paired with a weightlifting routine.
C	Power Output	—	—	1 study	No significant influence on power output and strength associated with glutamine supplementation over placebo.
D	Symptoms of Crohn's Disease	↓	★☆☆ Minor	3 studies	A possible reduction of symptoms associated with

					Crohn's disease may occur, but this appears to be unreliable

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Glycine

Glycine is an amino acid and neurotransmitter that serves both stimulatory and depressant roles in the brain. While supplementation of this amino acid is mostly limited due to such a high intake being needed (usually over 40g), three grams may improve sleep quality.

See [Glycine on Examine.com](#)

How to Take

The lowest active dose of glycine supplementation in humans tends to be the 1-3g dosage range, although doses of up to 45g have been used without apparent side-effects.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Symptoms of Schizophrenia	↓	★☆☆ Minor	1 study	Is able to decrease symptoms of schizophrenia similar to both D-serine and sarcosine, but this occurs at an impractically high dose (minimum effective dose being around 800mg/kg bodyweight)
C	Cognition	↑	★☆☆ Minor	2 studies	There are improvements in cognition due to glycine being able to treat schizophrenia and due to glycine being able to improve sleep; two states of impaired cognition.
C	Sleep Quality	↑	★☆☆ Minor	3 studies	In persons undergoing mild sleep deprivation, 3g of glycine an hour prior to sleep is able to increase sleep quality and improve self-reports of fatigue and well being the next day due to better sleep.
C	Fatigue	↓	★☆☆ Minor	2 studies	The reduction in fatigue may solely be secondary to how Glycine supplementation can improve sleep quality

Grape Seed Extract

Also known as: GSE, OPC-3, Oligomeric Procyanidins, Procyanidin

Grape Seed Extract is a mixture of tannins and procyanidins (chains of catechins) that appears to exert anti-estrogenic effects and may enhance blood flow. More related to Green Tea Catechins than to Resveratrol mechanistically.

See [Grape Seed Extract on Examine.com](#)

How to Take

Studies conducted in humans used in the range of 150-300mg Grape Seed extract daily for heart health purposes, while doses up to 600mg have been used with no reported side effects.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Total Cholesterol	↓	★☆☆ Minor	3 studies	May decrease total cholesterol to an unremarkable degree when taken either at high (600mg) doses or in high risk populations; reductions in cholesterol are definitely not reliable
B	Triglycerides	—	—	3 studies	No significant influence of grape seed extract on triglycerides even in a high risk population at a high oral intake of GSE (600mg)
B	HDL-C	—	—	3 studies	No significant influence on HDL-C even at up to 600mg GSE daily in a high risk population
B	Blood Pressure	↓	★☆☆ Minor	2 studies	The meta-analysis conducted noted a pooled reduction of 1.54mmHg systolic associated with standard doses of grape seed extract; something, but a small reduction.
B	Heart Rate	↓	★☆☆ Minor	1 study	A small decrease in heart rate

					may occur following grape seed extract, although the studies are currently in persons with metabolic syndrome and not healthy persons
C	C-Reactive Protein	↓	★☆☆ Minor	1 study	May reduce levels of C-reactive protein
C	General Oxidation	↓	★☆☆ Minor	3 studies	A decrease in whole body oxidation appears to occur following ingestion of grape seed extract
C	LDL-C	—	—	2 studies	No significant interactions with LDL-C even in high risk persons
C	Oxidation of LDL	—	—	1 study	Does not appear to influence oxidation rates of LDL cholesterol
C	Blood Flow	↑	★★★☆☆ Notable	2 studies	An increase in blood flow appears to be reliable following ingestion of high dose procyanidins; this is likely the same increase seen with Pycnogenol due to the same molecules being bioactive
C	Food Intake	↓	★☆☆ Minor	1 study	A decrease in voluntary food intake has been noted with grape seed extract ingestion, appetite <i>per se</i> not measured
C	Leg Swelling	↓	★☆☆ Minor	1 study	A reduction in leg swelling has been noted in sedentary women (sitting for a day or so), thought to be indicative of better blood flow with grape seed extract
D	Symptoms of Chloasma	↓	★☆☆ Minor	1 study	A decrease in chloasma has been noted in following orally consumed low doses of grape seed extract

Grapefruit

Grapefruit is a food product known for having a high level of bioactives, similar to the Pomegranate. It does appear to be effective at reducing fat mass when a mixture of polyphenols are used, and may work nicely with Caffeine.

See [Grapefruit on Examine.com](#)

How to Take

Studies that use the grapefruit itself (whole fruit) tend to use one half of a grapefruit at 2-3 meals throughout the day.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Weight	↓	★☆☆ Minor	3 studies	There appears to be a weight reducing effect of grapefruit consumption relative to isocaloric controls (such as apple juice)
C	Blood Flow	—	—	1 study	No significant influence on blood flow noted
C	LDL-C	↓	★☆☆ Minor	1 study	A decrease in LDL cholesterol has been noted, but may be due to weight loss
C	Total Cholesterol	↓	★☆☆ Minor	1 study	A decrease in total cholesterol has been noted, this is confounded with weight loss (also occurred)
C	Insulin Sensitivity	↑	★☆☆ Minor	1 study	Improvement in insulin sensitivity may be secondary to weight loss
C	Fat Mass	↓	★☆☆ Minor	1 study	Fat mass appears to be reduced more in groups consuming grapefruit relative to placebo

D	Heart Rate	-	-	1 study	No significant alterations in heart rate associated with grapefruit ingestion

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Green Coffee Extract

Green Coffee Extract is a concentrated source of dietary Chlorogenic Acid and is currently being used for heart health and fat loss as a supplement; it seems weakly to moderately effective on these parameters.

See [Green Coffee Extract on Examine.com](#)

How to Take

Studies using Green Coffee Extract (GCE) tend to be dosed based on their Chlorogenic Acid content, which in isolation are taken in the 120-300mg range. Based on this, recommended intakes of GCE would be approximately: 1,200-3,000mg for a 10% chlorogenic acid supplement 600-1,500mg for a 20% chlorogenic acid supplement 240-600mg for a 50% chlorogenic acid supplement The optimal dosage of both GCE and isolated chlorogenic acid is not known at this moment in time.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Weight	↓	★☆☆ Minor	3 studies	There may be a weight reducing effect, but currently the literature is too influenced by industrial producers of GCE and the magnitude of effect seems too large. Independent replication is needed.
C	Blood Pressure	↓	★★★☆☆ Notable	1 study	Decrease in blood pressure noted with green coffee extract ingestion, due to the Chlorogenic Acid component. Degree of reduction reached 10mmHg (from just above 145mmHg to just above 135mmHg) and is quite notable.
C	Heart Rate	↓	★☆☆ Minor	1 study	A decrease has been noted in hypertensives alongside a reduction in blood pressure; no studies in otherwise healthy persons
C	Liver Enzymes	—	—	1 study	No significant influence noted for liver enzymes when tested in part of a safety assay

C	White Blood Cell Count	—	—	1 study	No significant alterations in WBC count
C	Creatinine	—	—	1 study	No alterations noted in creatinine associated with green coffee extract intake
C	Total Cholesterol	—	—	1 study	No significant alterations in total cholesterol seen with green coffee extract
C	Triglycerides	—	—	1 study	No significant influence on triglycerides following oral intake
C	HDL-C	—	—	1 study	No significant alterations in HDL cholesterol noted following consumption of GCE
C	LDL-C	—	—	1 study	LDL cholesterol appears unaffected
C	Blood Glucose	—	—	1 study	No significant influence noted on fasting glucose levels (may reduce postprandial slightly)
C	Fat Mass	↓	★☆☆ Minor	1 study	Lone study to measure fat mass noted a decrease associated with green coffee extract consumption, but this is similarly confounded with industrial influence.
C	Vascular Function	↑	★☆☆ Minor	1 study	An increase in vascular responsiveness has been noted with green coffee extract, thought to be due to the metabolite ferulic acid
C	Homocysteine	↓	★☆☆ Minor	1 study	Decrease in homocysteine noted, thought to be indicative of cardioprotection

Green Tea Catechins

Also known as: Camellia sinensis, Green Tea Extract, GTE

Green tea catechins are four molecules, high amounts of which are present in green tea and other sources. The most potent one is EGCG. It is effective in respect to most claims and potent in a few. Any fat burning benefits are dependent on being Caffeine naive.

See [Green Tea Catechins on Examine.com](#)

How to Take

Most doses are standardized against EGCG. Although the amount of EGCG-equivalent varies from one cup of tea to another, depending on many factors (species of tea, length of steeping, time spent oxidizing), one cup of camellia sinensis green tea contains approximately 50mg of EGCG-equivalent. Fat burning: The benefits of green tea catechins on lipid oxidation and related fat-burning pathways are achieved in a dose dependent manner. Significant effects in humans are noted only at high doses, such as 400-500mg EGCG equivalent per day (most Green Tea Extract supplements are roughly 50% EGCG). Fat burning effects are highly synergistic, almost dependent, on not consuming caffeine habitually. Cancer Prevention: Cancer prevention effects are quite dose-dependent, and would be better to consume all catechins (as green tea extract) rather than isolated EGCG. Minimal doses would be good (200mg or higher) but with more frequency (3+ times a day). High, frequent doses may make one prone to nausea

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Fat Mass	↓	★☆☆ Minor	6 studies	There appears to be a fat reducing effect associated with green tea, but it is minor and unreliable
A	Fat Oxidation	↑	★☆☆ Minor	8 studies	There appears to be a slight but unreliable increase in fat oxidation (percentage of overall calories used coming from fatty acids rather than glucose) associated with consumption of green tea catechins
B	LDL-C	↓	★☆☆ Minor	4 studies	There appears to be somewhat of a reduction in LDL-C associated with consumption of green tea polyphenolics (5% or so with 500mg catechin intake)

B	Insulin Sensitivity	↑	★☆☆ Minor	3 studies	Mixed effects on insulin sensitivity, possible improvements seen in unhealthy persons
B	HDL-C	↑	★☆☆ Minor	3 studies	Mixed effects with somewhat of an increase, not to a remarkable magnitude
B	Metabolic Rate	—	—	3 studies	No significant influences on metabolic rate overall
B	Blood Flow	↑	★☆☆ Minor	1 study	Appears to somewhat increase blood flow
C	Heart Rate	↓	★☆☆ Minor	2 studies	Mixed influence on heart rate, a possible decrease secondary to weight loss and blood pressure reduction but no apparent alteration <i>per se</i> (possible increases with overdoses of green tea catechins)
C	Cerebral Blood Flow	↓	★☆☆ Minor	1 study	A reduction in cerebral blood flow has been noted with green tea catechins; a simultaneous reduction in cognitive performance was not noted.
C	Cognition	↑	★☆☆ Minor	2 studies	Mixed results, but may improve cognitive performance acutely in persons with poorer cognition at baseline
C	Estrogen	—	—	1 study	No significant influence on serum estrogens
C	Testosterone	—	—	1 study	No significant influence on serum testosterone
C	Blood Glucose	↓	★☆☆ Minor	1 study	A decrease in fasting blood glucose is noted with green tea catechin ingestion
C	Insulin	—	—	2 studies	No significant influence on

					fasting insulin levels
C	Exercise-Induced Oxidation	↓	★☆☆ Minor	1 study	A decrease in the oxidation that occurs during exercise may occur following acute ingestion of green tea catechins
C	Skin Quality	↑	★☆☆ Minor	1 study	Oral ingestion of high dose catechins (1400mg) has been shown to improve skin quality
C	Photoprotection	↑	★☆☆ Minor	1 study	An increase in photoprotection (protection of the skin from the sun) has been found with green tea catechin ingestion
C	Thermic Effect of Food	—	—	1 study	No significant influence on the thermic effect of food
C	Oxygen Uptake	↑	★☆☆ Minor	1 study	An increase in oxygen uptake has been noted with green tea catechin ingestion
C	VO2 Max	↑	★☆☆ Minor	1 study	An increase in VO2 max has been noted in untrained persons
C	Triglycerides	—	—	1 study	No apparent influence on triglycerides
C	Total Cholesterol	↓	★☆☆ Minor	1 study	A decrease in cholesterol is noted with green tea catechins, but to a small degree
C	Blood Pressure	↓	★☆☆ Minor	1 study	Possible decrease in blood pressure noted with green tea catechin consumption
C	Subjective Well-Being	↑	★☆☆ Minor	1 study	An increase in well being has been noted in unhealthy persons given green tea catechins
C	Weight	—	—	2 studies	
C	Muscle Soreness	↓	★☆☆	1 study	A decrease in muscle

			Minor		A decrease in muscle soreness has been noted with catechin ingestion
C	Adiponectin	↑	★☆☆ Minor	1 study	Possible increase in adiponectin associated with green tea ingestion
C	Insulin Secretion	↓	★☆☆ Minor	1 study	A minor decrease in insulin secretion has been noted associated with green tea catechin ingestion
C	Iron Absorption	↓	★☆☆ Minor	1 study	A decrease in iron absorption associated with green tea catechins has been noted
D	General Oxidation	↓	★☆☆ Minor	1 study	Can decrease oxidation in the body (assessed via oxidative biomarkers)
D	Lipid Peroxidation	↓	★☆☆ Minor	1 study	Can decrease biomarkers of lipid peroxidation

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Guggul

Also known as: Commiphora mukul, Commiphora Wightii, Guggulsterones, pregna-4,17-diene-3,16-dione

Guggul is a product of the Guggul tree, Commiphora Mukul. Guggul and its active guggulsterones have been investigated for their usage in elevating thyroid function, but with lacklustre results.

See [Guggul on Examine.com](#)

How to Take

A standard dose of guggul (plant extract) is 400-500mg taken thrice daily with meals, totaling 1,200-1,500mg daily (although doses up to 2,000mg have been used before) If using the guggulsterones in isolation, a dose of 25mg taken thrice a day with meals is used. Sometimes 'gum guggul' is used in doses of 2-4.5g a day (total), and while it is not sure if guggul needs to be consumed with meals it still tends to be recommended out of prudence.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Total Cholesterol	↓	★☆☆ Minor	2 studies	Possible decrease in total cholesterol, but this is unreliable (and paired with a possible increase in LDL-C, this is likely to be not desirable)
C	HDL-C	↓	★☆☆ Minor	2 studies	Either no significant change associated with Guggul supplementation or a small decrease is observed
C	LDL-C	↑	★☆☆ Minor	2 studies	Although unreliable, there is a possible increase in LDL cholesterol from Guggul supplementation
C	Triglycerides	—	—	2 studies	No significant influence of Guggul on triglycerides is detectable
C	vLDL-C	—	—	1 study	No significant influence on vLDL cholesterol levels

D	Symptoms of Osteoarthritis	↓	★☆☆ Minor	1 study	Possible reductions in the symptoms associated with osteoarthritis

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Gynostemma pentaphyllum

Also known as: Southern Ginseng, Jiao Gu-lan, Giao-Co-Lam (Tea), jiaogulan

Gynostemma pentaphyllum (Southern Ginseng) is a herb given Ginseng status although not related to Panax ginseng. It appears to share some saponins though, and is investigated for similar effects as True Ginseng.

See [Gynostemma pentaphyllum on Examine.com](#)

How to Take

Although not too many trials have been conducted, the two studies noting that Gynostemma Pentaphyllum could be useful to help diabetes used 6g of the leaves (dry weight) and made tea from that. The leaves themselves are a good source of both classes of active ingredients (the saponins, of which Gypenosides are a subset, and the flavonoids), and this is currently the best known dosage to use. Alternatively, due to the similarity between Gynostemma pentaphyllum gyphenosides and Panax ginseng ginsenosides they may have a similar active level for isolated alkaloids. 100-500mg gyphenosides may be a good educated guess to start from.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	HbA1c	↓	★★★☆☆ Notable	2 studies	Preliminary evidence in diabetics suggest potent HbA1c reducing effects (6g of the root reducing HbA1c by 2% over a few months)
C	Blood Glucose	↓	★★★☆☆ Notable	2 studies	Decrease in blood glucose in diabetics given gynostemma tea or root appears to be greater than other supplements; currently no studies in otherwise healthy persons.
C	Triglycerides	—	—	1 study	No significant alterations in triglycerides noted with supplementation
C	HDL-C	—	—	1 study	HDL appears unaffected
C	LDL-C	—	—	1 study	LDL cholesterol appears unaffected

C	Insulin Sensitivity	↑	★★★☆☆ Notable	2 studies	An improvement in insulin sensitivity is noted in diabetics which is fairly notable; no studies in otherwise healthy persons at this time
C	Insulin	↓	★★☆☆☆ Minor	1 study	A decrease in fasting insulin has been noted with supplementation in diabetics
C	Weight	↓	★★☆☆☆ Minor	1 study	Long term, but not short term, ingestion of gynostemma tea appears to reduce fat mass in diabetics; no studies in healthy persons yet
C	Liver Enzymes	↓	★★☆☆☆ Minor	1 study	Liver enzymes in a model of fatty liver are decreased with gynostemma ingestion
C	Uric Acid	—	—	1 study	No significant influences on uric acid

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Harpagophytum procumbens

Also known as: Devil's Claw, Grapple plant, Duiwelsklou, Wood Spider

Harpagophytum Procumbens (Devil's Claw) is a tuber that has traditional usage for musculoskeletal disorders, pain relief, and appetite stimulation; it appears to have preliminary evidence for its benefits to osteoarthritis and pain.

See [Harpagophytum procumbens on Examine.com](#)

How to Take

Studies conducted on humans using Devil's Claw tend to use a brand called Doloteffin, where 6,000mg of Devil's Claw root is taken daily which totals 50mg Harpagoside (tends to be used as an indicator of efficacy). It was taken in three divided doses, with 2,000mg taken at each of the three major meals. Benefits of Devil's Claw extract, as it pertains to arthritis and inflammation, may take upwards of 1-4 months to achieve maximal efficacy.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Lower Back Pain	↓	★☆☆ Minor	1 study	A decrease in back pain has been noted (with a greater frequency of pain abolishment than placebo) which needs to be replicated
D	Symptoms of Osteoarthritis	↓	★☆☆ Minor	3 studies	Symptoms of osteoarthritis appear to be reduced following ingestion of devil's claw, but insufficient robust evidence exists

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Hemp Protein

Also known as: Hemp, Cannabis sativa, Hempseed meal

Hemp is a food product derived from the same plant of which Marijuana originates from, but without intoxicating components; the protein fragment appears to be a popular meal replacement supplement but is not yet linked to unique properties (relative to other Protein supplements).

See [Hemp Protein on Examine.com](#)

How to Take

Like any Protein Supplement, hemp protein supplements are dosed in relation to dietary protein goals and how much dietary protein is consumed via other sources. Protein goals vary from person to person, but a general guide is: If you are an athlete or highly active person currently attempting to lose body fat while preserving lean muscle mass, a daily intake of 1.5-2.2g/kg bodyweight (0.68-1g/lb bodyweight) would be a good target. If you are an athlete or highly active person, or you are attempting to lose body fat while preserving lean mass, then a daily intake of 1.0-1.5g/kg bodyweight (0.45-0.68g/lb bodyweight) would be a good target. If you are sedentary and not looking to change body composition, a daily target of 0.8g/kg bodyweight (0.36g/lb bodyweight) and upwards would be a good target. Supplementation of hemp protein should be in the dose that is required to meet these ranges after dietary protein has been accounted for. If dietary protein has adequately reached these ranges, then protein supplementation is not required. Obese individuals (body fat over 20/30% for males and females or a BMI greater than 30 without significant levels of muscle mass) should not follow the above recommendations exactly as the state of obesity would overshoot requirements. In these instances, calculate your targets based upon what your weight would be assuming an overweight BMI.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	LDL-C	—	—	2 studies	No significant modifications in LDL-C levels
C	HDL-C	—	—	2 studies	No detectable differences in HDL-C levels
C	Triglycerides	—	—	2 studies	No significant influence of oral hemp seeds on triglycerides
D	Skin Quality	—	—	1 study	No significant influence of topical hemp oil on skin quality
D	Symptoms of Atopic dermatitis	↓	★☆☆ Minor	1 study	Topical application of the oil of hemp may confer some aid to

					atopic dermatitis; oral intake of the protein not tested

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Hesperidin

Also known as: 5,7,3'-trihydroxy-4'-methoxyflavanone, hesperitin-7-O-rutinoside, Hesperitin glycoside, glucosyl hesperidin, Vitamin P, hesperitin, G-hesperidin,

Hesperidin is a compound in orange peels that gives the flavonoid hesperitin to the body, and this flavonoid mediates most benefits of hesperidin including an increase in circulation and possible brain protective effects. Hesperidin, alongside naringenin, are known as the main citrus flavonoids.

See [Hesperidin on Examine.com](#)

How to Take

Most studies using hesperidin tend to use 500mg of supplemental hesperidin, and use the standard form of hesperidin if taking it as a daily preventative. If using it for acute improvements in blood flow (ie. before a workout) then the form of G-Hesperidin may be preferred since it is absorbed faster and reaches higher levels in the blood. It does not have significantly better absorption overall, but it is faster at peaking in the blood. Supplementation of hesperidin should be around 500mg and preferably taken with food In regards to food products, the lowest known beneficial dose of hesperidin in rodent studies is around 25mg/kg oral intake daily. This is approximately 4mg/kg oral intake for an adult human which may be a bit too high to consume via orange juice products (in optimal conditions, a 150lb man would need to consume 1,800mL) and orange fruits (1,800g of the fresh fruit). The exception to the above is the antiallergic effects, which have occurred at a fifth of the aforementioned dose. The peels of tangerines, however, appear to have 5-10% of their weight as hesperidin after 5-7 days of drying (to remove water content and concentrate the hesperidin) and as such a 500mg supplemental dose of hesperidin can be achieved by 5-10g of the dried tangerine peel. This is a low cost alternate assuming that the peel is thoroughly scrubbed prior to drying to remove possible contamination and grime collected on the peel. When looking at food products, it is unlikely that the benefits of hesperidin can be mediated by standard orange consumption except maybe for antiallergic effects. Sundrying the peels of tangerines or oranges, however, can yield enough hesperidin for supplemental purposes

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	C-Reactive Protein	↓	★☆☆ Minor	3 studies	There is a decrease in C-Reactive Protein (inflammatory biomarker) in those with higher baseline inflammation or inflammatory disease conditions, but not in healthy persons.
B	Total Cholesterol	—	—	5 studies	While there may be a slight decrease which only applies to those with very elevated cholesterol at baseline, in normal persons or those with

					mild to moderately high cholesterol there is no significant influence.
B	LDL-C	—	—	5 studies	Similar to total cholesterol, while there may be a minor reduction in those at the worst levels of LDL cholesterol those with minor increases fail to find benefit.
B	HDL-C	—	—	5 studies	There is no significant or long lasting effect on HDL cholesterol seen with hesperidin, except maybe a very small (less than 5%) increase in those with the lowest levels of HDL which fades after cessation of supplementation.
B	Triglycerides	—	—	6 studies	There is no significant influence on triglycerides noted with supplementation of hesperidin; if an effect occurs, it is of very minor magnitude and only lasts for as long as supplementation persists.
C	Cell Adhesion Factors	↓	★☆☆ Minor	2 studies	There is a mild decrease in E-selectin and perhaps sCAM-1 seen with oral supplementation of hesperidin, but not ICAM or VCAM; this is thought to be a mechanism underlying atherogenesis prevention.
C	Homocysteine	—	—	1 study	There was no influence on homocysteine seen with supplementation of hesperidin relative to placebo, despite subjects being in an inflammatory state.
C	Blood Flow	↑	★★★☆☆ Notable	2 studies	An increase in blood flow has been noted in persons with metabolic impairments, and was fairly notable in the lone study due to reaching 24.5% over placebo.

C	Blood Pressure	↓	★☆☆ Minor	2 studies	There is a mild decrease in blood pressure seen with supplementation of Hesperidin; like blood flow, this is acute (within an hour with hesperitin and G-hesperidin; about 6-8 hours with hesperidin) and does not persist after supplementation ceases.
C	Fibrinogen	—	—	1 study	No significant alterations in fibrinogen content have been noted with oral supplementation of hesperidin
C	Weight	—	—	2 studies	In studies measuring weight as well as other parameters, weight is not influenced by supplementation of hesperidin relative to placebo
C	Blood Glucose	—	—	2 studies	There are no known significant alterations in blood glucose seen with supplementation of hesperidin
C	Insulin	—	—	2 studies	Similar to blood glucose, there is no significant influence on basal insulin concentrations in otherwise healthy persons or those with metabolic diseases.
C	HbA1c	—	—	1 study	Alongside a failure to improve insulin sensitivity or to reduce glucose was a failure to reduce HbA1c concentrations in the plasma of those with metabolic syndrome given 500mg hesperidin.
C	Apolipoprotein A	—	—	1 study	No significant influence on Apolipoprotein A seen with supplementation of hesperidin.
C	Apolipoprotein B	↓	★☆☆ Minor	3 studies	There appear to be mild decreases of circulating Apolipoprotein B seen with supplementation of hesperidin

					in the populations with poor baseline cholesterol that actually see benefit from supplementation.
C	Insulin Sensitivity	—	—	1 study	There is no significant change in insulin sensitivity in persons with metabolic syndrome given 500mg of hesperidin daily.
C	Liver Enzymes	↓	★☆☆ Minor	1 study	In men with high triglycerides and cholesterol, the serum liver enzymes appear to be reduced suggesting protective effects at the level of the liver.
C	Oxidation of LDL	↓	★☆☆ Minor	1 study	There is a mild increase in particulate size of LDL cholesterol, indicative of less oxidation of these particulates and less atherogenicity, with hesperidin supplementation.
C	Neutrophil Activity	—	—	1 study	The activity of neutrophils taken from subjects consuming hesperidin does not appear to be significantly altered when stimulated relative to placebo.
C	Natural Killer Cell content	—	—	1 study	The overall cell population of Natural Killer (NK) cells does not appear to be influenced with supplementation of Hesperidin
C	Natural Killer Cell Activity	—	—	1 study	Natural Killer (NK) cell activity does not appear to be influenced with supplementation of hesperidin, with the count also remaining unchanged.
C	White Blood Cell Count	—	—	1 study	No significant influence on total white blood cell count is seen with supplemental hesperidin.
C	T cell count	—	—	1 study	There do not appear to be any significant influence on the overall count of T Lymphocytes

					(collectively referring to Th1 and Th2 cells) with hesperidin supplementation.
C	B cell count	—	—	1 study	Overall B-cell count does not appear to be influenced with supplementation of hesperidin.
C	Neutrophil count	—	—	1 study	There are no significant alterations in the amount of neutrophils seen in subjects consuming hesperidin.
C	Symptoms of Rheumatoid Arthritis	↓	★☆☆ Minor	1 study	Preliminary evidence suggests a mild decrease in symptoms of rheumatoid arthritis seen with high (3,000mg) supplemental doses of G-hesperidin.
C	Nitric Oxide	—	—	1 study	The increase in nitric oxide (and nitrate) seen with supplementation of hesperidin failed to reach statistical significance.
C	Interleukin 6	—	—	1 study	No significant influence on interleukin 6 (IL-6) is seen with oral supplementation of hesperidin.
C	General Oxidation	—	—	1 study	General oxidative parameters do not appear to be significantly altered with supplementation of hesperidin under resting conditions.
C	Microcirculation	↑	★☆☆ Minor	1 study	While hesperidin does not influence basal (fasting) microcirculation, there is an acute increase in circulation seen with supplementation of hesperidin at the time of peak blood concentrations.

Hibiscus sabdariffa

Also known as: Roselle, Isakpa, Krachiap daeng, Sour Tea

Hibiscus Sabdariffa (Roselle or Sour Tea) is a tea where the usually dark colored flowers are used to brew. It appears to inhibit carbohydrate absorption to a degree and appears to be effective in reducing blood pressure.

See [Hibiscus sabdariffa on Examine.com](#)

How to Take

When using Hibiscus Sabdariffa as a tea, a dried calyx (the part of the blooming top of a flower that is not the petals, but beneath them) weighing about a gram is steeped into tea; drunk either once in the morning or twice a day with 8 hours between doses. Supplemental Hibiscus Sabdariffa is taken according to the content of anthocyanins; 10mg of anthocyanins derived from Hibiscus Sabdariffa (which would be 1g of a 1% extract or 500mg of a 2% extract) appears to be effective. Higher doses are associated with toxicity in rats, and it would be prudent to not exceed the above doses unnecessarily.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Blood Pressure	↓	★★★☆☆ Notable	6 studies	The decrease in blood pressure seen with roselle tea and supplements is notable and is greater than that seen with other supplements
C	Weight	—	—	2 studies	Weight appears to be unaffected following ingestion of Roselle tea
C	Triglycerides	↓	★★★☆☆ Notable	4 studies	Mixed effects on triglycerides, but the lone study that noted a decrease noted comparable potency to pravastatin; requires more literature
C	Blood Glucose	—	—	2 studies	No significant alterations in blood glucose noted
C	HDL-C	—	—	3 studies	HDL cholesterol appears to be unaffected following roselle ingestion

C	LDL-C	—	—	3 studies	LDL cholesterol appears to be unaffected following Roselle ingestion
C	Total Cholesterol	—	—	3 studies	No significant changes in total cholesterol noted
D	General Oxidation	↓	★☆☆ Minor	1 study	Appears to reduce oxidative biomarkers in the body, surprisingly not the potency one would expect from <i>in vitro</i> evidence
D	Uric Acid	—	—	1 study	Does not appear to influence uric acid concentrations in serum
D	Lipid Peroxidation	↓	★☆☆ Minor	1 study	Has been noted to reduce lipid peroxidation
D	Urea	—	—	1 study	No significant influence on urea
D	Creatinine	—	—	1 study	No significant influence on creatinine
D	Liver Enzymes	↓	★☆☆ Minor	1 study	A decrease in liver enzymes has been reported
D	Inflammation	↓	★☆☆ Minor	1 study	Possible decreases in MCP-1 with mixed or no influence on other inflammatory cytokines
D	Apolipoprotein A	—	—	1 study	No significant influence on apolipoprotein A levels in serum
D	Apolipoprotein B	—	—	1 study	No significant influence on Apolipoprotein B levels in serum

HMB

Also known as: Hydroxy-MethylButyrate, beta-hydroxy-beta-methylbutyrate

HMB is an active metabolite of Leucine that reduces muscle protein breakdown. It appears to have an anticatabolic role for muscle, but fails to be more effective than its parent amino acid for inducing muscle protein synthesis.

See [HMB on Examine.com](#)

How to Take

Supplementation of HMB tends to be in the dosage range of 1-3g daily for the purpose of reducing muscle mass losses over time (anti-catabolic). As HMB is said to be 20-fold more potent than leucine for this purpose, it is seen as equivalent to 20-60g of leucine supplementation. For the purpose of muscle protein synthesis, HMB and leucine are fairly equivalent if not the latter (Leucine) being more potent on a gram basis. HMB is not advised for inducing muscle protein synthesis since leucine is likely more effective as well as cheaper. Supplementation of HMB prior to an exercise session would require the usage of an HMB free acid rather than a calcium salt, and the above dosage range still holds. For this specific purpose, HMB is to be taken 30-45 minutes before a workout.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Power Output	—	—	12 studies	Limited evidence supports the increase in power output, which may be due to chance; more often than not, there is no significant influence
B	Fat Mass	↓	★☆☆ Minor	7 studies	There may be a decrease in fat mass associated with HMB supplementation when combined with resistance training, but this reduction is not a large magnitude and usually does not occur; quite unreliable
B	Lean Mass	—	—	8 studies	No significant influences on lean body mass associated with HMB supplementation
B	Food Intake	—	—	4 studies	Although there are sporadic alterations seen in food intake in studies using HMB

					supplementation, they are not reliable and the exact change observed changes. It is likely that there is no significant effect per se and this is due to the study population
B	Cortisol	—	—	3 studies	No significant influence on cortisol levels following acute ingestion
B	Testosterone	—	—	3 studies	No significant influence of acute usage on testosterone levels
B	Muscle Damage	↓	★★★☆☆ Notable	3 studies	Decrease creatine kinase exists following acute supplementation (15-30 minutes before a workout) of HMB free acid to about a third of control, and is effective in trained individuals
B	Training Volume	—	—	3 studies	No significant influence on training volume when used acutely
C	Total Cholesterol	↑	★★☆☆☆ Minor	2 studies	One underpowered study noted an increase in total cholesterol while another suggested no significant effect. The exact effect of HMB on total cholesterol is not currently known and required replication
C	HDL-C	—	—	2 studies	No significant influence on HDL cholesterol levels
C	LDL-C	—	—	2 studies	No significant influence on LDL cholesterol levels
C	Muscle Soreness	—	—	2 studies	No significant influence on perceived muscle soreness following exercise with HMB supplementation
C	Range of Motion	—	—	1 study	No significant influence on range of motion (impaired in

					both groups due to soreness post workout)
C	C-Reactive Protein	—	—	1 study	No significant influence on C-reactive protein
C	Fatigue	—	—	2 studies	No significant reduction in exercise-induced fatigue associated with HMB supplementation in athletes
C	IGF-1	—	—	1 study	No significant alterations in circulating IGF-1 concentrations
C	Growth Hormone	—	—	1 study	Serum growth hormone is not significantly altered with HMB supplementation in athletes
C	Interleukin 6	—	—	1 study	No significant alterations in circulating IL-6 concentrations
C	Liver Enzymes	—	—	2 studies	No significant alterations in serum liver enzymes are noted with HMB supplementation
C	Bone Mineral Density	—	—	2 studies	Studies that assess bone mineral density via DEXA, albeit short in duration and in athletes rather than populations at risk for osteoporosis, fail to find significant alterations in bone mineral density.
C	Anaerobic Running Capacity	—	—	1 study	No significant improvement in sprint capacity in trained persons supplementing HMB
D	Blood Glucose	↓	★☆☆ Minor	1 study	A lone study that is underpowered suggest a decrease in blood glucose (measured by chance during a blood panel); not enough robust evidence supports a reduction in blood glucose but it cannot be ruled out

D	Urea	↑	★☆☆ Minor	1 study	A slight increase in urea has been noted, requires replication
D	VO2 Max	—	—	1 study	No significant influence on VO2 max in trained athletes
D	Triglycerides	—	—	1 study	No significant influence on triglycerides

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Holy Basil

Also known as: Ocimum sanctum, Green Tulsi, Sacred Basil, Tulsi, Ocimum tenuiflorum

A traditional anti-fertility agent and libido enhancer in Ayurveda, Holy Basil (also known as Tulsi) is currently being investigated for these two claims and its general health properties. A good source of dietary Ursolic Acid, which may cause the anti-fertility aspects.

See [Holy Basil on Examine.com](#)

How to Take

500mg of the leaf extract taken twice daily appears to be recommended for neurological and adaptogenic effects of holy Basil, whereas the only evidence on other health effects or testosterone boosting are done in rats with the dosages of 100-200mg/kg and 500mg/kg respectively. This leads to an estimated human dose of: 1,100-2,200mg for a 150lb person for general health and 5,500mg for testosterone boosting 1,500-2,900mg for a 200lb person for general health and 7,300mg for testosterone boosting 1,800-3,600mg for a 250lb person for general health and 9,100mg for testosterone boosting These are estimated human dosages based on animal research, and it is unsure if they are the optimal doses for humans.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Immunity	↑	★☆☆ Minor	1 study	Appears to induce proliferation of T cytokines and T lymphocytes
C	Natural Killer Cell Content	↑	★☆☆ Minor	1 study	An increased level of NK cell count has been noted following ingestion of Tulsi leaves
D	Anxiety	↓	★☆☆ Minor	1 study	A decrease has been noted, but the studies are not overly robust at this moment in time
D	Depression	↓	★☆☆ Minor	1 study	A decrease in depressive symptoms during generalized anxiety disorder has been noted
D	Blood Glucose	↓	★☆☆ Minor	1 study	May reduce blood glucose, with the potency demonstrated (fairly good) limited by the quality of the evidence currently

Hoodia gordonii

Also known as: Hoodia, Veldkos, Slimming cactus, Trichocaulon gordonii, Stapelia gordonii

Hoodia gordonii is a small shrub (falsely said to be a cactus) that is claimed to suppress appetite. It seems the main bioactive (P57) cannot easily reach the brain to do this, and aside from failures of hoodia to suppress the appetite it may also be mildly toxic and imprudent to supplement.

See [Hoodia gordonii on Examine.com](#)

How to Take

Recommended doses of Hoodia Gorgonii tend to be around one gram of an extract of 70% steroidal glycosides or more, taken twice a day with each dose about an hour before a meal. There is no evidence to suggest an optimal dose nor to support the above as being active, and the toxic dose in mice (as well as preliminary human evidence) is the exact same as the supplemental dose.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Blood Pressure	↑	★★★☆☆ Notable	1 study	The increase in blood pressure noted with <i>hoodia gordonii</i> in otherwise healthy persons reached 5.9-15.9mmHg systolic and 4.6-11.5mmHg diastolic; a worrying increase
C	Heart Rate	↑	★☆☆☆☆ Minor	1 study	Both heart rate and pulse rate are increased with hoodia ingestion, which are thought to be related to toxic effects of the herb
C	Bilirubin	↑	★☆☆☆☆ Minor	1 study	The increase in bilirubin seen with hoodia is thought to be a biomarker of possible hepatotoxicity, although it was not met with hemolysis (usually accompanies)
C	Liver Enzymes	↑	★☆☆☆☆ Minor	1 study	ALP was noted to be increased in otherwise healthy women given the standard dose of hoodia, although the other liver enzymes were not affected

					significantly
C	Lean Mass	—	—	1 study	No significant modifications in lean mass during weight loss with hoodia relative to placebo
C	Fat Mass	—	—	1 study	No significant reductions in fat mass are noted, secondary to a lack of influence on appetite
C	Weight	—	—	1 study	No significant influence on overall body weight (due to no fluctuations in appetite and thus no significant fat loss)
C	Appetite	—	—	1 study	No significant reduction in appetite was seen with hoodia relative to placebo

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Horny Goat Weed

Also known as: Epidemium, Herba Epimdii, Icariin, Yinyanghuo, Fairy Wings, Rowdy Lamb Herb

Epimedium, known as Horny Goat Weed, is an erectile aid and aphrodisiac used in Traditional Chinese Medicine that just so happens to also increase Testosterone in research animals (has not been looked at in humans). May also be a cognitive booster and heart health agent.

See [Horny Goat Weed on Examine.com](#)

How to Take

Testosterone boosting effects in rats have been noted at a dosage of 200mg/kg of a 40% extract (80mg/kg Icariin), and based on body weight conversions from rats to humans[1] this results in an estimated human dose of: 900mg Icariin for a 150lb person 1,200mg Icariin for a 200lb person 1,500mg Icariin for a 250lb person Studies that use a lower dosage of Icariin (1-10mg/kg) are approximately equal to: 11-110mg Icariin for a 150lb person 15-150mg Icariin for a 200lb person 18-180mg Icariin for a 250lb person The human study on postmenopausal women and bone health noted that 60mg Icariin daily was active, and might serve as the lowest active dose currently known. It also appears to fall within the above range of lower active dosages which show benefits in rats.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Estrogen	—	—	2 studies	No significant influence on serum estrogen levels
C	Bone Mineral Density	↑	★☆☆ Minor	1 study	The rate of bone loss over 2 years has been noted to be reduced with icariin supplementation, although not to a remarkable degree

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Horse Chestnut

Also known as: Aesculus hippocastanum, Conker tree, Rosskastanie, venostasin

Horse Chestnut (*Aesculus hippocastanum*) is a plant extract with a group of molecules known as aescins, which are beneficial to circulatory health. Supplementation of horse chestnut appears to be beneficial for varicose veins and venous insufficiency.

See [Horse Chestnut on Examine.com](#)

How to Take

Horse chestnut tends to be taken in the 400-600mg range, although it seems that the overall dose is less important than the standardization for aescin which should ultimately reach 100-150mg daily. Supplementation tends to be divided into two daily doses divided by 12 hours (so, a morning and evening dose at 8am and 8pm as an example), which is due to the active components (aescins) requiring about 12 hours to reach baseline concentrations.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Chronic Venous Insufficiency	↓	★★★☆☆ Notable	3 studies	Due to the venotrophic effects of aescin supplementation, disease states associated with blood pooling in extremities are significantly and fairly reliably treated with horse chestnut.
B	Leg Swelling	↓	★★★☆☆ Notable	3 studies	Symptoms of leg swelling and varicose veins appear to be fairly reliably reduced with the recommended oral doses of horse chestnut supplementation.
B	Pain	↓	★★☆☆☆ Minor	1 study	The pain associated with chronic venous insufficiency may be alleviated when that condition is treated by horse chestnut extract.
C	Hemorrhoids	↓	★★☆☆☆ Minor	1 study	Preliminary evidence suggests that the classical usage of horse chestnut for the treatment of hemorrhoids may

					be relevant to oral supplementation, with benefits within a week of usage.
D	HDL-C	—	—	1 study	No significant influence on HDL-C levels associated with horse chestnut extract supplementation.
D	LDL-C	—	—	1 study	No detectable influence on LDL cholesterol concentrations associated with horse chestnut extract.

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Inositol

Also known as: Myoinositol, Cyclohexanehexol, 1,2,3,4,5,6-cyclohexanehexol

Inositol usually refers to Myo-inositol, a small molecule structurally similar to glucose that is involved in cellular signalling. It appears to be an effective anxiolytic at higher doses, and is quite effective in treating insulin resistance and PCOS with standard doses.

See [Inositol on Examine.com](#)

How to Take

For the treatment of polycystic ovarian syndrome (PCOS), myo-inositol is taken in the range of 200-4,000mg once daily before breakfast; the higher dose seems to be used more often and seems more effective. Neurological usage of inositol tends to require higher doses, and while antidepressant effects have been noted as low as 6g at times the standard dose is between 14-18g daily. If using a soft gel formulation rather than powdered myo-inositol, then only 30% of the same dose is required to be equivalent. This would mean the 14-18g range for psychopharmacological effects is now reduced to 4.2-5.4g of myo-inositol soft gels.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Treatment of PCOS	↑	★★★☆☆ Notable	14 studies	Supplementation of inositol in the range of 200-4,000mg daily appears to be effective in improving fertility in women with PCOS, while doses in the 2,000-4,000mg range appear effective in improving testosterone levels and insulin sensitivity.
B	Panic Attacks	↓	★★★☆☆ Notable	3 studies	Chronic ingestion of high doses of inositol (18g) is associated with reductions in panic attack frequency to a level greater than the reference drug fluvoxamine; acute usage does not appear effective.
B	Anxiety	↓	★★★☆☆ Notable	4 studies	There appears to be a decrease in anxiety symptoms associated with high dose inositol, and it has been noted to be comparable to fluvoxamine in potency.

B	Symptoms of Schizophrenia	—	—	3 studies	At the dose that showed anti-depressant effects, inositol failed to improve any symptoms associated with schizophrenia.
B	Depression	↓	★☆☆ Minor	8 studies	There appears to be a reduction in depressive symptoms associated with inositol supplementation, although it is less potent than the benefits of inositol on anxiety and panic attacks.
B	Blood Pressure	↓	★☆☆ Minor	6 studies	There may be a slight decrease in blood pressure in women with PCOS who are having it treated with inositol therapy.
B	Insulin Sensitivity	↑	★☆☆ Minor	12 studies	Insulin sensitivity appears to be reliably improved following the treatment of PCOS in women.
B	Weight	↓	★☆☆ Minor	7 studies	Decreases in body weight have been noted in women with PCOS, as inositol is effective in treating PCOS. They seem to influence leaner and overweight women more than obese women.
B	Blood Glucose	↓	★☆☆ Minor	9 studies	Blood glucose can be reduced in women with PCOS secondary to treating that condition.
B	Insulin	↓	★☆☆ Minor	7 studies	Secondary to treating symptoms of PCOS, fasting insulin concentrations are fairly reliably reduced.
B	HDL-C	↑	★☆☆ Minor	5 studies	An increase in circulating HDL-C is seen in women with PCOS getting inositol therapy
B	Fertility	↑	★★★☆☆	9 studies	

B	Inositol	↓	★★★★ Notable	1 study	In women with PCOS, very low doses of inositol (200mg) and greater can reliably and significantly increase ovulation and fertility rates.
B	Triglycerides	↓	★★☆☆ Minor	4 studies	There may be a small decrease in triglycerides associated with supplementation of inositol to women with PCOS
C	Liver Enzymes	—	—	1 study	No adverse effects to the liver during human toxicology testing.
C	Symptoms of OCD	↓	★★☆☆ Minor	1 study	Although a small decrease, there appear to be benefits to OCD symptoms associated with high dose inositol supplementation
C	Symptoms of Bipolar Disorder	—	—	2 studies	Although a beneficial effect cannot fully be ruled out, the best evidence currently available does not support a significant role for inositol in the treatment of bipolar disorder.
C	General Oxidation	↓	★★☆☆ Minor	1 study	There may be a reduction in oxidation associated with PCOS when the condition is being treated by inositol
C	Total Cholesterol	↓	★★☆☆ Minor	4 studies	A small decrease in total cholesterol has been noted with supplementation of inositol in women with PCOS
C	Insulin Secretion	↓	★★☆☆ Minor	3 studies	The amount of insulin secreted in response to orally ingested glucose is attenuated after supplementation of inositol to insulin resistant persons
C	Gestational Diabetes Risk	↓	★★☆☆ Minor	2 studies	The limited evidence on the topic suggests that supplementation of inositol

					throughout pregnancy can reduce the risk of developing gestational diabetes by half.
C	Adiponectin	↑	★☆☆ Minor	1 study	An increase in adiponectin has been noted in women with PCOS
C	Symptoms of PMS	↓	★☆☆ Minor	2 studies	<i>Myo</i> -inositol supplementation appears to be effective in reducing dysphoric and depressive symptoms during PMS
C	Symptoms of Alzheimers	—	—	2 studies	The preliminary evidence at this point in time using <i>scyllo</i> -inositol has failed to find a significant therapeutic benefit and <i>myo</i> -inositol shows a nonsignificant trend for improvement based on preliminary evidence.
C	Forgetting	—	—	1 study	Electroconvulsion therapy induced amnesia is not prevented with oral administration of 6g <i>myo</i> -inositol preloaded for five days
C	Binge-eating	↓	★☆☆ Minor	1 study	Symptoms of bulimia and binge-eating in diagnosed women have been significantly improved with high dose inositol therapy (18g daily)
C	Symptoms of Post Traumatic Stress Disorder	—	—	1 study	Despite the notable improvements in general panic disorders and anxiety, the lone study specifically looking at PTSD failed to find any significant benefits of inositol therapy.
C	Psoriasis	↓	★☆☆ Minor	1 study	Lithium-induced psoriasis is reduced with supplemental inositol at 6g daily. Inositol may only be effective in this particular scenario
D	Acne	↓	★★★☆☆	1 study	

D			Notable		Although this may only apply to acne in women with PCOS, supplementation of normal doses of <i>myo</i> -inositol can abolish acne in over half of subjects within 3-6 months.
D	Symptoms of Hirsutism	↓	★☆☆ Minor	2 studies	The hair growth associated with high androgen levels in women (hirsutism) appears to be reduced secondary to reducing androgens in women with PCOS or hyperandrogenemia
D	LDL-C	↓	★☆☆ Minor	3 studies	A decrease in LDL-C has been noted alongside other improvements in lipid parameters.
D	Plasmalogens	↑	★☆☆ Minor	2 studies	An increase in choline plasmalogen has been noted with <i>myo</i> -inositol oral ingestion, which is thought to underlie the reductions in LDL-C seen in persons with metabolic syndrome only.
D	C-Reactive Protein	—	—	1 study	No significant influence on C-reactive protein concentrations even in persons with metabolic syndrome.
D	Risk of Lung Cancer	↓	★☆☆ Minor	1 study	Although much more evidence is required in humans, there has been a high rate of regression seen with lung dysplasia in smokers due to ingestion of 18g <i>Myo</i> -inositol
D	Symptoms of Autism	—	—	1 study	The preliminary evidence on autism does not support a role for inositol therapy

Iodine

Iodine is a mineral for thyroid function found mostly in iodized table salt, fish, and highest in seaweed. Despite most first world diets being sufficient in iodine, it may benefit those who do not consume seafood and are also in a high risk population (pregnancy and intentional salt restriction).

See [Iodine on Examine.com](#)

How to Take

Supplementation of iodine is designed to circumvent a deficiency, and deficiencies of iodine are quite rare in first world countries. For those in a first world country, iodine should only be considered if you meet all of the following requirements: You are a vegetarian or vegan who actively avoids processed foods, or a meat eater who never eats fish and avoids processed foods You avoid adding additional salt to your diet You avoid consumption of seaweed or seaweed based products (such as sushi, which are wrapped with Nori) Assuming all the criteria are met, recommendations for iodine intake tend to be in the range of 75-150 µg (micrograms) or 0.075-0.15 mg daily while higher doses are not inherently dangerous although there may be a slight suppression of thyroid hormones (T3 and T4) at 500 µg or above.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Serum T4	↓	★☆☆ Minor	5 studies	Supplemental iodine above 500µg appears to be capable of suppressing T4 to a small degree whereas lower doses are not associated with such an effect.
B	Thyroid-Stimulating Hormone	↑	★☆☆ Minor	3 studies	An increase in Thyroid Stimulating Hormone (TSH) occurs both at the doses that suppress T3 and T4 and sometimes at lower doses where thyroid function is not impaired
B	Serum T3	↓	★☆☆ Minor	3 studies	500µg iodine or higher (in addition to the diet) appears to have a slight suppressive effect on thyroid function in otherwise healthy persons
C	Thyrotropin Releasing Hormone	↑	★☆☆ Minor	1 study	Alongside the suppression of circulating thyroid hormones

					and TSH, there is a mild and transient increase in levels of the hormone that stimulates TSH known as thyrotropin releasing hormone (TRH)
D	Interleukin 6	↓	★☆☆ Minor	1 study	There is a minor decrease in circulating IL-6 associated with iodine supplementation, thought to be indicative of a minor antiinflammatory effect.
D	C-Reactive Protein	↓	★☆☆ Minor	1 study	There may be a small decrease in C-reactive protein associated with moderate iodine supplementation in otherwise healthy persons, indicative of an antiinflammatory effect.

Irvingia gabonensis

Also known as: African Wild Mango, African Mango Extract, African Bush Mango, Dika nut

Irvingia Gabonensis (African Mango) is a supplement derived from the seeds of the plant known as African Mango (not related to common Mango fruits); there is insufficient evidence to support its usage as a fat burning supplement, and it may merely be a vessel for fiber and fatty acids.

See [Irvingia gabonensis on Examine.com](#)

How to Take

Supplemental dosages of irvingia gabonensis are quite variable, being anywhere between 150-3,200mg taken daily alongside meals. The optimal or effective dose is not currently known, but since the dietary fiber may be the active ingredient then supplementing in the higher end of the aforementioned range may be prudent.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Weight	↓	★☆☆ Minor	2 studies	Decreased body weight has been noted when african mango is consumed before meals, which may be secondary to reduced food intake; studies are somewhat confounded by industry influence.
C	Fat Mass	↓	★☆☆ Minor	1 study	A decrease in fat mass has been detected, but may be due to industry influence; independent trials are needed. Mechanism appears to be from suppressing food intake
C	LDL-C	↓	★☆☆ Minor	2 studies	A decrease in LDL-C has been noted, confounded with both weight loss and industry influence.
C	HDL-C	↑	★☆☆ Minor	2 studies	An increase has been noted, but not to a remarkable degree. Independent trials need to be conducted to confirm.

C	Total Cholesterol	↓	★☆☆ Minor	2 studies	A decrease in total cholesterol has been noted, but is confounded with weight loss
C	Leptin	↓	★☆☆ Minor	1 study	May decrease leptin, but is confounded with weight loss
C	Adiponectin	↑	★☆☆ Minor	1 study	An increase in adiponectin is noted with irvingia gabonensis, but this result is somewhat unreliable due to being confounded with both weight loss and industry influence
C	C-Reactive Protein	↓	★☆☆ Minor	1 study	A decrease in C-reactive protein has been noted, confounded with weight loss and industry influence
C	Blood Pressure	↓	★☆☆ Minor	1 study	A decrease in blood pressure has been noted with weight loss associated with this supplement; no inherent blood pressure reduction has been demonstrated
C	Triglycerides	↓	★☆☆ Minor	1 study	A decrease in triglycerides has been noted, confounded with weight loss
C	Blood Glucose	↓	★☆☆ Minor	1 study	May reduce fasting blood glucose following prolonged supplementation; confounded with both weight loss (seen in trials) and industry influence

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Japanese Knotweed

Also known as: Polygonum Cuspidatum, Huzhang, Fleeceflower, Monkeyweed, itadori, Polygonum Japonicus, Kudzu

Japanese Knotweed, or Polygonum Cuspidatum, is a Traditional Chinese Medicine used for circulation and heart health. It is a very good source of Resveratrol, and most benefits of Japanese Knotweed may actually just be benefits of Resveratrol.

See [Japanese Knotweed on Examine.com](#)

How to Take

The only current human study used Japanese Knotweed at 200mg daily and standardized to 40mg Resveratrol which was effective. Although there are other bioactives in Japanese Knotweed, it may be prudent to dose it in accordance to the dosing guidelines on the resveratrol page.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	HDL-C	—	—	1 study	No significant influence on HDL-C in otherwise healthy lean persons
C	LDL-C	—	—	1 study	LDL-C appears to be unaffected, but testing has not been conducted in metabolically unwell persons
C	Total Cholesterol	—	—	1 study	No significant alterations in cholesterol seen with Japanese Knotweed ingestion
C	Triglycerides	—	—	1 study	No significant influence of Japanese Knotweed on triglycerides
C	Insulin Sensitivity	—	—	1 study	Insulin sensitivity is unaffected in otherwise healthy lean persons given this supplement
C	Blood Glucose	—	—	1 study	Blood glucose appears to be unaffected following ingestion of Japanese knotweed in

					otherwise healthy lean persons
C	Insulin	—	—	1 study	No significant alterations in fasting insulin levels seen with treatment
C	Leptin	—	—	1 study	No significant influence on leptin in otherwise healthy and lean individuals
C	TNF-Alpha	↓	★☆☆ Minor	1 study	A decrease in TNF-a has been noted following oral consumption of japanese knotweed
C	Inflammation	↓	★★★☆☆ Notable	1 study	The study in question measured nF-kB activity and noted a 25% decrease, which is somewhat novel (not a common measurement) and to quite a large degree; may be related to the Resveratrol or stilbene content
C	General Oxidation	↓	★☆☆☆☆ Minor	1 study	Appears to reduce oxidative biomarkers, requires more evidence to gauge potency and reliability thereof

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Kaempferia parviflora

Also known as: Krachai Dum, Black Turmeric, Black Galingale, Thai Ginseng

Kaempferia Parviflora (Thai Ginseng) is a root plant that is touted to be an aphrodisiac and glucose support agent, with its effects on Testosterone and aphrodisia relatively unresearched; it may be (slightly) erectogenic by various mechanisms.

See [Kaempferia parviflora on Examine.com](#)

How to Take

According to traditional usage of Kaempferia Parviflora,[1] 0.5-1 teaspoon of ground power is made into a tea and drank about 1-2 hours before physical performance. This is similar to the recommended daily dose from the Thai traditional medicine institute of 1.2g daily, and the one human study on the matter (failing to note benefit acutely) used 1.35g. General health protective effects have been noted at lower doses, although not enough evidence exists to suggest an optimal dose.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Functionality in Elderly or Injured	↑	☆☆☆ Minor	1 study	Grip strength has been found to be increased in elderly persons associated with supplementation at low doses
C	Anti-Oxidant Enzyme Profile	↑	☆☆☆ Notable	1 study	The lone study to assess superoxide dismutase found a doubling after 8 weeks of supplementation (in older individuals); needs replication in youth
C	Lipid Peroxidation	↓	☆☆☆ Minor	1 study	A minor decrease in lipid peroxidation has been noted with supplementation of low doses
C	Power Output	—	—	1 study	No significant influence on power output when taken acutely before exercise
C	Rate of Perceived Exertion	—	—	1 study	No significant influence on the rate of perceived exertion when a single dose is taken acutely

C	Aerobic Exercise	-	-	1 study	No significant influence on aerobic exercise when taken acutely before exercise in youth

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Kava

Also known as: Piper methysticum, Kava Pepper, Ava Pepper, Kava Kava, Intoxicating Pepper, Awa, rauschpfeffer, sakau, tonga, wurzelstock, yangona

Kava is a herb that has traditionally been drunk as a hypnotic and Anxiety reducer. It has been shown effective in reducing anxiety, sometimes at a potency similar to pharmaceuticals; may be a cognitive enhancer, but not completely safe.

See [Kava on Examine.com](#)

How to Take

When supplementing Kava, initially an extract known as WS1490 should be sought out. 300mg of this extract daily (in three divided doses of 100mg) appears to be reliable and effective for the treatment of anxiety and other cognitive issues. Doses of up to 800mg of the WS1490 extract have been tolerated for short periods of time. Otherwise, supplementation of any product conferring 250mg collective kavalactones (the active ingredients) is used. Although it is usually taken at multiple times throughout the day with meals, if a single dose per day is being used it tends to be used prior to sleep.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Anxiety	↓	★★★☆☆ Notable	8 studies	Appears to be quite reliable and effective in treating non-psychotic anxiety, with less reliability on the topic of generalized anxiety (which Lavender shows some promise for). It is possible that long-term usage of kava may have similar side-effects as long term usage of benzodiazepines (note demonstrated, but wholly logical) and most studies on kava are of a few weeks in duration without any problems.
B	Subjective Well-Being	↑	★★★☆☆ Notable	4 studies	The increase in well being appears to be quite large, but secondary to reducing anxiety. At least one study has noted that, in healthy persons subject to a minor stressor (testing) that kava enhanced cheerfulness

C	Depression	↓	★☆☆ Minor	2 studies	Depressive symptoms have been reduced vicariously through reductions in anxiety; <i>per se</i> antidepressant effects of kava uncertain
C	Liver Enzymes	—	—	2 studies	No significant influence on liver enzymes assuming the water extract (WS1490) is being used
C	Cognition	↑	★☆☆ Minor	1 study	Possibly secondary to the antianxiety effects, kava taken prior to a test is able to enhance cognition related to mood during the stressful test.
C	Reaction Time	↓	★★★☆☆ Notable	1 study	The one study to measure reaction time noted an astounding decreased (approximately 40% reduction), which needs to be replicated
C	Sleep Quality	↑	★☆☆ Minor	2 studies	Sleep quality is enhanced via reducing the symptoms of anxiety which impair sleep
C	Aggression	↓	★☆☆ Minor	1 study	Aggressive symptoms of anxiety have been noted to be decreased following kava ingestion, an outright reduction of anxiety (without treating anxiety) is uncertain
D	Stress	↓	★☆☆ Minor	2 studies	Possible antistress effects of kava that requires larger studies
D	Blood Pressure	↓	★☆☆ Minor	1 study	One study has noted a reduction in blood pressure associated with kava, of minor magnitude

Krill Oil

Also known as: Euphausiacea superba

Krill oil is a mixture of fatty acids high in EPA and DHA (Fish Oil fatty acids) in the form of phospholipids, mostly as Phosphatidylcholine; it appears to be better absorbed than fish oil, may be more cardioprotective, and has some unique (unexplored) fat burning effects.

See [Krill Oil on Examine.com](#)

How to Take

Supplementation of Krill oil tends to be in the range of 1-3g daily (overall oil weight), which has been used in the clinical trails of krill oil supplementation. If supplementing in accordance with the omega-3 content, the omega-3 content that is supplemented from krill oil should be equal to approximately 2/3rds that used with basic Fish Oil supplementation to account for the increased absorption. If one were to normally supplement 1000mg EPA plus DHA, then 660mg of EPA and DHA from krill oil would be equivalent.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	C-Reactive Protein	↓	★★★☆☆ Notable	2 studies	A decrease in C-Reactive protein has only been noted in rheumatoid arthritis (none in obese but healthy persons) but reached 30% within 30 days of 500mg krill oil, a very significant reduction
C	Triglycerides	↓	★★☆☆☆ Minor	2 studies	A decrease in triglycerides has been noted with krill oil
C	Total Cholesterol	↓	★★☆☆☆ Minor	2 studies	A decrease in total cholesterol has been noted with krill oil, to a fairly normal degree (reduction is lessened from the remarkable increase in HDL)
C	HDL-C	↑	★★★☆☆ Notable	2 studies	Although one study suggest no such increase (healthy persons), the increase seen in hyperlipidemics exceeded 50% and was remarkable; requires replication
C	LDL-C	↓	★★★☆☆	2 studies	

C			Notable		A decrease in LDL-C has been noted with krill oil, which appears to be to quite a significant degree
C	Weight	—	—	1 study	No significant influence on weight over time
C	Blood Glucose	—	—	1 study	No significant influence on blood glucose levels
C	Insulin	—	—	1 study	No significant influence on fasting insulin levels
C	2-Arachidonoylglycerol Acid	↓	★☆☆ Minor	1 study	On obese subjects, this endocannabinoid has been found to be reduced somewhat
C	Symptoms of Rheumatoid Arthritis	↓	★★★☆☆ Notable	1 study	500mg Krill oil reduced symptoms of osteoarthritis up to 30%, which is a pretty significant effect size that requires future research to investigate.
C	Functionality in Elderly or Injured	↑	★☆☆ Minor	1 study	The increase in functionality appears to be secondary to reductions in symptoms of rheumatoid arthritis
C	Symptoms of PMS	↓	★☆☆ Minor	1 study	PMS and its symptoms (breast tenderness, stress, and irritability mostly) have been reduced with krill oil supplementation
C	Breast Tenderness	↓	★☆☆ Minor	1 study	Secondary to reducing symptoms of PMS, a reduction in breast tenderness has been reported
C	Irritability	↓	★☆☆ Minor	1 study	Irritability as a side-effect of PMS has been reduced with supplemental krill oil
C	Stress	↓	★☆☆ Minor	1 study	Stress as a side-effect of PMS has been reduced with

					supplemental krill oil
D	Lipid Peroxidation	—	—	1 study	Despite containing PUFAs, no significant changes in lipid peroxidation
D	Apolipoprotein A	↓	★☆☆ Minor	1 study	A decrease in Apolipoprotein A has been noted with krill oil supplementation
D	Apolipoprotein B	—	—	1 study	No significant influence on Apolipoprotein B noted

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L-Carnitine

Also known as: Acetyl-L-Carnitine, ALCAR, Acetylcarnitine, L-Carnitine, L-Carnitine-L-Tartrate, LCLT, Glycine Propionyl-L-Carnitine, GPLC, Levocarnitine, Levacecarnine, L-3-hydroxytrimethylamminobutanoate

L-Carnitine is involved in energy metabolism and mitochondrial protection. It is made in the body, but can also be consumed through food. Supplementation of L-carnitine does not burn fat unless the individual is deficient in L-carnitine.

See [L-Carnitine on Examine.com](#)

How to Take

The standard dose for L-carnitine is between 500-2,000mg. There are various forms of carnitine supplementation available. Acetyl-L-Carnitine (ALCAR) is used for cognitive enhancement. L-Carnitine L-Tartrate (LCLT) is typically used for physical performance and power output. Glycine Propionyl L-Carnitine (GPLC) is used to alleviate intermittent claudication and blood flow issues. L-carnitine is supplemented daily. The equivalent dosage range for other forms of L-carnitine are as follows: 630-2,500mg (ALCAR), 1,000-4,000mg (LCLT) and 1,000-4,000mg (GPLC).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Treatment of Hepatic Encephalopathy	↑	★☆☆ Minor	4 studies	Cognitive side effects of hepatic encephalopathy are alleviated with carnitine supplementation, notably fatigue and cognitive performance.
B	Ammonia	↓	★★★☆☆ Notable	4 studies	A decrease in ammonia has been noted, and appears to influence both hepatic encephalopathy as well as persons with no significant liver damage
B	Blood Glucose	↓	★☆☆ Minor	3 studies	A decrease in blood glucose has been noted with carnitine supplementation
B	Fatigue	↓	★☆☆ Minor	7 studies	Carnitine appears to be somewhat effective in reducing fatigue in elderly persons with low muscular endurance and perhaps in chronic fatigue

					syndrome; there is insufficient evidence to support a role of carnitine in reducing exercise-induced fatigue
B	Muscle Carnitine Content	↑	★☆☆ Minor	3 studies	Unreliable and mixed effects, but some studies do note that muscular carnitine levels can be increased with carnitine supplements.
B	Power Output	—	—	5 studies	Highly mixed effects on power output, with mostly no significant influence but a possible increase in mean power output occurring in short-term anaerobic endurance exercise secondary to reducing the rate of perceived exertion
B	Lactate Production	↓	★☆☆ Minor	5 studies	Lactate production appears to be decreased in studies that note an increase in muscular carnitine stores, although the decrease is not overly notable
B	Muscle Damage	↓	★☆☆ Minor	4 studies	Biomarkers of muscle damage including creatine kinase and muscle soreness are both fairly reliably reduced following ingestion of carnitine and pairing with exercise
B	Exercise-Induced Oxidation	↓	★☆☆ Minor	5 studies	A decrease in the exercise-induced increase in MDA levels is seen with carnitine supplementation, possibly secondary to reducing damage to muscle tissue. The degree of MDA reduction is not overly remarkable
B	Lipid Peroxidation	↓	★☆☆ Minor	3 studies	The reduction in MDA that occurs during exercise may also occur at rest, suggesting a per se effect
B	Triglycerides	—	—	2 studies	No significant influence on triglycerides

B	LDL-C	—	—	2 studies	No detectable influence on LDL-C levels
B	HDL-C	—	—	2 studies	No significant changes in HDL cholesterol seen with supplementation
B	Total Cholesterol	—	—	4 studies	For the most part, there does not appear to be a significant influence of carnitine on total cholesterol levels
B	Symptoms of Intermittent Claudication	↓	★★★☆☆ Notable	3 studies	Symptoms of intermittent claudication are notably reduced with L-Carnitine supplementation (the rate of improvement over time, as assessed by walking distance, seems to be doubled; ie. from 40% to 60% or 60% to 90%) and associated with the Propionyl-L-Carnitine form (found in the supplement GPLC). The role of propionic acid cannot be ruled out at this time, and studies have not used basic L-carnitine or ALCAR
B	Sperm Quality	↑	★★★☆☆ Notable	5 studies	Carnitine at 3g daily appears to increase sperm quality mostly related to sperm morphology; there are mixed effects on sperm motility
B	Aerobic Exercise	—	—	5 studies	More evidence than not suggest no significant influence on low intensity and high duration cardiovascular exercise
B	Fat Mass	↓	★★☆☆☆ Minor	3 studies	There appears to be a fat reducing effect of L-Carnitine supplementation, but this may be limited to elderly persons; limited studies in otherwise healthy youth and adults fail to note an effect

B	Fat Oxidation	—	—	3 studies	Rates of fat oxidation appear unaffected following carnitine supplementation
B	Insulin Sensitivity	↑	★☆☆ Minor	4 studies	An increase in insulin sensitivity appears to exist with carnitine supplementation, and at least once has been noted in otherwise healthy lean males. This may be secondary to glucose disposition into tissues
B	Hematocrit			2 studies	
B	C-Reactive Protein			1 study	
B	Hemoglobin			1 study	
B	Serum Albumin			1 study	
C	Heart Rate	↓	★☆☆ Minor	2 studies	A decrease in heart rate has been noted associated with supplementation
C	Symptoms of Autism	↓	★★★☆☆ Notable	1 study	High dose carnitine (50mg per kilogram) appears to reduce some symptoms of autism as assessed by rating scales; notable due to the rarity of a supplement towards this goal
C	Subjective Well-Being	—	—	3 studies	No significant changes in subjective well being associated with carnitine intake
C	Cognition	↑	★☆☆ Minor	2 studies	Improvements in general cognitive capacity has been noted in elderly persons and in disease models (hepatic encephalopathy); lack of literature on otherwise healthy youth
C	Anaerobic Running Capacity	↑	★☆☆ Minor	2 studies	An increase in anaerobic cardiovascular exercise has been noted with carnitine ingestion
C	VO2 Max	—	—	1 study	

					No detectable influence on VO2 max associated with carnitine supplementation
C	Rate of Perceived Exertion	↓	★☆☆ Minor	1 study	A reduction in the rate of perceived exertion appears to exist following carnitine supplementation
C	Uric Acid	↓	★☆☆ Minor	1 study	A decrease in uric acid has been noted
C	Muscle Soreness	↓	★☆☆ Minor	2 studies	The decrease in muscle soreness appears to correlate with the reduced muscle damage
C	Testosterone	—	—	1 study	No significant alterations noted
C	IGF Binding Protein	↑	★☆☆ Minor	1 study	An increase in IGF binding protein (3) has been noted following carnitine supplementation in otherwise healthy youth
C	IGF-1	—	—	1 study	No significant changes in IGF-1 seen with carnitine supplementation; IGF-2 also appears unaffected
C	Muscle Oxygenation	↓	★☆☆ Minor	1 study	A decrease in muscle oxygenation has been noted during occlusion, but not during squat exercise; practical significance of these results unknown
C	Androgen Receptor Density	↑	★☆☆ Minor	1 study	At least one study has noted an increase in androgen receptor density in skeletal muscle tissue
C	Nitric Oxide	↑	★☆☆ Minor	1 study	An increase in nitric oxide has been noted, thought to be secondary to increases in plasma nitrate

C	Plasma Nitrate	↑	★☆☆ Minor	2 studies	Plasma Nitrate appears to be increased following carnitine ingestion, although not to the same degree as nitrate supplementation itself
C	Symptoms of Fibromyalgia	↓	★☆☆ Minor	1 study	Fibromyalgic symptoms are reduced with carnitine ingestion
C	Alcohol Dependence	↓	★☆☆ Minor	1 study	A reduced rate of relapse and alcohol cravings was noted with ALCAR ingestion relative to placebo
C	Symptoms of Multiple Sclerosis	↓	★☆☆ Minor	1 study	Some symptoms associated with multiple sclerosis are noted to be reduced with carnitine ingestion.
C	Symptoms of Hyperthyroidism	↓	★☆☆ Minor	1 study	Some symptoms of hyperthyroidism are reduced following carnitine supplementation
C	TNF-Alpha	—	—	1 study	No significant influence on TNF-a
C	Blood Flow	↑	★☆☆ Minor	1 study	Increases in blood flow appear to occur following carnitine supplementation, which may be related to the increases in nitrate
C	Lean Mass	↑	★☆☆ Minor	2 studies	An increase in lean mass has been noted in elderly persons. This may not apply to lean healthy individuals, and no research assesses youth
C	Metabolic Rate	—	—	1 study	No significant influence on metabolic rate noted with carnitine supplementation
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	2 studies	An increase in all three main enzymes (SOD, glutathione peroxidase, catalase) has

					been detected following ingestion of carnitine
C	Liver Enzymes	↓	★☆☆ Minor	1 study	A decrease in liver enzymes has been noted in a model of hepatic encephalopathy, a per se reducing effect is uncertain
C	Inflammation	↓	★☆☆ Minor	1 study	Possible antiinflammatory effect on exercise-induced inflammatory biomarkers
C	Adiponectin	↑	★☆☆ Minor	1 study	An increase in adiponectin has been noted
C	Blood Pressure	↓	★☆☆ Minor	1 study	May reduce blood pressure
C	ADHD in Children	↓	★☆☆ Minor	2 studies	At least one study has noted reduction in ADHD symptoms in children
C	Insulin	↓	★☆☆ Minor	1 study	Fasting insulin has been noted to be decreased in diabetics given carnitine
C	Attention	↑	★☆☆ Minor	2 studies	An increase in attention has been noted to be secondary to reductions in the symptoms of chronic fatigue
C	Aggression	↓	★☆☆ Minor	1 study	Secondary to reducing symptoms of ADHD, L-carnitine may reduce aggression in children.
D	Erections	↑	★☆☆ Minor	1 study	One study has noted an improvement in erections in persons thought to have impaired blood flow
D	General Oxidation	↓	★☆☆ Minor	1 study	Reduction in general oxidation seems to be secondary to antioxidant enzyme induction
D	Total Iron Binding Capacity			1 study	

L-Tyrosine

L-Tyrosine is an amino acid that is used to produce noradrenaline and dopamine; supplemental appears to be anti-stress for acute stressors (which tend to deplete noradrenaline) and may preserve stress-induced memory deficits.

See [L-Tyrosine on Examine.com](#)

How to Take

Anecdotally, L-Tyrosine tends to be taken in doses of 500-2000mg approximately 30-60 minutes before any acute stressor (this tends to be exercise) Studies in humans showing most anti-stress promise for acute supplemental L-Tyrosine use a dosage range of 100-150mg/kg bodyweight which can be taken 60 minutes before exercise; this is a dosage range of 9-13.5g for a 200lb person and 7-10g for a 150lb person. If using higher doses and finding digestive issues, this may be split into two doses separated by half an hour (30 and 60 minutes prior to acute stress).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Blood Pressure	—	—	3 studies	It is possible that Tyrosine can reduce blood pressure during stress, but the one study that noted this also noted a reduction in blood pressure in the stressed placebo; other studies have found no influence.
B	Cognition	↑	★☆☆ Minor	3 studies	Tyrosine appears to effectively improve cognition during acute stressors (altitude and cold being tested most); this appears reliable if the acute stressor is present, but may not be an inherent increase in cognition and it is unsure if it applies to chronic stress and fatigue.
C	Working Memory	↑	★☆☆ Minor	2 studies	Appears to preserve working memory during acute stressors without inherently having a memory boosting effect

C	Noradrenaline	—	—	1 study	No significant influence on plasma noradrenaline levels (despite increased plasma tyrosine) during rest or during a cold stress test (which increases noradrenaline)
C	Subjective Well-Being	↑	★☆☆ Minor	2 studies	There appears to be an increase in subjective well being during stress when tyrosine is preloaded (perhaps secondary to the antistress effects of tyrosine), although this is not overly reliable
C	Stress	↓	★☆☆ Minor	2 studies	Perceptions of stress during acute stressors, as well as related symptoms of acute stress, appear to be reduced following tyrosine ingestion
C	Heart Rate	—	—	1 study	No significant influences of Tyrosine on heart rate has been noted
C	Depression	—	—	1 study	Depressive symptoms that occur during acute stressors have not been affected by Tyrosine supplementation; chronic depression not yet researched
C	Fatigue	—	—	1 study	No significant influence has been noted on fatigue from L-Tyrosine supplementation during acute stresses

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Lavender

Lavender is a 'calming' essential oil and aroma derived from the Lavandula family of plants, and appears to have some anxiety reducing properties following oral ingestion.

See [Lavender on Examine.com](#)

How to Take

For oral ingestion, Lavender essential oil tends to be consumed in the range of 80-160mg daily (for a product with 25-46% linalool by weight). Aromatherapeutic administration of lavender involves evoking a pleasant scent of Lavender in a moderately well ventilated room, the exact dose is hard to control in this scenario. Topical administration of Lavender involves a diluted oil given via massage, but may not be the ideal method of administration due to possible skin agitation and damaging effects (mostly underresearched, but some evidence to support this effect)

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Anxiety	↓	★★★☆☆ Notable	5 studies	There appears to be a notable decreased in symptoms of generalized anxiety disorder and with oral ingestion of lavender supplements; aromatherapy seems effective and implicated in reducing state anxiety (acute, situation based, anxiety), but has less robust evidence to support it. One study suggesting oral supplementation was comparable to lorazepam
C	Dysmenorrhea	↓	★★☆☆☆ Minor	1 study	Lavender as aromatherapy is able to reduce pain associated with menstruation
C	Blood Pressure	↓	★★☆☆☆ Minor	1 study	A reduction in blood pressure is noted alongside reduced autonomic nervous system activation and increased relaxation; this is likely to not affect the body over the long term
C	Calmness	—	—	1 study	Despite the increase in

					'relaxation', there does not appear to be an increase in calmness
C	Relaxation	↑	★☆☆ Minor	3 studies	An increase in the magnitude of self-reported 'relaxation' is noted with lavender aromatherapy more than placebo
C	Stress	—	—	1 study	No significant influences on stress
C	Sedation	↑	★☆☆ Minor	1 study	An increase in sedation has been noted with aromatherapy, but not with oral usage of lavender supplements
C	Heart Rate	↓	★☆☆ Minor	2 studies	A decrease in heart rate has been noted at rest over a long period of time (12 weeks in insomniacs) and acutely; both studies have used aromatherapy
C	Body temperature	↓	★☆☆ Minor	1 study	A decrease in body temperature is seen with lavender ingestion
C	Sleep Quality	↑	★☆☆ Minor	7 studies	Improvements in sleep quality have been noted in insomniacs and persons with generalized anxiety disorder mostly, with some limited evidence suggesting this may benefit generally healthy persons. Both oral supplements and aromatherapy are implicated in these benefits, but overall the quality of the studies is somewhat less than desirable. The parameters that see benefit are less waking up during the night and reduction in insomniac symptoms
C	Migraine	↓	★☆☆ Minor	1 study	Acute inhalation of lavender at the onset of a migraine is associated with less pain

					symptoms than placebo scent
C	Canker Sores	↓	★☆☆ Minor	1 study	A reduction in canker sore size and the pain associated with them are observed with topical lavender application
D	Heart Rate variability	↓	★☆☆ Minor	1 study	Lavender aromatherapy has once been noted to reduce heart rate variability
D	Restlessness	↓	★☆☆ Minor	1 study	A decrease in restlessness has been noted, but may be from symptom reduction of neurasthenia
D	Subjective Well-Being	↑	★☆☆ Minor	1 study	An increase in well being has been noted with lavender aromatherapy, possible secondary to the relaxing effects
D	Depression	↓	★☆☆ Minor	1 study	Depression as a side effect of anxiety appears to be reduced
D	Symptoms of Neurasthenia	↓	★☆☆ Minor	1 study	Both anxiety and restlessness associated with neurasthenia have once been noted to be beneficially influenced with lavender
D	Insomnia	↓	★☆☆ Minor	1 study	May be effective in reducing insomnia when measured
D	Infantile colic	↓	★☆☆ Minor	1 study	Reduction in infantile colic and improvements in mother-child interaction has been noted with adding the aroma of lavender to a bathing period
D	Cortisol	↓	★☆☆ Minor	1 study	A decrease in cortisol has been noted acutely with aromatherapy

Leucic Acid

Also known as: Alpha-Hydroxy-isocaproic acid, DL-alpha-Hydroxy-isocaproic acid, HICA

Leucic acid (also known as α -hydroxyisocaproic acid or HICA) is a Leucine metabolite touted to have anabolic properties. Although it appears to be effective following oral supplementation, comparisons to leucine or HMB do not exist.

See [Leucic Acid on Examine.com](#)

How to Take

The only human evidence currently uses a daily dose of 1,500mg HICA, split into three divided doses of 500mg. There is not enough evidence to suggest if this is the optimal dose nor is there evidence to assess the comparative potency of HICA against leucine or HMB supplementation.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Muscle Soreness	↓	★☆☆ Minor	1 study	A decrease in muscle soreness has been noted in the one study conducted in athletes (when measured at week 4 only) to the degree of around 23%, but muscle soreness was not overly high in the study to begin with
C	Power Output	—	—	1 study	Power output as assessed by jumping tasks and weightlifting is unaffected
C	Anaerobic Running Capacity	—	—	1 study	No significant influence on anaerobic running capacity
C	Fat Mass	—	—	1 study	No significant interaction between leucic acid and body fat has yet to be detected
C	Bone Mineral Density	—	—	1 study	No significant alterations in bone mineral density
C	Lean Mass	↑	★☆☆ Minor	1 study	An increase in lean mass has been noted in the legs of

					soccer players to the degree of 0.4kg over 4 weeks; this study currently stands alone
C	Weight	↑	★☆☆ Minor	1 study	The lone study using leucic acid in athletes has noted a minor but statistically significant increase in weight, attributable to lean mass (muscle plus water; bone mass unchanged)

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Licorice

Also known as: Licorice, Liquorice, Yashtimadhu, Glycyrrhiza, Glycyrrhiza Uralensis, Glycyrrhiza Glabra

Licorice is the common name for plants of the Glycyrrhiza family. It may contain protective flavanoids. Glycyrrhetic acid (a component of licorice) may decrease testosterone and increase cortisol.

See [Licorice on Examine.com](#)

How to Take

Prior to supplementing Licorice, please be aware of Glycyrrhizin (the agent that increases cortisol and reduces testosterone) and, if these results are not desired, try to get products with low Glycyrrhizin content (less than 500mg total dose daily). 150mg has been confirmed to not influence these hormones Traditional Chinese Medicine recommends a decoction of 8-15g Licorice for health protection and up to 100g for disease states. Consumption of licorice in these doses as a food product does confer the same properties as supplementation, but the caloric and carbohydrate intake from either the root of confectionaries derived from the root need to be accounted for. With supplementation, intakes of Licorice in the range of 150-300mg daily appear to be most commonly used and intakes of Deglyccyrhizinated (without Glycyrrhizin) up to 1800mg daily for 4 weeks are not associated with toxicity in humans.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Testosterone	↓	☆☆☆ Minor	6 studies	There appears to be a testosterone reduction associated with intake of licorice above 500mg, but the magnitude of this reduction is quite variable and there is no robust information on the topic
C	Cortisol	↑	☆☆☆ Minor	3 studies	Appears to increase cortisol at higher doses (500mg or more), with no significant influence at lower doses; this is related to the glycyrrhizin content, and would not occur in deglycyrrhizinated supplements
C	Weight	—	—	1 study	No significant interactions with body weight associated with licorice ingestion
C	Fat Mass	—	—	1 study	No significant influence on fat

					mass
C	Lean Mass	—	—	1 study	No significant alterations in lean mass associated with licorice
C	Insulin	—	—	1 study	No significant changes in fasting insulin levels
C	Insulin Sensitivity	—	—	1 study	No significant changes in insulin sensitivity following licorice ingestion
C	Adiponectin	—	—	1 study	No significant interaction between adiponectin and licorice
C	HDL-C	—	—	1 study	No significant influence of licorice on HDL
C	LDL-C	—	—	1 study	No significant influence on LDL cholesterol seems apparent
C	Total Cholesterol	—	—	1 study	No significant influence on total cholesterol is observed following licorice ingestion
C	Triglycerides	—	—	1 study	No significant influence on triglycerides
C	Oxidation of LDL	↓	★★★☆☆ Notable	2 studies	The decrease in oxidation of LDL seen with either licorice or isolated Glabridin appears to exceed 20% and is more than other supplements
C	Lipid Peroxidation	↓	★★☆☆☆ Minor	2 studies	A decrease in lipid peroxidation is noted with licorice consumption, not to a remarkable degree
C	DHEA	↑	★★☆☆☆ Minor	1 study	An increase in serum DHEA has been noted following licorice consumption

C	Canker Sores	↓	★☆☆ Minor	1 study	Topical application of licorice is able to reduce canker sore size and pain associated with canker sores
D	Estrogen	—	—	2 studies	No significant alterations in serum estrogen
D	Luteinizing Hormone	—	—	3 studies	More evidence than not suggests no significant changes in lutenizing hormone, although limited evidence suggests an increase of minor magnitude.
D	Follicle-Stimulating Hormone	—	—	1 study	No significant alterations in follicle stimulating hormone seen with licorice consumption
D	Prolactin	—	—	1 study	Prolactin appears unaffected following licorice consumption
D	Sex Hormone Binding Globulin	—	—	1 study	No significant alterations in SHBG levels following supplementation
D	Blood Pressure	↑	★★★☆☆ Notable	2 studies	Has the potential to increase blood pressure secondary to increasing cortisol; this is notable as it seems hypertensives are at greater risk from an adverse reaction to high dose licorice and as such should exert caution when using this herb (related to the glycyrrhizin content, and deglycyrrhizinated supplements should not have the same risk)
D	Parathyroid Hormone	↑	★☆☆ Minor	1 study	An increase in parathyroid hormone has been noted with consumption of licorice

Maca

Also known as: Lepidium meyenii, Maca root, Peruvian Ginseng

Maca (*Lepidium Meyenii*) is a vegetable in the broccoli family resembling a turnip, it is grown in Peru where it has a history of usage as an aphrodisiac. It appears to benefit both genders in this regard, and is not known to interact with any hormone.

See [Maca on Examine.com](#)

How to Take

Currently, all human studies that show benefit use 1,500-3,000mg Maca daily and usually alongside food; this appears to be well-tolerated and effective, with the higher dose sometimes being more effective. If looking for maca extracts, a water or an ethyl acetate extract seem to be recommended. Animal studies tend to use Maca in the dosage range of 1,000-2,200mg/kg bodyweight which correlates to an estimated human dose of: 10.9-24g of the maca vegetable for a 150lb person 14.5-32g of the maca vegetable for a 200lb person 18.1-40g of the maca vegetable for a 250lb person These higher dosage ranges tend to reflect traditional usage of maca, which is treated and consumed as a food product rather than a dietary supplement.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Estrogen	—	—	3 studies	No significant influence on circulating estrogen noted
B	Luteinizing Hormone	—	—	3 studies	No significant influence on luteinizing hormone noted with maca ingestion
B	Testosterone	—	—	4 studies	No significant influences on testosterone in any tested demographic
B	Follicle-Stimulating Hormone	—	—	3 studies	No significant influence on follicle stimulating hormone noted
B	Libido	↑	★★★☆☆ Notable	3 studies	An increase in libido appears to occur following Maca ingestion, which is notable as it appears to influence all demographics and is not

					associated with systemic hormones
C	Symptoms of Menopause	↓	★☆☆ Minor	1 study	One study noted reduced symptoms associated with menopause; libido was possibly independently increased, but anxiety and depression appear to also be reduced.
C	Depression	↓	★☆☆ Minor	2 studies	May reduce depression in postmenopausal women, unlikely to occur in otherwise healthy youth
C	Anxiety	↓	★☆☆ Minor	2 studies	An anxiety reducing effect has been noted in postmenopausal women but not otherwise healthy young men
C	Prolactin	—	—	2 studies	No significant influence on prolactin levels
C	Erections	↑	★☆☆ Minor	1 study	An increase in erection frequency has been noted in men, likely related to the libido enhancing properties
C	Subjective Well-Being	↑	★☆☆ Minor	1 study	An increase in well being has been noted
C	Sexual Function	↑	★☆☆ Minor	1 study	An improvement in SSRI induced sexual dysfunction has been noted with Maca supplementation
C	Anaerobic Running Capacity	—	—	1 study	No significant influence on anaerobic running capacity associated with Maca
C	Rate of Perceived Exertion	—	—	1 study	No significant influence on the rate of perceived exertion associated with Maca root
C	Heart Rate	—	—	1 study	No significant influence on

					heart rate noted with Maca ingestion

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Magnesium

Magnesium is a dietary mineral which is the second most common deficiency in the first world (first being Vitamin D), deficiency appears to increase blood pressure and reduce insulin sensitivity mostly. Superloading Magnesium for cognition or sports is understudied.

See [Magnesium on Examine.com](#)

How to Take

Magnesium doses range from 200-450mg Magnesium, when looking at the weight of the ion itself (known as Elemental Magnesium). Depending on what the ion is ingested as (see: forms of Magnesium) this dose is increased by a variable amount. For the purposes of relieving a deficiency or maintaining Magnesium status, any form of Magnesium may be used but Magnesium L-Threonate may not be the best choice (due to the low amount of elemental Magnesium per dose). Although all forms appear to be able to attenuate a deficiency, gastrointestinal side-effects such as diarrhea and bloat are more common with the forms that have less absorption rates; oxide and chloride. Citrate tends to be a good choice in these instances. For any attempt of superloading Magnesium above and beyond dietary sufficiency, more bioavailable forms of Magnesium such as Diglycinate or Gluconate (taken with food) should be used in moderate to high doses. Magnesium L-Threonate appears to be able to enhance neural magnesium levels to a supraphysiological level even when at a moderate dose and may be a good choice for cognitive enhancement.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Blood Glucose	↓	☆☆☆ Minor	8 studies	There appears to be some reduction in blood glucose in diabetics and persons with elevated glucose with magnesium supplementation, which may be secondary to better insulin functioning from the pancreas. The reduction in glucose is not overly impressive and is somewhat unreliable, and increases in glucose have been noted to occur during exercise when magnesium is supplemented in healthy persons
B	Insulin Sensitivity	↑	☆☆☆ Minor	4 studies	There appears to be increases in insulin sensitivity as assessed by HOMA-IR, which is thought to be secondary to aiding pancreatic function

B	Insulin	↓	★☆☆ Minor	6 studies	Decreases in fasting insulin appear to occur over long term supplementation with magnesium in persons at risk for diabetes or already with the disease state; decreases in insulin may not occur in normoglycemic persons
B	Blood Pressure	↓	★★★☆☆ Notable	9 studies	There appears to be a significant reduction in blood pressure assuming one of two conditions is met, either the subject is low in magnesium levels in the body (deficient) or if the subject has elevated blood pressure (140/90 or above), with the latter not requiring a deficiency to precede the blood pressure reducing effects
B	Weight	—	—	4 studies	No evidence to support a role for magnesium in inducing alterations in body weight
B	HDL-C	—	—	4 studies	For the most part, there is no significant direct influence of magnesium on HDL-C levels. Some counter evidence suggests it may occur vicariously through betterment of glycemic control in diabetics, but that is not always seen
B	Triglycerides	—	—	6 studies	For the most part, no significant influence of magnesium supplementation on triglycerides
B	Serum Magnesium	↑	★★★☆☆ Notable	6 studies	Has the capacity to increase serum magnesium stores, but this is somewhat unreliable and may be dependent on the person being deficient in magnesium prior to supplementation
B	Asthma	↓	★☆☆ Minor	4 studies	There appears to be a reduction in asthmatic symptoms associated with

					magnesium supplementation to a low degree, with the one study using corticosteroids alongside magnesium finding no effect. There may be a role for magnesium in aiding untreated asthma, but already medicated situations are not certain
B	HbA1c	↓	★☆☆ Minor	3 studies	More evidence than not suggest no significant effect on HbA1c levels, but one study suggests a decent decrease with the other two studies trending towards a decrease. There may be a role for magnesium in reducing HbA1c levels to a minor degree
C	Sleep Quality	↑	★☆☆ Minor	2 studies	An improvement in sleep quality has been noted in persons with poor sleep quality, no studies assess persons with normal sleep function
C	LDL-C	—	—	2 studies	No significant influence on LDL cholesterol levels seen with magnesium supplementation
C	Total Cholesterol	—	—	2 studies	No significant influence on total cholesterol levels seen with magnesium supplementation
C	C-Reactive Protein	↓	★☆☆ Minor	2 studies	Possible reduction in C-Reactive protein, but these changes are unreliable
C	Testosterone	—	—	2 studies	No significant influences on testosterone levels noted with magnesium intake
C	Osteocalcin	↑	★☆☆ Minor	2 studies	Possible but unreliable increases in osteocalcin
C	Migraine	↓	★☆☆ Minor	1 study	One study has noted a reduction in symptoms of migraines associated with oral

					magnesium supplementation
C	Cramps	—	—	1 study	No evidence to support a reduction in pregnancy related leg cramps
C	Cortisol	—	—	1 study	No significant influence on cortisol seen with magnesium supplementation
C	Bone Mineral Density	↑	★☆☆ Minor	1 study	An increase in bone mineral density has been noted with magnesium supplementation
C	Symptoms of Diabetic Neuropathy	↓	★☆☆ Minor	1 study	A reduction in symptoms associated with diabetic neuropathy has been noted with magnesium supplementation
C	Aerobic Exercise	↑	★★★☆☆ Notable	1 study	The one study to assess aerobic exercise capacity noted a significant improvement during extreme physical stress (triathletes), which is notable and needs replication
C	Muscle Oxygenation	↑	★★★☆☆ Notable	1 study	The one study to measure muscle oxygenation in high intensity exercise noted quite a remarkable increase in oxygenation in healthy athletes; this needs to be replicated
D	Symptoms of Tinnitus	↓	★☆☆ Minor	1 study	Decreased symptoms associated with tinnitus have been noted following magnesium supplementation
D	Depression	↓	★☆☆ Minor	1 study	Reduced depressive symptoms have been found in elderly diabetics
D	Symptoms of PMS	↓	★☆☆ Minor	1 study	A slight reduction in symptoms of PMS has been noted with magnesium supplementation

D	Oxidation of LDL	-	-	1 study	No significant influence on oxidation rates of LDL cholesterol

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Magnolia officinalis

Also known as: Saiboku-to, Magnolia Bark Extract, Honokiol, Magnolol

Magnolia officinalis is a Traditional Chinese Medicine known for its neuroprotective and relaxing properties, being used to treat depression and anxiety as well as acting as a slight sedative. It may also possess anti-cancer effects in higher doses.

See [Magnolia officinalis on Examine.com](#)

How to Take

The dosage of magnolia officinalis to take varies on goal. For those related to GABA (including anxiety, sedation, stress, and epilepsy) an oral dose of 0.2mg/kg in mice appears effective and suggests very low doses (5-10 mg) are effective in humans. For those goals related to learning or depression, higher doses may be required. This usually means 15-30mg/kg in rats, and suggests a human dose of: 160-330 mg for a 150lb person 220-440 mg for a 200lb person 270-550 mg for a 250lb person The above doses refer to the total neolignans (usually magnolol plus honokiol), which are usually at 1-10% of a basic bark extract unless otherwise concentrated.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Dental Health	↑	★★★☆☆ Notable	1 study	An improvement in dental health is noted with gum containing magnolia bark, which outperforms that of Xylitol in regards to reducing acid, plaque, and gum bleeding

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Melatonin

Also known as: N-Acetyl-5-Methoxytryptamine, Melatonine, Melovine, Melatol, Melatonex, Circadin

Melatonin is a hormone secreted in the brain that regulates sleep. It appears to be highly sensitive to Light Therapy and Dark Therapy. Oral ingestion of melatonin may be used as a sleep aid. It is non-addictive.

See [Melatonin on Examine.com](#)

How to Take

For regulating the sleep cycle, doses of melatonin between 500mcg (0.5mg) and 5mg seem to work. Start with 500mcg, and if it doesn't work, work up to 3-5mg. The benefits of melatonin are not dose-dependent - taking more will not help you fall asleep faster. To help with sleep, take roughly 30 minutes before going to bed. Growth hormone appears to spike slightly better at 5mg than 500mcg, although both doses are fairly effective.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Stomach Ulcers	↓	★★★☆☆ Notable	3 studies	A notable protective effect against both aspirin and <i>heliobacter pylori</i> induced stomach ulceration is seen with melatonin either alone or with other agents (such as omeprazole) nearing absolute protection in some instances. Although less researched, these may apply to duodenal ulcers as well
B	Plasma Melatonin	↑	★★★★★ Strong	6 studies	Plasma melatonin is increased at both night and daylight following supplementation of melatonin. Although the degree of increase is a tad unreliable, it seems to always occur and to a fairly large magnitude
B	Gastrin	↑	★★★☆☆ Notable	4 studies	There appears to be an increase in serum gastrin levels following ingestion of melatonin in persons with stomach ulceration, this increase is thought to be

					related to the ulcer healing effects of melatonin
B	Leptin	↑	★☆☆ Minor	3 studies	Mixed influences on leptin, but melatonin may be able to increase leptin levels following acute administration
B	Symptoms of Tinnitus	↓	★☆☆ Minor	4 studies	Melatonin may reduce symptoms associated with tinnitus in persons who suffer from the state, as assessed by questionnaire
B	Sleep Quality	↑	★☆☆ Minor	4 studies	An increase in sleep quality can occur following treatment of conditions known to impair sleep quality (insomnia and tinnitus)
B	Symptoms of Jet Lag	↓	★★★☆☆ Notable	1 study	Insomnia related to jet lag is reliably reduced with melatonin supplementation taken in accordance to the destination's time zone; secondary to better sleep, many other symptoms are reduced
B	Blood Pressure	↓	★☆☆ Minor	4 studies	An acute decrease in blood pressure occurs following melatonin ingestion, but this decrease is temporary and abolished upon standing; likely not practically relevant in an ambulatory population
B	Insomnia	↓	★★★★ Strong	4 studies	Melatonin is the reference drug for insomnia related purposes, and appears to be highly effective at 3mg (time release formulation) or lower concentrations when taken before sleep.
B	Adrenaline	—	—	4 studies	There do not appear to be any influence of melatonin ingestion on plasma adrenaline, either inherently or from influencing the spike in

					adrenaline from stress
B	Noradrenaline	↓	★☆☆ Minor	4 studies	A decrease in noradrenaline appears to reliably occur after melatonin ingestion, but only at rest; this reduction is abolished upon moving
B	Cancer Mortality	↓	★☆☆ Minor	1 study	There appears to be a significant protective effect on life in cancer patients with solid tumors, although the protective effect does not reach 'half risk' (RR of 0.50) and fluctuates in the range of quarter risk.
C	IGF-1	—	—	1 study	No significant influence on IGF-1 levels
C	Estrogen	—	—	1 study	No significant influence on circulating estrogen levels
C	Ghrelin	↑	★☆☆ Minor	2 studies	An increase in Ghrelin appears to exist following acute supplementation of melatonin
C	Insulin Sensitivity	↑	★☆☆ Minor	1 study	An increase in insulin sensitivity has been noted to be secondary to reducing liver fat; an inherent influence on insulin sensitivity is uncertain
C	Adiponectin	↑	★☆☆ Minor	1 study	An increase in adiponectin has been noted following acute ingestion of melatonin
C	Liver Enzymes	↓	★☆☆ Minor	1 study	A decrease in liver enzymes has been noted in persons with fatty liver given melatonin supplementation, although not to a remarkable degree
C	Resistin	—	—	1 study	No significant influence on resistin noted
C	Insulin	—	—	1 study	No significant influence on fasting insulin levels noted with

					melatonin
C	Exercise-Induced Oxidation	↓	★☆☆ Minor	2 studies	Related to the antioxidative effects, a reduction in exercise-induced oxidation has been noted
C	Lipid Peroxidation	↓	★☆☆ Minor	1 study	A reduction in lipid peroxidation has been noted with melatonin
C	Inflammation	↓	★☆☆ Minor	1 study	A reduction in inflammatory cytokines is noted with melatonin supplementation
C	Muscle Damage	↓	★☆☆ Minor	1 study	A decrease in muscle damage biomarkers (creatine kinase) has been noted with melatonin supplementation
C	Intraocular Pressure	↓	★☆☆ Minor	1 study	Oral supplementation of melatonin (500mcg) is able to reduce intraocular pressure in otherwise healthy persons
C	Growth Hormone	↑	★☆☆ Minor	2 studies	Appears to increase circulating levels of growth hormone
C	Cortisol	↑	★☆☆ Minor	2 studies	Mixed results, a possible increase when measuring whole-day cortisol levels (when taken in the AM) with no augmentation of stress-induced cortisol increases; may reduce cortisol if taken prior to sleep, however
C	Prolactin	—	—	1 study	No significant influence on prolactin concentrations
C	Triglycerides	↓	★☆☆ Minor	2 studies	A possible reduction in triglycerides to a minor degree is noted with melatonin supplementation, but this is not reliable
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	2 studies	Mixed effects on antioxidant enzymes, but there appears to

					be potential for melatonin to increase their content
C	LDL-C	—	—	1 study	No significant influence on LDL cholesterol is noted with melatonin
C	HDL-C	—	—	1 study	No significant influences on HDL-C are noted with melatonin supplementation
C	Total Cholesterol	—	—	1 study	No significant influence on total cholesterol levels
C	General Oxidation	↓	★☆☆ Minor	1 study	May decrease biomarkers of oxidation in serum
C	Fibrinogen	↑	★☆☆ Minor	1 study	An increase in fibrinogen has been noted
C	Blood Glucose	—	—	1 study	No significant influence on blood glucose levels
C	C-Reactive Protein	—	—	1 study	No significant influence on C-reactive protein
C	Migraine	—	—	1 study	No detectable influence of melatonin on migraines that exceeds placebo
C	Symptoms of GERD	↓	★★★☆☆ Notable	1 study	Symptoms of GERD, most notably heart burn, are reduced significantly following daily melatonin ingestion at 3mg
C	Heartburn	↓	★★★☆☆ Notable	1 study	A notable decrease in heartburn symptoms occurs after melatonin supplementation, thought to be related to a strengthening of the lower esophageal sphincter
C	Lower Esophageal Pressure	↑	★★★☆☆ Notable	1 study	Has been noted to increase LES pressure, which is thought to underlie symptoms

					reduction in GERD
C	Memory	↑	★☆☆ Minor	1 study	An increase in memory retention under periods of stress has been noted
C	Alertness	↓	★☆☆ Minor	1 study	A decrease in alertness has been noted with melatonin supplementation
C	Attention	—	—	1 study	Despite the reduction in alertness, no significant influence on sustained attention tests
C	Anxiety	—	—	1 study	No significant influence on state anxiety during stress testing
C	Heart Rate	—	—	2 studies	No significant influence of melatonin on heart rate during waking either at rest or ambulation
C	Blood Flow	↑	★☆☆ Minor	1 study	Has been noted to increase blood flow at rest
C	Dopamine	↓	★☆☆ Minor	1 study	Serum dopamine has been noted to be slightly reduced (37%) during waking at rest, but this decrease was eliminated upon walking
C	Cerebral Blood Flow	—	—	1 study	No significant influence on cerebral blood flow rates
D	Breast Cancer Risk	—	—	1 study	Too preliminary to conclude any relation to breast cancer, but urinary melatonin metabolites are positively correlated with breast cancer risk (not applied yet to supplementation)

Melissa officinalis

Also known as: Lemon Balm, Melissengeist, Bee balm, Garden Balm, Melissa, Erva-cidreira

Melissa officinalis (Lemon Balm) is a herb/tea traditionally said to induce calmness and improve cognition. It does appear effective at inducing calmness and reducing anxiety, but the cognitive enhancing properties are variable (appears to benefit if stressed, but otherwise it is merely sedative).

See [Melissa officinalis on Examine.com](#)

How to Take

The lowest active supplemental dose appears to be 300mg, and supplementation above this dose appears to confer dose-dependent effects although it is not very reliable (ie. one study says that 1200mg gives thrice as much benefit as 300mg while another suggests 1.4x benefit) Lemon Balm bioactives may also be consumed via tea or acquired via aromatherapy, although it is much harder to quantify 'the right dose' via these two methods.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Memory	↑	★☆☆ Minor	3 studies	Mixed influences on memory, with one study noting a decrease in 'total' memory formation and two studies noting improvements in 'quality' of memories formed. There is likely a modulatory effect associated with lemon balm.
C	Anxiety	↓	★☆☆ Minor	2 studies	A decrease in anxiety has been noted with lemon balm extract, although not to a remarkable degree
C	Calmness	↑	★★★☆☆ Notable	2 studies	An increase in self-reported ratings of 'calmness' appears to exist following ingestion of lemon balm single doses
C	Stress	↓	★☆☆ Minor	1 study	A decrease in self-reported stress has been reported with lemon balm
C	Alertness	↓	★★★☆☆ Notable	2 studies	A decrease in alertness

					appears to occur alongside lemon balm ingestion (with or without sedation)
C	Attention	—	—	1 study	Despite the decrease in alertness seen with lemon balm, there does not appear to be any alterations in intentional attention
C	Working Memory	—	—	2 studies	No significant influence appears to exist on working memory associated with lemon balm
C	Processing Speed	↓	★☆☆ Minor	1 study	A decrease in processing speed appears to occur following lemon balm ingestion, which may be related to the sedation effects
C	Contentment	—	—	1 study	No significant influence on self-ratings of contentment despite the increase in calmness
D	General Oxidation	↓	★☆☆ Minor	1 study	A decrease in general oxidation occurs following lemon balm ingestion
D	DNA Damage	↓	★☆☆ Minor	1 study	A reduction in DNA damage has been noted with lemon balm tea in persons exposed to high levels of radiation
D	Lipid Peroxidation	↓	★☆☆ Minor	1 study	A slight decrease in biomarkers of lipid peroxidation occurs following ingestion of lemon balm
D	Insomnia	↓	★☆☆ Minor	1 study	A decrease in insomnia has been noted to be to quite a large degree in one open-label trial, but may be secondary to anxiety reduction
D	Relaxation	↑	★☆☆ Minor	1 study	An increase in self-reports of relaxation occur, which may be

					related to the increased calmness and sedation ratings also seen
D	Aggression	↓	★☆☆ Minor	1 study	A reduction in agitation has been noted with lemon balm in stressed and anxious subjects, perhaps secondary to alleviating anxiety
D	Fatigue	↓	★☆☆ Minor	1 study	A decrease in fatigue associated with anxiety has been noted, no research looking at the <i>per se</i> influence of lemon balm on fatigue

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Methylsulfonylmethane

Also known as: MSM, dimethyl sulfone, dimethylsulfone

Methylsulfonylmethane (Dimethylsulfone or, more commonly, MSM) is a small sulfur containing molecule related to DMSO which is used for its antioxidative and antiinflammatory properties. It holds potential for joint health (not significantly different than Glucosamine sulfate).

See [Methylsulfonylmethane on Examine.com](#)

How to Take

Supplementation of MSM tends to be taken at up to 3,000mg daily, which seems to be effective for reducing symptoms of osteoarthritis and conferring some antioxidant protection to the body. It is unsure if higher supplemental doses are better than 3,000mg, so sticking to that dose may be prudent.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Muscle Soreness	↓	★☆☆ Minor	1 study	A decrease in muscle soreness has been noted with MSM preloads before exercise
C	Fatigue	—	—	1 study	No significant influence on exercise related fatigue
C	Training Volume	—	—	1 study	No significant influence on the total training volume able to be conducted
C	General Oxidation	↓	★☆☆ Minor	2 studies	A reduction in oxidative biomarkers has been noted following MSM ingestion
C	Muscle Damage	↓	★☆☆ Minor	1 study	Biomarkers of muscle damage such as creatinine and bilirubin are decreased following exercise with an MSM preload
C	Edema	↑	★☆☆ Minor	1 study	One study that used MSM as a placebo noted that there was an increase in edema relative to baseline; not known why.

C	Symptoms of Osteoarthritis	↓	★☆☆ Minor	1 study	A decrease in symptoms of osteoarthritis has been noted and seems to be somewhat comparable in potency to Glucosamine sulfate
C	Pain	—	—	1 study	No significant influence on pain symptoms in osteoarthritis
C	Exercise-Induced Oxidation	↓	★★★☆☆ Notable	1 study	A decrease in exercise induced oxidation is noted with MSM supplementation and thought to be the underlying reason for reductions in muscle damage and soreness. The degree of reduction seems to be notable, as the increase in MDA and protein carbonylation were fully abolished
C	Protein Carbonyl Content	↓	★☆☆ Minor	1 study	A decrease in protein carbonylation is noted with MSM supplementation
C	Lipid Peroxidation	↓	★☆☆ Minor	1 study	A decrease in exercise-induced lipid peroxidation is noted as assessed by serum MDA
D	Nasal Congestion	↓	★☆☆ Minor	1 study	Decreases upper respiratory symptoms have been noted with MSM supplementation, although not to a remarkable degree.
D	Allergies	↓	★☆☆ Minor	1 study	A decrease in pollen-induced allergies has been noted with MSM supplementation, with efficacy within one week

Microlactin

Also known as: Hyperimmune Milk

Microlactin (Hyperimmune milk) is a form of milk that is acquired by giving lactating cows immunostimulants, which produces a larger amount of antibodies in their secreted milk. It appears to be effective in reducing symptoms of osteoarthritis and may support the immune system.

See [Microlactin on Examine.com](#)

How to Take

Microlactin has shown benefit following oral ingestion of both 2,000mg and 9,000mg when taken daily over the course of a few weeks. The optimal dose is currently not known.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Pain	↓	★☆☆ Minor	2 studies	Possible pain reduction associated with reducing symptoms of osteoarthritis, with one study suggesting comparable efficacy to Glucosamine sulfate
C	Symptoms of Osteoarthritis	↓	★☆☆ Minor	2 studies	Appears to reduce pain symptoms and improve functionality associated with osteoarthritis, with one study suggesting comparable efficacy to Glucosamine sulfate
C	Total Cholesterol	↓	★☆☆ Minor	2 studies	May be able to reduce total cholesterol by a moderate to low degree (8-10%), but requires more robust evidence
C	Blood Pressure	↓	★☆☆ Minor	1 study	Has been noted to reduce blood pressure in persons with hyperlipidemia
C	LDL-C	↓	★☆☆ Minor	1 study	A reduction in LDL-C is seen in hyperlipidemics associated with hyperimmune milk consumption

C	HDL-C	—	—	1 study	Despite reductions in LDL and total cholesterol, there do not appear to be significant influences on HDL-C levels
C	Triglycerides	—	—	1 study	No significant influence on fasting triglycerides noted

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Minoxidil

Also known as: Rogaine

Commonly known as Rogaine (brand name), Minoxidil is a topical application that enhances hair growth. Less effective in Male Pattern Baldness than 'Bald patches', Minoxidil is the most commonly used topical hair growth compound.

See [Minoxidil on Examine.com](#)

How to Take

Usage of minoxidil as a topical formulation in the concentration range of 2-5%, with 5% being slightly better than 2% at promoting hair growth. Although oral supplementation technically aids hair growth, it is not advised due to possible complications with blood pressure.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Hair Regrowth	↑	★★★☆☆ Notable	8 studies	Topical application of Minoxidil (oral administration as well, but that is associated with more side-effects) appears to be highly effective in increasing the rate of hair regrowth and can reverse hair loss associated with non-androgenic hair loss (bald patch, rather than a receding hair line which is related to androgens)

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Modafinil

Also known as: 2-[(Diphenylmethyl) sulfinyl]acetamide, Provigil, Modalert, Modapro, Alertex

Modafinil is a prescription medicine for narcoleptics that increases alertness and prevents sleep. It just so happens to also increase cognition and memory, and is a potent and highly regarded supplement in the category of nootropics.

See [Modafinil on Examine.com](#)

How to Take

Standard dosages are 100-200mg, or perhaps 4mg/kg bodyweight, either taken in a sleep deprived state (if the user desires to not fall asleep) or taken first thing in the morning if the user does not wish to impair sleep.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Cognition	↑	★☆☆ Minor	4 studies	Cognition is significantly improved in persons undergoing sleep deprivation or other conditions in which attention processing is highly impaired, while other conditions (cognitive decline or drug dependence) experience minor improvements in cognition that are lesser than those seen in sleep deprivation.
B	Blood Pressure	↑	★☆☆ Minor	3 studies	There may be a slight increase in systolic blood pressure with acute usage of modafinil (when measured at its peak blood levels), although it does not appear to modify basal blood pressure values
B	Heart Rate	—	—	3 studies	Heart rate and pulse do not appear to be influenced from modafinil supplementation, despite a small increase in systolic blood pressure.
B	Working Memory	↑	★☆☆	5 studies	

			Minor		An improvement in working memory is noted in most persons tested, even otherwise healthy and nonfatigued controls.
B	Reaction Time	↓	★☆☆ Minor	3 studies	An improvement in reaction time (decrease) is noted in both healthy and normal persons as well as those undergoing either drug addiction or sleep deprivation. This may be related to the alertness promoting effects of the compound.
B	Fatigue	↓	★★★☆☆ Notable	6 studies	Fatigue is notably reduced with modafinil supplementation, particularly during instances of sleep deprivation or hypersomnia.
C	ADHD in Children	↓	★★★☆☆ Notable	1 study	Modafinil appears to be able to reduce symptoms of ADHD in children when taken as a daily preventative at the lowest active dose
C	Appetite	↓	★☆☆☆☆ Minor	1 study	Modafinil appears to be able to reduce appetite, and 'loss of appetite' is a common side-effect of modafinil supplementation.
C	Weight	—	—	1 study	There is currently no evidence to suggest a significant reduction of weight associated with modafinil, although as a trend to reduce weight has been noted alongside appetite reduction it is thought that modafinil could have a role in weight control.
C	Attention	↑	★☆☆☆☆ Minor	2 studies	There appears to be somewhat of an increase in subjective attention with modafinil secondary to its arousal promoting effects
C	Subjective Well-being	↑	★★★☆☆	2 studies	

			★★★ Notable		Subjective well being and enjoyment during cognitive tasks appears to be significantly improved with modafinil supplementation, and this is notable as it has been noted to occur in otherwise healthy persons taking modafinil for nootropic purposes
C	Sedation	↓	★★★★ Strong	2 studies	Modafinil (300mg) taken prior to sleep is as potent as 20mg D-amphetamine in reducing the need to sleep and improving cognitive performance during intentional sleep deprivation. Occasionally, this potency manifests itself as the 'side-effect' of insomnia in some persons who take it in the AM
C	Alcohol Dependence	↓	★☆☆ Minor	1 study	Alcohol dependence, particularly the impulsivity thereof, appears to be slightly reduced with modafinil administration
C	Impulsivity	↓	★☆☆ Minor	2 studies	Modafinil can decrease impulsivity in studies assessing addiction, although it appears to only significantly affect those with higher baseline impulsivity (more impulsive at the start of the study) rather than all persons.
C	Symptoms of Multiple Sclerosis	↓	★☆☆ Minor	2 studies	Memory impairment in multiple sclerosis may be attenuated with supplementation of modafinil (250mg armodafinil), although other cognitive impairments associated with MS do not appear significantly affected.
C	Processing Speed	—	—	1 study	There does not appear to be a significant influence on processing speed, with some evidence suggesting a possible reduction thereof.

C	Memory	↑	★☆☆ Minor	2 studies	Memory (usually studies investigate short term) appears to be beneficially influenced with modafinil supplementation, possible secondary to the improvements in working memory and attention.
C	Motivation	↑	★☆☆ Minor	1 study	Motivation to complete a cognitive task appears to be improved in persons supplementing modafinil.
C	Calmness	—	—	1 study	There do not appear to be any significant influences on self-reported ratings of calmness with supplementation of modafinil.
C	Processing Accuracy	↑	★☆☆ Minor	1 study	There is a possible improvement in processing accuracy with supplementation of modafinil.
C	Alertness	↑	★☆☆ Minor	1 study	An increase in alertness has been reported in persons using modafinil supplementation.

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Moringa oleifera

Also known as: Moringa pterygosperma, Ben Oil Tree, Horse Radish Tree, Tree of Life, Miracle Tree, Drumstick Tree, Jiksna gandha, Akshiva, Mochak, Sahijan, Zogale

Moringa oleifera is an economically important tree and vegetable, and preliminary evidence suggests that it has a respectable antioxidant and antiinflammatory potency. It contains compounds structurally similar to Sulforaphane and appears to be protective when orally ingested.

See [Moringa oleifera on Examine.com](#)

How to Take

There is not a lot of human evidence at this point in time, but the majority of animal evidence uses rats as the models and uses a water extract of the leaves. When those conditions are met, it appears that 150-200mg/kg oral intake is deemed as optimal (greater potency than higher and lower doses) and in this case a preliminary human dose can be estimated at: 1,600-2,200 mg for a 150lb person 2,100-2,900 mg for a 200lb person 2,700-3,600 mg for a 250lb person Due to the above ranges being the most potent antioxidative doses (with higher doses being less antioxidative) and the human studies currently in existence either using 500mg of the leaf extract of 3 grams of the seeds, it may be prudent to treat the ranges mentioned above as a maximal level of intake since higher doses have been noted to be genotoxic.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Milk Production	↑	★★★☆☆ Notable	1 study	When 250mg of <i>moringa oleifera</i> is taken twice daily, there is a time dependent increase in milk production; the lone study noted that the increase relative to placebo on the third day of supplementation was to 265% of placebo (a 165% increase).
D	Asthma	↓	★★☆☆☆ Minor	1 study	Non-allergic asthmatic symptoms were reduced in a pilot study using the seeds of <i>moringa oleifera</i>
D	White Blood Cell Count	—	—	1 study	No significant alterations in white blood cell count following ingestion of the seeds of <i>Moringa oleifera</i>
D	Lymphocyte Count	—	—	1 study	No significant alterations in

					Lymphocyte count following continued supplementation of the seeds of <i>Moringa oleifera</i>
D	Lung Function	↑	★☆☆ Minor	1 study	Respiratory capacity (as assessed by breath testing) in persons with nonallergic asthma (most of whom were smokers) appears to be enhanced following supplementation of the seeds of Moringa
D	Blood Glucose	↓	★☆☆ Minor	2 studies	There appears to be a decrease in postprandial blood glucose following a meal in type II diabetics (21%), and this hypoglycemia may apply to non-diabetics based on rodent research, and appears to increase with time.
D	Insulin Secretion	—	—	1 study	The hypoglycemic properties of this supplement do not appear to be related to an increase in insulin secretion from the pancreas following a meal
D	HbA1c	↓	★☆☆ Minor	1 study	The reduction of HbA1c noted is minor, from 7.8% down to 7.4% with 90 days supplementation of the leaf extracts

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Morus alba

Also known as: White Mulberry, Karayamaguwa, Sohakuhi, Sang-Bai-Pi, Ramulus Mori

Morus Alba (White Mulberry) is a plant where both the fruit and roots have been used traditionally for vitality and immune support; it may have cognitive enhancing properties (mostly unexplored) and anti-cancer effects.

See [Morus alba on Examine.com](#)

How to Take

For the purpose of reducing carbohydrate absorption and glucose spikes following a meal, morus alba must be consumed alongside said carbohydrate source. The dosage appears to be 500-1,000mg/kg in rat studies (assuming about a 0.11% 1-deoxynojirimycin content) which is an estimated human dose of: 5,400-11,000mg for a 150lb person 7,300-14,500mg for a 200lb person 9,000-18,000mg for a 250lb person Concentrated extracts may reduce the above requirement, so a 10:1 concentrated extract (for the 1-deoxynojirimycin content) would then require 900-1,800mg at the heaviest weight. For inflammation and other health related issues (such as uric acid), the rat dose appears to be in the range of 20-200mg/kg which is an estimated human dose of: 220-2,200mg for a 150lb person 300-2,900mg for a 200lb person 400-3,600mg for a 250lb person

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Symptoms of Melasma	↓	☆☆☆ Minor	1 study	A decrease in symptoms of melasma and subsequent improvement of skin quality has been noted with mulberry oil dissolved in Coconut Oil relative to coconut oil itself, topical application

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Mucuna pruriens

Also known as: Velvet Bean, Cowitch, Werepe, Karara, Agbara

Mucuna Pruriens, or Velvet Bean, is a bean that grows from trees and is very itchy to touch due to serotonin on its surface. It is a good source of L-DOPA, and contains some other molecules that may aid the benefits of L-DOPA. The other psychoactives in Mucuna are dosed too low to be relevant.

See [Mucuna pruriens on Examine.com](#)

How to Take

Supplement-wise, 5g of Mucuna Pruriens dried powder has been used with efficacy in some human studies on Parkinson's Disease and Fertility. This dose or doses upwards of it should be a good starting point. If your supplement is standardized for L-DOPA and you are supplementing for an effect attributed to L-DOPA, then start with about 1/2 the L-DOPA equivalent and work up if needed (this is due to the same amount of L-DOPA in Mucuna being more bioactive relative to isolated L-DOPA without carbidopa). Mucuna Pruriens can be eaten isolated as a food product, but cooking is required to destroy trypsin inhibitors in the beans (so protein absorption is not hindered) yet cooking also destroys L-DOPA. Some supplements use the cotyledon of Mucuna Pruriens, which may have different nutrient profiles relative to the bean or whole root.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Sperm Quality	↑	★☆☆ Minor	3 studies	There appears to be an increase in seminal quality and oxidative parameters following 3-month ingestion of Mucuna pruriens, which is thought to be secondary to correcting the hypothalamic-pituitary-testes axis
C	Testosterone	↑	★☆☆ Minor	2 studies	An increase in testosterone is seen in infertile men. It is unsure if this increase in testosterone occurs in fertile and otherwise healthy men
C	Prolactin	↓	★☆☆ Minor	2 studies	A decrease in prolactin appears to occur following Mucuna or L-DOPA ingestion
C	Dopamine	↑	★☆☆ Minor	1 study	The reduction in dopamine seen in infertility seems to be

					reversed with L-DOPA ingestion; theoretically L-DOPA ingestion should unilaterally increase dopamine
C	Adrenaline	↑	★☆☆ Minor	1 study	The decrease in adrenaline seen in infertility is normalized with mucuna
C	Noradrenaline	↑	★☆☆ Minor	1 study	The reduction in noradrenaline levels seen in infertility is normalized following mucuna ingestion
C	Symptoms of Parkinsons Disease	↓	★★★☆☆ Notable	3 studies	Possible symptoms reduction in Parkinson's Disease related to the L-DOPA content and theorized (but not proven) peripheral dopamine decarboxylase inhibitor; this is notable as a L-DOPA and carbidopa combination supplement is the reference for reducing parkinson's symptoms
C	Subjective Well-Being	↑	★☆☆ Minor	1 study	An increase in well being has been noted to be secondary to a reduction in cortisol
C	Seminal Motility	↑	★☆☆ Minor	2 studies	An increase in seminal motility is observed following mucuna ingestion
C	Cortisol	↓	★☆☆ Minor	1 study	In chronically stressed men, prolonged ingestion of mucuna pruriens appears to be able to reduce cortisol concentrations

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N-Acetylcysteine

Also known as: N-Acetyl Cysteine, NAC, N-Ac

N-Acetylcysteine (NAC) is a prodrug for L-cysteine, which is used for the intention of allowing more glutathione to be produced when it would normally be depleted. Through glutathione buffering, NAC provides antioxidative effects and other benefits.

See [N-Acetylcysteine on Examine.com](#)

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Treatment of COPD	↑	☆☆☆ Minor	4 studies	N-Acetylcysteine may reduce some symptoms of COPD by acting as a mucolytic agent and reducing sputum formation, but it does not appear to be effective at aiding the lungs themselves or reducing disease progression.
B	Symptoms of Autism			3 studies	
C	Anti-Oxidant Enzyme Profile	↑	☆☆☆ Notable	1 study	NAC supplementation is able to reliably increase glutathione concentrations in cells specifically
C	Mineral Bioaccumulation	↓	☆☆☆ Minor	1 study	NAC supplementation appears to reduce lead bioaccumulation in red blood cells, although the magnitude is statistically significant it is not overly large
C	Lipofuscin	↓	☆☆☆ Minor	1 study	A decrease in red blood cell (RBC) lipofuscin content has been seen, which is thought to be secondary to reducing lead toxicity and increasing antioxidative defenses
C	Nicotine Addiction	↓	☆☆☆ Minor	1 study	After about two weeks of 2,400mg NAC supplementation, cigarette usage appears to be reduced

					voluntarily by around 25%.
C	Anaerobic Running Capacity			1 study	
C	Power Output			1 study	
C	Neutrophil Activity			1 study	
C	Lung Function			1 study	
C	Symptoms of OCD			1 study	
C	Treatment of Trichotillomania	↓	★☆☆ Minor	1 study	Preliminary evidence suggests a 31-45% reduction in hair pulling symptoms in persons with trichotillomania when supplementing with 1,200-2,400mg NAC for twelve weeks.
C	Depression			1 study	
C	Anxiety			1 study	
C	Subjective Well-Being			1 study	
C	Irritability			2 studies	
D	Marijuana Addiction	↓	★☆☆ Minor	1 study	Supplementation of 2,400mg appears to reduce symptoms of marijuana addiction, although the reductions in symptoms are not overly prominent based on the limited evidence so far.
D	Cocaine Addiction	↓	★☆☆ Minor	1 study	Self-reported cravings for cocaine during one day of withdrawal appear to be significantly reduced following 12 hours (although acute cravings after 2 hours of supplementation are not affected); this lasts for 24 hours after cessation.

Nattokinase

Also known as: Natto extract, subtilisin NAT, Orokinase, NSK-SD

Nattokinase is one of many enzymes derived from the food product Nattō (boiled soybeans fermented by the bacteria *Bacillus subtilis*) and appears to have some direct fibrinolytic activity (fibrin degrading). It is thought to reduce the risk of cardiovascular events, but is fairly underresearched.

See [Nattokinase on Examine.com](#)

How to Take

There is not enough evidence to suggest the optimal dose of oral nattokinase, but studies in humans tend to use around 500mg or 5,000 FU (Fibrinolysis Units) daily, usually divided into two separate doses taken with meals. Nattō itself can be used, and some anti-clotting effects have been noted with 12g of nattō daily over 2 weeks.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Blood Pressure	↓	★☆☆ Minor	1 study	A possible blood pressure reducing effect seen with nattokinase, notable but with high variability
C	Renin Activity	↓	★☆☆ Minor	1 study	In hypertensive persons, there is a decrease in renin activity seen with nattokinase ingestion
C	HDL-C	—	—	1 study	No significant influence on HDL-C levels
C	LDL-C	—	—	1 study	No significant influence on LDL cholesterol
C	Triglycerides	—	—	1 study	No significant influence on triglycerides
C	Liver Enzymes	—	—	1 study	No significant influence on liver enzymes noted
C	Total Cholesterol	—	—	1 study	No significant influence on total

					cholesterol seen with supplementation
D	Fibrinolysis	↑	★☆☆ Minor	1 study	The rate of degradation of fibrin appears to be enhanced slightly following nattokinase ingestion
D	Factor VII	↓	★☆☆ Minor	1 study	Factor VII (involved in blood clotting) has been noted to be reduced with nattokinase ingestion
D	Factor VIII	↓	★☆☆ Minor	1 study	Factor VIII (involved in blood clotting) appears to be reduced following nattokinase ingestion
D	Fibrinogen	↓	★☆☆ Minor	1 study	A decrease in fibrinogen appears to exist following nattokinase ingestion

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Nicotine

Nicotine is the main stimulatory compound found in cigarettes and is now sold in vaporizers and patches in isolation. It works on the acetylcholine system, and is implicated in cognitive enhancement.

See [Nicotine on Examine.com](#)

How to Take

Nicotine can be administered via several methods (excluding cigarettes, which are not recommended due to risks greatly exceeding benefits): An inhaler, which lets you rapidly feel the effects of nicotine (and inherently carries more risk than other forms due to the speed at which it works) Topical patches, which have about a 1 hour delay between application and absorption and maintain constant serum levels of nicotine but with less cognitive spike (least risk potential, least nootropic potential) Chewing gums, which are sort of an intermediate between the two There is currently insufficient evidence to suggest an 'optimal dose' of nicotine for non-smoking individuals. For non-smoking individuals, it would be prudent to follow stimulant usage guidelines and start with a low dose and work up. This includes buying 2mg gums or cutting a 24mg nicotine patch into quarters to start, then work up to what is seen as the minimum effective dose. There is currently no established 'threshold' for when risk becomes too great as it varies between individuals. If using nicotine as Nicotine Replacment Therapy (to curb smoking cravings), then following the instructions on the product is sufficient. These instructions may be excessive for a non-smoking individual.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Blood Pressure	—	—	4 studies	Mixed effects on blood pressure
B	Insulin Sensitivity	—	—	3 studies	Long term insulin sensitivity does not appear to be highly affected, but acutely nicotine exposure can reduce insulin sensitivity
C	Heart Rate	↑	★☆☆ Minor	2 studies	An increase in heart rate is present after nicotine ingestion due to the stimulatory properties
C	Libido	—	—	2 studies	There do not appear to be any significant interactions with nicotine and libido
C	Penile Girth	↓	★☆☆ Minor	1 study	A decrease in penile girth in

					the flaccid state is noted, which is thought to be secondary to reduced blood flow
C	Depression	—	—	1 study	No significant influence on depressive symptoms
C	Anxiety	↓↑	★☆☆ Minor	2 studies	Reduced anxiety symptoms have been noted in persons with cognitive decline, where anxiety was relieved as a symptoms of cognitive decline. In otherwise healthy persons prone to anxiety attacks, nicotine may be able to cause them.
C	Cognition	↑	★☆☆ Minor	1 study	An improvement in cognition has been noted in persons with mild cognitive impairment
C	Memory	↑	★☆☆ Minor	1 study	An increase in memory has been noted with ingestion of nicotine in persons with mild cognitive impairment
C	Weight	↓	★☆☆ Minor	2 studies	Possible minor weight reducing effects occur in interventions using nicotine, but they are highly unreliable and likely mediated by lesser food intake rather than inherent fat burning effects
C	Reaction Time	↓	★☆☆ Minor	1 study	A decrease in reaction time is noted with acute nicotine ingestion
C	Self Control	—	—	1 study	No significant influence on self control and inhibitions
C	Testosterone	—	—	1 study	No significant influence on testosterone levels
C	Prolactin	↑	★☆☆ Minor	1 study	An increase in prolactin has been noted with nicotine ingestion

C	Luteinizing Hormone	↑	★☆☆ Minor	1 study	An increase in luteinizing hormone has been noted
C	Growth Hormone	↓	★☆☆ Minor	1 study	An acute suppression of growth hormone has been noted with nicotine to a small degree
C	Insulin	—	—	1 study	No significant influence on fasting insulin levels
C	Blood Glucose	—	—	1 study	No significant influence on fasting glucose levels
C	Cortisol	—	—	1 study	No significant influence on cortisol levels
C	Fat Oxidation	—	—	1 study	When nicotine increases metabolic rate, there is no change in rates of fat or glucose oxidation.
C	Metabolic Rate	↑	★☆☆ Minor	1 study	Chewing gum containing nicotine can increase the metabolic rate in a dose-dependent manner (3.7-4.9% with 1-2mg nicotine) when measured for the 180 minutes following 20 minutes of chewing.
D	Attention	—	—	1 study	No significant influence on attention in otherwise healthy persons

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Nigella sativa

Also known as: Nigella cretica, Black cumin, Black seeds, Roman coriander, Nutmeg flower, Fennel flower, Ajaji

Nigella sativa (Black Cumin) is a medicinal Spice that appears to be active in the dose used to season food products. It has a potent bioactive known as thymoquinone which shows promise in treating epilepsy, allergies, and boosting the immune system.

See [Nigella sativa on Examine.com](#)

How to Take

Supplementation of the seeds of nigella sativa usually use the basic seed extract (a crushed powder of the seeds with no further processing or concentration) or the seed oil, both of which do not require a large degree of processing as the medicinal dosage is close to the raw product's natural state. While 1 gram of the seed tends to always underperform relative to 2-3 grams, there is not sufficient evidence to suggest which of those two higher doses is 'better' and thus something within that range is recommended. As the seeds are about a quarter to one third fatty acids (ie. the seed oil) then supplementation of any black seed oil product would be 3-4 times lower than the aforementioned range (giving a recommended range of 250-1,000 mg daily).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	HDL-C	—	—	8 studies	Mild increases have been reported in some cases, but for the most part <i>nigella sativa</i> does not influence HDL cholesterol in the active dosage range.
B	LDL-C	↓	★☆☆ Minor	8 studies	Reductions in LDL-C are mild at best and only occur in persons with impaired lipid profiles (high cholesterol or dyslipidemia), but they do appear to occur with ingestion of the seed extract
B	Total Cholesterol	↓	★☆☆ Minor	8 studies	Decreases have been sporadically noted in persons with high cholesterol initially, the cholesterol reductions are mild at best and do not affect persons with normal cholesterol.

B	Triglycerides	↓	★☆☆ Minor	8 studies	The decreases in triglycerides only affect those with high triglycerides, and the decrease scales with severity of hyperlipidemia (mild elevation of TGs is met with a 1-5% decrease, significantly elevated TGs are met with a 15-20% reduction).
B	Blood Pressure	↓	★☆☆ Minor	4 studies	The reduction in blood pressure is only seen in hypertensives and very mild (1-3mmHg), likely not practically relevant at all.
B	Weight	↓	★☆☆ Minor	4 studies	One study has noted weight loss, but due to the reduction in appetite and no records of food intake the possibility of subjects losing weight due to eating less cannot be ruled out. Other studies have failed to find an influence of treatment.
B	Liver Enzymes	—	—	5 studies	There may be a reducing effect in instances of liver damage (this curative effect needs to be explored more), and there are no alterations in liver enzymes that would be indicative of liver damage.
C	Blood Glucose	—	—	5 studies	Although the best evidence to date shows no change in blood glucose, these studies were not structured to assess the influence on diabetics; in diabetics, there appears to be a significant reduction in glucose.
C	Symptoms of Rheumatoid Arthritis	↓	★☆☆ Minor	1 study	A modest reduction in symptoms of rheumatoid arthritis (9%) has been noted with ingestion of the seeds
C	Pain	↓	★☆☆ Minor	1 study	Pain as a side-effect of rheumatoid arthritis is

					modestly reduced.
C	Allergies	↓	★★★☆☆ Notable	4 studies	Supplementation of the seed appears to beneficially influence most symptoms associated with allergies and most causes of the allergies (rhinitis, eczema, asthma, etc.), with the magnitude being somewhat notable among supplements.
C	Nasal Congestion	↓	★☆☆☆☆ Minor	1 study	Nasal congestion as a side-effect of allergic rhinitis is slightly reduced following the treatment of rhinitis with <i>nigella sativa</i> seeds
C	Seizure Frequency	↓	★☆☆☆☆ Minor	1 study	Seizure frequency in children with poorly controlled epilepsy is significantly reduced with a seed extract, and while it was quite notable in some children it was variable enough to also be quite modest in others. Needs more research to assess potency.
C	Food Intake	—	—	1 study	No significant alterations in food intake associated with ingestion of <i>nigella sativa</i> .
C	Creatinine	—	—	2 studies	No significant influence on serum creatinine
C	Heart Rate	—	—	1 study	No significant influence on heart rate or pulse rate.
C	Serum Albumin	↑	★☆☆☆☆ Minor	3 studies	An increase in serum albumin has been noted, and the reason for this currently unknown.
C	Proteinuria	—	—	1 study	No significant influence on the rate of proteinuria, suggesting no kidney damage associated with supplementation.
C	Uric Acid	—	—	2 studies	

					No statistically significant alterations in uric acid concentrations in serum
C	Pulmonary Function	↑	★☆☆ Minor	2 studies	While the magnitude of benefit has not yet been compared to reference drugs, <i>nigella sativa</i> extracts appear to benefit lung function in both asthmatics and persons with otherwise damaged lung function; no studies in otherwise healthy persons.
C	Subjective Well-being	↑	★★★☆☆ Notable	1 study	Although only based on one study, in men with central obesity and a wide variety of general health complaints supplementation has outright abolished all measured complaints such as loss of libido, high appetite, pain, and forgetfulness.
C	Adiponectin	—	—	1 study	No significant influence on adiponectin concentrations
C	C-Reactive Protein	—	—	1 study	The alterations in C-reactive protein failed to reach statistical significance, but are otherwise not very well explored.
C	Free Testosterone	—	—	1 study	No significant influence on circulating free testosterone concentrations in men with central obesity
C	Appetite	↓	★☆☆ Minor	1 study	The side-effect of 'high appetite' was effectively abolished in men with central obesity, which may underlie the observed weight loss; food intake was not reported in this study.
C	Bilirubin	—	—	2 studies	Despite treating the viral load of hepatitis C, no significant changes in serum bilirubin exist.

C	Processing Speed	↑	★☆☆ Minor	1 study	Trail making test time in older adult men appears to be reduced modestly with daily supplementation of nigella seed extract
C	Processing Accuracy	—	—	1 study	No significant improvements in the accuracy of cognitive processing appears to occur with supplementation of nigella sativa seeds.
C	Attention	↑	★☆☆ Minor	1 study	Attention processing on trail making tests appears to be increased.
C	Cognition	↑	★☆☆ Minor	1 study	A slight improvement in cognition has been noted with supplementation of nigella seed extract in older persons
C	Memory	↑	★☆☆ Minor	1 study	There appears to be a small but respectable (15-20% higher than baseline) improvement in logical memory and 30 minute recall in older subjects supplementing the seeds in their daily lifestyle.
C	Working Memory	—	—	1 study	Despite improvements in logical memory and 30 minute recall, digit span tests are not affected by supplementation of <i>nigella sativa</i> .
D	HbA1c	↓	★☆☆ Minor	1 study	A mild decrease in HbA1c has been noted in diabetics given the seeds as an adjuvant to standard therapy
D	Cortisol	—	—	1 study	No significant alterations in cortisol concentrations seen with supplementation of the seeds.
D	Asthma	↓	★☆☆ Minor	2 studies	Asthmatic symptoms appear to

					be reduced with supplementation of <i>nigella sativa</i> seeds, in part due to benefits to lung function and in part due to its anti-allergic properties. Potency has not been adequately assessed
D	Immunity	↑	★☆☆ Minor	1 study	Macrophage phagocytic activity and killing potential is increased following oral ingestion of the seed extract.
D	Viral Load	↓	★★★☆☆ Notable	1 study	A pilot study in hepatitis C noted that the viral load was reduced to 38.6% of baseline with a modest dosage of the seed oil, a fairly drastic reduction.
D	Red Blood Cell Count	↑	★☆☆ Minor	1 study	A normalization of RBC count has been noted in the treatment of hepatitis C with the seed oil of <i>nigella sativa</i>
D	White Blood Cell Count	↑	★☆☆ Minor	1 study	A normalization of WBC count has been noted in persons with hepatitis C being treated with the seed oil.

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Nitrate

Also known as: Beetroot extract

Inorganic nitrate (NO₃⁻) is an endogenously produced food product that appears to have a critical role in blood pressure and cardiovascular health management; the main ingredient in Beet Root, nitrate converts to Nitric Oxide by various means independent of the NOS enzyme and may aid exercise.

See [Nitrate on Examine.com](#)

How to Take

The optimal dosage of nitrate supplementation tends to be 0.1-0.2mmol/kg (or 6.4-12.8mg/kg), which is the range of: 440-870mg for a 150lb person 580-1,160mg for a 200lb person 730-1,450mg for a 250lb person
Supplementation of nitrates via Beet Root is equally feasible, and beet root itself is dosed according to its nitrate content.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Blood Pressure	↓	★★★☆☆ Notable	6 studies	Appears to be a fairly potent blood pressure reducing agent during periods of high blood pressure (at rest during disease states or during exercise in healthy persons) without having a reducing effect when blood pressure is normalized.
C	Plasma Nitrate	↑	★★★★★ Strong	1 study	Nitrate ingestion strongly and fairly reliably increases plasma nitrate and nitrite.
C	Insulin Sensitivity	—	—	1 study	No significant observed effects on insulin sensitivity.
C	Blood Flow	—	—	1 study	No significant influence on blood flow in studies that use flow-mediated vasodilation
C	Anaerobic Running Capacity	↑	★★★☆☆ Notable	1 study	The increase in performance on a sprint test appeared to be fairly significant, and pending more evidence nitrates may be

					a reference comparator.
C	Power Output	—	—	1 study	No significant effect on acute power output
C	Heart Rate	—	—	2 studies	Does not appear to significantly influence heart rate
C	Aerobic Exercise	↑	★☆☆ Minor	2 studies	The performance enhancing aspect of nitrate supplementation in prolonged aerobic exercise is less than that seen in shorter duration cardiovascular exercise, and is only somewhat effective for longer periods.
C	Rate of Perceived Exertion	↓	★☆☆ Minor	2 studies	May reduce the rate of perceived exertion in some instances (prolonged cardiovascular exercise), but is not highly reliable.
C	Oxygenation Cost of Exercise	↓	★★★☆☆ Notable	2 studies	A notable reduction in the oxygenation cost of exercise associated with nitrate supplementation.
C	Functionality in Elderly or Injured	—	—	1 study	No significant influence has been noted on functional tests in elderly persons given nitrate supplementation
C	Cognitive Decline	—	—	1 study	Short-term supplementation failed to restore cognitive decline in older persons, no evidence as to whether nitrate exerts a preventative effect.
C	Exercise performance during hypoxia	↑	★☆☆ Minor	2 studies	Appears to preserve exercise performance during insufficient oxygen, but not to a remarkable degree

Noopept

Also known as: N-phenylacetyl-L-prolylglycine ethyl ester, Noopeptide, Ноопепт, GVS-111

Noopept (N-phenylacetyl-L-prolylglycine ethyl ester) is a racetam molecule which appears to be similar to Piracetam in effects, but at a lower oral dose. Noopept similarly is highly neuroprotective in research animals, and may enhance cognition in those with cognitive decline.

See [Noopept on Examine.com](#)

How to Take

The recommended oral intake is between 10 and 30mg, which is from the manufacturer of Noopept for the purposes of treating cerebrovascular and posttraumatic cognitive deficiency. Optimum human dose for cognitive enhancement is not currently known.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Rehabilitation of Cerebral Trauma	↑	★★★☆☆ Notable	1 study	The one trial with Noopept suggests surprisingly effective rehabilitative effects, outperforming Piracetam as comparator.

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Olive leaf extract

Also known as: Olive polyphenols

Olive leaf extract comes from the leaves of olive plants, and is distinct from Olive Oil; the leaf extract contains phenolics such as oleuropein, and appears to have highly protective effects against LDL oxidation and may also benefit glucose metabolism and skin health.

See [Olive leaf extract on Examine.com](#)

How to Take

Supplemental olive leaf is taken in the 500-1000mg range daily, although supplements with even as low as 10mg (as seen in olive oil products) may confer good protection against LDL oxidation. At least for LDL oxidation, olive food products may suffice rather than supplementation.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Oxidation of LDL	↓	★★★☆☆ Notable	8 studies	The decrease in LDL oxidation seen with olive oil phenolics appears to be of notable potency due to its reliability (occurring in both healthy persons and diseased persons, chronically and acutely) and a reduction in LDL oxidation rates can exceed 25% in some studies with low intakes of olive phenolics (enough from virgin olive oil consumption)
B	LDL-C	↓	★★☆☆☆ Minor	5 studies	A decrease in LDL-C seems to be somewhat consistent, but the magnitude of decrease is not overly impressive relative to other agents
B	HDL-C	↑	★★☆☆☆ Minor	7 studies	The increase in HDL seen with olive phenolics is somewhat inconsistent and not to a large magnitude when it occurs
B	Total Cholesterol	↓	★★☆☆☆ Minor	4 studies	There appears to be somewhat of a decrease in

					total cholesterol (mostly due to LDL) with olive leaf consumption; it is not overly reliable
B	Triglycerides	—	—	5 studies	The majority of the evidence suggests that there is no impressive effect on triglycerides with olive phenolic consumption
B	Blood Pressure	↓	★★★☆☆ Notable	4 studies	One study assessing the potency in hypertensive persons noted it was comparable to Captopril, and olive leaf appears to be potent when it can reduce blood pressure. It does not appear to reduce blood pressure in normotensive persons, however
C	Liver Enzymes	—	—	2 studies	No significant influences on liver enzymes have been noted in trials that assess them (safety reasons)
C	Insulin Sensitivity	↑	★★☆☆☆ Minor	1 study	An increase in insulin sensitivity has been noted in otherwise healthy persons (Matsuda Index and oral glucose tolerance test) and thought secondary to the pancreas; may be relevant to otherwise healthy persons
C	Blood Glucose	↓	★★☆☆☆ Minor	2 studies	There appears to be significant interactions with olive leaf and diabetes, and research is too preliminary to come to conclusions. Olive leaf may reduce blood glucose in diabetics only
C	Insulin	↓	★★☆☆☆ Minor	2 studies	A decrease of fasted and postprandial insulin with olive leaf consumption has been noted, not to a remarkable degree
C	IGF Binding Protein	↑	★☆☆☆☆	1 study	

C	IGF-1	—	Minor	1 study	An increase in IGF binding proteins has been noted in one study (which would sequester and reduce the activity of IGF hormones); potency of this interaction unable to be determined (no reference drug)
C	Inflammation	—	—	1 study	No significant influence on circulating IGF-1 nor IGF-2 levels
C	Weight	—	—	2 studies	Overall, there does not appear to be a significant effect of olive phenolic consumption on weight
C	General Oxidation	↓	★☆☆ Minor	1 study	Is able to reduce oxidative parameters in the blood when they are measured.
C	Lipid Peroxidation	↓	★☆☆ Minor	2 studies	Appears to reduce biomarkers of lipid peroxidation.
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	2 studies	Appears to induce the activity of the enzyme known as glutathione peroxidase
C	DNA Damage	↓	★★★ Notable	1 study	The one study to measure DNA damage (via 8-oxo-dGF as a biomarker) noted up to 50% reductions in mitochondrial and urine measurements; a fairly significant reduction.
C	HbA1c	↓	★☆☆ Minor	1 study	A minor decrease in HbA1c has been noted with olive leaf consumption
C	Cell Adhesion Factors	↓	★★★ Notable	1 study	A decrease was noted in CD40 and MCP1 adhesion factors, and this is notable as this downregulation was dose-dependently related to

					ingested tyrosol/hydroxytyrosol and may explain the reduced LDL oxidation
D	Carbohydrate absorption	↓	★☆☆ Minor	1 study	There appears to be a decrease in either the rate or overall amounts of carbohydrate absorption seen with olive leaf consumption

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Origanum vulgare

Also known as: Oregano, Oil of Oregano, Wild Marjoram

Origanum vulgare (Oregano) is a spice. Its essential oil component, oil of oregano, is sold as an immune booster. The oil has various antimicrobial properties and can preserve food quality during storage. Human evidence for supplementation is lacking.

See [Origanum vulgare on Examine.com](#)

How to Take

The only study on using oil of oregano for oral supplementation used a dose of 600mg. To make tea, steep 15g of oregano leaves in 250mL of water. The tea is traditionally used to aid digestion, while the oil has antibacterial properties that may boost the immune system. Both the tea and oil is usually supplemented once a day.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Intestinal Parasites	↓	★★★☆☆ Notable	1 study	One lone study (potential financial influence) has noted ablation of parasites in infected humans (77% of study group) and a reduction otherwise as assessed by stool samples.

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Ornithine

Also known as: L-Ornithine

Ornithine is one of the three amino acids involved in the Urea cycle, alongside L-Arginine and L-Citrulline; this amino acids appears to reduce elevated ammonia levels when supplemented, and preliminary evidence suggests an ergogenic role due to this.

See [Ornithine on Examine.com](#)

How to Take

Ornithine supplementation (as hydrochloride) is taken in the range of 2-6g daily. Most studies use a dose in this range, but despite serum levels being somewhat dose dependent there is a chance of intestinal distress at doses above 10g. Most studies use Ornithine hydrochloride (Ornithine HCl) which appears to be effective. Ornithine HCl is 78% Ornithine by weight, and so for the 2-6g range an equivalent dose for L-Ornithine L-Aspartate (50% Ornithine) would be 3.12-9.36g and an equivalent dose for L-Ornithine α -ketoglutarate (47% Ornithine) would be 3.3-10g. These two forms are theoretically more effective, but lack sufficient comparative testing.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Heart Rate	—	—	3 studies	For the most part there is no significant effect, although one trial did not that after exercise during a recovery period ornithine had a higher heart rate. The reason for this is not known
C	Ammonia	↓ ↑	★☆☆ Minor	2 studies	Although supplementation of Ornithine is recommended to reduce ammonia (which it appears to do in both models of hepatic encephalopathy and prolonged physical exercise) at least one study noted that for short term strenuous exercise ornithine caused an increase in ammonia
C	Urea	↑	★☆☆ Minor	2 studies	Mixed effects, but it appears that when ammonia is decreased that urea is also increased but if ammonia is unchanged whatever reason

					for this also means that urea is unchanged.
C	Anaerobic Running Capacity	—	—	1 study	Performance during short term cardiovascular exercise (assessed by time to exhaustion) does not appear to be significantly affected.
C	Oxygen Uptake	—	—	1 study	Oxygen uptake during exercise does not appear to be significantly altered
C	Training Volume	—	—	1 study	No significant influence on the amount of work that can be conducted on a cycle ergometer during short-term testing
C	Fatigue	↓	★☆☆ Minor	2 studies	A reduction in fatigue has been noted for both prolonged exercise, hepatic pathology, and for hangovers; all situations characterized by excessive ammonia concentrations in the blood.
C	Blood Pressure	—	—	1 study	No significant interactions with blood pressure
C	Sleep Quality	↑	★☆☆ Minor	1 study	The increase in sleep quality was secondary to reducing the adverse effects of excessive drinking, and was measured by self-report
C	Cortisol	↓ ↑	★☆☆ Minor	1 study	Increases have been noted with intravenous ornithine (not in human trials table) while decreases have been noted following treatment of hangovers. The most practical study of using ornithine as a preworkout supplement failed to find any effect

Orthosiphon stamineus

Also known as: Java, Misai kucing, Kumis kucing, cats whiskers, rau meo, cay bac, remujung, moustaches de chat, yaa nuat maeo

Orthosiphon stamineus (Java or Cat's Whiskers) is a plant whose leaves make a health tea, used mostly for its antiinflammatory and urinary health properties. It appears to be a large source of both Rosmarinic Acid and methylated flavonoids.

See [Orthosiphon stamineus on Examine.com](#)

How to Take

There is not enough information to get an ideal dose, but at this moment it seems that a 70% ethanolic extract would be the most prudent supplemental dosage for the production of leptin in the body. Since this has been noted in a highly variable range (as low as 20mg/kg in mice, as high as 450mg/kg in rats) it is uncertain what the best oral dose to take would be. Nonetheless, human equivalents for the above range are: 110-4,900 mg for a 150lb person 150-6,500 mg for a 200lb person 180-8,100 mg for a 250lb person The diuretic effect has been noted with tea, and thus brewing a tea from the leaves may be sufficient.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Diuresis	—	—	1 study	Despite both traditional usage and rat studies, the lone study assessing the diuretic effects of 10g of the fresh leaves has failed to find any effect.
D	Skin quality	↑	★★★☆☆ Notable	1 study	The lone study in women with oily skin noted that improvements in skin quality with a 2% <i>orthosiphon</i> cream were greater than the reference drug of 1% zinc gluconate on all parameters.

Oxiracetam

Also known as: 4-hydroxy-2-oxo-pyrrolidinoacetamide, ISF-2522

Oxiracetam is one of the three first-tier Racetam compounds, being produced after both Piracetam and Aniracetam. Oxiracetam appears to enhance the release of excitatory neurotransmitters and can aid in memory formation, but lacks human studies.

See [Oxiracetam on Examine.com](#)

How to Take

Supplementation of Oxiracetam tends to be in the dosage range of 1,200-2,400mg taken over the course of a day, either in two to three evenly spread dosing periods (such as three doses of 400mg or 800mg). No studies have assessed whether or not oxiracetam would benefit from being taken with a meal, but it should be taken approximately one hour prior to a learning activity.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Cognitive Decline	↓	☆☆☆ Minor	5 studies	Appears to reliably reduce the cognitive decline and related symptoms seen in dementia and other organic brain deterioration states, with particular efficacy towards verbal skill in doses above 1,200mg
C	Memory	↑	☆☆☆ Minor	2 studies	Although it has mechanisms and animal evidence to support improvements in memory in healthy youth, all human studies are currently in those with cognitive decline
C	Functionality in Elderly or Injured	—	—	1 study	The one study to note functional capabilities in persons with dementia given oxiracetam failed to find a significant treatment effect
C	Verbal Fluency	↑	☆☆☆ Minor	2 studies	Appears to favor improvements in verbal fluency in persons with cognitive dementia, despite benefiting most

					parameters measured
C	Quality of Life	↑	★☆☆ Minor	1 study	The one study to measure subjective quality of life in persons with dementia found a significant improvement with supplementation
C	Symptoms of Alzheimers	—	—	1 study	The lone study in persons with Alzheimer's rather than organic cognitive decline has failed to find any benefit associated with supplementation

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Panax ginseng

Also known as: True Ginseng, Ginseng, Panax, Mountain Ginseng, Wild Ginseng

Panax Ginseng is commonly referred to as the 'True Ginseng' (being the most researched 'Ginseng' actually belonging to the plant family of 'Ginseng') and appears to be effective for mood, immunity, and cognition; subpar for erections, testosterone, and exercise.

See [Panax ginseng on Examine.com](#)

How to Take

Panax Ginseng tends to be taken in doses of 200 to 400mg daily for general 'preventative' medicine, although some studies on the inclusion of Panax Ginseng in a multivitamin suggest doses as low as 40mg might be bioactive. The 400mg dose appears to confer most cognitive benefit. These doses refer to standard 'Ginseng Extract' which is around 2-3% total Ginsenosides, and is a once daily dosage. Trials using Korean Red Ginseng extract for erectile health and libido enhancement tend to use 3g of total KRG extract daily, in three doses of 1000mg.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Blood Glucose	↓	★☆☆ Minor	10 studies	A decrease in fasting blood glucose has been noted over time with standard supplemental doses of panax ginseng in diabetics, with this dose being ineffective in altering the blood glucose of non-diabetics; high (20g) doses may acutely reduce blood glucose in healthy persons
B	Insulin Sensitivity	—	—	3 studies	More evidence than not suggests no significant improvement in insulin sensitivity, although it is still a minor possibility
B	Blood Pressure	—	—	4 studies	Although there may be a slight blood pressure reducing effect in persons with the highest blood pressure, overall there is not a significant reducing effect of panax ginseng

B	Subjective Well-Being	↑	★☆☆ Minor	5 studies	There appears to be an increase in well being and happiness in persons who either have a disease state treated (ie, better glycemic control in diabetes or less erectile dysfunction) and this may also apply to acute usage of 400mg panax ginseng during acute mental stress. In an unstressed and healthy person, panax ginseng is unlikely to have benefit
B	Cognition	↑	★☆☆ Minor	4 studies	An increase in cognition is seen acutely and thought to be due to anti-fatigue effects, with nonfatigued individuals not experiencing an increase in cognitive performance
B	Symptoms of Menopause	↓	★☆☆ Minor	3 studies	May decrease some symptoms associated with menopause, mostly related to libido, but this is unreliable.
B	Erections	↑	★☆☆ Minor	4 studies	An improvement in erectile dysfunction is seen with 3g of Korean Red Ginseng (fermented panax ginseng, regular panax ginseng not as well tested) which is thought to be secondary to anti-fatigue effects and improved blood flow
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	2 studies	An increase in all three main antioxidant enzymes (SOD, glutathione peroxidase, and catalase) appear to occur to a small degree following ingestion of Panax ginseng
C	General Oxidation	↓	★☆☆ Minor	1 study	Oxidation in the body appears to be reduced, which is thought to be secondary to induction of antioxidant enzymes
C	Inflammation	↓	★☆☆ Minor	1 study	A decrease in IL-6 concentrations has been noted

C	Muscle Damage	↓	★☆☆ Minor	1 study	A decrease in biomarkers of muscle damage (creatine kinase) has been noted 72 hours after exercise in which panax ginseng was preloaded
C	Anaerobic Running Capacity	—	—	1 study	Insufficient evidence to support a role of panax ginseng in improving exercise performance
C	Fat Oxidation	—	—	1 study	Rates of fat oxidation during exercise appear unchanged
C	Oxygenation Cost of Exercise	—	—	1 study	No significant influence on oxygen uptake during exercise
C	Heart Rate	—	—	1 study	No significant influence on heart rate
C	Lactate Production	↓	★☆☆ Minor	1 study	A decrease in lactate has been noted one hour into training in heat, with no significant influence prior to one hour
C	Rate of Perceived Exertion	—	—	1 study	No significant influence on the rate of perceived exertion during exercise
C	Endothelial Function	↑	★☆☆ Minor	2 studies	A possible increase in endothelial reactivity is noted with panax ginseng supplementation
C	Triglycerides	—	—	2 studies	No significant alterations in triglycerides and fatty acids in the fasted state or during exercise
C	Calmness	↑	★☆☆ Minor	1 study	Has been noted to improve self-reported calmness
C	Blood Flow	↑	★☆☆ Minor	2 studies	An increase in blood flow has been noted with panax ginseng supplementation

C	Libido	↑	★☆☆ Minor	1 study	May increase libido as a side-effect of reducing the symptoms associated with menopause, may not work inherently in youth or men
C	Sleep Quality	↑	★☆☆ Minor	1 study	Has been noted to improve the first-night effect (impaired sleep when sleeping in a new location) after a week of supplementation; possibly of interest to frequent travellers
C	HbA1c	↓	★☆☆ Minor	2 studies	A possible reduction in HbA1c, but small in magnitude and unreliably seen
C	Insulin	—	—	2 studies	No significant influence on fasting insulin levels seen with panax ginseng
C	Testosterone	↑	★☆☆ Minor	2 studies	May increase testosterone in infertile men, has also failed in fertile men to influence testosterone; likely a mere antioxidative effect in damaged testicles
C	Prolactin	—	—	1 study	No significant influence on prolactin in men
C	HDL-C	↑	★☆☆ Minor	2 studies	May increase HDL-C levels, seems unreliable in doing so
C	LDL-C	↓	★☆☆ Minor	2 studies	May reduce LDL-C levels to a very small degree, seems unreliable in doing so
C	Weight	—	—	2 studies	Does not appear to have any weight reducing properties, although it has been reported in one study secondary to improving the glycemic profiles of diabetics
C	Depression	↓	★☆☆ Minor	1 study	Anti-depressive effects may be

			Minor		secondary to reducing menopausal symptoms
C	Estrogen	—	—	1 study	No significant influence on estrogen levels in women
C	Total Cholesterol	↓	★☆☆ Minor	2 studies	Possible cholesterol reducing effect, but appears unreliable
C	C-Reactive Protein	—	—	2 studies	No significant influence on C-reactive protein levels
C	Vaccine Augmentation	↑	★☆☆ Minor	1 study	Has been noted to increase the antibody response to vaccinations when taken prior
C	Reaction Time	↓	★☆☆ Minor	2 studies	Mixed effects on reaction time, with a possible decrease occurring
C	Oxidation of LDL	↓	★☆☆ Minor	2 studies	A possible reducing effect on the oxidation of LDL, secondary to reduction of oxidation in general; however, this appears to be unreliable
C	DNA Damage	↓	★☆☆ Minor	1 study	Can decrease the rates of DNA damage noted in lymphocytes, which may be related to the anticancer effects of panax ginseng
D	Overall Cancer Risk	↓	★★★☆☆ Notable	2 studies	Has been associated with over half the risk of all tested forms of cancer, possibly confounded with a healthy lifestyle in general (as the study in question did not exert many controls)
D	Cognitive Decline	↓	★☆☆ Minor	1 study	A decrease in symptoms associated with cognitive decline has been noted
D	Pancreatic Cancer Risk	↓	★★★☆☆ Notable	1 study	More than a halving of pancreatic cancer risk has been noted with panax ginseng

D	Ovarian Cancer Risk	↓	★★☆ Notable	1 study	More than a halving of ovarian cancer risk has been associated with daily panax ginseng ingestion
D	Colorectal Cancer Risk	↓	★★☆ Notable	1 study	More than a halving of the risk of colorectal cancer has been noted with panax ginseng daily ingestion

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Patchouli

Also known as: Pogostemon cablin, Patchouly, Patchy

Patchouli is the name given to the herb Pogostemon cablin and has a history of usage for aromatherapy and as a perfume cosmetic ingredient; it may possess anti-viral and anti-inflammatory properties.

See [Patchouli on Examine.com](#)

How to Take

There is no human evidence at this moment in time, but oral ingestion of patchouli to rats at 40mg/kg is associated with anti-depressive effects. This is an approximate human dose of: 440mg for a 150lb person 580mg for a 200lb person 730mg for a 250lb person These are estimated human dosages based on the animal evidence.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	CNS activity	↓	★☆☆ Minor	1 study	The decrease in CNS activity was not overly remarkable with Patchouli aromatherapy

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Pelargonium sidoides

Also known as: African Geranium, South African Geranium, Kaloban EPs7630, EPs 7630, Umckaloabo, rabas

Pelargonium sidoides (African Geranium) is a German phytopharmaceutical for the treatment of acute bronchitis. Secondary to its antiinfective effects it can greatly reduce all symptoms of acute bronchitis and may be of use to the common cold, herpes, and general immune support.

See [Pelargonium sidoides on Examine.com](#)

How to Take

Supplementation of pelargonium sidoides almost always uses the patented extract known as EPs7630, which is an 11% ethanolic extract of the roots where either 4.5mL of the tincture (30 drops) or 30mg of the capsules is approximately equal to 800mg of the root extract (since it is concentrated to 1:8-10, there is some inherent variability). The dosage to taken varies based on age, and as follows: 10 drops (1.5mL) or 10mg of EPs7630 is taken thrice daily before meals for those under six years of age 20 drops (3.0mL) or 20mg of EPs7630 is taken thrice daily before meals for those between six and twelve 30 drops (4.5mL) or 30mg of EPs7630 is taken thrice daily before meals for those above twelve years of age While the vast majority of studies have used EPs7630 specifically, any hydroalcoholic (water and ethanol) extraction which equals around 800mg of the plant daily.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Symptoms of Acute Bronchitis	↓	★★★ Strong	11 studies	The standard dose of EPs7630 appears to greatly reduce all symptoms of acute bronchitis, being able to outright eliminate symptoms in as little as 60% of patients (cough and hoarseness related) and up to 95% of persons (sputum and rhonchi related) with efficacy within three days increase over two weeks.
A	Lung Function	↑	★☆☆ Minor	10 studies	Secondary to treating sickness (bronchitis, URTIs, common cold) there is improvement in sputum content, rhonchi, breathing, coughing, and chest pain while coughing relative to placebo; while the improvements are marked, they only occur secondary to treating illness.

A	Cough	↓	★☆☆ Minor	12 studies	Symptoms of cough, <i>in the context of acute bronchitis</i> , are reduce in most subjects with around 50-60% of subjects reporting remission. There isn't an improvement in other lung disorders though, so this is more reflective of treatment of acute bronchitis.
A	Treatment of Headaches	↑	★☆☆ Minor	10 studies	Headaches as a side effect of acute bronchitis are pretty much abolished with the treatment of acute bronchitis from this herb; it is doubtful that headaches from other causes aside from sickness are treated in a similar manner.
B	Fever	↓	★★★☆☆ Notable	9 studies	Fever as a side effect of acute bronchitis is reduced quite potently (80-90% of persons reporting elimination of fever) due to the potent treatment of acute bronchitis, but there is no inherent anti-pyretic effect of this herb in other instances.
B	Fatigue	↓	★☆☆ Minor	7 studies	Fatigue as a side-effect of acute bronchitis is reduced quite respectably relative to placebo.
B	Rhonchi	↓	★★★☆☆ Notable	5 studies	Rhonchi (coarse rattling sound associated with mucus in the airway, similar to wheezing and crackles) appears to be eliminated in more than 90% of persons (with bronchitis) using the standard dose of this supplement within a week.
B	Subjective Well-being	↑	★☆☆ Minor	4 studies	Alongside improvements in sickness comes improved well being and vitality associated with supplementation over placebo.
B	Nasal Congestion	↓	★★★☆☆ Notable	4 studies	Nasal congestion appears to be decreased with

					supplementation of this herb, and while this is noted in acute bronchitis (most potently) it also affects other bacterial or viral instances such as the common cold and acute rhinosinitus.
C	Severity of Sickness	↓	★☆☆ Minor	1 study	In children with upper respiratory tract infections (URTIs), supplementation is effective in reducing symptom severity.
C	Appetite	↑	★☆☆ Minor	2 studies	There appears to be an increase in appetite during sickness in those given this supplement, and surprisingly this may not be limited to acute bronchitis.
C	Nausea	↓	★☆☆ Minor	2 studies	Nausea as a side-effect of acute bronchitis may be reduced, although studies assessing nausea/vomiting outside of acute bronchitis have failed to find an effect despite the subjects being sick.
C	Asthma	↓	★☆☆ Minor	1 study	In children with upper respiratory tract infections <i>and</i> asthma, the amount of asthmatic attacks during sickness appears to be slightly but significantly reduced relative to placebo.
C	Exercise-Induced Immune Suppression	↓	★☆☆ Minor	1 study	Although rates of sickness were not assessed, the alterations in the cytokine/immunoglobulin profile (increase in Immunoglobulin A, suppressing of IL-6 and IL-15) suggest less immunosuppression from exercise.
C	Immunoglobulin A	↑	★★★☆☆ Notable	1 study	The decrease in Immunoglobulin A noted with

					exercise in one study in marathon runners (60% relative to baseline) was reversed to a large increase (194% relative to baseline) when measured after exercise.
C	Aerobic exercise	—	—	1 study	There are no improvements in running performance in otherwise healthy athletes given this supplement for one month
C	Symptoms of the Common Cold	↓	★★★☆☆ Notable	1 study	All symptoms appear to be reduced with treatment of the standard dose of EPs7630. With symptom reduction after five days and the amount of persons with full resolution of symptoms being more than doubled relative to placebo.

Peppermint

Also known as: Menthol, Mentha piperita, Mentha balsamea

Peppermint (*Mentha piperita*) is a hybrid plant that is used for its sensory properties (aroma and taste) and the oil is used internally as a carminative and intestinal aid. It appears to be well supported for relaxing the stomach and intestines, and effectively reduces abdominal pain in IBS.

See [Peppermint on Examine.com](#)

How to Take

Oral supplementation of peppermint oil for the purpose of gastrointestinal health and motility involves consuming anywhere between 450-750mg of the oil daily in 2-3 divided doses, and this is around 0.1-0.2mL of the oil itself per dosage. The exact optimal dosage of peppermint is not known, and the numbers reflect a menthol content somewhere between 33-50%. Usage of peppermint for the treatment of headaches involves having a solution of 10% peppermint oil and applying a relatively thin layer to the front of your head upon the start of a headache, with another application after 15 minutes and 30 minutes (for three applications in total). Usage of peppermint for Aromatherapy does not follow any particular dosing, and similar to other forms of aromatherapy it should be used as either an oil or in a diffuser until a pleasant aroma permeates the vicinity. Any form of peppermint oil should be effective although for persons who experience heartburn (acid reflux) and wish to supplement with peppermint oil for their intestines, then an enteric coated capsule would be useful (since the muscle relaxing effects may affect the esophagus if the capsule breaks prematurely).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Symptoms of Irritable Bowel Syndrome	↓	★★★☆☆ Notable	8 studies	In persons with IBS, supplementation of peppermint oil appears to reliably and effectively reduce abdominal pain for as long as it is taken. Benefits are no longer seen two weeks after supplement cessation and abdominal pain is the only symptom notably reduced.
B	Nausea	↓	★★☆☆☆ Minor	5 studies	There appears to be interactions with peppermint as aromatherapy and reducing nausea, but the best evidence at this point in time is mixed and with some faults. More research is needed to see the potential role of peppermint aromatherapy in nausea

					reduction
C	Rate of Gastric Emptying	↑	★☆☆ Minor	1 study	A slight increase in the rate of gastric emptying is noted with peppermint oil, which is thought to be of benefit to persons with GERD
C	Subjective Well-being	↑	★☆☆ Minor	3 studies	Although mood state during cognitive testing is unaffected, quality of life is increased when headaches or abdominal pain is being treated with peppermint oil.
C	Colonic Tension	↓	★☆☆ Minor	1 study	Supplementation of peppermint oil four hours prior to a colonoscopy eases tension in the colon and aids reduces complaints associated with treatment.
C	Pain	↓	★☆☆ Minor	1 study	Pain has been noted to be reduced in instances where pain is associated with tightened intestinal tissue (ie. during a colonoscopy) or during tension headaches. No inherent analgesic effect is known
C	Treatment of Headaches	↑	★★★☆☆ Notable	2 studies	Preliminary evidence suggests that topical application of peppermint oil is effective in reducing tension headache severity when applied at the start of the headache (can work within 15 minutes), and is comparable to 1,000mg acetaminophen in potency
C	Irritability	↓	★☆☆ Minor	1 study	Irritability as a side-effect of tension headaches is reduced secondary to the treatment of tension headaches
C	Nipple Cracks	↓	★☆☆ Minor	2 studies	Topical application of peppermint oil or water appears to be more effective than placebo in alleviating

					nipple cracks in breastfeeding women
C	Flatulence	↓	★☆☆ Minor	1 study	Flatulence as a side-effect of IBS is reduced with ingestion of peppermint oil
D	Attention	↑	★☆☆ Minor	2 studies	Although there is no influence acutely in cognitive testing, there appears to be improvements in sustained attention processing with prolonged testing (10-40 minutes) with the aroma of peppermint. Suggesting an anti-fatigue effect.
D	Memory	—	—	1 study	The aroma of peppermint has been unable to influence memory processing (quantity or quality of memory formation) relative to control
D	Working Memory	—	—	1 study	Working memory does not appear to be influenced with the aroma of peppermint
D	Processing Accuracy	—	—	1 study	Processing accuracy does not appear to be significantly influenced with acute inhalation of peppermint extract during cognitive testing
D	Processing Speed	—	—	1 study	Processing speed is not significantly influenced with the aroma of peppermint during cognitive testing
D	Calmness	—	—	1 study	Subjective ratings of calmness during cognitive testing are not significantly influenced with the aroma of peppermint
D	Sedation	—	—	1 study	Peppermint aromatherapy does not appear to significantly influence the state of wakefulness
D	Treatment of Diffuse	↑	★★★☆☆	1 study	

	Esophageal Spasms		Notable		The pilot study on this topic did not have a placebo control, but noted complete resolution of spasms in all persons following a single supplemental dose of peppermint oil; a large amount of promise

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Phenylpiracetam

Also known as: Phenotropil, Carphedon, (RS)-2-(2-oxo-4-phenylpyrrolidin-1-yl)acetamide

Phenylpiracetam (Phenotropil) is a racetam drug derived from Piracetam in where the only modification is the addition of a phenyl group to its structure. It appears to require much lower doses for similar properties, and appears to have psychostimulatory effects.

See [Phenylpiracetam on Examine.com](#)

How to Take

Phenylpiracetam is taken at a dosage of 100-200mg acutely, and this dose is taken 2-3 times per day (totalling a daily range of 200-600mg). The lower range seems effective, but the optimal dosage is not yet known. The R-isomer appears to be more active on the common usages of phenylpiracetam (stimulation and cognition) than does the S-isomer, and while the racemic mixture (commonly sold version) is effective for cognitive decline it is not certain if it works for nootropic purposes in youth.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Stroke Recovery Rate	↑	★☆☆ Minor	1 study	Symptoms (cognitive and physical) seen after a stroke appear to be more rapidly recovered with daily usage of phenylpiracetam than with placebo
C	Functionality in Elderly or Injured	↑	★☆☆ Minor	1 study	Physical function and activities of daily living in elderly persons after a stroke appear to be benefitted with phenylpiracetam. While it should work in elderly persons without cognitive impairment, this has not been tested
C	Cognition	↑	★☆☆ Minor	3 studies	Cognition is improved in persons suffering from cognitive decline, organic brain lesions, and epilepsy. There are currently no studies conducted in otherwise healthy youth for the purpose of cognitive enhancement
D	Coanitive Decline	↓	★☆☆ Minor	1 study	

D	Cognitive decline	↓	★☆☆ Minor	1 study	The rate of cognitive decline appears to be significantly reduced following usage of phenylpiracetam
D	Anxiety	↓	★☆☆ Minor	1 study	Anxiety as a symptom of stroke has been reduced with phenylpiracetam. No studies currently exist in otherwise healthy persons with anxiety symptoms
D	Depression	↓	★☆☆ Minor	1 study	Depressive symptoms following a stroke appear to be reduced following ingestion of phenylpiracetam. Currently, there are no studies on otherwise healthy persons with depressive symptoms
D	Fatigue	—	—	1 study	Despite the usage of phenylpiracetam to treat asthenia, the lone study assessing this in persons with traumatic brain injuries failed to find a benefit (which may be a false negative if phenylpiracetam is inactive on brain injuries in the first place).

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Phosphatidylserine

Also known as: PS

Phosphatidylserine (PS) is an amino acid derivative compound that is fat-soluble and found in high amounts in the brain, where it contributes to cognitive functioning. Found in high amounts in fish, it may improve memory in the elderly and lowers Cortisol.

See [Phosphatidylserine on Examine.com](#)

How to Take

A standard dose of phosphatidylserine (PS) is 100mg, taken 3 times a day to total 300mg daily. This dose seems to be effective as a daily preventative against cognitive decline, and 100mg once daily may provide some degree of benefit (but may be lesser than 300mg). Studies in children and adolescents for the purpose of attention improvement tend to use 200mg, and a dose of 200-400mg has been used in adult non-elderly humans with success. Animal evidence tends to use a dose correlating to 550mg as well.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Cognition	↑	★☆☆ Minor	3 studies	The interactions of supplemental PS with cognition in healthy persons is not fully researched, but there appears to be a positive influence; this may be secondary to a reduction in stress and excitation (the latter resulting in an increase in attention) but increased glucose utilization is an unexplored possibility
B	Cortisol	—	—	4 studies	A decrease in exercise-induced cortisol has been noted with the bovine cortex sourced PS only, soy based supplements (which are usually the only ones sold now due to fear of Creutzfeldt–Jakob disease) have been shown to have outright no effect at doses up to 750mg
B	Cognitive Decline	↓	★☆☆ Minor	5 studies	There appears to be a protective effect against

					cognitive decline with PS supplementation above 300mg when using the bovine cortex form; usage of the soy based PS is not yet confirmed to have these effects, although it is possible
C	ADHD in Children	↓	★☆☆ Minor	2 studies	There appears to be reduced symptoms of both hyperactivity and attention deficit in children given PS, which may be more effective when the PS is complexed with fish oils
C	Attention	↑	★☆☆ Minor	1 study	The improvement in attention is associated with reducing the symptoms of attention deficit, an increase in attention outright has not yet been demonstrated
C	Working Memory	↑	★☆☆ Minor	1 study	Improvement in working memory may be due to improved attention
C	Stress	↓	★☆☆ Minor	2 studies	Possible stress reducing effects that appear independent of cortisol and heart rate, although these effects are unreliable
C	Golf performance	↑	★☆☆ Minor	1 study	Improved accuracy of golf swings thought to be due to a stress reducing effect
C	Subjective Well-Being	—	—	1 study	No significant influence on subjective well being noted
C	Processing Accuracy	↑	★☆☆ Minor	1 study	Increased processing accuracy has been noted in otherwise healthy persons at 400mg PS daily when testing was conducted in a fatigued state (post exercise)
C	Processing Speed	↑	★☆☆ Minor	1 study	Increased processing speed has been noted in otherwise healthy persons at 400mg PS

					daily when testing was conducted in a fatigued state (post exercise) which coincided with increase accuracy as well.
C	Testosterone	—	—	1 study	No significant influence on testosterone noted with PS supplementation
C	Fatigue	↓	★☆☆ Minor	2 studies	Unreliable effects, but a quite notable reduction in fatigue has been noted during intense exercise (85% VO2 max) which resulted in increased time to exhaustion. This was not present at lower intensities
C	Memory	↑	★☆☆ Minor	3 studies	Increases in memory have been noted in persons with cognitive decline. A memory improving effect in otherwise healthy people is theoretical (secondary to reducing stress, has been noted in rodents), but not demonstrated in humans yet
C	HDL-C	—	—	1 study	No significant influence on HDL-C with PS supplementation
C	LDL-C	—	—	1 study	No significant influence on LDL-C with PS supplementation
C	Total Cholesterol	—	—	1 study	No significant influence with PS supplementation on total cholesterol
C	Triglycerides	—	—	1 study	No significant influence on triglycerides seen at rest or during exercise with PS supplementation
C	Blood Pressure	—	—	1 study	No significant alterations in blood pressure noted with PS supplementation

C	Heart Rate	—	—	2 studies	No significant influence on heart rate with PS supplementation
C	Liver Enzymes	—	—	1 study	No significant influence on liver enzymes seen with PS supplementation
C	Reaction Time	—	—	1 study	No significant alterations in reaction time during treatment of cognitive decline
C	Anaerobic Running Capacity	↑	★★★☆☆ Notable	1 study	An increase in time to exhaustion has been noted in cycling at 85% of VO2 max with soy based phosphatidylserine (750mg) to the degree of 29+/-8%, which is quite notable. This is independent of cortisol, and requires further investigation
C	Fat Oxidation	—	—	1 study	No significant influence on fat oxidation during exercise
C	Oxygenation Cost of Exercise	—	—	1 study	No significant influence on oxygenation cost of exercise
C	Exercise-Induced Oxidation	—	—	1 study	No significant influence on oxidation biomarkers that are increased during exercise
C	Inflammation	—	—	1 study	No significant influence on inflammatory cytokines
C	Muscle Damage	—	—	1 study	No significant influence on serum biomarkers of muscle damage such as creatinine
C	Muscle Soreness	—	—	1 study	No significant influence on perceived muscle soreness
D	Forgetting	↓	★★☆☆☆ Minor	1 study	A reduced rate of forgetting immediate information (results in 'grasping' information easier) has been noted during

					treatment of cognitive decline with PS; an inherent anti-amnesiac effect is not known
D	Cerebral Glucose Utilization	↑	★☆☆ Minor	1 study	An increase in glucose utilization has been noted in persons with Alzheimer's to the degree of around 15%; this has not been investigated in otherwise healthy persons
D	Growth Hormone	—	—	1 study	No significant influence on exercise-induced growth hormone
D	Prolactin	—	—	1 study	No significant influence on exercise-induced prolactin
D	Lactate Production	—	—	1 study	No significant influence on exercise-induced lactate production

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Picrorhiza kurroa

Also known as: Kutki, Picrorhiza scrophulariiflora, Katuki, Kurro, Kutkin, Picroliv, Picrolax

Picrorhiza kurroa (Kutki or Picroliv) is a liver tonic from Ayurveda that, when used at low doses, appears to exceed Milk Thistle silymarins in potency. It is underresearched, but its liver protective effects and some other immunomodulatory properties hold potential.

See [Picrorhiza kurroa on Examine.com](#)

How to Take

Supplementation of picroliv (picroside I plus picroside II) appears to be most effective in at 12mg/kg (the higher dose, 24mg/kg, is not significantly more effective than 12mg/kg in most cases) and this leads to a preliminary human dosage of: 130 mg for a 150lb person 170 mg for a 200lb person 220 mg for a 250lb person Although the above dosage levels are ideal, lower doses also appear to be effective and the lone human study used a total picroside I and II dosage of around 25mg. If using an extract of picrorhiza kurroa, then the above dosage refers to the total picroside I and II content (kutkin or picroliv) rather than the weight of the plant itself. For example, a plant extract that is 1,000 mg and contains 4% picroliv will confer 40 mg picroliv.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Bilirubin	↓	☆☆☆ Minor	1 study	Supplemental <i>picrorhiza kurroa</i> can reduce bilirubin in a model of acute viral hepatitis, although no comparisons to reference drugs have yet been made.
C	Liver Enzymes	↓	☆☆☆ Minor	1 study	Supplementation of <i>picrorhiza kurroa</i> is able to reduce circulating liver enzymes in acute viral hepatitis. While animal research suggests it is more potent than Milk Thistle , the human evidence is not yet able to directly compare the two.
C	Symptoms of Vitiligo	↓	☆☆☆ Notable	1 study	The one study using <i>picrorhiza kurroa</i> for the purpose of treating vitiligo noted that after daily usage that 27% of the subjects experienced complete resolution of symptoms

					(curative effect)

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Piracetam

Also known as: Pyracetam, Pyrrolidone acetamide, 2-Oxo-1-pyrrolidine, Memotopril, Fezam (with cinnarizine), UCB6215

Piracetam is the parent compound of the Racetam class of Nootropic supplements, which somewhat controls excessive excitation in neurons. Touted as a subtle brain booster, it appears to increase cognitive capacities in elderly persons but awaits more testing in healthy persons.

See [Piracetam on Examine.com](#)

How to Take

Doses used in Piracetam, if the target is children (for Breath Holding Spells), vary from 40-100mg/kg with the lower end of the range (40-50mg/kg) usually being used. Similar doses are used for youth with Dyslexia. For adults, doses range from 1200-4800mg per day; the largest effective dose appears to be 1600mg of Piracetam taken thrice a day in divided doses to total 4800mg overall.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Cognitive Decline	↓	★★★☆☆ Notable	6 studies	There appears to be a notable reduction in the rate of cognitive decline (or rehabilitation of aged cognition) associated with high dose Piracetam over time and in a general manner. Piracetam is sometimes used as a comparator for cognitive decline.
C	Breath Holding Spells	↓	★★★★★ Strong	3 studies	Remarkably effective in reducing breath holding spells in infants at feasible dosages, nearly absolutely reducing the presence of breath holding spells with no apparent side-effects noted.
C	Stroke Recovery Rate	—	—	1 study	Ineffective in the one study where stroke recovery rate was assessed
C	Memory	↑	★★★☆☆ Minor	2 studies	Small increase in backwards recall with piracetam; nothing

					remarkable and overall very limited evidence in otherwise healthy individuals to draw from.
C	Aggression	↓	★☆☆ Minor	1 study	In persons with cognitive decline, supplementation of Piracetam was able to reduce aggression and agitation symptoms.
D	Cognition	—	—	1 study	No significant influence on cognition and neural functioning has been noted in otherwise healthy persons following piracetam ingestion.

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Policosanol

Also known as: Cane Sugar Extract

Policosanol is a mixture of oils from Cuban Cane Sugar; touted as a cholesterol lowering agent, it shows potency at this claim in several studies released from Cuba. Other studies undermine the quality of these, however, and it remains controversial.

See [Policosanol on Examine.com](#)

How to Take

The standard supplemental dosage of policosanol is 5-10mg taken twice daily (for a daily total of 10-20mg), although due to the state of the research on this supplement it is not sure if it is bioactive in this range.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	LDL-C	↓	★☆☆ Minor	13 studies	It is possible that policosanol is either effective or totally ineffective due to older Cuban studies being remarkably different than more recent replications; high probability of publicity bias
A	HDL-C	↑	★☆☆ Minor	12 studies	Unlikely to be potent, either small or no increases in HDL-C are likely to occur after policosanol ingestion. A good deal of the literature is based upon some highly suspicious past research from Cuba
A	Total Cholesterol	↓	★☆☆ Minor	12 studies	There may be some limited efficacy of policosanol on cholesterol (when excluding the studies from cuba, which are highly suspicious, there is still some scattered but unreliable evidence) whereas it does not appear to be potent in any way.
B	Triglycerides	—	—	5 studies	When excluding older cuban

					studies (which are highly suspicious) there is no evidence to support a reduction of triglycerides.
C	Reaction Time	↓	★☆☆ Minor	1 study	Reductions in reaction time were not overly significant.
C	Blood Flow	—	—	1 study	No significant influence detected on blood flow
C	Symptoms of Intermittent Claudication	↓	★☆☆ Minor	2 studies	Possible benefits to intermittent claudication, 'notable' rating is being held until it is replicated outside of Cuba
C	Oxidation of LDL	↓	★☆☆ Minor	2 studies	Mixed evidence, possibly an effect but needs to be replicated
C	Blood Pressure	↓	★☆☆ Minor	1 study	Possibly a small effect in persons with high blood pressure.

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Polypodium leucotomos

Also known as: Phlebodium aureum, Golden Polybody, Cabbage palm fern, Golden serpent fern, Calaguala, Anapsos

Polypodium Leucotomos (Calaguala) is the commonly referred to name of a herb that appears to possess moderately potent protective effects against sun-induced skin damage; may also be an immune booster.

See [Polypodium leucotomos on Examine.com](#)

How to Take

Polypodium leucotomos supplementation has shown benefit in humans with oral supplementation of 7.5mg/kg for skin health (dose based on weight due to correlating with the amount of skin somebody has); this results in a dosage of: 500mg for a 150lb person 700mg for a 200lb person 850mg for a 250lb person Or alternatively, a topical skin cream containing 0.1% polypodium leucotomos appears effective. For supplementation of leucotomos for other purposes (or if you do not wish to calculate the optimal dose) then the dosage range of 360-720mg appears to be used clinically for skin conditions with the lower dose being beneficial for neurology.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Psoriasis	↓	★★★☆☆ Notable	1 study	Limited evidence suggests potent anti-psoriatic effects.
C	Symptoms of Vitiligo	—	—	1 study	Currently no evidence to support a role of <i>polypodium leucotomos</i> in the treatment of vitiligo
C	Cognitive Decline	↓	★☆☆☆☆ Minor	1 study	360mg anapsos daily appears to be somewhat benefit for persons with senile dementia.
C	Cerebral Blood flow	↑	★☆☆☆☆ Minor	1 study	In persons with senile dementia, supplementation of 360mg anapsos may increase blood flow in both hemispheres of the brain (720mg being less effective).
C	T cell count	—	—	1 study	The increase in T cell count does not appear to be statistically significant,

					although a possibly relevant increase cannot be ruled out.
C	Natural Killer Cell content	—	—	1 study	Although it cannot yet be ruled out, the best evidence currently suggests that the increase in NK cell activation seen with this herb does not apply after oral supplementation.
C	Cell Adhesion Factors	↓	★☆☆ Minor	1 study	Even in healthy persons, cell adhesion factor expression on immune cells appears to be reduced with supplementation of the herb at 720mg.
D	Upper Respiratory Tract Infection Risk	↓	★☆☆ Minor	1 study	Appears to reduce infection risk, although it did not appear to be overly remarkable in doing so.
D	Polymorphic Light Eruptions	↓	★★★☆☆ Notable	3 studies	Appears to be notably effective against those that are sensitive to sunlight following oral ingestion of Polypodium
D	UV Damage	↓	★★★☆☆ Notable	1 study	Preliminary evidence suggests that oral supplementation is a bit more effective than other supplements for reducing UV damage

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Pramiracetam

Also known as: CI-879, Diisoprop-yl-(2-oxopyrrolidin-1-yl)acetamide, CI879

Pramiracetam is a synthetic racetam derivative for the purpose of cognitive enhancement, with preliminary evidence to support its usage in aiding long-term memory formation. Although the mechanisms are not well known at all, it might enhance acetylcholine synthesis.

See [Pramiracetam on Examine.com](#)

How to Take

Currently, the evidence using pramiracetam in humans uses either 400mg thrice daily or 600mg twice daily; both of these dosing regiments totals 1,200mg of pramiracetam daily. It is unsure if pramiracetam should be taken with meals, and it is not clear if 1,200mg is the optimal dosage or not. This does, however, does appear effective.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Forgetting	↓	☆☆☆ Minor	1 study	Appears to decrease the influence of amnesiac drugs (scopolamine), and is effective when loaded over a few days rather than relying on acute administration
D	Memory	↑	☆☆☆ Minor	2 studies	While it appears effective in promoting memory formation in elderly persons and cognitively injured youth, there is currently no evidence in otherwise healthy use for nootropic purposes
D	Cognition	↑	☆☆☆ Minor	1 study	Cognitive ability in youth who experienced brain trauma is improved with prolonged usage of pramiracetam, suggesting neuroprotective effects

PRL-8-53

Also known as: Methyl 3-(2-(benzyl(methyl)amino)ethyl)benzoate

PRL-8-53 is a synthetic supplement with potential benefits for short term memory. More evidence is needed for its effects, since all current evidence comes from a study funded by the patent holder.

See [PRL-8-53 on Examine.com](#)

How to Take

More evidence is needed to determine the ideal dosage for PRL-8-53. The effective dosage may vary, since the only human study on PRL-8-53 used a single dose of 5mg, while patent information on PRL-8-53 suggests a dosage range of 0.01-4mg/kg, with an 'ideal' range of 0.05-1.2mg/kg.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Reaction Time	—	—	1 study	The dose of PRL-8-53 that improves memory formation does not appear to have any significant influence on reaction time.
C	Working Memory	↑	★☆☆ Minor	1 study	Memory acquisition appears to be mildly increased in the range of 18-31% in persons with poorer performance on a word recollection memory test, but is not improved in high performers.
C	Memory	↑	★★★☆☆ Notable	1 study	The lone study noted mild increases in memory (14%) bordering on statistical significance in high performers on a word recollection test, with higher performances in subjects over the age of 30 regardless of initial performance (108-152% increase over placebo performance) and in poor performers (87.5-105%).
C	Motor Control	—	—	1 study	Supplementation of 5mg PRL-

					8-53 has failed to improve hand motor control following supplementation.

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Psyllium

Also known as: Psyllium Husk, Psyllium Fiber, Metamucil (brand name), ispaghula, plantago psyllium, plantago ovata, plantago

Psyllium (usually as husk or powder) is a fiber derived from the plant *Plantago psyllium* that is able to bind to fatty acids and cholesterol from the diet; it can increase fecal moisture and weight.

See [Psyllium on Examine.com](#)

How to Take

On the lower end of dosing, 5g of psyllium is taken once with meals alongside some form of liquid (200mL of water or more) and can be taken at every meal if desired; coingestion of psyllium with a meal is not mandatory although coingestion with water is highly advised. Acute doses of up to 30g appear to be well tolerated assuming enough water (in these instances, around 500mL or so) are also coingested. If using psyllium for the fecal forming properties, a daily dose of 15g (thrice daily dosing of 5g) is a good starting point and then the dose can be titrated up or down depending on its effects on fecal formation.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	LDL-C	↓	★☆☆ Minor	6 studies	Not overly potent reductions of LDL-C, although they seem to reliably occur in persons with high cholesterol
B	Blood Glucose	↓	★☆☆ Minor	4 studies	Reductions in blood glucose seen with psyllium seem to occur reliably in persons with high blood glucose, but are transient benefits and not of a remarkable magnitude.
B	Triglycerides	—	—	4 studies	Currently, it does not seem like there is a significant influence of psyllium on circulating triglycerides
B	HDL-C	↓	★☆☆ Minor	3 studies	Similar to the reductions in LDL-C and total cholesterol, the reduction in HDL-C is seemingly small in magnitude and likely not much to be concerned about

B	Weight	—	—	4 studies	No convincing evidence for a weight reducing effect of psyllium.
B	Total Cholesterol	↓	★☆☆ Minor	4 studies	Not unique to psyllium, but has the standard slight reduction of cholesterol that affects persons with high cholesterol. Not strong enough for monotherapy, can be a nice addition to more potent supplements or drugs
B	Blood Pressure	—	—	3 studies	No real significant effect of psyllium on blood pressure directly, although there may be an insignificant reduction seen with correcting other parameters of metabolic syndrome.
B	HbA1c	↓	★☆☆ Minor	2 studies	Reduction seen in HbA1c was not overly remarkable
C	Fecal Weight	↑	★★★★ Strong	4 studies	Psyllium tends to be the reference drug for increasing fecal weight, and due to that and the reliability of which this occurs it gets a strong rating
C	Fecal Moisture	↑	★★★★ Strong	4 studies	Psyllium is the reference drug for increasing water content of stool.
C	Iron Absorption	—	—	2 studies	No significant influence on iron absorption; it is possible the inhibitory effect of phytates in the small intestine are negated by the reduced pH in the colon that enhances mineral reuptake
C	Appetite	↓	★☆☆ Minor	3 studies	Studies that report appetite note that there is a significant reduction after a meal containing psyllium (relative to no fiber ingestion) although it does not appear to be too remarkable in potency as

					overall food intake does not appear influenced.
C	Rate of Gastric Emptying	↓	★☆☆ Minor	1 study	No reference drug to compare it to, and thus the potency in psyllium delaying gastric emptying is not certain.
C	Blood Flow	↑	★☆☆ Minor	1 study	Study noted an improved augmentation index by 22% alongside a reduction in blood pressure, mechanisms unknown and no reference drug for comparison.
C	Insulin	↓	★☆☆ Minor	2 studies	A minor decrease in diabetics following supplementation, although it is small in magnitude and does not carry over to nondiabetics.
C	Insulin Sensitivity	—	—	1 study	No significant alterations of insulin sensitivity in those who are not insulin resistant at baseline
C	Carbohydrate absorption	↓	★☆☆ Minor	1 study	Supplementation of 12g psyllium husk with a test breakfast is able to reduce carbohydrate absorption by around 12% relative to control.
C	Fructosamine	↓	★☆☆ Minor	1 study	A decrease in fructosamine has been noted in diabetics supplementing psyllium husk.
C	Uric Acid	↓	★☆☆ Minor	1 study	An 11% decrease in uric acid has been noted in diabetics supplementing with psyllium husk.
D	Lipid Absorption	—	—	1 study	A significant reduction of lipid absorption (assessed via fecal lipids) is not yet supported.
D	Intestinal Motility	↑	★☆☆ Minor	1 study	Increases intestinal motility due to being a bulk laxative, but is unlikely to have a strong

					laxative effect.
D	Food Intake	—	—	1 study	Failed to significantly influence food intake
D	Flatulence	↓	★★★☆☆ Notable	1 study	Notably effective as dietary fibers should normally enhance flatus (almost being a 'per se' effect of dietary fiber) yet psyllium has noted the opposite effect.
D	Thermic Effect of Food	—	—	1 study	Failed to modify the thermic effect of food.
D	Symptoms of Ulcerative Colitis	↓	★★★☆☆ Notable	1 study	The potency of psyllium husk in controlling remission of ulcerative colitis is comparable to the reference drug mesalamine.

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Pueraria lobata

Also known as: Kudzu, Gegen

Pueraria Lobata (Kudzu) is a root plant that appears to have traditional usage in alleviating migraines and hangovers.

See [Pueraria lobata on Examine.com](#)

How to Take

The lone study on Kudzu root used a product containing 100mg of isoflavone equivalents, which appeared to be slightly effective for promoting cognition in postmenopausal women. It is unsure if this is near the optimal dosage or not.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Cognition	↑	★☆☆ Minor	1 study	A small boost in cognition in menopausal women given the supplement; needs to be replicated and uncertain if it applies to otherwise healthy youth.
D	Attention	↑	★☆☆ Minor	1 study	Small boost in attention in menopausal women (independent of reductions in symptoms of menopause); needs to be reinvestigated
D	LDL-C	—	—	1 study	No significant influence on circulating LDL-C has been noted with supplementation
D	HDL-C	—	—	1 study	No detectable influence on HDL-C levels
D	Total Cholesterol	—	—	1 study	No significant influence have been detected on total cholesterol
D	Estrogen	—	—	1 study	No significant influence of Pueraria lobata on circulating

					estrogen levels (although it itself may be a phytoestrogen; weak)
D	Follicle-Stimulating Hormone	—	—	1 study	No significant alterations have been noted in follicle-stimulating hormone concentrations following pueraria lobata ingestion.
D	Luteinizing Hormone	—	—	1 study	No significant alterations in luteinizing hormone has been detected with pueraria lobata ingestion.
D	Symptoms of Menopause	—	—	1 study	No significant influence detected on symptoms of menopause (as assessed by rating scales)
D	Apolipoprotein B	—	—	1 study	No alterations in Apolipoprotein B have been noted

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Pueraria mirifica

Also known as: White Kwao Krua

Pueraria Candollei var. Mirifica (White Kwao Krua) is a highly estrogenic herb (main bioactive, Deoxymiroestrol, being more potent than estrogen itself) which is used as herbal estrogen replacement therapy. It appears effective, but lacks blinded studies.

See [Pueraria mirifica on Examine.com](#)

How to Take

In regards to Pueraria Mirifica (White Kwao Krua), a dose of 20-50mg of the herb is taken daily once in the morning. This appears to be significantly bioactive, and it would be advisable to not exceed this dosage. And if you are a man who wants to take 'Pueraria' for hangovers, ensure you don't get the estrogen replacement therapy (this supplement) by accident. The herb touted to cure hangovers is Pueraria lobata (Kudzu), and although it is not a common mistake it is indeed a critical one to make.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Symptoms of Menopause	↓	★★★☆☆ Notable	4 studies	The effects of Pueraria Mirifica on menopausal symptoms appear to be potent, with one study suggesting comparable efficacy to estrogen replacement therapy itself. Requires more robust evidence, however.
C	LDL-C	↓	★★☆☆☆ Minor	1 study	Somewhat effective in menopausal women.
C	Apolipoprotein B	↓	★★☆☆☆ Minor	1 study	A slight decrease in Apolipoprotein B has been noted with Pueraria Mirifica
C	HDL-C	↑	★★☆☆☆ Minor	1 study	Not overly potent, only testing in menopausal women has been conducted
C	Bone-specific Alkaline Phosphatase	↓	★★☆☆☆ Minor	1 study	Efficacy has been noted (and suggests long term bone regenerative properties) but requires more evidence to

					establish overall potency relative to other estrogenic agents
C	Vaginal Dryness	↓	★☆☆ Minor	1 study	Was able to reduce vaginal dryness (due to estrogenic effects, perhaps) although potency cannot be judged well due to no comparator.

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Punicalagins

Also known as: Pomegranate Extract, Punica Granatum L., Pomegranate Juice

Punicalagins are really big molecules found in pomegranate juice that are somehow absorbed; they are potent anti-oxidants, and alongside Punicic Acid confer many of the benefits associated with pomegranates, of which many studies conducted with are here.

See [Punicalagins on Examine.com](#)

How to Take

Anti-oxidant potential of the blood increases at an oral dose of 800mg Pomegranate Extract (318mg punicalagins), which may be a good starting point for a bioactive dose. The optimal dose is currently not known.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Prostate Cancer Risk	↓	★★★☆☆ Notable	2 studies	Notable as consumption of pomegranate juice is associated with a prolongation in the time require for PSA (biomarker of prostate cancer) to double, from 15 months to 54 months
D	Prostate Specific Antigen	↓	★☆☆☆☆ Minor	2 studies	Does not appear to be able to reduce PSA levels outright, although it can attenuate the rate of which PSA increases over time (relative to untreated control, this is a reduction)
D	Testosterone	—	—	1 study	No significant influence on testosterone levels in men at risk for prostate cancer
D	Estrogen	—	—	1 study	No significant influence on estrogen
D	Nitric Oxide	↑	★★☆☆☆ Minor	1 study	An increase in metabolites of nitric oxide metabolism have been noted and thought to be indicative of increased nitric

					oxide production
D	Lipid Peroxidation	↓	★☆☆ Minor	1 study	A decrease in lipid peroxidation has been noted
D	General Oxidation	↓	★☆☆ Minor	1 study	A decrease in general oxidation has been noted with punicalagins

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Punicic Acid

Also known as: Pomegranate Seed Oil

Punicic Acid is the main fatty acid found in Pomegranate Seed Oil and found in Pomegranates, it may contribute to many of the health benefits associated with Pomegranates.

See [Punicic Acid on Examine.com](#)

How to Take

Studies that use pomegranate seed oil use 400mg of a 72% punicic acid seed oil. While this appears to be in the bioactive range of punicic acid, it is not known if this is an optimal dosage or not.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	HDL-C	↑	★☆☆ Minor	2 studies	Although there are possible increases in HDL-C with punicic acid, this has not been noted all the time and may be unreliable
C	LDL-C	—	—	2 studies	No significant influences on LDL-C levels
C	Triglycerides	↓	★☆☆ Minor	2 studies	A possible slight reduction in triglycerides has been noted with pomegranate oil, but this appears to be unreliable
C	Total Cholesterol	—	—	1 study	No significant influence on total cholesterol levels
C	Weight	—	—	1 study	No significant influence on weight has been noted
C	Fat Mass	—	—	1 study	No significant influence on fat mass by itself
C	Lean Mass	—	—	1 study	No significant influence on lean mass has been noted with punicic acid

					supplementation
C	Insulin Sensitivity	—	—	1 study	No significant alterations in insulin sensitivity noted
C	Insulin	—	—	1 study	No significant influence on fasting insulin levels
C	TNF-Alpha	—	—	1 study	No significant influence on serum TNF-a levels

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Pycnogenol

Also known as: Pine Bark Extract, Pine Bark Procyanidins, Procyanidins

Pine Bark Extract; Pycnogenol is investigated for its general health and anti-diabetic properties and its ability to enhance Nitric Oxide, which appears to significantly help erectile dysfunction.

See [Pycnogenol on Examine.com](#)

How to Take

Although doses in the range of 40-60mg have been noted to be effective over a prolonged period of time, standard doses of Pycnogenol appear to be in the range of 100-200mg. Studies have used twice daily dosing (dividing the daily total into two even doses to be taken with breakfast and dinner) as well as once daily dosing with breakfast, both appear effective and no comparative studies have been conducted to see which is better. Although it is usually recommended to be taken with meals out of prudence, this does not appear to be an absolute requirement.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Blood Flow	↑	★★★☆☆ Notable	3 studies	An improvement in nitric oxide dependent blood flow appears to occur following procyanidin supplementation which has been noted in both unhealthy persons as well as healthy controls; there does not appear to be a per se hypotensive effect either.
C	Blood Pressure	—	—	1 study	Despite the improvement in blood flow, no significant alterations noted in resting blood pressure
C	General Oxidation	↓	★★☆☆☆ Minor	2 studies	A reduction in general oxidation is noted following prolonged Pycnogenol supplementation
C	Inflammation	—	—	2 studies	No significant influence on standard inflammatory cytokines
C	Heart Rate	—	—	1 study	No significant alterations in

					heart rate noted
C	C-Reactive Protein	—	—	1 study	No significant alterations in C-Reactive protein noted
C	Symptoms of Menopause	↓	★☆☆ Minor	1 study	A decrease in some symptoms of menopause has been noted with Pycnogenol supplementation
C	Subjective Well-Being	↑	★☆☆ Minor	1 study	An increase in well being and mood has been noted in students undergoing academic testing, which correlated with improved test scores
C	Cognition	↑	★☆☆ Minor	1 study	An improvement in cognitive function has been noted in students during academic testing
C	Attention	↑	★☆☆ Minor	1 study	An improvement in attention has been noted, possibly secondary to improvements in general cognition, in students during prolonged academic testing
C	Skin Elasticity	↑	★☆☆ Minor	1 study	An improvement in skin elasticity has been noted with Pycnogenol supplementation
C	Skin Quality	↑	★☆☆ Minor	1 study	Oral supplementation of standard doses of procyanidins can improve skin quality in elderly women, other demographics not tested
C	Asthma	↓	★☆☆ Minor	2 studies	A slight reduction in asthmatic symptoms has been noted with Pycnogenol supplementation
C	Leg Swelling	↓	★★★☆☆ Notable	2 studies	Appears to reduce leg swelling secondary to the enhancement of blood flow. While the evidence is not overly robust, it is comparable if not better than

					the reference supplement of Horse Chestnut
C	Nitric Oxide	—	—	1 study	Despite one study establishing the blood flow effects are dependent on nitric oxide, there do not appear to be any significant differences in nitric oxide quantities in saliva
C	Pain	↓	★☆☆ Minor	1 study	A reduction in pain secondary to improvements in symptoms of osteoarthritis has been noted, and while notable in this certain instance it is not certain if there are inherent analgesic effects
C	Symptoms of Osteoarthritis	↓	★★★☆☆ Notable	2 studies	The preliminary evidence at this point in time (promising and independent, but limited) support the usage of pycnogenol in reducing all symptoms of osteoarthritis, reaching up to a halving of symptoms but requiring 90 days for effects to occur
D	Erections	↑	★☆☆ Minor	1 study	May be proerectile in persons with organic erectile dysfunction (due to poor blood flow)
D	HDL-C	↑	★☆☆ Minor	2 studies	May increase HDL cholesterol, but has mixed evidence to support it and may be unreliable
D	LDL-C	↓	★☆☆ Minor	2 studies	May reduce LDL cholesterol for as long as pycnogenol is taken (some evidence to suggest a normalization after supplement cessation)
D	Triglycerides	—	—	1 study	No significant alterations on triglycerides
D	Total Cholesterol	↓	★☆☆ Minor	2 studies	Possible cholesterol lowering effects of small magnitude, but

					these are not wholly reliable
D	Chronic Venous Insufficiency	↓	★★★☆☆ Notable	1 study	Appears to reduce symptoms of chronic venous insufficiency, and preliminary evidence suggests a greater potency than the reference supplement of Horse Chestnut
D	nF-kB Activity	↓	★★☆☆☆ Minor	1 study	A decrease in nF-kB activity has been confirmed in humans given 200mg pycnogenol daily for five days, to the degree of around 15%

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Pygeum

Africanum Pygeum is a tree bark that is commonly sold as a prostatic health supplement (usually alongside Saw Palmetto); components of Pygeum appear to possess anti-androgenic properties, and the efficacy of this compounds on benign prostatic hyperplasia is not fully established.

See [Pygeum on Examine.com](#)

How to Take

Most supplements and studies using a dose of 50-100mg of Pygeum bark extract daily, and there does not appear to be much difference between these two doses. The optimal dose of Pygeum bark is not currently known

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Symptoms of Benign Prostate Hyperplasia	↓	☆☆☆ Minor	1 study	Urinary complications with Benign prostatic hyperplasia appear to be reduced with Pygeum supplementation in the range of 19-23% (including nocturia, residual urine volume, and urinary flow rate).

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Pyrroloquinoline quinone

Also known as: PQQ, Methoxatin

PQQ is a small molecule once thought to be a vitamin, although its actions in the human body are not related to this hypothesized vitamin-like mechanism. Via its actions as a REDOX agent in cells, it can modify signalling and is thought to support mitochondrial function.

See [Pyrroloquinoline quinone on Examine.com](#)

How to Take

The optimal dosage of Pyrroloquinoline quinone (PQQ) to be taken daily is currently not known, but extrapolations from animal studies suggest that doses as low as 2mg are somewhat bioactive while most dietary supplements are sold in the 20-40mg range.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Stress	↓	★☆☆ Minor	1 study	A reduction in self-reported stress has been noted after 8 weeks in persons with self-reported sleep problems; this study also noted improvements in sleep
D	Fatigue	↓	★☆☆ Minor	1 study	A decrease in fatigue has been noted in older adults with self-reported energy problems
D	Sleep Quality	↑	★☆☆ Minor	1 study	An improvement in sleep quality has been noted in persons with impaired sleep; it is not certain how PQQ affects persons with normal sleep cycles
D	Pain	↓	★☆☆ Minor	1 study	In persons with sleep disorders taking PQQ (which improved sleep) there were reductions in pain ratings at the end of the trial
D	TMAO	↓	★☆☆ Minor	1 study	A decrease in urinary TMAO has been noted with

					supplementation of PQQ, which is thought to be due to increased activity of the FMO3 enzyme.
D	C-Reactive Protein	↓	★★☆ Notable	1 study	The decrease in C-reactive protein seen in one study in otherwise healthy humans reached 45% after three weeks of supplementation.
D	Interleukin 6	↓	★☆☆ Minor	1 study	IL-6 appeared to be significantly reduced in the serum of adults given PQQ supplementation relative to baseline.
D	General Oxidation	—	—	1 study	Overall oxidation in serum as assessed by TRAP has failed to be significantly influenced by PQQ supplementation in otherwise healthy adults.
D	Lipid Peroxidation	↓	★☆☆ Minor	1 study	Although a decrease technically exists as assessed by TBARS, the decrease was measured at around 0.2% and is practically irrelevant.
D	Liver Enzymes	—	—	1 study	Serum ALT is not affected by supplementation of PQQ for up to three weeks.
D	HDL-C	—	—	1 study	Three weeks supplementation of PQQ has failed to significantly influence HDL cholesterol levels in otherwise healthy adults.
D	LDL-C	—	—	1 study	No apparent changes to LDL cholesterol exist in otherwise healthy adults given PQQ supplementation daily for up to three weeks.
D	Triglycerides	—	—	1 study	Short term supplementation of PQQ has failed to significantly influence triglycerides in otherwise healthy adults

D	Blood Glucose	—	—	1 study	Short term ingestion of PQQ supplementation in otherwise healthy adults has failed to significantly influence serum glucose concentrations.

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Pyruvate

Pyruvate is an energy intermediate in cells, derived from both glucose and fatty acids to produce ATP. Despite this importance, human studies are not overly promising and the high doses needed are sometimes limited by intestinal side-effects.

See [Pyruvate on Examine.com](#)

How to Take

Most studies on pyruvate substituted dietary carbohydrates for pyruvate as pyruvate itself does contain calories. The dose used in studies showing most fat loss is in the range of 20-50g daily, or replacing 10-20% of caloric intake (initially from carbohydrates) with supplemental pyruvate. The lowest effective range noted in the aforementioned studies is replacing 6-12g of carbohydrates with pyruvate, but even then the results seen with pyruvate are variable and lacklustre enough to warrant caution in buying this supplement.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Fat Mass	—	—	5 studies	The majority of the evidence currently does not support a role for supplemental Pyruvate in weight loss. The limited evidence to suggest fat loss are in obese women under severe caloric restriction, of which pyruvate was twice linked to increase the already drastic weight loss
B	Weight	—	—	5 studies	Most evidence suggests that standard oral doses of Pyruvate supplementation do not have a reducing effect on weight, but the effects of high dose pyruvate during severe caloric restriction cannot be ruled out
C	Training Volume	—	—	1 study	No significant influence on training volume in otherwise healthy persons given an exercise protocol
C	Fatigue	↓	★☆☆ Minor	1 study	May reduce fatigue during weight loss periods

C	Subjective Well-Being	↑	★☆☆ Minor	1 study	An increase in well being may occur secondary to weight loss, although due to the complications in weight loss with pyruvate this may not be feasible
C	Power Output	—	—	1 study	No significant influence on power output noted with pyruvate supplementation in healthy athletes
C	HDL-C	—	—	2 studies	No significant influence on HDL-C levels
C	LDL-C	↓	★☆☆ Minor	2 studies	A reducing effect on LDL-C has been noted once during caloric surplus; practical relevance of this information unknown
C	Total Cholesterol	↓	★☆☆ Minor	1 study	A reduction in total cholesterol has been noted once in response to a high fat hypercaloric diet; practical relevance unknown
C	Heart Rate	↓	★☆☆ Minor	1 study	May decrease heart rate alongside blood pressure in hyperlipidemics according to one trial
C	Blood Pressure	↓	★☆☆ Minor	1 study	May reduce blood pressure in hyperlipidemics, relation to weight loss not known
C	Aerobic Exercise	—	—	1 study	No significant influence on aerobic exercise performance

Quercetin

Also known as: Apple extract, 3,4,5,7-pentahydroxyflavone

Quercetin is the most well researched of all Bioflavonoids. It is not actually that good of a supplement on its own, but is an interesting research topic. Tons of interactions, and synergistic with other Bioflavonoids and increases absorption of Resveratrol and Green Tea Catechins.

See [Quercetin on Examine.com](#)

How to Take

Dosages of quercetin used are in the range of 12.5 to 25mg per kg body weight, which translates to a range of 1,136-2,272mg daily consumption of quercetin when in isolation. It is suggested to supplement with other Bioflavonoids such as Resveratrol, genistein, or Green Tea Catechins to increase the potency synergistically and theoretically get the benefits at a reduced level of intake. When looking for quercetin, the form of dihydrate has the apparent best bioavailability followed by glycosides, aglycone, and finally rutinose.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Blood Pressure	—	—	3 studies	No acute alterations in blood pressure following Quercetin supplementation
C	Sleep Quality	—	—	1 study	No significant influence on sleep quality
C	Fatigue	—	—	1 study	No significant influence on fatigue nor vitality in otherwise healthy persons
C	Anaerobic Running Capacity	—	—	2 studies	No significant influence on anaerobic exercise capacity when preloaded
C	Interleukin 6	—	—	1 study	The alterations in IL-6 concentrations seen with exercise are unchanged with quercetin supplementation.
C	Rate of Percieved Exertion	—	—	2 studies	There is no significant influence of quercetin

					supplementation on the rate of perceived exertion (RPE)
C	Uric Acid	—	—	1 study	No significant influence on uric acid concentrations
C	LDL-C	↓	★☆☆ Minor	2 studies	A decrease in LDL-C has been noted in persons with high blood lipids, although this decrease is not observed in persons who do not have high LDL-C concentrations.
C	HDL-C	↑	★☆☆ Minor	2 studies	An increase in HDL-C has been noted following quercetin supplementation
C	Intestinal Permeability	↑	★☆☆ Minor	1 study	An increase in the amount of intestinal permeability induced by training in the heat has been noted with quercetin supplementation, which is an adverse event; the influence of quercetin at rest is uncertain
C	Exercise-induced Stress Response	↓	★★★☆☆ Notable	1 study	The exercise-induced increase in HSP70 expression is abolished with quercetin preloading
C	General Oxidation	↓	★☆☆ Minor	2 studies	May reduce oxidative biomarkers in serum and urine, but is a tad unreliable in doing so.
C	Inflammation	—	—	1 study	Mixed influence on inflammation, but does not appear to at all be practically significant
C	Metabolic Rate	—	—	1 study	No significant influence on metabolic rate following acute Quercetin supplementation
C	Fat Oxidation	—	—	1 study	No significant alterations in fat oxidation noted with quercetin supplementation

C	Training Volume	—	—	1 study	Training volume does not appear to be significantly influenced with quercetin supplementation.
C	Hydration	—	—	1 study	Hydration during exercise in the heat is unaffected by quercetin supplementation.
C	Weight	—	—	1 study	No significant alterations detected in body weight with quercetin supplementation.
C	Heart Rate	—	—	1 study	No significant influence on heart rate either acutely or with prolonged supplementation.
C	8-isoPGF2a	—	—	1 study	Urinary 8-isoPGF2α is unchanged with prolonged quercetin supplementation.
C	vLDL-C	—	—	1 study	No significant changes in vLDL-C are detected with quercetin supplementation.
C	Blood Glucose	—	—	1 study	No significant alterations in blood glucose are detected with quercetin supplementation.
D	Total Cholesterol	↑	★☆☆ Minor	1 study	An increase in total cholesterol has been noted, but mostly attributed to HDL

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Raspberry Ketone

Also known as: 4-(4-hydroxyphenyl) butan-2-one, p-hydroxybenzyl acetone

Raspberry ketone is a molecule marketed as a fat burning compound. Oral doses of this supplement are not effective.

See [Raspberry Ketone on Examine.com](#)

How to Take

There is no human evidence for the effects of raspberry ketones. Studies on rats have used a dosage range of .545-2.18g/kg, which correlates to a human estimated dose of 80-340mg/kg for humans. This dose is very high compared to other fat burning compounds, so for that reason the standard supplemental dose of raspberry ketones for humans is in the 100-200mg range. There is no solid evidence for the effectiveness of the doses listed below. Rat dosages correlate to the following human doses: 870-3,700mg for a 150lb person 1,100-5,000mg for a 200lb person 1,500-6,200mg for a 250lb person There is no human evidence for the effectiveness of raspberry ketones. Raspberry ketones cannot be concentrated in the human body the same way they are concentrated during studies done outside the body, on single cells.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Skin Elasticity	↑	★☆☆ Minor	1 study	Appears to benefit the skin when topically applied as part of a cream
D	Hair Regrowth	↑	★☆☆ Minor	1 study	May induce hair growth when topically applied

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Red Clover Extract

Also known as: trifolium pratense, biochanin A, Formononetin Promensil (brand name), Menoflavon (brand name)

Red Clover Extract (Promensil or Menoflavon) are isoflavones including the Soy Isoflavones in low amounts and some similar structures such as Biochanin A; used as a therapy for menopause, red clover appears to have minor yet unreliable benefits in improving health and reducing hot flashes.

See [Red Clover Extract on Examine.com](#)

How to Take

Supplementation of Red Clover Extract tends to be 40mg of total isoflavones taken once a day, or two doses totalling 80mg a day. This can be reached through: Supplementing pure isoflavones (in which case the range is 40-80mg) Supplementing brand name products such as Promensil, which confer 40mg isoflavones per 500mg capsule (so, around 8% isoflavones by weight) Approximately 5 grams of the whole plant without any particular extraction techniques

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	LDL-C	—	—	11 studies	Although a minor effect may occur in those with high blood cholesterol concentrations, the majority of evidence does not support a role of Red Clover Extract in reducing LDL-C when supplemented.
A	HDL-C	—	—	13 studies	Similar to other lipid parameters, despite an increase (10-20%) being noted in a few studies the best evidence to date does not support this conclusions and the benefits, when they occur, are unreliable.
A	Total Cholesterol	—	—	14 studies	The majority of evidence does not support a role for reducing total cholesterol with supplementation of red clover extract, except perhaps a minor (less than 10%) reduction in overweight postmenopausal women.

A	Triglycerides	—	—	11 studies	Isolated reports have noted minor (less than 10%) reductions in triglycerides in overweight or hyperlipidemics mostly, but overall there is not a significant reduction in triglycerides noted with Red clover extract.
A	Symptoms of Menopause	—	—	12 studies	While isolated studies have noted some benefits, the best evidence at this moment in time (Independently conducted and larger, better conducted, studies) tend to note no significant influence on the main climacteric symptoms such as hot flashes with supplementation.
B	Weight	—	—	7 studies	No studies, even those using up to 120mg total isoflavones for up to a year, have noted significant weight loss associated with Red Clover supplementation in postmenopausal women.
B	Blood Pressure	—	—	7 studies	The one study in diabetics found a reduction in blood pressure, and due to no studies in hypertensives all other studies have failed to find an influence on blood pressure.
B	Sex Hormone Binding Globulin	—	—	6 studies	There are no significant alterations in the circulating levels of SHBG seen with red clover supplementation.
B	Follicle-Stimulating Hormone	—	—	6 studies	No significant influence on FSH seen with oral supplementation of red clover to postmenopausal women
B	Luteinizing Hormone	—	—	3 studies	Luteinizing hormone does not appear to be significantly influenced with oral supplementation of red clover extract in postmenopausal

					women.
B	Testosterone	—	—	3 studies	The majority of evidence has suggested no significant influence of red clover supplementation on the testosterone concentrations in postmenopausal women
B	Estrogen	—	—	6 studies	Regardless of any direct estrogenic effects (which also do not appear to occur) there are no changes in circulating estrogen seen with oral supplementation of red clover extract.
B	Apolipoprotein A	—	—	4 studies	A large decrease has been noted in one study in overweight postmenopausal women, although three other studies failed to replicate this decrease.
B	Bone Mineral Density	—	—	4 studies	Beyond a small (less than 5%) attenuation in the rate of lumbar bone mineral density losses, standard supplementation does not appear to significantly influence bone mass or the rate of bone loss.
B	IGF-1	—	—	3 studies	Supplementation does not appear to significantly influence circulating IGF-1 concentrations, although equol (a possible metabolite of formononetin) has been associated with a reduction not observed to a significant degree in most trials on red clover extract.
B	IGF Binding Protein	—	—	3 studies	No influence of supplementation on circulating concentrations of any measured IGF binding protein (IGFBP-1, IGFBP-2, IGFBP-3) in any tested population.

C	Liver Enzymes	—	—	1 study	Liver function does not appear to be significantly altered with supplementation of red clover.
C	Breast Density	—	—	2 studies	Breast density, as a measure of estrogenicity, has failed to be significantly influenced with supplementation of red clover extract in postmenopausal women.
C	Insulin Sensitivity	↓	★☆☆ Minor	2 studies	While one study has noted no significant effect, another has noted a minor reduction in sensitivity as assessed by QUICKI; reasons underlying this are unknown.
C	Blood Glucose	—	—	2 studies	No significant influence on fasting blood glucose concentrations are known with supplementation of red clover extract.
C	Insulin	—	—	2 studies	Fasting blood insulin concentrations do not appear to be significantly influenced with supplementation of red clover extract.
C	Osteocalcin	—	—	1 study	Circulating osteocalcin does not appear to be influenced with supplementation of red clover extract.
C	General Oxidation	—	—	1 study	There does not appear to be a significant influence on oxidative parameters seen with supplementation of red clover isoflavones.
C	Lipid Peroxidation	—	—	1 study	No known interactions with serum MDA concentrations, a biomarker of lipid peroxidation.
C	Arterial Stiffness	↓	★☆☆ Minor	2 studies	Short term supplementation of red clover isoflavones appears to reduce arterial stiffness in a

					manner independent of changes in blood pressure or flow.
C	Blood Flow	—	—	2 studies	The reduction in arterial stiffness (increase in arterial compliance) sometimes seen with supplementation of red clover extract does not necessarily coincide with improved blood flow.
C	Cell Adhesion Factors	↓	★☆☆ Minor	1 study	Isolated formononetin has been noted to reduce circulating VCAM-1 levels by approximately 11% in one study.
C	Fibrinogen	—	—	2 studies	No known changes to circulating fibrinogen concentrations.
C	HbA1c	—	—	1 study	No significant changes in HbA1c seen with supplementation of red clover in diabetics.
C	Plasminogen Inhibitor 1	—	—	1 study	Circulating levels of PAI-1 (plasminogen activation inhibitor 1) have not been altered with supplementation of red clover isoflavones.
C	Homocysteine	—	—	1 study	There do not appear to be changes to circulating homocysteine in premenopausal women given supplementation of red clover extract.
C	Serum Folate	—	—	1 study	There do not appear to be any significant changes to circulating folate seen with supplementation of red clover extract.
C	Anxiety	↓	★★★☆☆ Notable	2 studies	A minor reduction in anxiety (associated with menopause) has been noted in one

					independent trial while it was much more significant (near 80%) in a study with a potential conflict of interest; requires more research.
C	Depression	↓	★★★☆☆ Notable	1 study	Depression as a side-effect of menopause has been noted to be decreased to quite a significant level (around 80%) which needs to be replicated due to possible funding issues.
C	Attention	—	—	1 study	No significant influence on attention processing in older women in a postmenopausal state with supplementation of red clover isoflavones.
C	Memory	↓ ↑	★★☆☆☆ Minor	1 study	The lone study to assess cognition in older women in menopause has noted an increase in visuospatial processing yet a reduction in digit span and verbal memory tests; uncertain implications.
C	Heart Rate	—	—	1 study	No significant influence on resting heart rate is seen with supplementation of red clover extract.
C	Dry Eyes	↓	★★☆☆☆ Minor	1 study	The complaint of 'dry eyes' appears to be slightly reduced in postmenopausal women given 80mg of the isoflavones as a supplement.
C	Skin quality	↑	★★☆☆☆ Minor	1 study	There appears to be an overall increase in skin texture and moisture content associated with oral supplementation of the isoflavones, and a depigmenting activity should also apply (not yet shown in humans)
C	Subjective Well-Being	—	—	1 study	Two differing studies have noted either no improvement of

					well being in menopausal women, or a significant (near 80%) improvement; more research is needed to refine the actual effect, but the study noting no effect is considered higher quality.
C	Sleep Quality	↑	★☆☆ Minor	1 study	In post menopausal women, there appears to be an increase in self reported sleep quality that was quite notable, reaching 70-73 points of improvement on a 0-100 rating scale (placebo at 10-16) although this needs to be replicated (independently) to assure quality of data.
C	Subjective Well-being	—	—	1 study	Two differing studies have noted either no improvement of well being in menopausal women, or a significant (near 80%) improvement; more research is needed to refine the actual effect, but the study noting no effect is considered higher quality.
D	Apolipoprotein B	↓	★☆☆ Minor	1 study	One preliminary study has noted a reduction in Apolipoprotein B concentrations with supplementation of a Formononetin rich red clover supplement.

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Resveratrol

Also known as: Red Wine Extract, 3,5,4'-trihydroxystilbene

A molecule known for its content in Wine, and falsely said to increase lifespan (does not appear to do so in mammals). It appears to be effective at protecting the heart and blood flow, and may be an insulin sensitizer. Does not add years to life, but may add life to years.

See [Resveratrol on Examine.com](#)

How to Take

The lower end of supplementation tends to be for cardiovascular health, insulin sensitivity, and longevity for somebody who is otherwise unhealth is 5-10mg daily. For persons who are otherwise healthy, dosages between the range of 150-445mg have been used (with no clear indication for what is the optimal dose). Supplementing for cerebral blood flow requires a dose in the 250-500mg range whereas supplementation for aromatase inhibition requires 500mg as well. Supplementation of resveratrol refers to trans-resveratrol exclusively.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Insulin Sensitivity	↑	★☆☆ Minor	3 studies	There appears to be an increase in insulin sensitivity seen with resveratrol at doses low enough to be achieved via wine consumption, all tests currently in obese and unhealthy persons
C	Blood Pressure	↓	★☆☆ Minor	1 study	Blood pressure has been reduced with resveratrol in persons with high blood pressure; influence on otherwise healthy persons unknown
C	Metabolic Rate	↓	★☆☆ Minor	1 study	A decrease in the metabolic rate has been noted in humans, thought to be related to the caloric restriction mimetic aspect
C	Triglycerides	↓	★☆☆ Minor	1 study	A decrease in triglycerides has been noted with resveratrol supplementation

C	Insulin	↓	★☆☆ Minor	1 study	A decrease in insulin (fasting) has been noted in persons with metabolic syndrome
C	Blood Glucose	↓	★☆☆ Minor	1 study	A decrease in blood glucose has been noted, practical significance unknown
C	TNF-Alpha	↓	★☆☆ Minor	1 study	A significant decrease in circulating TNFα levels have been detected with resveratrol supplementation; linked to antiinflammatory effects of resveratrol
C	Liver Enzymes	↓	★☆☆ Minor	1 study	In persons with elevated liver enzymes (not pathological, just metabolic syndrome) there appeared to be a protective effect on the liver from resveratrol supplementation
C	DNA methylation	↓	★☆☆ Minor	1 study	A decrease in DNA methylation rates has been noted
C	Blood Flow	↑	★☆☆ Minor	1 study	An improvement in blood flow (secondary to Nitric Oxide interactions) has been noted with low dose resveratrol, possibly relevant to high wine and grape product consumption
C	Left Ventricular Ejection Fraction	↑	★☆☆ Minor	1 study	10mg resveratrol appears to improve left ventricle function slightly
C	LDL-C	↓	★☆☆ Minor	1 study	Possible decreases in LDL-C in persons at risk for heart disease, but it does not appear to be of large magnitude
C	HDL-C	—	—	1 study	No significant influence on HDL cholesterol
C	Total Cholesterol	—	—	1 study	No significant effect on total

					cholesterol levels
C	C-Reactive Protein	—	—	1 study	No significant effect on C-reactive protein
C	General Oxidation	↓	★☆☆ Minor	1 study	A decrease in oxidative biomarkers has been noted following resveratrol supplementation
C	Cognition	—	—	1 study	No significant influence on cognition in otherwise healthy persons (despite an increase in cerebral blood flow)
C	Cerebral Blood Flow	↑	★☆☆ Minor	1 study	500mg of resveratrol (high dose) has been confirmed to increase cerebral blood flow
C	Fatigue	—	—	1 study	No significant influence on self-reported ratings of fatigue at rest
C	Adaptations to Exercise	↓	★★★☆☆ Notable	1 study	Supplementation of resveratrol before exercise can fairly effectively prevent the benefits associated with intense exercise (increases in oxygen capacity and HDL-C, reductions in LDL-C and blood pressure) in otherwise healthy men. Theoretically, the mTOR inhibition of resveratrol may also inhibit muscle protein synthesis.
C	Exercise-induced Oxidation	↓	★★★☆☆ Notable	1 study	The oxidation induced by exercise is effectively diminished with resveratrol, which is thought to underlie the inhibitory effects on exercise-induced adaptations.
D	Acne	↓	★★★☆☆ Notable	1 study	Topical application of resveratrol in a cream more than halved the rating scores of acne, and reductions in lesion count were also noted (but only to 10%)

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Rhodiola Rosea

Also known as: Rosavin, Rosenroot, Rhodiola Rhizome, Golden Root, Arctic Root, Rhidola

Rhodiola rosea is a Traditional Chinese Medicine and Scandinavian herb touted to promote physical/cognitive vitality. It appears to be proven for reducing fatigue and exhaustion in prolonged stressful situations. Rhodiola is also neuroprotective and promotes longevity in preliminary evidence.

See [Rhodiola Rosea on Examine.com](#)

How to Take

Supplementation of rhodiola rosea tends to refer to either the SHR-5 extract in particular or an equivalent extract, any that confers both 3% rosavins and 1% salidroside. Usage of rhodiola as a daily preventative against fatigue has been reported to be effective in doses as low as 50mg. Acute usage of rhodiola for fatigue and anti-stress has been noted to be taken in the 288-680mg range. As rhodiola has been shown to have a bell-curve response before, it is recommended to not exceed the aforementioned 680mg dosage as higher doses may be ineffective.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Fatigue	↓	★★★☆☆ Notable	7 studies	The decrease in fatigue appears to be quite strong and reliable, rhodiola may be an active control on this parameter
B	Subjective Well-Being	↑	★★★☆☆ Notable	4 studies	Increases in subjective well being and contentment in fatigued or stressed individuals appears to be greater than other supplements.
B	Cognition	↑	★★★☆☆ Notable	4 studies	Notably effective assuming fatigue is being reduced. There is insufficient evidence to evaluate rhodiola's effects on cognition without the fatigue reduction aspect
C	Depression	↓	★★★☆☆ Notable	1 study	Limited evidence, but up to a halving of symptoms has been noted with higher doses of Rhodiola

C	Stress	↓	★☆☆ Minor	2 studies	Might be effective, but the reduction in stress (rating scale) appears to be less than that seen with fatigue
C	Heart Rate	—	—	2 studies	No significant influences on heart rate found so far
C	Rate of Perceived Exertion	↓	★☆☆ Minor	1 study	Possibly effective if confounded with fatigue (the antifatigue effects may reduce the rate of perceived exertion during submaximal exercise) but there does not appear to be strong effects in maximal effort trials
C	VO2 Max	—	—	1 study	May slightly improve oxygen consumption during submaximal exercise in untrained persons, but overall the improvement in VO2 max does not appear to be highly potent or reliable.
C	Lactate Production	↓	★☆☆ Minor	1 study	A decrease in lactate production has been noted with rhodiola supplementation; practical significance unknown
C	Lipid Peroxidation	—	—	2 studies	No significant influences on lipid peroxidation biomarkers in serum
C	Muscle Damage	↓	★☆☆ Minor	2 studies	Able to reduce circulating levels of creatine kinase following exercise
C	Attention	—	—	1 study	No significant influences on attention
C	Reaction Time	—	—	1 study	No significant influences on reaction time
C	Power Output	—	—	1 study	No significant influences on power output

C	Weight	—	—	1 study	Unable to modify weight over time
C	Processing Accuracy	↑	★☆☆ Minor	1 study	Increases in processing accuracy are likely secondary to reductions in fatigue
C	C-Reactive Protein	↓	★☆☆ Minor	1 study	A decrease in C-reactive protein has been noted with rhodiola supplementation; practical significance of these results unknown
C	Blood Pressure	—	—	1 study	No significant effects yet noted on blood pressure
C	Muscle Oxygenation	—	—	1 study	No significant effects on oxygenation during exercise or simulated altitude tests

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Rooibos

Also known as: Aspalathus linearis, Red Bush Tea

Rooibos (*Aspalathus linearis*) is a semi-sweet tea touted for its potent antioxidant properties; despite being highly palatable and marketed, the poor absorption of the main bioactive (aspalathin) suggests a limit to its health promoting properties.

See [Rooibos on Examine.com](#)

How to Take

Not enough information is known to evaluate the optimal dosage or Rooibos as a tea or as a supplement, although it appears that the minimum effective dose in humans has been a cup of tea brewed from 750mg of the plant. A daily intake of 750-3,000mg of the tea leaves, preferably in multiple doses with meals, might be optimal

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	General Oxidation	↓	★☆☆ Minor	3 studies	A decrease sometimes occurs, although this has not been noted in all instances. The decrease in healthy persons is minor and lasts for about 5 hours, whereas it may be more prominent in persons at risk for cardiovascular disease
C	Blood Glucose	↓↑	★☆☆ Minor	2 studies	A decrease may occur in persons at risk of cardiovascular disease with daily ingestion of Rooibos tea, although at least one study noted an inexplicable acute increase in otherwise healthy persons (faded within an hour of ingestion).
C	Triglycerides	↓	★☆☆ Minor	2 studies	A minor reduction of triglycerides occurs with daily ingestion of Rooibos tea only in unhealthy persons
C	LDL-C	↓	★☆☆ Minor	2 studies	A decrease in LDL-C has been noted to a minor degree in

					persons at risk for cardiovascular disease, but there is no inherent reduction in LDL-C in otherwise healthy persons.
C	Total Cholesterol	↓	★☆☆ Minor	2 studies	May decrease total cholesterol to a small degree in unhealthy persons
C	HDL-C	↑	★☆☆ Minor	2 studies	Increases HDL-C in persons at risk for cardiovascular disease to a small amount, does not appear effective in otherwise healthy persons
C	Lipid Peroxidation	↓	★☆☆ Minor	1 study	A decrease in lipid peroxidation has been noted following oral ingestion of Rooibos tea
C	C-Reactive Protein	—	—	1 study	No significant alteration in C-reactive protein
C	Uric Acid	—	—	1 study	No significant influence on uric acid is seen with Rooibos tea ingestion.
C	Nitric Oxide	—	—	1 study	No significant alterations in nitric oxide levels with acute ingestion of Rooibos tea to otherwise healthy persons.
C	Blood Pressure	—	—	1 study	Despite ACE inhibition, Rooibos tea does not appear to significantly reduce blood pressure
C	Heart Rate	—	—	1 study	No significant alterations in heart rate are seen with Rooibos ingestion
D	Hydration	—	—	1 study	Rooibos tea does not appear to be significantly better than the water it is brewed in at restoring hydration in athletes

Rose Essential Oil

Also known as: Rose, Rosa damascena, Rosa alba, Rosa gallica, Rosa centifolia, Rose Oil

Rose oil is an oil derived from roses (plant genus Rosa) used in aromatherapy and romance. The essential oil appears to be rich in Citronellol, and preliminary evidence suggests sedative, stress relieving, and anti-depressive effects from the aroma.

See [Rose Essential Oil on Examine.com](#)

How to Take

(There is overall a lack of highly quantifiable information regarding the dosing of Rose essential oil) For the purposes of Aromatherapy, rose essential oil should be applied (or rose aromatics lit) to a degree where the aroma is detectable but not adverse. The room should be poorly to moderately ventilated. Topical administration of rose essential oil for large body surfaces (massage) should be diluted (up to 1%) in a cream or lather prior to administration, while pure essential oil may suffice for small body surface areas for the purposes of aromatherapy (if a wafting aroma from the body is desired over having the rose placed somewhere in the room).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Calmness	↑	★☆☆ Minor	1 study	Self-reported ratings of calmness increase following application of rose oil topically
C	CNS activity	↓	★☆☆ Minor	1 study	A decrease in CNS activity has been noted following topical application of rose oil (in which aroma was controlled with gas masks)
C	Blood Pressure	↓	★☆☆ Minor	1 study	A small reduction in blood pressure was noted, possibly secondary to reductions in CNS activity
C	Breathing Rate	↓	★☆☆ Minor	1 study	A decrease in breathing rate has been noted to be secondary to relaxing effects of rose oil topical application
C	Stress	↓	★☆☆ Minor	1 study	Self-reported ratings of stress are reduced with rose oil

					inhalation
C	Cortisol	↓	★☆☆ Minor	1 study	A decrease in cortisol appears to result from the anti-stress response of rose oil inhalation
C	Pain	↓	★☆☆ Minor	1 study	Inhalation of rose may confer pain relieving properties in emergency situations, although potency relative to other agents is not assessed

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Rose Hip

Also known as: Rosa canina, Dog Rose, Cynosbati fructus, Fructae cynosbati

Rose hip, the fruit of Rosa canina, is a dietary supplement for joint health. It appears to have mild benefits to arthritis when consumed as a daily supplement and the reported antiobese properties are not yet proven.

See [Rose Hip on Examine.com](#)

How to Take

Rose hip supplementation (referring to the water extract of rosa canina) tends to be consumed as a powdered supplement in the dosage range of 5-10g daily, divided into two doses and taken alongside food. This dosage appears to be beneficial, although benefits associated with it are more time-dependent than dose dependent (requiring a long duration of supplementation for benefits to arise). Doses of 40g daily have been used before, and aside from some intestinal distress from taking a high dose at once it does not appear to be harmful to health.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Symptoms of Osteoarthritis	↓	☆☆☆ Minor	3 studies	There appears to be benefit to osteoarthritis symptoms with supplementation of rose hip relative to placebo, with benefits more apparent over longer periods of supplementation.
C	C-Reactive Protein	—	—	5 studies	Preliminary studies showed marked reductions in C-reactive protein concentrations in healthy persons, although more recently conducted blinded studies have failed to replicate such a large decrease.
C	Pain	↓	☆☆☆ Minor	4 studies	Pain is reduced alongside improvements in osteoarthritic and rheumatoid arthritis, and at least one study (cohort) noted benefits in persons without these diseases yet with high labour jobs. No studies in athletes to assess the analgesic properties yet.
C	Liver Enzymes	—	—	2 studies	No significant influence on the liver

					enzymes of otherwise healthy persons subject to rose hip supplementation
C	Total Cholesterol	↓	☆☆☆ Minor	3 studies	A decrease in total cholesterol has been noted to a mild degree in obese persons, although a study in rheumatic patients without any abnormalities in cholesterol metabolism failed to find such an effect.
C	Symptoms of Rheumatoid Arthritis	↓	☆☆☆ Minor	2 studies	There appears to be mild benefits to joint symptoms in rheumatoid arthritis when rose hip is supplemented over the course of months, and these benefits may be seen at low (5g) dosages. Short term supplementation has not shown much benefit.
C	TNF-Alpha	—	—	1 study	At this point in time, there is no evidence to suggest modifications in the circulating levels of TNF-α relative to control.
C	Triglycerides	—	—	1 study	No significant influence of rose hip on triglyceride concentrations has been noted.
C	Blood Pressure	↓	☆☆☆ Minor	1 study	A mild (3.7%) decrease in systolic blood pressure has been noted in obese persons given supplementation of rose hip.
C	HDL-C	—	—	1 study	No significant alteration of HDL-C concentrations has been noted with limited evidence investigating rose hip supplementation.
C	LDL-C	↓	☆☆☆ Minor	1 study	A mild reduction in LDL cholesterol levels seen in obese persons with rose hip supplementation explains the reduction in total cholesterol, as HDL-C appears to be unaffected.
C	Adiponectin	—	—	1 study	No significant modifications in adiponectin concentrations when rose hip supplementation is given to humans.

C	Blood Glucose	—	—	1 study	Both fasting and postprandial glucose in persons given prolonged rose hip supplementation is not affected relative to placebo.
C	Insulin	—	—	1 study	No significant influence on circulating (basal) insulin has been noted with rosehip supplementation.
C	Insulin Sensitivity	—	—	1 study	No significant influence on insulin sensitivity has been noted in obese humans relative to placebo.
C	Weight	—	—	1 study	Despite some evidence to suggest antiobese effects in the mouse, limited human evidence has failed to find evidence in otherwise healthy but obese humans.
C	HbA1c	—	—	1 study	No significant influence of rose hip on HbA1c concentrations in the blood of non-diabetic yet obese persons relative to placebo
D	Chemotaxis	↓	★☆☆ Minor	2 studies	Chemotaxis of immune cells appears to be reduced with oral ingestion of rose hip supplements. This antiinflammatory/immunosuppressive mechanism is thought to underlie in part the benefits of rose hip against arthritic symptoms
D	Creatinine	↓	★☆☆ Minor	1 study	Creatinine, a biomarker of kidney damage and muscle damage, has been noted to be reduced with rose hip supplementation in one preliminary trial
D	Anti-oxidant Enzyme Profile	—	—	1 study	Limited evidence has failed to find any significant changes in antioxidant enzyme profiles in the red blood cells of those given rose hip extract

Rosmarinic Acid

Also known as: Rosmarinus Officinalis Extract, Rosemary Extract, Perilla Frutescens extract. Perilla Extract

Rosmarinic Acid is a polyphenol similar to caffeic acid (found in Coffee) and is in high levels in Perilla Oil and Rosemary, from which it draws its name from. It is a general anti-oxidant and health compound, and seen as 'healthy'.

See [Rosmarinic Acid on Examine.com](#)

How to Take

A standard dose is 200-300mg active Rosmarinic acid (check source for extract percentage) for oral ingestion.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Nasal Congestion	↓	★☆☆ Minor	1 study	Nasal congestion is reduced secondary to reducing pollen allergies
C	Allergies	↓	★☆☆ Minor	1 study	Rosmarinic acid appears to be effective in suppressing the response to pollen allergies in persons with seasonal rhinitis
D	Symptoms of Atopic dermatitis	↓	★☆☆ Minor	1 study	Topical application of rosmarinic acid may aid symptoms of atopic dermatitis

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Royal Jelly

Royal Jelly is essentially the breast milk of Bees. The 'Royal' refers to how the Queen lives on it, and the 'Jelly' refers to the consistency. It is a nutritive jelly with a composition similar to pollen, and is being investigated for effects on Testosterone and longevity.

See [Royal Jelly on Examine.com](#)

How to Take

It is unclear what dosage of Royal Jelly is seen as optimal, as benefits have been reported in the low milligram range (50-300mg) when taken daily as well as the lower gram range (6g daily).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Total Cholesterol	↓	☆☆☆ Minor	2 studies	A decrease in total cholesterol is noted in the range of 10% associated with 50-100mg of Royal Jelly daily; the evidence this conclusion was drawn from (via a meta-analysis) is a bit lacklustre
C	Triglycerides	—	—	3 studies	Although there may be a reduction in triglycerides associated with Royal Jelly, currently the best evidence suggests no such change
C	LDL-C	—	—	3 studies	Although a reduction in LDL-C cannot be ruled out (due to the reduction in total cholesterol), the best evidence currently suggest no effect while uncontrolled studies confirm a reduction of minor magnitude
C	HDL-C	—	—	3 studies	No significant influences on HDL-C detectable
C	Allergies	—	—	1 study	No detectable benefit to hay fever or pollen allergies in youth

C	Blood Glucose	↓	★☆☆ Minor	2 studies	May slightly reduce blood glucose in otherwise healthy older persons, but not to a remarkable degree
C	Testosterone	↑	★☆☆ Minor	1 study	A small increase in testosterone has been noted with 3g Royal Jelly for 6 months in older men and women, no studies in youth currently and practical significance of such a small increase unknown
C	Insulin Sensitivity	—	—	1 study	Despite a slight reduction in blood glucose, no significant influence on insulin sensitivity noted
C	HbA1c	—	—	1 study	No significant alterations in HbA1c levels following Royal Jelly ingestion for 6 months
C	Red Blood Cell Count	↑	★☆☆ Minor	1 study	At least one study has noted an increase in red blood cell count following ingestion of Royal Jelly
C	Estrogen	—	—	1 study	No significant alterations in estrogen seen with Royal Jelly
C	Weight	—	—	1 study	No significant alterations in weight over the long term with Royal Jelly supplementation
C	Blood Pressure	—	—	1 study	No significant alterations in blood pressure observed over long term supplementation with Royal Jelly
D	Symptoms of Menopause	↓	★☆☆ Minor	1 study	A decrease in symptoms related to menopause have been noted with Royal Jelly ingestion
D	Depression	↓	★☆☆ Minor	1 study	Reduction in irritability noted with Royal Jelly may be

					secondary to reducing symptoms associated with menopause
D	Irritability	↓	★☆☆ Minor	1 study	Decrease in irritability seen with Royal Jelly may be secondary to reducing the symptoms of menopause
D	Cell Adhesion Factors	—	—	1 study	No significant alterations in VCAM-1 levels in menopausal women, although a trend towards reduction was noted
D	C-Reactive Protein	—	—	1 study	No significant alterations in serum C-rp levels
D	Liver Enzymes	—	—	1 study	In safety testing, supplemental Royal Jelly does not appear to increase liver enzymes

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Rubus coreanus

Also known as: Korean Black Raspberry, Rubus tokkura, Cha tian pao, bokbunja, Rubi Fructus

Rubus coreanus (Korean Black Raspberry) is a dark berry sometimes brewed as a wine called bokbunja ju; it has a high levels of anthocyanins of the Cyanidin type, and other tannin structures that underlie its antioxidant and proerectile properties.

See [Rubus coreanus on Examine.com](#)

How to Take

The one human study on the subject matter used 30g of the freeze dried berries and noted antioxidative and liver benefits associated with that dose. For the food product it is probably a good starting point, and there is not enough information to assess if one can use bokbunja ju for health reasons. Many other studies in rats use the supplemental doses of 100-500 mg/kg of the unripe berry powder. In human terms, this gives us estimates of (the following is dry weight of the berry): 1,100-5,450 mg for a 150lb person 1,450-7,300 mg for a 200lb person 1,800-9,000 mg for a 250lb person If using unripe berries with a water content, it will need to be recalculated.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Liver Enzymes	↓	★☆☆ Minor	1 study	In otherwise healthy men with no health problems, the mild reduction in lipid peroxidation seen was associated with a mild reduction in circulating ALP levels (6%) although AST and GST were unaffected.
D	Testosterone	—	—	1 study	Despite the highly promising evidence in rats, there is no significant influence of the berries on testosterone levels of otherwise healthy men.
D	Blood Glucose	—	—	1 study	No significant alterations in fasting blood glucose are noted with daily berry consumption in otherwise healthy persons.
D	C-Reactive Protein	—	—	1 study	In otherwise healthy men, there are no changes in C-reactive protein levels seen with berry

					consumption.
D	Triglycerides	—	—	1 study	No significant influence of this berry on the triglycerides of otherwise healthy men.
D	HDL-C	—	—	1 study	No significant influence of the berries on HDL cholesterol levels in men who are otherwise healthy.
D	LDL-C	—	—	1 study	No significant influence of <i>rubus coreanus</i> on LDL cholesterol levels in otherwise healthy persons.
D	Total Cholesterol	—	—	1 study	Currently the only study is in otherwise healthy men with no cholesterol problems, and there was no influence of berry consumption.
D	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	1 study	There appears to be a mild increase in glutathione peroxidase with no significant influence on catalase nor SOD in otherwise healthy men.
D	Lipid Peroxidation	↓	★☆☆ Minor	1 study	In otherwise healthy men with no apparent health problems, there is a mild decrease in lipid peroxidation associated with consumption of the berries (12% reduction in MDA)

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Rubus suavissimus

Also known as: Chinese sweet leaf tea, Ten-cha

Rubus suavissimus (Chinese sweet leaf) is a plant whose leaves are used to brew a sweetened tea, and it is currently thought to be a decent weight loss aid in part due to suppressing the formation of body fat and in part due to its sweetness helping with food cravings.

See [Rubus suavissimus on Examine.com](#)

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Allergies	—	—	1 study	Although this tea appears to be a popular tea for the purpose of treating allergic rhinitis, the currently available human evidence does not support this conclusion.
C	Nasal Congestion	—	—	1 study	Due to the lone study failing to find benefit to allergic symptoms with 400mg of the leaf extract, there are no reported benefits to allergic rhinitis

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Ruscus aculeatus

Also known as: Butcher's Broom, Jew's Myrtle, Knee Holly, Kneeholm, Pettigree, Sweet Broom

An herb more commonly known as Butcher's Broom, *ruscus aculeatus* is traditionally used for circulation and appears to constrict veins. This is thought to reduce pooling of blood in extremities, and the limited evidence appears to be promising.

See [Ruscus aculeatus on Examine.com](#)

How to Take

Supplementation of *ruscus aculeatus* tends to use the rhizome (vertical root above the ground) of the plant, and when using this extract it tends to be at concentrations above 10-fold (10:1) to 20-fold (20:1), in order to concentrate the main bioactives which are the ruscogenins. In the above extract range, doses of 37.5mg are taken twice daily to total 75mg daily. This equates to approximately 750-1,500mg of the rhizome's unextracted dry weight daily. There is not enough evidence to suggest whether it is better to take *ruscus aculeatus* on an empty stomach or with a meal, and while the above dosing appears effective there is not enough evidence to suggest if it is the optimal dosage.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Leg Swelling	↓	★☆☆ Minor	1 study	Secondary to its venotropic actions in persons with chronic venous insufficiency, supplementation of <i>ruscus aculeatus</i> appears to reduce leg swelling and edema (thigh and ankle).
C	Chronic Venous Insufficiency	↓	★☆☆ Minor	1 study	<i>Ruscus aculeatus</i> appears to be more effective than placebo for treating chronic venous insufficiency, although the degree of benefit relative to other treatments is not established.
C	Subjective Well-being	—	—	1 study	Despite improving symptoms of chronic venous insufficiency in the afflicted persons, supplementation failed to lead to an increase in quality of life relative to placebo.

D	Visual Acuity	—	—	1 study	The improvement in visual acuity seen with supplementation of this herb failed to reach statistical significance in diabetic persons with retinopathy.
D	Fructosamine	↓	★☆☆ Minor	1 study	A 7.8% reduction in fructosamine has been noted with supplementation of <i>ruscus aculeatus</i> in diabetic persons.
D	Blood Glucose	↓	★☆☆ Minor	1 study	A reduction reaching 10.2% blood glucose has been noted with continual supplementation of <i>ruscus aculeatus</i> in type II diabetic persons in this non-placebo controlled study; requires replication.
D	HbA1c	↓	★★★☆☆ Notable	1 study	The decrease in HbA1c noted in this pilot study (15.6%) was fairly marked and requires replication.
D	Total Cholesterol	↓	★☆☆ Minor	1 study	A decrease in total cholesterol (9.4%) has been noted in diabetic persons alongside an increase in HDL-C. Requires replication.
D	HDL-C	↑	★★★☆☆ Notable	1 study	A fairly notable increase in HDL-C (23%) in the lone (but not placebo controlled) study with <i>ruscus aculeatus</i> , requires replication
D	Triglycerides	—	—	1 study	No significant influence on circulating triglycerides in diabetic persons given <i>ruscus aculeatus</i> supplementation.

S-Adenosyl Methionine

Also known as: SAME, S-AdoMet, Ademetionine, S-adenosyl-L-methionine, Adomet

S-Adenosylmethionine (S-AdoMet) is a methyl donating compound that circulates in the blood and provides methyl groups to maintain other metabolic reactions. Lowered S-AdoMet levels are associated with depressive symptoms, and supplementation may aid a partial deficiency.

See [S-Adenosyl Methionine on Examine.com](#)

How to Take

Supplementation of S-adenosylmethionine tends to be in the 600-1,200mg range over the course of a day, divided into two or three separated doses with meals. The higher dosage (1,200mg) tends to be used more often, with the lower dosage (600mg) being used to cut costs. For S-adenosylmethionine to benefit osteoarthritis, it appears to require a few weeks or up to a month of continual usage for benefits to show. Benefits to depressive symptoms may be much more rapid.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Symptoms of Osteoarthritis	↓	★★★☆☆ Notable	4 studies	Decreases in symptoms of osteoarthritis appear to be reduced to similar levels with S-AdoMet as with pharmaceuticals like Naproxen, although S-AdoMet requires a longer period of time for efficacy to occur
B	Functionality in Elderly or Injured	↑	★☆☆☆☆ Minor	3 studies	Somewhat of an increase in functionality of elderly persons, most likely secondary to the beneficial effects on joint health.
C	Liver Enzymes	—	—	3 studies	No significant rehabilitative effects on liver function in persons with impaired liver function, and no significant alterations in serum liver enzymes in otherwise healthy persons
C	Bilirubin	—	—	1 study	No significant alterations in serum bilirubin seen with supplementation

C	Liver Damage	—	—	1 study	Supplemental SAME in a study of persons with liver damage failed to confer rehabilitative effects
C	Attention	—	—	1 study	No significant alterations in attention in persons given SAME in conjunction with their SSRI antidepressant medication
C	Memory	↑	★☆☆ Minor	1 study	In persons with SSRIs, adding SAME confers a cognitive promoting effect; it is unsure if this persists in persons without SSRIs, and this augmenting effect with SSRIs is only seen in limited other instances (ie. with Creatine)
C	Motivation	—	—	1 study	No significant differences in self-reported motivation
C	Depression	↓	★★★☆☆ Notable	2 studies	Has been noted to augment SSRI therapy (similar to Creatine) and monotherapy with SAME appears to be of similar potency to tricyclic antidepressants for some studies.
C	Pain	↓	★★★☆☆ Notable	2 studies	The decrease in pain associated with osteoarthritis appears to be similar to the reference drugs Aleve (Naproxen) and Celecoxib, but requires more time to act (up to one month)
C	Homocysteine	—	—	3 studies	No significant alterations in plasma homocysteine occur following supplemental SAME ingestion
C	C-Reactive Protein	—	—	1 study	No significant influence on C-Reactive Protein
C	Numerical Memory	↓	★☆☆☆☆	1 study	

			 Minor		A decrease in numerical memory has been noted once in elderly subjects, which is thought to be secondary to some sedation rather than indicative of damaging effects
C	Symptoms of Fibromyalgia	↓	 Minor	1 study	A decrease in soreness symptoms of fibromyalgia (with no apparent effect on force production) has been noted with SAMe supplementation.
D	Early Virologic Response	↑	 Minor	1 study	An increase in the time taken to achieve a virological response was reduced, and SAMe is thought to confer an anti-viral effect
D	Cholestasis	↓	 Minor	1 study	Cholestasis is somewhat reduced with supplemental SAMe

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Saffron

Also known as: Crocus sativus

Crocus sativus is a stemless flower commonly known as saffron and used as a Spice. Low dose supplementation appears to confer antidepressive properties.

See [Saffron on Examine.com](#)

How to Take

For chronic supplementation, take 15mg of saffron, twice a day. This is the advised upper limit for constant supplementation. Preliminary evidence suggests that doubling this dose may have a toxic effect after eight weeks of continuous usage. Acute, single doses of saffron, can be as high as 200mg. Saffron can be supplemented by taking water extracts of the stigma (the red part of the plant, used as a spice) or by using the dehydrated stigma itself. Some evidence suggests that the petals of saffron may also be effective. Saffron can be taken twice a day in a supplement form, or at meals as a spice. Doses above 1,200mg may cause nausea and vomiting.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Depression	↓	★★★☆☆ Notable	9 studies	30mg saffron daily (both petals and stigma) appear to be effective in reducing depressive symptoms in persons with major depressive disorder, and the potency has been noted to be comparable to reference drugs (fluoxetine and imipramine).
C	Immunoglobulin A	—	—	1 study	No significant influence on circulating IgA concentrations following saffron ingestion.
C	Immunoglobulin G	↑	★★★☆☆ Minor	1 study	An increase in IgG concentrations has been noted to occur with saffron supplementation alongside a decrease in IgM and no influence on IgA.
C	Immunoglobulin M	↓	★★★☆☆ Minor	1 study	A decrease in IgM concentrations has been noted to occur following

					supplementation of saffron.
C	Neutrophil count	—	—	1 study	Neutrophil concentrations in serum are unaffected by supplementation of saffron.
C	Eosinophil count	—	—	1 study	Eosinophil concentrations are not affected by saffron supplementation in otherwise healthy persons.
C	Basophil count	↓	★☆☆ Minor	1 study	Basophil count has been noted to mildly decrease following saffron supplementation alongside a reduction in IgM concentrations.
C	Monocyte count	↑	★☆☆ Minor	1 study	Supplementation of saffron appears to be able to cause a mild increase in monocyte concentrations in serum.
C	White Blood Cell Count	↓	★☆☆ Minor	2 studies	A decrease in white blood cell count has been noted with supplementation of saffron at 60mg for over eight weeks.
C	Red Blood Cell Count	↓	★☆☆ Minor	2 studies	A decrease in RBCs has been noted in one study suggesting saffron toxicity with prolonged supplementation of a double dose (60mg).
C	Liver Enzymes	—	—	1 study	Supplementation of 100mg saffron extract for six weeks failed to increase liver enzymes in otherwise healthy persons.
C	Creatinine	—	—	1 study	Creatinine does not appear to be influenced in serum following supplementation of saffron.
C	Symptoms of Alzheimers	↓	★☆☆ Minor	2 studies	Mixed evidence on the efficacy of saffron, but it is possible that supplementation could delay an increase in symptoms without a therapeutic effect.

C	Visual Acuity	↑	★☆☆ Minor	2 studies	Supplementation of saffron appears to increase visual acuity in persons with age-related macular degeneration.
C	Sexual Function	↑	★☆☆ Minor	2 studies	SSRI related sexual dysfunction in both men and women appears to be reduced with coingestion of saffron, although saffron does not alter the efficacy of SSRI therapy on depression.
C	Erections	—	—	3 studies	The best evidence to date does not support a pro-erectile effect of saffron supplementation <i>per se</i> , although it may have a particular role in combating SSRI related sexual dysfunction that results in erectile dysfunction.
C	Weight	↓	★☆☆ Minor	1 study	A reduction in weight has been noted to a very mild degree which may be wholly related to a reduction in snacking that has been observed with saffron supplementation in overweight women.
C	Food Intake	↓	★☆☆ Minor	1 study	Secondary to reducing snacking (thought to be via increasing satiety from meals) saffron appears to reduce overall food intake.
C	Appetite	↓	★☆☆ Minor	1 study	High dose (176.5mg) saffron extract appears to be able to reduce snacking and increase self-reported satiety in otherwise healthy overweight women. It should be noted that with chronic supplementation of high doses (60mg) that have some minor toxic effects, that supplementation is associated with both increases and decreases in appetite.

C	Symptoms of PMS	↓	★★☆ Notable	1 study	One study assessing saffron on PMS symptoms noted that supplementation caused 76% of the participants to have more than a halving of overall symptoms (placebo reaching 8%), suggesting relatively potent effects.
C	Sperm Count	—	—	2 studies	Saffron supplementation does not appear to be effective in increasing sperm count in infertile men.
C	Seminal motility	—	—	2 studies	The best evidence to date does not support a role for saffron supplementation in increasing seminal motility.
C	Sperm Quality	—	—	2 studies	While preliminary evidence suggested benefit to seminal morphology, the best evidence to date does not support a role for saffron in enhancing seminal quality.
C	Testosterone	—	—	2 studies	Neither aromatherapy nor oral supplementation appear to significantly influence testosterone concentrations in serum.
C	Luteinizing Hormone	—	—	1 study	LH concentrations are unaffected by saffron supplementation at 60mg in infertile men.
C	Follicle-Stimulating Hormone	—	—	1 study	FSH is unaffected in infertile men given 60mg saffron daily over the course of 26 weeks.
C	Prolactin	—	—	1 study	Supplementation of 60mg saffron for 26 weeks does not significantly influence prolactin in infertile men.
C	Ejaculate Volume	—	—	1 study	Saffron does not appear to influence ejaculate volume in

					men with infertility.
C	Hemoglobin	↓	★☆☆ Minor	1 study	Hemoglobin has been noted to be decreased in one study and thought to be related to possible toxic effects of moderately high dose saffron (60mg for more than 8 weeks).
C	Serum Platelets	↓	★☆☆ Minor	1 study	Supplementation of 60mg saffron was able to reduce platelet counts in serum following eight weeks of exposure (increasing in magnitude until study cessation at 26 weeks) thought to be related to toxicity.
C	Blood Pressure	↓	★☆☆ Minor	1 study	A decrease in blood pressure was noted in otherwise healthy (normotensive) men following 26 weeks of saffron supplementation at 60mg daily, although this was thought to possibly be related to chronic toxicity of the higher than normal dose.
C	Estrogen	↑	★☆☆ Minor	1 study	The aroma of saffron appears to cause a mild increase in circulating estrogen concentrations in otherwise healthy women following 20 minutes of exposure.
C	Cortisol	↓	★☆☆ Minor	1 study	The aroma of saffron has been noted to reduce cortisol concentrations to a mild degree in otherwise healthy women, and this occurred alongside a reduction in state anxiety.
C	Anxiety	↓	★☆☆ Minor	1 study	The aroma of saffron has once been noted to cause a mild (approximately 10%) reduction in state anxiety following 20 minutes of exposure in otherwise healthy women.
D	Penile Girth	↑	★☆☆	1 study	

D		—	Minor		In men with erectile dysfunction, saffron appeared to increase nighttime tumescence at both the tip and base.
D	Oxidation of LDL	↓	★☆☆ Minor	1 study	Supplementation of saffron appears to be capable of reducing LDL oxidation when tested <i>ex vivo</i> in both healthy controls and persons with cardiovascular disease, although to a mild degree.
D	Skin Moisture	—	—	1 study	Acute topical application of a cream containing saffron has failed to cause significant changes in skin moisture content over the course of seven hours.

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Salacia reticulata

Also known as: Kothala himbutu

Salacia Reticulata is a medicinal herb from Ayurveda which appears to have anti-diabetic activities, namely by inhibiting carbohydrate uptake from the intestines; it appears quite effective at this, similar to Arcabose in potency.

See [Salacia reticulata on Examine.com](#)

How to Take

Supplementation of salacia herbs (reticulata or oblonga) seem to be effective in humans when taken at the oral dose of 240-1,000mg, with the higher dose being used more frequently for the purpose of reducing glucose absorption form the intestines. Due to this supplement acting as a carbohydrate absorption inhibitor, it needs to be taken alongside dietary carbohydrates.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Blood Glucose	↓	★★★☆☆ Notable	3 studies	The decrease in blood glucose is acute due to blocking carbohydrate absorption (no studies on long-term glucose influence) and standard supplemental doses range between 20-25% inhibition of carbohydrate absorption, with is quite reliable and significant. This has been noted in both diabetics as well as lean/healthy persons .
B	Insulin	↓	★★★☆☆ Notable	3 studies	A decrease in postprandial insulin has been noted with acute supplementation, which is thought to be secondary to the reduction in glucose absorption (as the two correlate highly). There are currently no studies assessing long term changes in fasting insulin
C	HbA1c	↓	★★☆☆☆ Minor	1 study	A decrease in HbA1c has been noted in diabetics given a tea

					of Salacia for months , but the decrease was minor in magnitude and outperformed by Glibenclamide

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Salvia hispanica

Also known as: Chia seeds, Mexican chia, Salba

Salvia hispanica (Chia) are seeds commonly used to supplement Dietary Fiber and are claimed to have other health promoting properties. Its mechanical properties may provide use during baking and the fiber content good for bowel health with health promoting effects not yet demonstrated.

See [Salvia hispanica on Examine.com](#)

How to Take

25g of chia tends to be used once daily with a meal for the purposes of general health and intestinal motility. There is no evidence to suggest if this is the optimal dose.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	C-Reactive Protein	↓	★☆☆ Minor	2 studies	It is possible that a decrease in C-Reactive protein may exist but evidence is contradictory at this moment in time
C	Inflammation	—	—	1 study	No significant alteration in serum biomarkers noted with chia seeds
C	Blood Glucose	↓	★☆☆ Minor	3 studies	Has been implicated in reducing postprandial glucose while having no significant influence on fasting glucose levels.
C	Blood Pressure	—	—	2 studies	No significant influence on blood pressure noted with long term chia ingestion
C	Triglycerides	—	—	2 studies	No significant influence on triglycerides
C	LDL-C	—	—	2 studies	LDL-C appears to be unaffected with chia ingestion when compared to similar macronutrient sources

C	HDL-C	—	—	2 studies	HDL-C appears to be unaffected with chia ingestion when compared to similar macronutrient sources
C	Total Cholesterol	—	—	2 studies	No significant influence on total cholesterol levels after inclusion of chia seeds into the diet
C	Appetite	↓	★☆☆ Minor	1 study	The decrease in appetite in one study was notable, but longer term studies do not note weight loss when diet is uncontrolled (which undermines the idea that chia is a potent appetite suppressant)
D	HbA1c	—	—	1 study	No significant influence on HbA1c levels of diabetics given chia seeds
D	Insulin	—	—	1 study	No significant influence on fasting insulin levels following chronic consumption of chia seeds in the diet
D	Fibrinogen	↓	★☆☆ Minor	1 study	A decrease in fibrinogen has been noted with chia seed ingestion according to one study
D	Symptoms of Xerotic Pruritus	↓	★☆☆ Minor	1 study	Topical application of chia seed oil to the skin appears to confer some symptom reduction in xerotic pruritus
D	Skin moisture	↑	★☆☆ Minor	1 study	An increase in skin moisture has been noted with topical chia seed application (4% of the solution being chia oil)

Salvia sclarea

Also known as: Clary Sage

Salvia sclarea (Clary Sage) is a herb commonly used as an aromatic. Belonging to the Mint family of plants, the 'relaxing' effects of the aromas may be related to preliminary evidence suggesting anti-depressant effects.

See [Salvia sclarea on Examine.com](#)

How to Take

If using Clary Sage for aromatherapy, enough should be lit (if using incense) to confer a pleasant aroma. The two studies using combination therapy noted that a cream containing 1 concentration drop of Clary Sage to 2 drops of Lavender in 5cc of volume was rubbed on the abdomen (the scent would remain on the body for a while). Due to the exact bioactives not being known, quantifying the right dose for aromatherapy is difficult. There is insufficient evidence to suggest an optimal oral dose of Clary Sage for any purpose.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Heart Rate	↓	★☆☆ Minor	1 study	A decrease in heart rate has been noted acutely in response to the aroma of clary sage
C	Blood Pressure	↓	★☆☆ Minor	1 study	A decrease in systolic blood pressure resulted in response to clary sage aromatherapy, to a small degree and likely not able to exert long-term benefit (probably more indicative of short-term CNS depression)
C	Cortisol	↓	★☆☆ Minor	1 study	A decrease in cortisol may result following inhalation of clary sage, but the magnitude of reduction (2.5%) is very small

Sarcosine

Also known as: N-methylglycine, Methylglycine

Sarcosine (N-methylglycine) is a product of glycine that is able to inhibit glycine reuptake, thus promoting the effects of glycine. It has potential usage as a cognitive enhancer and for schizophrenia, perhaps with more potency than D-Serine.

See [Sarcosine on Examine.com](#)

How to Take

Sarcosine is taken at the same oral doses as D-Serine, with 2,000mg daily appearing to be effective for cognitive purposes.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Symptoms of Schizophrenia	↓	★★★☆☆ Notable	4 studies	While the magnitude of benefit seen with Sarcosine is comparable to both D-serine and glycine, it appears to require a much lower (more practical) dose than does glycine and is more reliable than D-serine
C	Cognition			2 studies	

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Schisandra chinensis

Also known as: Omija, Omija Cha, Gomishi, Repnihat, Wuweizi, Lemonwood, Northern Magnolia Vine, Chinese Magnolia Vine, Matsbouza

Schizandra berries have been used traditionally as performance enhancers and as an Adaptogen. Lots of human evidence from many decades ago in Russia that cannot be accessed, and limited Western evidence. Appears to also reduce anxiety and cortisol, with a tart taste.

See [Schisandra chinensis on Examine.com](#)

How to Take

Clinical trials done in the West are lacking or confounded, and thus optimum doses cannot really be extrapolated from these. The best estimate at this moment in time may be falling back on traditional preparation methods, which are various: Dried fruit extract in a 1:6 w/v ratio against liquid (95% ethanol) and administered at 20-30 drops daily Dried fruit extract in a 1:20 w/v ratio against water, 150mL drank twice a day with meals Eating the powdered fruit or fruit extract (this is what is usually found in pills) at 1-3g daily, with meals Schisandra Chinensis fruits can be brewed into wines or teas as well.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Nitric Oxide	↑	★☆☆ Minor	1 study	An increase in serum nitric oxide has been detected in one study in elite athletes
C	Cortisol	↓↑	★☆☆ Minor	1 study	Conditional influences on cortisol, with an apparent increase in cortisol of beginner atheltes at rest with decreases in exercise-induced cortisol in beginners and lower overall cortisol exposure in trained athletes

Sea Buckthorn

Also known as: Hippophae rhamnoides

Sea buckthorn (Hippophae rhamnoides) is a plant whose leaves are sometimes supplemented (or the berries consumed as juice) for general antiinflammatory and antioxidative purposes. Though healthy, it does not appear to have any unique literature on it to support supplementation.

See [Sea Buckthorn on Examine.com](#)

How to Take

Sea buckthorn is supplemented as either a dry plant extract (of which both the berries and the leaves are viable options) or as an oil made from the berries. When supplementing dry extracts, the range of 500-2,000mg is used for both the berry extracts and the leaf extracts. For the oil, slightly higher dosage ranges (2,000-5,000mg) are used daily.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Inflammation	—	—	1 study	Supplementation of sea buckthorn in persons on hemodialysis has failed to significantly influence any inflammatory biomarker measured at the standard supplemental dosage.
C	C-Reactive Protein	—	—	1 study	2,000mg of the sea buckthorn supplement has failed to significantly influence C-reactive protein concentrations in serum
C	DNA Damage	—	—	1 study	DNA damage as measured in lymphocytes does not appear to be significantly affected by supplementation of sea buckthorn
C	Blood Glucose	↑	★☆☆ Minor	1 study	An increase in glucose has been noted with sea buckthorn, but it was from one study which had the control group (coconut oil) also raise blood glucose; this may just be due to added

					calories.
C	Platelet Aggregation	↓	★☆☆ Minor	1 study	5g of the oil daily is able to reduce platelet aggregation in otherwise healthy persons.
C	Triglycerides	—	—	1 study	Although it may attenuate postprandial lipidemia (spikes in triglycerides following a meal), supplementation does not appear to significantly affect fasting triglyceride concentrations.
C	Total Cholesterol	—	—	1 study	Total cholesterol does not appear to be affected with supplementation of sea buckthorn in otherwise healthy persons.
C	HDL-C	—	—	1 study	No significant influence on circulating HDL-C levels
C	LDL-C	—	—	1 study	No significant influence on LDL-C levels in otherwise healthy men
C	Dry Eyes	↓	★☆☆ Minor	1 study	2g of the oil daily is able to reduce symptoms of dry eyes, particularly reddening and the actual perceived dryness
D	Insulin Secretion	↓	★☆☆ Minor	1 study	Secondary to reducing the absorption of carbohydrates from a test meal, insulin secretion is attenuated
D	Carbohydrate absorption	↓	★☆☆ Minor	1 study	Carbohydrate absorption appears to be attenuated with oral ingestion of sea buckthorn berries alongside a meal, which is thought to be due to the fiber component.

Senna alexandrina

Also known as: Senna alexandrina, Daio

Senna Alexandria is a plant containing Sennosides, which are laxatives. Nothing more special about Senna root or Sennosides, they just are very effective at clearing your bowels and are at a level of potency where they are sometimes given before a colonoscopy.

See [Senna alexandrina on Examine.com](#)

How to Take

In accordance with clinical usage, the correct dose is the "lowest dose required to produce the desired effects (soft-formed and comfortable stool)". This is either 1-2g of the powdered extract or fruit usually standardized to 10-30mg active Sennosides. Higher doses are used only if the aforementioned lower dose is not effective (it should be noted that senna alexandrina is a delayed laxative unlike the immediate effects of Caffeine and it may take a few hours to assess whether a dose is effective or not). Senna alexandrina tends to be taken prior to bed in order to time its laxative effect with a morning bowel movement.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Intestinal Motility	↑	★★★ Strong	10 studies	Senna Alexandria is a reference drug for its laxative effects, with comparable efficacy to oral polyethylene glycol (PEG; used before colonoscopies) and lactulose, but more cost-effective than the latter
B	Constipation	↓	★★★ Strong	6 studies	Due to the strong laxative effect, constipation is greatly reduced with supplemental Senna Alexandria. Has been noted effective against regular, postpartum, and opioid-induced constipation and appears to not require a context-specific cause of constipation (ie. reliable) but appears to be associated with more cramping than placebo.

Serrapeptase

Also known as: Serratiopeptidase, Serratia E-15, serralysin, serratiaprotease, Serratiopeptidase, Silk worm enzymes

Serrapeptase (Serralysin) is an enzyme derived from the silkworm that is thought to confer anti-fibrinolytic and anti-inflammatory effects. It appears to be absorbed and have some efficacy, but seems unreliable with mediocre quality evidence.

See [Serrapeptase on Examine.com](#)

How to Take

Serrapeptase tends to be recommended to be ingested at 10-60mg daily, taken on an empty stomach (30 minutes before a meal or 2 hours after the last meal) and divided into up to three daily doses; most studies used a protocol where 10mg serrapeptase was taken every 8 hours (starting upon waking). There is insufficient evidence to suggest if this is the optimal dose, and 10mg of serrapeptase is equivalent to approximately 20,000 enzymatic units.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Inflammation	↓	★☆☆ Minor	4 studies	Appears to reduce swelling and inflammation following surgery or trauma, although to a lesser degree than corticosteroids. There is a lack of practical evidence for the claims behind serrapeptase (instead, studies tend to only look at post-surgery inflammation)
B	Pain	↓	★☆☆ Minor	5 studies	When a decrease in inflammation occurs post surgery, there appears to be a concomitant reduction in pain; it tends to hover around a 1 point reduction on a VAS scale (scale of 1-10).
C	Edema	↓	★☆☆ Minor	2 studies	Related to the antiinflammatory effects, swelling and edema post surgery appear to be reduced.
C	Breast Tenderness	↓	★☆☆	1 study	

			 Minor		A decrease in breast tenderness and soreness has been noted with serrapeptase treatment in one study.
C	Mucus Production	↓	 Notable	4 studies	A somewhat notable decrease in mostly the viscosity of mucus (elasticity is somewhat unreliably decreased), due to the mucolytic properties of serrapeptase. This may be of use for both nasal discharge and lung sputum (cystic fibrosis)
D	Symptoms of Carpal Tunnel	↓	 Minor	1 study	A decrease in symptoms has been noted, but the study was not structurally a good one; requires replication
D	Symptoms of Superficial Thrombophlebitis	↓	 Minor	1 study	There appears to be a small decrease in symptoms, which is thought to be due to fibrinolytic properties of serrapeptase

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Sesamin

Sesamin is a lignan derived from sesame seeds (*Sesamum indicum*) that appears to inhibit vitamin E metabolism, which causes a relative increase in circulating levels of γ -tocopherol and γ -tocotrienol; it shows most promise in augmenting the efficacy of vitamin E supplements.

See [Sesamin on Examine.com](#)

How to Take

There are limited human studies on sesamin, but it appears that oral ingestion of around 100-150mg of sesamin is sufficient to raise bodily sesamin stores to the level where it can preserve Vitamin E in the body; this indirect antioxidative effect may be the most practical reason to supplement sesamin. If using sesame seeds to get your sesamin from, human studies have used 50-75g of sesame seeds with some success and rat studies tend to use 100-fold the oral dose of sesame seeds relative to sesamin (which would make the aforementioned dose of 100-150mg as minimum being 10-15g of sesame seeds).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Blood Pressure	↓	★☆☆ Minor	1 study	A small decrease in blood pressure has been noted with sesamin supplementation

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Shilajit

Also known as: Mineral Pitch, Jew's Pitch, Ozokerite, Mineral Wax, Shilajita Mumiyo

Shilajit is a mixture of minerals used traditionally in Ayurveda, with the main bioactive of Fulvic Acid. It appears to be heralded, but is currently in the preliminary stages of research in the West.

See [Shilajit on Examine.com](#)

How to Take

Currently, the only human study conducted used 200mg of Shilajit with 50% Fulvic acid content in two divided doses with meals for a period of 90 days.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Testosterone	↑	★☆☆ Minor	1 study	A 23.5% increase has been noted in infertile men, it is not certain if this applies to fertile men.
C	Sperm Quality	↑	★☆☆ Minor	1 study	Sperm quality (and thought to apply to fertility) has been improved with shilajit supplementation
C	Follicle-Stimulating Hormone	↑	★☆☆ Minor	1 study	An increase in follicle-stimulating hormone has been detected with shilajit consumption
C	Luteinizing Hormone	—	—	1 study	No significant influence on luteinizing hormone
C	Lipid Peroxidation	↓	★☆☆ Minor	1 study	A decrease in lipid peroxidation (assessed by MDA) has been noted in serum and semen following oral ingestion of shilajit
C	Triglycerides	↓	★☆☆ Minor	1 study	Minor decrease in triglycerides has been noted with shilajit

C	LDL-C	↓	★☆☆ Minor	1 study	Minor decrease in LDL has been noted with shilajit
C	HDL-C	↑	★☆☆ Minor	1 study	Minor increase in HDL-C has been detected in persons after shilajit consumption
C	vLDL-C	↓	★☆☆ Minor	1 study	Minor decreases in vLDL concentrations have been noted
C	Weight	—	—	1 study	No significant influence detected on weight
C	Blood Pressure	—	—	1 study	No significant effect has been detected on blood pressure
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	1 study	An increase in superoxide dismutase has been noted with Shilajit consumption

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Sodium Bicarbonate

Also known as: Baking Soda, Bicarb, Bicarbonate

Sodium Bicarbonate (baking soda) is a molecule that acts as a buffering agent against acidity in the human body, and appears to enhance physical performance in elite and novice athletes. It also may have health benefits and intestinal side effects.

See [Sodium Bicarbonate on Examine.com](#)

How to Take

Supplemental sodium bicarbonate can be baking soda bought from the grocery store; they are the same molecule, so store-bought baking soda will work. Supplemental dosages of sodium bicarbonate are in the 200-300 mg/kg range when used before exercise. Although 500 mg/kg is slightly more effective, it tends to be associated with a higher degree of intestinal side effects if taken all at once. If taking sodium bicarbonate acutely for exercise, a dose should be taken 60-90 minutes before anaerobic activities associated with metabolic acidosis (i.e.. "the burn") for maximum benefit. For other activities that might be longer in duration, sodium bicarbonate should be taken 45-60 minutes before. Sodium bicarbonate can be taken with meals rather than acutely before exercise, and should be similarly effective. In this case, up to 500 mg/kg can be well tolerated if divided into three doses throughout the day (just over 150 mg/kg per dose) with no inherent need to take bicarbonate on the day of activity. Some health effects (increase in metabolic rate or attenuation of metabolic acidosis) can be achieved at more reasonable doses, such as 5-10g, and may be more practical for nonathletes. Additionally, as 27.3% of sodium bicarbonate's weight is due to sodium, every 100 mg/kg confers about 27 mg/kg sodium to the diet; this needs to be accounted for, and severely limits usage by persons with salt-sensitive hypertension. As the doses are measured in reference to body weight, obesity may result in a falsely high oral dose. If you are not within a normal or overweight BMI range, estimate your oral dose based on your "ideal weight" instead. The means of consuming bicarbonate is important, as excessively high doses or rapid ingestion can cause gastric upset due to a reaction between bicarbonate and stomach acid. Bicarbonate should be sipped slowly over a period of a few minutes with a moderate amount of water (500 mL), and the first time bicarbonate is used a half-dose should be ingested to assess tolerance. Rapidly ingesting the drink, or taking too much, is likely to induce stomach pain and nausea within an hour followed by increased diarrhea and flatulence; sticking to 200 mg/kg may alleviate the risk of these side effects. Independent of the dose taken, caution should be exercised with the manner by which sodium bicarbonate is ingested, so as to minimize intestinal and gastric side effects; these side effects occur with rapid or excessive consumption of bicarbonate, and include nausea and diarrhea.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Anaerobic Running Capacity	↑	★☆☆ Minor	34 studies	Cardiovascular exercise where failure is associated with metabolic acidosis (ie. 'the burn') appear to get benefit with bicarbonate supplementation to a small degree but reliably.

					For other exercises (rowing, sprinting, swimming) not characterized by the burn, the benefits are much less reliable
A	Power Output	—	—	28 studies	Although <i>technically</i> an increase in average power output may occur during exercise associated with the 'burn' (metabolic acidosis) to the degree of 1-2%, saying this is an inherent or reliable increase in power would be misleading; it is an attenuation of the decrease in power that acidosis is able to induce
A	Lactate Production	↓ ↑	★★★☆☆ Notable	37 studies	Increases of lactate production are noted in short intense exercises (due to allowing more work to be conducted, and the work produces more lactate) while prolonged exercise is associated with a decrease in lactate concentrations relative to placebo
A	Serum Bicarbonate	↑	★★★★ Strong	47 studies	For the purpose of increasing serum bicarbonate concentrations, orally ingested bicarbonate is the reference compound for it. The increases tend to be around a 30% increase from baseline values (as there is always a circulating bicarbonate concentration)
A	Blood Acidity	↓	★★★☆☆ Notable	46 studies	Although the magnitude of decrease is somewhat minor, this is due to blood pH being highly regulated in the body. pH appears to be reliably reduced following supplementation of 300mg/kg sodium bicarbonate
B	VO2 Max	—	—	7 studies	For the most part, peak VO2 consumption is not significantly influenced by supplemental sodium bicarbonate (although VO2 kinetics that are not referring to

					VO2 max may be influenced somewhat)
B	Aerobic Exercise	↑	★☆☆ Minor	3 studies	For cardiovascular exercise that is prolonged in nature (45m or greater) and not exceeding the lactate threshold, there appears to be a small beneficial effect of sodium bicarbonate supplementation on improving time to fatigue or time to complete a test
B	Heart Rate	—	—	5 studies	There is no significant effect of sodium bicarbonate on heart rate at rest or during exercise
B	Rate of Perceived Exertion	—	—	10 studies	Although there is some limited evidence that sodium bicarbonate can increase 'percieved readiness' for a task and ample evidence that it can reduce the rate of neuromuscular decline (seen with fatigue), the actual rate of percieved exertion (how hard an exercise feels) is wholly unaffected.
B	Training Volume	↑	★☆☆ Minor	10 studies	There might be an increase in work output conducted in tests that are anaerobic (high intensity) and associated with metabolic acidosis ('the burn') but may not extend to other contexts
B	Neuromuscular Function	↑	★☆☆ Minor	3 studies	Sports requiring hand-eye coordination (boxing and tennis) appear to be enhanced with supplemental sodium bicarbonate, with improved punch and tennis swing accuracy
B	Teeth Whitening	↑	★★★☆☆ Notable	3 studies	There appears to be a time dependent benefit on stain reduction when gum containing sodium bicarbonate is used, with efficacy at 4

					weeks (around 30-50% stain reduction) but more at 12 weeks (around 70%)
C	Insulin Sensitivity	↑	★☆☆ Minor	2 studies	Mixed effects on insulin sensitivity in persons who may be suffering from metabolic acidosis, with one positive and one null result
C	Blood Glucose	—	—	2 studies	No significant effect on blood glucose concentrations at rest or during exercise is seen with sodium bicarbonate supplementation
C	Insulin	—	—	1 study	Fasting insulin concentrations are not affected with sodium bicarbonate supplementation
C	Blood Pressure	—	—	1 study	No significant influence on blood pressure
C	Hydration	—	—	1 study	The addition of sodium bicarbonate to a pre-testing rehydration protocol does not enhance hydration more than the protocol itself (mostly water and carbohydrates)
C	Judo Performance	↑	★☆☆ Minor	1 study	During a simulated throwing test (throwing one of two partners for time), sodium bicarbonate ingestion is able to improve the amount of throw conducted in a set time
C	Fat Oxidation	↑	★☆☆ Minor	2 studies	An increase in fat oxidation has been noted at rest with supplemental sodium bicarbonate which contributed solely to the increase in metabolic rate
C	Lipid Absorption	↓	★☆☆ Minor	1 study	One study in menopausal women with a modest dose of sodium bicarbonate (less than 100mg) noted a reduction in lipid absorption from a meal.

C	Plasma Endorphins	↓	★★★☆☆ Notable	1 study	The exercise-induced spike in endorphins appears to be related to the spike in acidity, and supplementation of bicarbonate is able to potentially suppress the spike (although not abolish it)
C	Ammonia	—	—	2 studies	No significant effects on plasma ammonia detected with supplemental bicarbonate
C	Adrenaline	—	—	2 studies	Mixed effects, but one intravenous study (not in the human effect matrix) that also noted no significant differences suggest that the increase in catecholamines during exercise is not associated with acidity and thus not suppressed by sodium bicarbonate
C	Noradrenaline	↓	★★☆☆☆ Minor	1 study	A decrease in exercise-induced noradrenaline has been noted before, but it is unsure if this is correct information (as this was the lone study to measure noradrenaline, three studies have measured adrenaline and are split with the only one noting a decrease in adrenaline also being this study)
C	Muscle Oxygenation	↑	★★☆☆☆ Minor	1 study	The rate of muscle deoxygenation is reduced with attenuation of acidosis (which can be achieved with sodium bicarbonate), and in later stretches of exercise this can be manifest as a relative increase in oxygenation
C	Oxygen Uptake			1 study	
D	Metabolic Rate	↑	★★☆☆☆ Minor	1 study	An increase in metabolic rate has been noted and calculated (extrapolated) to be approximately 0.5% extra over

					the course of 24 hours, associated with a low dose of sodium bicarbonate (17mg/kg)
D	Weight	—	—	1 study	Despite the potential increase in metabolic rate and increase in ketone body production, there is currently no evidence to support more fat loss with sodium bicarbonate over placebo
D	Ketone Bodies	↑	★☆☆ Minor	2 studies	During fasting or ketogenic diets, sodium bicarbonate supplementation may be able to increase ketone body production. This appears to be of somewhat small magnitude and was not associated with additional fat loss
D	Insulin Secretion	—	—	1 study	No significant influence of supplementaion sodium bicarbonate on insulin secretion

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Soy lecithin

Soy lecithin is a lecithin (a structural term for a triglyceride with one fatty acid replaced by phosphatic acid conjugates) which delivers a high level of Phosphatidylserine (PS), Phosphatidylcholine (PC), and phosphatidylinositol (PI).

See [Soy lecithin on Examine.com](#)

How to Take

Supplementation of soy lecithin seems to be in the range of 500-2,000mg. While it does not require to be taken with a meal, it is usually recommended to do so out of prudence. Alternatively, soy lecithin can be dosed in accordance with Phosphatidylcholine dosing.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Cortisol	↓	★☆☆ Minor	1 study	May reduce cortisol during a social stress test at 2g
C	Stress	↓	★☆☆ Minor	1 study	May reduce perceived stress during stressful situations
C	Heart Rate	—	—	1 study	Despite the reduction in perceived stress, heart rate does not appear to be affected by supplemental soy lecithin
C	HDL-C	—	—	1 study	No significant influence on HDL-C levels
C	LDL-C	↓	★★★☆☆ Notable	1 study	A decrease in LDL-C has been noted with soy lecithin ingestion to the degree of 42.05-56.15% in hypercholesterolemics, which is a remarkable decrease. Requires replication.
C	Total Cholesterol	↓	★★★☆☆ Notable	1 study	A decrease in total cholesterol, mostly due to LDL-C, has been noted to the magnitude of 40.66-42.00% which is astounding; requires

					replication.
C	Triglycerides	-	-	1 study	No significant influence on triglycerides

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Spirulina

Spirulina is a non-toxic blue-green algae. It is a source of phycocyanobilin. Preliminary evidence suggests spirulina is remarkably potent at protecting the brain and reducing liver fat.

See [Spirulina on Examine.com](#)

How to Take

A standard dose of spirulina is between 1-3g. Doses up to 10g have been used in studies effectively. Spirulina is about 20% C-phycocyanin by weight, and about 1% phycocyanobilin by weight. The dosage range of 200mg/kg C-phycocyanin (1g/kg spirulina) in rats is approximately: 10.9g for a 150lb person 14.5g for a 200lb person 18.2g for a 250lb person Further research is needed to determine whether spirulina should be taken once a day, or in smaller doses, multiple times per day. It is not recommended to exceed the highest dose mentioned above, as no clear benefits have been noted beyond that level.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Lipid Peroxidation	↓	★★★☆☆ Notable	3 studies	Although there is no reference drug to compare the effects of Spirulina against, the decrease in lipid peroxidation as assessed by serum MDA is quite notable and is likely stronger than other supplements. A comparative study would be needed
B	Muscular Endurance	↑	★★☆☆☆ Minor	3 studies	Studies currently assessing the effects of spirulina on muscular endurance are too heterogeneous to properly assess potency thereof. However, a positive effect does appear to exist
B	Triglycerides	↓	★★★☆☆ Notable	8 studies	In populations with metabolic syndrome or related morbidities (diabetes, hyperlipidemia, hypertension, etc.) spirulina in a variety of doses between 1-8g daily is able to reduce triglycerides up to 10-15%.

B	HDL-C	↑	★☆☆ Minor	7 studies	A positive influence of spirulina on HDL-C appears to be present, but the magnitude of benefit is not overly remarkable and varies depending on the disease state (with states associated with fatty liver having a much greater increase in HDL-C seen with spirulina)
B	LDL-C	↓	★☆☆ Minor	6 studies	Degree of efficacy seems variable and correlated with disease state (more drastic improvements when LDL-C is much higher) but currently does not appear to be overly remarkable unless fatty liver exists.
B	Total Cholesterol	↓	★☆☆ Minor	6 studies	Reductions in cholesterol seen are positive, but not overly remarkable
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	2 studies	Although increases have been noted in glutathione peroxidase and superoxide dismutase, it is difficult to assess potency thereof as there are no active controls and the two studies heterogenous.
C	Fat Oxidation	↑	★☆☆ Minor	1 study	Nothing remarkable in the one study on fat oxidation rates during exercise.
C	Inflammation	↓	★☆☆ Minor	2 studies	Some various and uncertain changes in cytokines that are seen as indicators of inflammation; not enough human interventions to draw conclusions.
C	General Oxidation	↓	★★★☆☆ Notable	1 study	Notable due to mechanisms, but requires studies with reference drugs and more biomarkers measured.
C	Allergies	↓	★★★★ Strong	1 study	The lone study suggests that spirulina is strongly effective in

					controlling allergies, with the symptoms of nasal discharge, sneezing, nasal congestion and itching being time-dependently reduced and self-reported satisfaction doubling more than double that in spirulina relative to placebo.
C	Nasal Congestion	↓	★★★ Strong	1 study	The decrease in nasal congestion seen in the one study was remarkably strong relative to placebo in a model of allergic rhinitis; it is not sure if this applies to other causes of nasal congestion.
C	Blood Pressure	↓	★★★☆☆ Notable	3 studies	Insufficient evidence to fully evaluate the effects on blood pressure, but given how 6 weeks supplementation reduced both systolic and diastolic in <i>nonhypertensive</i> persons by about 11/6 points it is notable
C	Insulin Sensitivity	↑	★★☆☆☆ Minor	1 study	Requires more evidence to establish its potency
C	Blood Glucose	↓	★★☆☆☆ Minor	3 studies	Reductions in blood glucose seen are not overly remarkable or noteworthy
C	Arsenic Poisoning	↓	★★☆☆☆ Minor	1 study	Somewhat effective, but requires more evidence; no reference drug was used to compare
C	Symptoms of Oral Cancer	↓	★★★☆☆ Notable	1 study	The lesions were fully healed in 44% of the 1g spirulina group relative to 7% of the placebo; although no reference drug was used.
C	Power Output	↑	★★★☆☆ Notable	1 study	Notable as acute power output (leg extension measurement) increased by 20-30% (more efficacy in untrained persons, some efficacy in trained persons) after 8 weeks

					whereas placebo failed to have an increase. Needs more research to fine-tune the efficacy.
C	Weight	—	—	2 studies	Currently not enough evidence to support any significant interaction with weight
C	HbA1c	↓	★★★☆☆ Notable	2 studies	Lone study noted a decrease from 9% to 8% with 2g spirulina, which is somewhat notable but requires more evidence to establish this.
C	White Blood Cell Count	↑	★☆☆☆☆ Minor	1 study	Minor increase, needs more evidence in a non-aged cohort to assess potency
C	Risk of Anemia	↓	★☆☆☆☆ Minor	1 study	Although there was some promising evidence, it did not appear overly remarkable and requires further evidence.
C	Red Blood Cell Count	—	—	1 study	Currently insufficient evidence to support a change in RBC count.
D	Natural Killer Cell Content	↑	★★★☆☆ Notable	1 study	The increases in mRNA content of natural killer cell content increased 37-55% (NKG2D) and 75% (perforin) which appeared to be dose-dependent, a possibly potent immunostimulatory effect.
D	Natural Killer Cell Activity	↑	★★★☆☆ Notable	1 study	NK cell activity against a tumor cell line (K562) increased 40% following a week ingestion of fairly reasonable oral dosing, suggesting that this is a notable increase of possible interest.
D	Fatigue	—	—	1 study	Currently no evidence to support an improvement in fatigue symptoms
D	Sustained Virologic	↑	★★★☆☆	1 study	

D	Response		 Notable		Notably effective as it trended to outperform Milk Thistle , which is a good reference supplement in regards to a sustained virologic response (not the best comparison, however)
D	Liver Enzymes	↓	 Notable	2 studies	Preliminary evidence suggests the reduction of liver enzymes correlates with the degree of liver damage somewhat, and this is notable since the reduction of liver fat seen is strongly effective at this moment in time.
D	Liver Fat	↓	 Strong	1 study	Although only based on a series of case studies at this moment in time, the reduction of liver fat seen after 3 months was remarkably effective

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Stephania tetrandra

Also known as: hangfangji, Fangchi, Hang Fang Chi

Stephania tetrandra (Fang Ji) is a medicinal herb from Traditional Chinese Medicine that is sometimes used alongside Astragalus membranaceus for kidney protection and diabetes prevention; it is moderately antiinflammatory.

See [Stephania tetrandra on Examine.com](#)

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Serum Elastase	↓	☆☆☆ Minor	1 study	A decrease in serum neutrophil elastase has been noted, and this is thought to be related to symptoms of rheumatoid arthritis
D	Lipid Peroxidation	↓	☆☆☆ Minor	1 study	A minor decrease in levels of lipid peroxidation in serum were noted, to the tune of 17%.
D	White Blood Cell Count	—	—	1 study	No significant alterations in white blood cell count are noted with oral supplementation of this plant.
D	Lymphocyte Count	—	—	1 study	Lymphocytes (both B and T cells) are unchanged in their overall quantity with 12 weeks of supplementation.

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Stevia

Also known as: Rebiana, rebaudioside A, stevioside, steviol, steviol glycosides, sweetleaf, sugarleaf,

Stevia rebaudiana (Stevia) is a herb where either the leaf extract or isolated 'steviosides' are used for sweetening. Unlike other sweeteners, stevia is 'natural' (rather than artificial) and associated with both beneficial pharmacological effects and some toxicity.

See [Stevia on Examine.com](#)

How to Take

Preferentially, stevia is dosed according to taste (as it is used as a sweetener). For prudence, and due to some toxicological data on this herb, an estimated upper daily intake of around 8mg/kg should be used (for a 150lb human, this is 540mg). This dose is within the current recommended intake limits, and is sufficient for anti-inflammatory and anti-oxidant effects but insufficient for any observed toxic or infertility inducing effects of stevia. That being said, some human studies using prolonged intake of up to 1.5g daily show no adverse effects.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Blood Pressure	↓	★☆☆ Minor	4 studies	There appears to be a reduction in blood pressure associated with stevia only in persons with high blood pressure, this may be a transient effect that is normalized upon supplement cessation.
B	Blood Glucose	↓	★☆☆ Minor	3 studies	There may be a very small glucose reducing effect of stevia consumption, but it does not appear to apply to everybody and is unreliable. Requires more evidence.
C	Appetite	—	—	1 study	No significant influence on appetite have been detected with stevia (in isolation)
C	Food Intake	↓	★☆☆ Minor	1 study	Stevia, in place of caloric sweeteners, has been associated with reducing whole-day food intake.

C	Heart Rate	—	—	2 studies	No significant influence on heart rate detected with stevia consumption
C	HbA1c	—	—	1 study	No significant influence on HbA1c serum levels has been detected
C	Cardiac Mass	↓	★☆☆ Minor	1 study	A reduction of cardiac mass has been detected over long term usage with stevia, which is thought to be secondary to a reduction in blood pressure
C	HDL-C	—	—	1 study	No significant influence on HDL-C has been detected with stevia
C	Total Cholesterol	—	—	1 study	No significant effect on total cholesterol levels have been detected with stevia consumption
C	Triglycerides	—	—	1 study	No significant influence on circulating triglycerides has been noted with stevia consumption

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Stinging Nettle

Also known as: Urtica dioica, Radix Urticae, Common Nettle, Greater Nettle, Ortica, Tsuknida

Stinging Nettle is quite a nasty plant to touch, but oral ingestion of pills without spikes results in a moderately potent anti-inflammatory that can reduce the sniffles. Does not boost Testosterone despite being claims to, although it can help Benign Prostatic Hyperplasia and urine abnormalities.

See [Stinging Nettle on Examine.com](#)

How to Take

120mg of Stinging Nettle (root) taken three times a day (totalling 360mg) is associated with benefit in Benign Prostate Hyperplasia.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	1 study	An increase in glutathione peroxidase has been detected
C	Lipid Peroxidation	—	—	1 study	No significant effect on lipid peroxidation has been noted.
C	Inflammation	↓	★☆☆ Minor	2 studies	Appears to reduce LPS-stimulated proinflammatory cytokine release, and thus is likely to have anti-inflammatory effects. The potency of this is not overly remarkable
C	C-Reactive Protein	↓	★☆☆ Minor	1 study	Minor decrease in C-reactive protein concentrations
C	Weight	—	—	1 study	No significant influence on body weight with consumption of stinging nettle
C	Insulin Sensitivity	—	—	1 study	No significant interactions between insulin sensitivity and stinging nettle yet detected
C	TNF-Alpha	—	—	1 study	No apparent effect on

					circulating TNF-a at baseline (may reduce TNF-a secretion from proinflammatory signals, see inflammation)
C	Testosterone	—	—	1 study	No detectable influence on testosterone levels
C	Symptoms of Benign Prostatic Hyperplasia	↓	★☆☆ Minor	1 study	Appears to increase urinary flow rate in persons with benign prostatic hyperplasia
C	Prostate Hypertrophy	—	—	1 study	No significant influence on prostatic hypertrophy despite reducing symptoms
C	Symptoms of Osteoarthritis	—	—	4 studies	Highly difficult to assess the efficacy of stinging nettle on osteoarthritic symptoms due to a wide degree of variance in study methodology
C	Allergies	↓	★☆☆ Minor	1 study	A small decrease in allergic symptoms with oral stinging nettle consumption
C	Nasal Congestion	↓	★☆☆ Minor	1 study	A slight decrease in nasal congestion seen with stinging nettle

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Sulbutiamine

Also known as: Arcalion, Enerion, Bisibuthiamine, Youvitan

Sulbutiamine is a synthetic molecule which consists of two Thiamine (Vitamin B1) molecules bound together by a sulfur group, and appears to be somewhat useful in alleviating fatigue; especially that associated with infection.

See [Sulbutiamine on Examine.com](#)

How to Take

Human studies using sulbutiamine supplementation have used 400mg daily. It is not clear if this is near the optimal dosage, and an ideal dosing regimen (with or without meals and how many divided doses a day) is not currently known.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Symptoms of Diabetic Neuropathy	—	—	1 study	Insufficient evidence to support a role in diabetic neuropathy associated with sulbutiamine supplementation
D	HbA1c	—	—	1 study	No significant influence of sulbutiamine on HbA1c
D	Blood Glucose	—	—	1 study	No significant influence on blood glucose in diabetics detected

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Taurine

Also known as: 2-aminoethane sulphonic acid, L-Taurine

Taurine is not bull urine, it is an amino acid with a sulfur in it. It is found in foods, in highest amounts in meats, and is a heart and blood healthy agent that can confer a wide variety of health benefits. Its most well known usage is to reduce cramping caused by fat burners like Ephedrine.

See [Taurine on Examine.com](#)

How to Take

Dosages between 500mg-2,000mg have shown efficacy, although the upper limit for toxicity is placed at a much greater level and high doses are well-tolerated. The upper limit for which one can be relatively assured no side effects will occur over a lifetime has been suggested to be 3g a day.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Blood Pressure	—	—	2 studies	Despite the improvement in blood flow, no significant influence on blood pressure
C	Heart Rate	—	—	3 studies	No significant influence on heart rate following Taurine supplementation
C	Blood Flow	↑	★★★☆☆ Notable	1 study	The improvement in blood flow seen in type 1 diabetics was sufficient to normalize to a non-diabetic control group
C	Muscle Soreness			1 study	
C	Muscle Damage			1 study	
C	Fat Oxidation			1 study	
C	Rate of Perceived Exertion			1 study	
C	Anaerobic Running Capacity			1 study	
D	Exercise Capacity (with Heart Conditions)	↑	★★☆☆☆ Minor	1 study	An improvement in walking distance has been noted

D	Weight	-	-	1 study	No significant influence on weight noted with supplementation

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Tauroursodeoxycholic Acid

Also known as: TUDCA

TUDCA is a water soluble bile acid. It shows great potency in treating cholestasis (bile acid backup in the liver) as the water soluble bile acids counteract the toxicity of regular bile acids. Can also protect and rehabilitate the liver, and general protects cells; very promising molecule.

See [Tauroursodeoxycholic Acid on Examine.com](#)

How to Take

10-13mg daily has once been shown to improve liver regeneration rates in a clinically ill population, and may be the lowest estimate of an active oral dose. When looking at improving bile salt composition, a dose around 15-20mg/kg bodyweight TUDCA seems best according to one study. Benefits have been seen at 1,750mg daily for muscle and liver insulin sensitivity, which is the highest dose used for treatment of fatty liver disease.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Liver Enzymes	↓	★★★☆☆ Notable	5 studies	The decrease in liver enzymes associated with cholestasis is quite strong, and TUDCA is a reference drug for these effects
C	Insulin Sensitivity	↑	★★★☆☆ Notable	1 study	Notable due to reaching near 30% improvement in obese persons and only being localized to muscle tissue and the liver, but not adipose tissue
C	Fat Mass	—	—	1 study	No significant influence on fat mass in obese persons
C	Weight	—	—	1 study	No significant influence on weight in obese persons
C	Blood Glucose	—	—	1 study	No significant influence on fasting glucose levels
C	Insulin	—	—	1 study	No significant influence on fasting insulin levels

C	Cholestasis	↓	★★★☆☆ Notable	1 study	Is either comparable or exceeds the potency of ursodeoxycholic acid, the reference drug for cholestasis
D	Total Cholesterol	↓	★★☆☆☆ Minor	1 study	A decrease in total cholesterol in serum has been noted secondary to treating cholestasis
D	HDL-C	↓	★★☆☆☆ Minor	1 study	A decrease in HDL-C has been noted to be secondary to treating cholestasis
D	Liver Cell Content	↑	★★☆☆☆ Minor	1 study	An increase in hepatocyte regeneration has been noted with TUDCA in persons with liver disease

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Terminalia arjuna

Also known as: Arjuna, Dhavala, Kakubha, Nadisarja, Veeravriksha, Partha, Indradru

Terminalia arjuna (Arjuna) is a tree that has its bark used medicinally, usually for the purposes of cardioprotection. It appears to reduce pressure and pulse rate, and may increase aerobic exercise capacity.

See [Terminalia arjuna on Examine.com](#)

How to Take

A standard dose for the purposes of cardiac health appears to be 500mg of the bark (water extract) taken daily in the morning without food (no evidence exists to suggest that taking it with food is bad or anything). For persons who suffered cardiac trauma (such as Myocardial Infarction), this dose tends to be taken thrice a day every 8 hours. The leaf extracts and ethanolic extracts appear to be more related to the cytotoxic and anti-tumor effects, but not enough evidence exists to recommend an active dose of these extracts for human consumption.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Power Output	↑	★☆☆ Minor	1 study	Power output has been noted to be increased in sprint tests, which is thought to be secondary to pulmonary effects of terminalia
C	Anaerobic Running Capacity	↑	★☆☆ Minor	1 study	Able to increase intermittent sprint performance
C	Left Ventricular Ejection Fraction	↑	★☆☆ Minor	2 studies	Appears to increase LVEF in person suffering from cardiovascular ailments; preliminary evidence suggests that this is not limited to myocardial infarction
C	Mitral Regurgitation	↓	★☆☆ Minor	1 study	Appears to reduce mitral regurgitation in persons with cardiac complications
D	Cardiac Mass	↓	★☆☆ Minor	1 study	A decrease in cardiac mass has been noted in persons who suffered heart failure and

					were given Terminalia Arjuna
D	Liver Enzymes	—	—	1 study	No significant influence on liver enzymes during standard testing of safety

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Tetradecyl Thioacetic Acid

Also known as: TTA

Technically an Omega-3 fatty acid, TTA is a non-metabolizable fatty acid that cannot be used for energy and may be able to burn fat via mechanisms similar to Conjugated Linoleic Acid. Lacking studies in humans at the moment, TTA appears to be a promising future candidate for fat loss and health.

See [Tetradecyl Thioacetic Acid on Examine.com](#)

How to Take

Not much evidence currently exists in human, but the standard dose appears to be 1g of TTA daily taken in divided dosages with meals.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Total Cholesterol	↓	☆☆☆ Minor	3 studies	Possible reductions in total cholesterol with supplementation of TTA
C	Triglycerides	↓	☆☆☆ Notable	3 studies	The one trial using TTA to reduce triglycerides noted a reduction of around 15%, which is notable and requires replication
C	TNF-Alpha	↓	☆☆☆ Minor	2 studies	A decrease in serum levels of TNF-a has been noted with supplemental TTA
C	Cell Adhesion Factors	↓	☆☆☆ Minor	1 study	Expression of VCAM-1 has been noted to be decreased
D	LDL-C	↓	☆☆☆ Minor	3 studies	Possible reductions in LDL cholesterol seen with TTA consumption
D	Liver Enzymes	—	—	3 studies	No significant influence on liver enzymes in preliminary testing for possible toxicity
D	Uric Acid	—	—	2 studies	

D					No significant alterations in serum uric acid seen with supplemental TTA
D	C-Reactive Protein	—	—	2 studies	No significant influence on C-Reactive Protein levels
D	HbA1c	—	—	2 studies	No significant alterations in HbA1c concentrations
D	Blood Pressure	↓	★☆☆ Minor	2 studies	A slight reduction in blood pressure has been noted in dyslipidemic obese men with TTA supplementation
D	Weight	—	—	2 studies	Although increased mitochondrial fat oxidation was created for underlying the reductions in lipids and blood pressure, no significant influence on body weight was noted in obese men
D	HDL-C	↑	★☆☆ Minor	3 studies	An increase in HDL cholesterol has been noted with TTA consumption
D	Blood Glucose			1 study	
D	Kidney function			2 studies	
D	Red Blood Cell Count			1 study	
D	White Blood Cell Count			1 study	
D	Heart Rate			1 study	
D	Thyroid-Stimulating Hormone			1 study	
D	Serum T4			1 study	
D	Viral Load			1 study	
D	Apolipoprotein B			1 study	
D	Insulin Sensitivity			1 study	

Theaflavins

Theaflavins are a group of molecules that are found in black tea (due to an additional fermentation process from green tea) that are said to be the bioactives of black tea.

See [Theaflavins on Examine.com](#)

How to Take

Theaflavins for purposes that do not require absorption (oral health, stomach ulceration, intestinal or colonic interactions) can have bioactivity in the doses found in Black Tea (this may also be advisable as the capsule of a supplement would need to break for it to influence the stomach or oral cavity) There is currently no evidence to support the best oral dose of supplementation, although studies tend to use 700mg of Theaflavins once a day (this is said to be 30 cups of Black Tea, but that is a variable claim due to varying levels of Theaflavins in Black Tea to start) Currently no evidence to support the best time of day or manner to take Theaflavin supplementation, although if using it for the purposes of hindering fat or carbohydrate absorption it would need to be taken alongside a meal containing those nutrients.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Cortisol	↓	☆☆☆ Minor	1 study	A decrease in exercise-induced cortisol secretions has been noted with theaflavin consumption in high doses (above 1,800mg daily)
C	Power Output	↑	☆☆☆ Minor	1 study	An increase in power output on a Wingate test has been noted with theaflavins supplementation above 1,800mg daily; efficacy of lower doses is uncertain
C	Muscle Soreness	↓	☆☆☆ Minor	1 study	May decrease muscle soreness at high doses, with the efficacy of lower doses uncertain.
C	Inflammation	—	—	1 study	No significant influence on inflammatory cytokines noted with theaflavins supplementation
C	Total Cholesterol	—	—	1 study	

C					No significant influence on total cholesterol levels with theaflavins supplementation
C	LDL-C	—	—	1 study	No detectable influence on LDL-C levels following theaflavin consumption
C	HDL-C	—	—	1 study	No significant influence of theaflavins on HDL-C
C	Triglycerides	—	—	1 study	No significant influence of theaflavins on triglycerides (hypercholesterolemic persons)

Theanine

Also known as: L-Theanine, 5-N-Ethyl-Glutamine

L-Theanine is a relaxing and nondietary amino acid found pretty much exclusively in teas from *Camellia sinensis* (alongside Green Tea Catechins and Caffeine) and is known to promote relaxation without sedation. It appears to be effective at this as well as reducing stress at standard dosages.

See [Theanine on Examine.com](#)

How to Take

L-Theanine tends to be taken in the dosage of 100-200mg, usually alongside Caffeine

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Anxiety	↓	☆☆☆ Minor	4 studies	Possible anxiety reducing effects, although anticipatory anxiety appears to be unaffected.
B	Relaxation	↑	☆☆☆ Notable	3 studies	A notable increase in relaxation (usually without sedation) appears to occur, as assessed by neural measurements (such as alpha-waves) or self-report surveys. Occurs within 30 minutes to an hour
C	Symptoms of Schizophrenia	↓	☆☆☆ Minor	1 study	Activation and anxiety symptoms of schizophrenia appear to be reduced with high dose (400mg) Theanine
C	Subjective Well-Being	—	—	1 study	No significant influence on subjective well being and mood state per se
C	Sleep Quality	↑	☆☆☆ Minor	1 study	Sleep quality has been noted to improve in persons with hyperactivity during sleep (such as ADHD). Sleep duration and latency do not appear to be affected

C	Heart Rate			2 studies	
C	Sedation			1 study	
C	Attention			1 study	
C	Reaction Time			1 study	
C	Stress			1 study	

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Tinospora cordifolia

Also known as: Guduchi, makabuhay, Amrita, Giloya, Giloe

Tinospora cordifolia (Guduchi or Amrita) is an immunostimulant in Ayurveda mechanistically similar to Reishi that stimulates macrophages and potentially reduce symptoms of allergic rhinitis. It has some additional but lesser benefits to diabetes, and holds promise as an anti-cancer herb.

See [Tinospora cordifolia on Examine.com](#)

How to Take

Supplementation of Tinospora cordifolia tends to use the water extract of the stem, which is standardized to a minimum concentration of 5% bitters (referring to the bitter tasting alkaloids and diterpenes) and consumed at up to the dosage of 1g daily. Usually 300mg is taken thrice daily. If using Amrita Ghrta (Tinospora cordifolia with Ghee and some Ginger), a traditional dosage according to Ayurveda appears to be in the 10-15g range take once daily. Due to traditional usage of this herb being alongside Ghee (which serves as an absorption enhancer of sorts), it may be prudent to take this supplement alongside a meal.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Neutrophil count	—	—	3 studies	Although there was a reduction in neutrophils in the nasal mucosa, the two studies measuring neutrophils in serum failed to find any benefit.
C	Nasal Congestion	↓	★★★ Strong	1 study	In persons suffering from allergic rhinitis, nasal congestion is completely resolved in around two-thirds of persons. Currently no studies in nasal congestion for persons without allergies.
C	Allergies	↓	★★★ Strong	1 study	At least in regards to allergic rhinitis, oral ingestion of <i>tinospora cordifolia</i> appears to abolish symptoms in 61-83% of persons (depending on symptom) extending to nasal blockage, mucus, pruritis, and sneezing.
C	Lymphocyte Count	↓ ↑	★☆☆ Minor	2 studies	Variable effects on

					Lymphocytes, with both increases and decreases being noted in persons with allergic rhinitis and no effect being observed in those with HIV.
C	Eosinophil count	↓	★★★☆☆ Notable	2 studies	There appears to be a reduction in eosinophils in the range of 30% or greater, somewhat notable
C	T cell count	—	—	1 study	Overall concentrations of T-cells (including CD4+ Lymphocytes) do not appear to be significantly influenced
C	CD4 Lymphocytes	—	—	1 study	Limited studies looking into CD4+ Lymphocytes have failed to find a stimulatory effect.
C	Symptoms of HIV	↓	★★☆☆☆ Minor	1 study	Quite modest reductions in the reported symptoms of HIV when <i>tinospira cordifolia</i> is used as adjuvant therapy
C	Macrophage Activity	↑	★★☆☆☆ Minor	2 studies	Macrophage activity (phagocytosis and intracellular killing capacity) appears to be preserved when preloaded to surgery, which normally suppresses these parameters.
C	Diabetic Foot Ulceration	—	—	1 study	Although there were trends for improvement, they failed to be statistically significant and there doesn't seem to be a strong therapeutic effect of <i>tinospira cordifolia</i>
D	Scabies	↓	★★★☆☆ Notable	3 studies	Topical application of a <i>tinospira cordifolia</i> lotion to youth infected with scabies appears to be comparable in potency to a 5% permethrin lotion as well as Crothamiton (two reference drugs).
D	Bilirubin	—	—	1 study	The reduction in bilirubin seen

					with this herb failed to reach statistical significance when used in a clinical setting.

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Tribulus terrestris

Also known as: Trib, puncturevine, protodioscin

Tribulus terrestris is a plant from Ayurveda where the root and fruits are used for male virility and general vitality, respectively. The roots enhance libido and sexual well being without affecting testosterone while the fruits appear to be potently protective of organ function.

See [Tribulus terrestris on Examine.com](#)

How to Take

Given a 60% saponin extract, a dose of between 200-450mg a day is typically used for libido enhancement and sexuality. If rodent research applies to humans, then the dosage of 5mg/kg of tribulus terrestris saponins which is seen as the optimal dose would correlate to a human dose of: 55 mg saponins (90 mg of a 60% extract) 70 mg saponins (120 mg of a 60% extract) 90 mg saponins (150 mg of a 60% extract) Which suggests low doses are better. If a concentrated extract is not used, traditional dosages of the basic root powder are in the 5-6g range while the fruits are in the 2-3g range.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Testosterone	—	—	4 studies	In otherwise healthy males, testosterone is not influenced with supplementation of <i>tribulus terrestris</i> . There may be an increase in infertile men, but this is weak.
C	Lean Mass	—	—	2 studies	Insufficient evidence to support an increase of lean mass associated with tribulus relative to placebo during a training program.
C	Fat Mass	—	—	2 studies	No significant influences on fat mass are noted with tribulus terrestris
C	Power Output	—	—	2 studies	No significant alterations in power output associated with tribulus supplementation.
C	Luteinizing Hormone	—	—	1 study	No influence on luteinizing hormone has been detected

					with supplemental tribulus
C	Fatigue	—	—	2 studies	Exercise related fatigue and vigor is unaffected by tribulus supplementation in trained men
C	Blood Pressure	↓	★☆☆ Minor	1 study	A decrease in blood pressure has been noted in hypertensive subjects; insufficient evidence to address efficacy in normotensive persons
C	Heart Rate	↓	★☆☆ Minor	1 study	A decrease in heart rate has been observed in hypertensive persons given tribulus supplementation
C	Total Cholesterol	↓	★☆☆ Minor	1 study	A decrease in cholesterol levels has been noted with tribulus supplementation
C	Diuresis	↑	★☆☆ Minor	1 study	3g of the fruits or a water extract thereof appears to increase overall urine volume after a month of supplementation by around 200mL daily.
C	Erections	↑	★☆☆ Minor	1 study	In infertile men, supplementation of 6g tribulus root appears to increase rigidity of erections and improve performance (reduce anxiety while delaying ejaculation and improving orgasm).
C	Libido	↑	★☆☆ Minor	1 study	There appears to be an increase in frequency of coitus and improvement in sexual well being associated with supplementation of 6g of the basic root extract of tribulus.
C	Sperm Count	—	—	1 study	The increase in sperm count seen with tribulus failed to outperform placebo.

C	Sperm Quality	-	-	1 study	The increase in sperm quality seen with 6g tribulus root has failed to outperform placebo in infertile men.

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Trimethylglycine

Also known as: Betaine, TMG, Glycine betaine, oxyneurine, lycine

Trimethylglycine (commonly referred to as betaine) is an active metabolite of Choline in the body and a component of beetroot. It serves a vital role in methylation in the body alongside folate, and is an osmoregulator like Creatine; possible ergogenic aid as well.

See [Trimethylglycine on Examine.com](#)

How to Take

The lowest active dose of betaine is 500mg taken throughout the course of the day. This is a dose that appears to be minimally active in reducing homocysteine and may be healthy to take, and doses of this up to 1,000mg seem to be in the range of being minimally active but also able to be gained through food consumption (so supplementation may not be needed). The standard doses that seen to be used for dietary supplementation are in the range of 2,500-6,000mg taken in two divided doses daily, and taking said doses alongside a meal does not appear to be required. This is the dosage range which reliably reduces homocysteine, and is the dosage range where (unreliable and minimal) benefits to physical performance have been noted. Studies on liver fat and fibrosis, and in some clinical settings on homocysteine reduction where the subject appears to be resistant to the 6g dose, the dosage can be increased up to 20g daily; this does appears to be moderately well tolerated (like any osmolyte, it may cause diarrhea in this high of a dose).

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Lactate production	—	—	3 studies	An attenuation in the rise of lactate seen in more endurance based exercise may need to be replicated, since two other studies (majority of evidence) have failed to find an interaction with betaine ingestion and lactate.
B	Blood Glucose	—	—	4 studies	No known alterations in fasting blood glucose concentrations or glucose concentrations during exercise seen with betaine supplementation.
B	Homocysteine	↓	★★★ Strong	9 studies	Betaine (3g or more) appears to potently and reliable reduce homocysteine concentrations following a single dose and

					maintaining this reduction for as long as supplementation is continued. The magnitude is around 10% in persons with normal homocysteine levels, and greater (20-40%) in those with high homocysteine, and (unlike folate) works in instances of methionine loading tests. 500mg betaine can reduce homocysteine after a methionine load, but it too low to influence fasting homocysteine.
B	Serum Folate	—	—	4 studies	<i>Chronically</i> there are no changes to serum folate due to the body normalizing folate levels, but acute supplementation can reduce folate concentrations in serum sharply for a short time.
B	Weight	—	—	4 studies	No significant alterations in weight are seen with supplementation of betaine, which is different than what is seen with another popular sports osmolyte (creatine).
B	Fat Mass	—	—	3 studies	Fat mass does not appear to be significantly influenced with either short term (2 week) or long term supplementation.
B	HDL-C	—	—	3 studies	No significant alterations in circulating HDL-C are seen with prolonged supplementation of betaine in persons with metabolic impairment.
B	LDL-C	↑	★☆☆ Minor	3 studies	Similar to total cholesterol, one study noted a stasis in LDL when placebo decreased (a relative increase). Reasons for this unknown and the data needs to be replicated, and HDL was unaffected.
B	Total Cholesterol	↑	★☆☆ Minor	3 studies	One study noted a stasis in

					total cholesterol when placebo decreased (a relative increase). Reasons for this unknown and the data needs to be replicated.
B	Liver Enzymes	↓	☆☆☆ Minor	5 studies	Similar to liver fat and damage, the levels of liver enzymes in serum appears to be reduced potentially in preliminary evidence with the currently largest trial showing no significant influence; there may be a role, but it needs to be further elucidated.
B	Power Output	—	—	7 studies	There appear to be isolated cases of power output being increased which fail to be replicated elsewhere under similar experimental conditions, and the majority of evidence suggests that the power output increase seen is no greater than placebo; a potential ergogenic effect is either due to a currently unknown prerequisite (ie. parameter of the study population) or is not present.
B	Muscular Endurance	—	—	3 studies	There may be a small benefit in prolonged and exhaustive resistance training with betaine relative to placebo, but at this moment in time most evidence assessing muscular endurance has failed to find a statistically significant increase (trends to improve do seem apparent).
B	Fatigue	—	—	3 studies	One study noted a reduced <i>rate of change</i> in fatigue (no overall differences in fatigue outright though) seen with betaine, whereas the other two studies have failed to find benefit with betaine.
B	Anaerobic Running Capacity	—	—	3 studies	Studies assessing distance, time, or other parameters of performance during cycling

					tests have failed to find any significant benefit with betaine supplementation (one positive study measuring power output is pooled in that parameter).
C	Growth Hormone	—	—	1 study	The minor increase in growth hormone seen with betaine (6.1%), relative to placebo, failed to reach statistical significance and is too low of magnitude to consider it practically appreciable.
C	IGF-1	↑	★☆☆ Minor	1 study	IGF-1 appears to be minimally increased relative to placebo (7.8%) following two weeks supplementation of betaine and when tested after exercise in a fasted state.
C	Cortisol	↓	★☆☆ Minor	1 study	Cortisol appears to be minimally (6.1%) decreased with two weeks betaine supplementation when measured after exercise in a fasted state.
C	Insulin	—	—	1 study	Similar to blood glucose, there is currently no known influence of betaine supplementation on fasting insulin concentrations.
C	Dry Mouth	↓	★☆☆ Minor	4 studies	Symptoms of dry mouth either caused by a disease state (Sjögren's syndrome) or as a side-effect of pharmaceuticals appears to be significantly reduced when betaine is formulated into a toothpaste at 4%.
C	Serum Methionine	↑	★☆☆ Minor	2 studies	Secondary to reducing homocysteine (since betaine gives a methyl group to homocysteine to convert it into L-methionine) there is an increase in serum methionine seen with supplementation acutely; this is normalized somewhat after prolonged

					supplementation.
C	Serum Cobalamin	—	—	3 studies	Mixed evidence as to whether B12 is influenced with supplementation of betaine, but the higher quality study appears to show no effect (since the other study noted a decline in B12 in placebo).
C	Metabolic Rate	—	—	1 study	No significant influence of betaine on the metabolic rate of obese persons subject to chronic supplementation.
C	Blood Pressure	—	—	1 study	No significant influence of betaine supplementation on blood pressure is currently known.
C	Triglycerides	—	—	2 studies	No significant alterations in serum triglycerides are noted with prolonged supplementation of betaine supplementation.
C	Creatinine	—	—	1 study	No significant influence on circulating creatinine is seen with supplementation of betaine.
C	Thyroid-Stimulating Hormone	—	—	1 study	No significant influence of betaine on circulating TSH concentrations in serum.
C	Nitric Oxide	—	—	2 studies	A potent increase in nitric oxide seen in a pilot study has failed to be replicated in a controlled intervention.
C	Training Volume	↑	★☆☆ Minor	1 study	One study noted an increase in overall training volume (6.5%) when the whole workout was assessed, and this was without any apparent changes in the volume conducted in any individual set or any changes in the rate of perceived exertion.

C	Lipid Peroxidation	—	—	1 study	No significant alterations have been noted in circulating biomarkers of lipid peroxidation.
C	Heart Rate	—	—	2 studies	No significant influence on heart rate in subjects who are rehydrated and then subject to exercise.
C	Rate of Perceived Exertion	—	—	2 studies	No significant influence of betaine (acute or two weeks of supplementation) on the rate of perceived exertion.
C	Muscle Oxygenation	↑	★☆☆ Minor	1 study	There appears to be a minor increase in overall oxygen consumption during physical training (anaerobic) to fatigue associated with betaine supplementation, although this was alongside increased work volume (which may be the causative factor).
C	Muscle Soreness	—	—	1 study	No significant influence of betaine supplementation of subjective ratings of muscular soreness nor the pump relative to placebo.
C	Hydration	—	—	2 studies	Betaine supplementation does not appear to be significantly beneficial in improving hydration status of users either outright or after prior dehydration relative to water alone.
C	Hematocrit	—	—	2 studies	No significant influence on hematocrit is noted with supplementation of betaine.
C	Lean Mass	—	—	2 studies	In studies assessing lean mass, there are no apparent changes with supplementation of betaine.

C	Muscle Creatine Content	—	—	1 study	Betaine (2g) has failed to increase phosphocreatine levels in skeletal muscle and failed to augment the increase caused by 20g of creatine.
C	Liver Damage	↓	★☆☆ Minor	3 studies	Preliminary evidence showed a large decrease in fibrotic area and inflammation in the livers of persons with NAFLD given high dose (20g) betaine, but the best evidence failed to find a significant influence. An interaction is apparent, but the exact role is not known as this time.
C	Liver Fat	↓	★☆☆ Minor	3 studies	Preliminary evidence showed a major decrease in liver fat (normalization in over half of persons with fatty liver) but currently the best evidence suggests that this does not occur as potently; there may still be a role, but this requires more research.
C	Adiponectin	—	—	1 study	No significant influence on adiponectin concentrations in persons with fatty liver seen with betaine supplementation.
C	TNF-Alpha	—	—	1 study	No significant influence on TNF-α concentrations following supplementation of betaine to persons with fatty liver.
C	Rate of Percieved Exertion	—	—	1 study	No significant influence on the rate of perceived exertion is seen with supplementation of betaine in rehydrated athletes.
C	VO2 max	—	—	1 study	Although a minor increase in oxygen uptake was noted in certain situations (final sprint of testing), overall VO ₂ max is not significantly affected.
C	Oxygen Uptake	—	—	2 studies	A minor increase in oxygen uptake was noted in selective

					testing (final sprint of one, but not both, betaine conditions) which did not manifest over the whole study period and is likely practically insignificant.
C	Plasminogen Inhibitor 1	↑	★☆☆ Minor	1 study	An increase in PAI-1 concentrations has been noted with 4g of betaine supplementation daily over the course of six months in otherwise healthy adults.
C	Kidney function	—	—	1 study	No significant alterations of kidney function in healthy persons given betaine (4g) for six months.
C	Oxidation of LDL	—	—	1 study	No significant alterations in the overall oxidation of LDL cholesterol associated with supplementation of betaine.
C	Apolipoprotein A	↑	★☆☆ Minor	1 study	An increase in Apolipoprotein A1 has been noted with supplementation of betaine relative to placebo in otherwise healthy persons.
C	Fibrinogen	—	—	1 study	No significant alterations in fibrinogen concentrations seen with supplementation of betaine.
C	Blood Flow			1 study	
D	Salivation	↑	★☆☆ Minor	3 studies	Betaine containing toothpaste, in persons with xerostomia (dry mouth), can reduce symptoms of dry mouth possibly related to an increase in salivation (basal salivation, not in response to stimuli)

Uncaria tomentosa

Also known as: Cat's Claw, Vincaria

Uncaria Tomentosa (Cat's Claw) is an Amazonian vine that has been traditionally recommended for antiinflammatory and fatigue syndromes.

See [Uncaria tomentosa on Examine.com](#)

How to Take

Studies using Cat's Claw tend to use 250-350mg of the ethanolic extract once a day. This is usually standardized to a Pentacyclic Oxindole Alkaloid content.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	White Blood Cell Count	↑	☆☆☆ Minor	1 study	An increase in white blood cell count has been noted with Cat's Claw by 9% over 9 weeks with a water extract, which is thought to be related to the immunoenhancing properties. The white blood cells that were increased were not assessed

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Uridine

Also known as: UDP, UMP

Uridine is a nucleotide base found in high levels in beer which is used for increasing synthesis of cellular membranes and for other neurological properties. It appears to have potentially cognitive enhancing properties, and is synergistic with Fish Oil.

See [Uridine on Examine.com](#)

How to Take

Supplementation of uridine seems to be in the 500-1,000mg range, with the lone human study using the higher end of this range. It is recommended to take uridine with food out of prudence, but this has not been noted to be an absolute requirement.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
D	Symptoms of Bipolar Disorder	↓	★☆☆ Minor	1 study	Depressive symptoms of bipolar disorder are fairly strongly reduced with uridine supplementation, but currently only open label studies are in existence
D	Depression	↓	★☆☆ Minor	1 study	Depressive symptoms in bipolar disorder have been noted to be reduced

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Valeriana officinalis

Also known as: Valerian

Valeriana officinalis, also known as valerian, is an herbal tea and supplement. It is commonly used for its sedative and Anxiety-reducing effects.

See [Valeriana officinalis on Examine.com](#)

How to Take

A standard dose of valerian is 450mg. Daytime supplementation should consist of 2 to 3 doses of 300mg. Valerian supplements consist of the root, which is standardized to contain 0.8-1% valerenic acid. Valerian should be taken an hour before bed. If valerian is being supplemented during the daytime, it should be taken with meals.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Sleep Quality	—	—	4 studies	At least according to an overall meta-analysis on the topic, valerian does not appear to be much greater than placebo for aiding sleep in otherwise healthy persons. This may differ in persons with insomnia but that is not yet tested adequately
B	Sleep Latency	—	—	3 studies	There are isolated cases of minor reductions in the time taken to fall asleep (improvements in sleep latency), but the majority of the evidence and the only meta-analysis to date suggest no significant influence of valerian.
C	Symptoms of Menopause	↓	★☆☆ Minor	2 studies	Limited evidence suggests efficacy in the treatment of menopausal symptoms with valerian extract, with one study measuring benefits to hot flash frequency and the other insomniac symptoms.
C	Symptoms of PMS	↓	★☆☆	1 study	

			★☆☆ Minor		Abdominal pain associated with menstruation appears to be reduced relative to placebo in women who complained of above average levels of pain during their menstrual cycles.
C	Pain	↓	★☆☆ Minor	1 study	Menstrual pain appears to be reduced with supplementation of low dose valerian extracts.
C	Insomnia	↓	★☆☆ Minor	2 studies	Mixed evidence, with benefit to insomnia in menopausal women yet no apparent benefit in those with restless leg syndrome. Overall, a lack of evidence to conclude efficacy for this particular disorder.
C	Sedation	↑	★☆☆ Minor	2 studies	Doses above 750mg may be associated with the 'morning hangover' side effect (sleepiness upon waking) whereas lower doses of 400mg have not been associated with such.
C	Symptoms of OCD	↓	★☆☆ Minor	1 study	The lone study assessing the effects of valerian and OCD found a benefit with treatment relative to placebo.
C	Symptoms of Restless Leg Syndrome	↓	★☆☆ Minor	2 studies	There may be benefits to restless leg syndrome, although this was found only in persons with excessive daytime sleepiness; over the whole group, there was no significant benefit.
C	Fatigue	↓	★☆☆ Minor	1 study	One study assessing valerian in persons with cancer on chemotherapy (of which insomnia may be a side effect of chemotherapy) found reductions in sleep disturbances which manifested as less fatigue during the day; no other evidence at this point in time.

C	Anxiety	—	—	1 study	Valerian does not appear to be effective for the treatment of generalized anxiety disorder in the one study assessing its effects.

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Vanadium

Vanadium is a mineral that is not one of the Essential Mineral compounds, but is sometimes ingested in the diet. Can be found in bone tissues, Vanadium may influence glucose metabolism in an anti-diabetic manner.

See [Vanadium on Examine.com](#)

How to Take

The majority of research on vanadium uses an oral dose of 100mg as a once daily supplement in persons with poor glucose tolerance. It is unsure if this is the optimal dose, but it appears to be effective.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Insulin Sensitivity	—	—	5 studies	Although an insulin sensitizing effect cannot be fully ruled out at this point in time, the more robust evidence currently does not support this insulin sensitizing effect in obese persons with impaired glucose tolerance. It may be only in diabetics
C	Triglycerides	↑	★☆☆ Minor	2 studies	A slight increase in triglycerides has been noted with vanadium supplementation
C	LDL-C	—	—	3 studies	Mixed effects on LDL-C, likely no direct influence on LDL but may reduce overall LDL levels secondary to improving the diabetic state (which normally increases LDL)
C	HDL-C	—	—	2 studies	No significant influence on HDL-C levels in serum of obese subjects
C	Total Cholesterol	—	—	2 studies	No significant alterations in the levels of total cholesterol <i>per se</i> , but a decrease has been

					noted to be secondary to attenuating diabetic symptoms
D	Glycogen Resynthesis	↑	★☆☆ Minor	1 study	An increase in glycogen content has been noted in diabetic persons given vanadium, no studies in athletes currently
D	HbA1c	↓	★☆☆ Minor	2 studies	A decrease in HbA1c has been noted with vanadium supplementation
D	Blood Pressure	—	—	1 study	No significant influence on blood pressure noted
D	Blood Glucose	↓	★☆☆ Minor	1 study	A decrease in blood glucose has been noted in type II diabetics which is thought to be secondary to reducing hepatic synthesis of glucose

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Velvet Antler

Also known as: Deer Velvet Antler, Deer Antler, Elk Velvet Antler, Cervus, Lu Jiao Pan

Velvet Antler (usually from deer) is crushed antler that is orally consumed for preventative health purposes. Hailing from Traditional Chinese Medicine, velvet antler does not appear to influence hormones and is currently unsupported for muscle repair (although it may aid skin regeneration rates).

See [Velvet Antler on Examine.com](#)

How to Take

Due to a lack of human evidence to support benefits of this supplement, an optimal dosage cannot yet be ascertained. Two possible options exist: 500 mg once daily, which is what seems to be used in most dietary supplements 1,000-2,000 mg daily, which appears to be the recommendation from Traditional Chinese Medicine

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Testosterone	—	—	3 studies	Repeated trials have failed to find an increase in testosterone associated with velvet antler supplementation
C	IGF-1	—	—	1 study	No significant influence of velvet antler on IGF-1
C	Lean Mass	—	—	1 study	No interaction between velvet antler and lean mass accrual
C	Power Output	↑	★☆☆ Minor	2 studies	A lone study noted an increase in muscle torque associated with Velvet Antler supplementation, which needs to be replicated to see if it is a true effect.
C	Aerobic Exercise	—	—	1 study	No benefit of velvet antler on aerobic cardiovascular exercise
C	Red Blood Cell Count	—	—	1 study	No influence of this supplement on red blood cell

					count following prolonged supplementation
C	Erythropoietin	—	—	1 study	No influence on erythropoietin with velvet antler supplementation
C	Prolactin	—	—	1 study	No significant interactions with prolactin and velvet antler noted
C	Follicle-Stimulating Hormone	—	—	1 study	No alterations in FSH levels have been noted with velvet antler supplementation
C	Luteinizing Hormone	—	—	1 study	No significant influence on luteinizing hormone levels
C	Free Testosterone	—	—	1 study	Free testosterone was unaltered with velvet antler relative to placebo
C	Libido	—	—	1 study	There does not appear to be a significant influence of velvet antler supplementation on the libido
C	Symptoms of Rheumatoid Arthritis	—	—	2 studies	No significant influence of velvet antler on symptoms of rheumatoid arthritis
C	Growth Hormone	—	—	1 study	No significant influence on growth hormone levels
C	Anaerobic Running Capacity	—	—	1 study	No significant influence on anaerobic cardiovascular exercise capacity

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Vinpocetine

Also known as: Vincamine, Vinca Minor, Periwinkle Extract, Cavinton (Brand Name), ethyl apovincamate

Vinpocetine is a compound from the Periwinkle plant that is used as a cognitive protective and anti-aging agent. One of the more common of the nootropics, Vinpocetine may enhance blood flow and is touted to increase memory; this latter claim has not been investigated.

See [Vinpocetine on Examine.com](#)

How to Take

Vinpocetine is taken in the daily dosage range of 15-60mg, divided into three daily doses with meals. The standard low dose is 5mg at each of these three meals, with 20mg at each meal being seen as the higher end of efficacy. These doses are taken for the purposes of neuroprotection, enhancing cerebral blood flow, and reducing the rate of cognitive decline. Doses in the higher end of that range (30-45mg acute dosages) may be useful for promoting cognition and memory formation in otherwise healthy persons, but there is not a lot of evidence looking at this claim.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Pulse Rate	↓	★☆☆ Minor	1 study	A decrease in pulse rate has been noted with vinpocetine
C	Reaction Time	↓	★☆☆ Minor	1 study	High doses (40mg) may reduce reaction time during tested, with lower doses not being potent enough to influence reaction time
C	Processing Accuracy			1 study	
C	Memory	↑	★☆☆ Minor	1 study	An increase in acute memory formation has been noted in female volutneers given 40mg Vinpocetine
D	Subjective Well-Being	↑	★☆☆ Minor	2 studies	An increase in well being has been noted to be secondary to the reduced rate of cognitive decline
D	Functionality in Elderly or Injured	↑	★☆☆ Minor	1 study	An improvement in balance has been noted with

					vinpocetine ingestion in the elderly, which may be related to the attenuation of cognitive decline
D	Cognitive Decline	↓	★☆☆ Minor	2 studies	The rate of cognitive decline appears to be attenuated with vinpocetine administration, this may be related to blood flow
D	Isaac speech activity test	↑	★☆☆ Minor	1 study	Improvements in speech performance have been noted in the elderly, which may be more indicative of the reductions in cognitive decline

Vitamin B12

Also known as: Cyanocobalamin, cobalamin, methylcobalamin, 5-deoxyadenosylcobalamin, adenosylcobalamin, cobamamide, dibenzozide, hydroxocobalamin

Cobalamin (Vitamin B12) is a water-soluble essential vitamin that is known to play roles in neurology.

See [Vitamin B12 on Examine.com](#)

How to Take

Supplementation of vitamin B12 tends to be around 1,000mcg (1mg) of supplemental vitamin B12 to persons who are at risk for B12 insufficient or deficiency, mostly older individuals and vegans.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Homocysteine			1 study	
D	Fatigue			1 study	
D	Depression			1 study	
D	Stroke Recovery Rate	↑	★☆☆ Minor	1 study	A slight improvement in verbal learning associated with 1,000mcg of B12 supplementation in persons with lacunar stroke, according to at least one pilot study

Vitamin C

Also known as: Ascorbic Acid, Ascorbate, 2-oxo-L-threo-hexono-1,4-lactone-2,3-enediol, L-ascorbic acid

Vitamin C is an essential vitamin with antioxidant properties. It is frequently supplemented to ward off the common cold.

See [Vitamin C on Examine.com](#)

How to Take

The Recommended Daily Intake (RDI) of vitamin C is 100-200mg. This is easily attained through the diet, so supplementation of such low doses is usually unnecessary. Higher doses of vitamin C, up to 2,000mg, are used to support the immune system (for athletes) or reduce the duration of the common cold. Most studies on vitamin C prescribe one dose per day. The claim that taking 2,000mg up to five times a day to optimally reduce cold symptoms is not sufficiently tested and requires more evidence.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	General Oxidation	↓	★☆☆ Minor	6 studies	Surprisingly mixed influences on biomarkers of oxidation, with either a decrease or no significant influence the majority of the time (with limited evidence to hint at an increase being possible)
B	Lipid Peroxidation	↓	★☆☆ Minor	6 studies	Mixed and weak influences on lipid peroxidation, but a possible reduction exists
B	Blood Flow	↑	★☆☆ Minor	4 studies	An increase in blood flow is seen in instances of impaired blood flow (smoking, obesity, etc.) which may be due to preservation of nitric oxide function (via reducing oxidation thereof); this is a phenomena general to antioxidants and not unique to Vitamin C
B	Inflammation	—	—	4 studies	No significant alterations seen in inflammatory cytokines associated with Vitamin C supplementation

B	Muscle Damage	↓	★☆☆ Minor	4 studies	Although not acute, a possible reduction in biomarkers of muscle damage is sometimes noted with antioxidative supplementation which applies to Vitamin C; results are unreliable
B	Aerobic Exercise	—	—	4 studies	No significant influence on aerobic exercise performance
B	Cortisol	↓↑	★☆☆ Minor	6 studies	Vitamin C (500-1,500mg daily) appears to be associated with both increases and decreases in exercise-induced cortisol spikes, depending on whether it acts as a prooxidant or antioxidant (respectively). There is no influence on resting cortisol concentrations.
B	Exercise-Induced Immune Suppression	—	—	6 studies	More evidence suggests no significant effect than a possible protective effect, although the latter is possible
B	Heart Rate	↓	★☆☆ Minor	3 studies	A decrease in heart rate has been noted in exercising obese adults, a per se effect of Vitamin C on heart rate (rather than secondary to the rate of perceived exertion) seems unlikely.
B	Protection from Smoking	—	—	3 studies	There do not appear to be any inherent protective effects of Vitamin C against the oxidative and inflammatory changes associated with cigarette smoking, although the reduction in blood flow may be attenuated somewhat with antioxidants and this applies to Vitamin C
B	Plasma Vitamin C	↑	★★★ Strong	3 studies	For the purpose of increasing plasma Vitamin C concentrations, orally supplemented Vitamin C appears to be the best

					decision (second only to intravenous vitamin C).
C	Glycemic Control	—	—	1 study	No significant influence on glycemic control in diabetics with Vitamin C supplementation
C	Triglycerides	—	—	2 studies	No significant influence on fasting or postprandial triglycerides seems apparent with Vitamin C
C	Heart Palpitations	—	—	1 study	No significant influence on heart palpitations
C	Symptoms of Bacterial Vaginosis	↓	★☆☆ Minor	1 study	Vaginal bacterial infections are somewhat treatable with directly applied (via silicon coated tablets), as Vitamin C exerts some antioxidant effects against those bacterial strains
C	Microcirculation	↑	★☆☆ Minor	1 study	An increase in microcirculation has been noted secondary to increased blood flow, thought to be a general property of antioxidants
C	Fat Mass	—	—	1 study	Does not appear to significantly influence fat mass
C	Weight	—	—	2 studies	Vitamin C does not appear to have a weight reducing effect
C	Adaptations to Exercise	↓	★☆☆ Minor	2 studies	It is thought that, secondary to reducing the rate of muscular damage, that adaptations gained from exercise are attenuated; there is mixed evidence to support this, but is seems possible with antioxidants
C	VO2 Max	—	—	1 study	Does not appear to have a role in altering VO2 max

C	Total Cholesterol	—	—	2 studies	No significant influence on total cholesterol seems apparent with vitamin C supplementation
C	Symptoms of Charcot-Marie-Tooth Disease	—	—	1 study	Insufficient evidence to support a role
C	Insulin Sensitivity	—	—	1 study	No significant influence on insulin sensitivity
C	Pre-Eclampsia Risk	—	—	1 study	No significant influence on pre-eclampsia risk
C	Risk of Cataracts	—	—	1 study	No significant influence on the risk of cataracts
C	Spontaneous Birth Risk	—	—	1 study	No significant influence on spontaneous birthing
C	Upper Respiratory Tract Infection Risk	—	—	2 studies	No significant influence on the rate of acquiring sickness
C	Length of Sickness	—	—	2 studies	Mixed influences on the length one is sick for, with possibly no effect
C	Subjective Well-Being	↑	★☆☆ Minor	1 study	An improvement in mood has been noted in hospitalized persons
C	Bone Mineral Density	↑	★☆☆ Minor	2 studies	The rate of bone mineral density loss over time in elder women appears to be reduced with dietary antioxidants, and as such applies to Vitamin C supplementation. The protective effect is not remarkably large
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	1 study	An increase in antioxidant enzymes have been noted in elderly persons
C	Oxygenation Cost of			1 study	

	Exercise				
C	C-Reactive Protein	↓	★☆☆ Minor	1 study	A possible reduction in C-Reactive Protein exists with Vitamin C supplementation
C	DNA Damage	—	—	2 studies	No significant influences on DNA damage
C	Exercise-Induced Oxidation	—	—	2 studies	Highly mixed interactions with the exercise:oxidation axis with Vitamin C, with both increases and decreases being noted. Unlikely to have a reliable role
C	Muscle Soreness	↓	★☆☆ Minor	1 study	A possible reduction in muscle soreness the day after exercise may result when preloading exercise with Vitamin C
C	HbA1c	—	—	1 study	No significant influence of Vitamin C supplementation on HbA1c levels
C	Oxidation of LDL	—	—	2 studies	No significant influence on the oxidation rates of LDL cholesterol
C	HDL-C	—	—	1 study	No significant influence on HDL cholesterol
C	LDL-C	—	—	1 study	No significant alterations in LDL cholesterol seen with Vitamin C supplementation
C	Rate of Perceived Exertion	↓	★☆☆ Minor	2 studies	The rate of perceived exertion in obese adults appears to be attenuated with Vitamin C supplementation
C	Fatigue	↓	★☆☆ Minor	1 study	A decrease in fatigue has been noted in obese adults given Vitamin C in conjunction with exercise
C	Fat Oxidation	—	—	1 study	No significant influence on fat

					oxidation
C	Mineral Bioaccumulation			1 study	
C	Sperm Quality			1 study	
C	Seminal Motility			1 study	
C	Depression			1 study	
C	Frequency of Intercourse	↑	★☆☆ Minor	1 study	Supplementation of 3,000mg Vitamin C appears to increase sexual frequency from 4 times monthly to 14 times. No influence on masturbation frequency
D	Symptoms of Osteoarthritis	—	—	1 study	No significant influence on the symptoms of osteoarthritis
D	Interleukin 6			1 study	

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Vitamin D

Also known as: Cholecalciferol (Vitamin D3), Ergocalciferol (Vitamin D2)

Vitamin D is an essential vitamin known as the sunlight vitamin, due to the synthesis that occurs in the skin from the sun's radiation. It provides benefits for bone structure support, mood state, and much more. Vitamin D is generally seen as healthy and anticancer.

See [Vitamin D on Examine.com](#)

How to Take

The recommended daily allowance for Vitamin D is currently set at 400-800IU/day, but this is too low for adults. The safe upper limit in the United States is 2,000IU/day, while in Canada it is 4,000IU/day. Research suggests that the true safe upper limit is 10,000IU/day. For moderate supplementation, a 1,000-2,000IU dose of vitamin D3 is sufficient to meet the needs of most of the population. This is the lowest effective dose range. Higher doses, based on body weight, are in the range of 20-80IU/kg daily. Vitamin D3 supplementation (cholecalciferol) is recommended over D2 supplementation (ergocalciferol), since D3 is used more effectively in the body. Vitamin D should be taken daily, with meals or a source of fat, like Fish Oil.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Risk of Falls	↓	★★★☆☆ Notable	4 studies	The risk of falls in the elderly (and subsequently, rate of bone fractures) appears to be significantly reduced with Vitamin D supplementation at 700 IU or greater, with most research in the 700-1000 IU range. Lower doses do not appear effective, and a greater protective effect appears to exist alongside calcium supplementation (and possibly Vitamin K supplementation)
A	Cardiovascular Disease Risk	↓	★★☆☆☆ Minor	3 studies	There appears to be less risk of cardiovascular disease and related cardiovascular complications with supplementation of 1,000 IU of Vitamin D or higher serum levels of Vitamin D. The degree of prevention is borderline significant overall

B	Colorectal Cancer Risk	↓	★★★☆☆ Notable	1 study	The association between serum Vitamin D at 37ng/mL and colorectal cancer is approximately a halving of risk according to one meta-analysis, which is a notable risk reduction
B	Bone Fracture Risk	↓	★★☆☆☆ Minor	1 study	A decrease in bone fracture risk (nonvertebral and hip) appears to exist when supplemental doses of Vitamin D3 are taken above 800 IU, with this protective effect being highly correlated with the improvement in functionality and fall reduction risk
B	Blood Pressure	↓	★★☆☆☆ Minor	2 studies	Both correlational and intervention studies note that higher cohorts of serum Vitamin D have less blood pressure than lower cohorts, establishing a role for Vitamin D in blood pressure reduction. The magnitude of reduction is small, around 5mmHg systolic, and likely not potent enough to be a reference therapy
B	Parathyroid Hormone	↓	★★★★☆ Strong	4 studies	Vitamin D supplementation is the reference drug for reductions in parathyroid hormone due to directly negatively regulating its secretion
B	Fat Mass	↓	★★☆☆☆ Minor	3 studies	Mixed effects on overweight/obese persons, but it appears that normalizing a deficiency may aid fat loss in persons of higher body weight. Insufficient evidence to suggest the role of Vitamin D in lean persons
C	All-Cause Mortality	↓	★★☆☆☆ Minor	2 studies	Cohorts of people with higher serum Vitamin D appear to die less frequently than cohorts with less serum Vitamin D; this may be heavily influenced by reducing falls in the elderly

					(reduction of falls and subsequent hospitalizations reducing death rates)
C	Insulin Secretion	↑	★☆☆ Minor	3 studies	An improvement in insulin secretion is noted in diabetics (type II mostly) and in persons at risk for diabetes, which is thought to be secondary to protective effects at the level of the pancreas.
C	Insulin Sensitivity	↑	★☆☆ Minor	4 studies	Improvements in insulin sensitivity can occur secondary to increasing pancreatic insulin secretion
C	Weight	—	—	2 studies	No significant alterations noted in weight, even when fat mass is lost, in obese persons
C	Triglycerides	↓	★☆☆ Minor	1 study	The decrease in triglycerides is present after long term ingestion of Vitamin D, although it isn't to a highly significant degree
C	TNF-Alpha	↓	★☆☆ Minor	1 study	A decrease has been noted over time relative to placebo, of relatively minor magnitude
C	LDL-C	↑	★☆☆ Minor	1 study	Either no significant influence on LDL cholesterol or a slight increase (around 5%) has been noted; practical significance of this information unknown
C	Metabolic Rate	—	—	1 study	No detectable influence on metabolic rate over time
C	Influenza	↓	★☆☆ Minor	2 studies	May reduce the risk of catching the flu
C	Asthma	↓	★☆☆ Minor	1 study	Appears to be somewhat effective at reducing the occurrence of asthma attacks in youth

C	Testosterone	↑	★☆☆ Minor	1 study	An increase in testosterone has been noted in men with 3,332 IU of Vitamin D over the course of a year
C	Functionality in Elderly or Injured	↑	★★★☆☆ Notable	1 study	An improvement in muscular and neural functionality in the elderly is thought to underlie the reductions of fall risk and reduced bone fracture rate seen in elderly cohorts
C	HbA1c	—	—	2 studies	The decrease in HbA1c is statistically insignificant and very small in magnitude, likely not a concern.
C	Interleukin 5	↑	★☆☆ Minor	1 study	An increase in IL-5 has been noted with Vitamin D supplementation
C	Lean Mass	↓ ↑	★☆☆ Minor	2 studies	An increase in lean mass has been noted in dieting obese women relative to control (2,000IU) and a trend to reduce lean mass relative to control has been noted in exercising healthy persons (4,000IU); there appears to be potential for both effects with Vitamin D supplementation, but there is insufficient evidence to draw conclusions
C	Food Intake	—	—	1 study	No significant alterations in food intake noted with Vitamin D supplementation
C	Endothelial Function	—	—	1 study	No significant influence on endothelial function
C	Inflammation	—	—	1 study	No significant influence on select inflammatory cytokines
C	Calcium Absorption	—	—	1 study	Superloading Vitamin D (rather than staying sufficient) does not appear to further increase

					absorption rates of calcium, although normalizing a deficiency can aid in absorption which is hindered.
C	Symptoms of Systemic Lupus Erythematosus	↓	★☆☆ Minor	1 study	Inflammatory symptoms associated with Lupus appear to be reduced with Vitamin D ingestion
C	Upper Respiratory Tract Infection Risk	—	—	1 study	Lack of efficacy in reducing rate of sickness
C	Height	↑	★☆☆ Minor	1 study	A higher vitamin D level in serum during growth spurts in children is associated with greater heights during adulthood; currently no evidence to support the role of Vitamin D in inducing height growth in adults
C	Symptoms of Tuberculosis	↓	★☆☆ Minor	1 study	A decrease in symptoms associated with tuberculosis are noted with Vitamin D
C	Insulin	—	—	1 study	No significant influence on fasting insulin levels
C	Blood Glucose	—	—	1 study	No significant influence on fasting blood glucose levels
C	Power Output	—	—	1 study	Although a trend to increase power output has been noted, most research suggest no such benefit
C	Hip Fracture Risk			1 study	
C	Bone Mineral Density			1 study	
C	Symptoms of Osteoarthritis			1 study	
C	Collagen Content			1 study	
C	Pain			1 study	
D	Risk of Multiple Sclerosis	↓	★★★☆☆ Notable	1 study	The risk of developing MS is significantly reduced by both

					sunlight, latitude, and supplemental Vitamin D
D	Breast Cancer Risk	↓	★☆☆ Minor	2 studies	There is less risk of breast cancer associated with Vitamin D supplementation
D	Pancreatic Cancer Risk	↓	★☆☆ Minor	1 study	Appears to be associated with less risk of pancreatic cancer
D	Arthralgia	↓	★☆☆ Minor	2 studies	May reduce symptoms of arthralgia
D	Incidence of Type 1 Diabetes	↓	★☆☆ Minor	1 study	May reduce the incidence of type 1 diabetes in offspring and adults when supplemented (for the former, but the mothers)
D	Symptoms of Multiple Sclerosis	↓	★☆☆ Minor	1 study	There appears to be a lower relapse rate in multiple sclerosis patients when Vitamin D is present at higher concentrations

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Vitamin E

Also known as: Tocopherols, Tocotrienols

Vitamin E is a group of eight different compounds which, collectively, help support antioxidation in the body. Benefits of high doses have uncertain safety, and lower doses seem effective in boosting immunity in the elderly.

See [Vitamin E on Examine.com](#)

How to Take

Maintaining adequate levels of vitamin E in the body can be achieved through very low daily doses of 15mg (22.4 IU) or less. This dose of vitamin E can be acquired through the diet, making supplementation unnecessary in many cases. An elderly person supplementing vitamin E to improve immunity should take a 50-200mg dose. Vitamin E supplements should contain α -tocopherol. Avocados, olives, vegetable oils and almonds are all high in vitamin E. Vitamin E's antioxidant properties are improved when taken with unsaturated dietary fat. The minimum intake of vitamin E is 1 IU per gram of saturated fat. The ideal range is between 2-4 IU per gram of saturated fat. In regards to an upper limit, while doses above 400IU α -tocopherol (240mg) are well tolerated in the short term it is the smallest dose associated with potential long-term adverse effects. If taking vitamin E as a daily supplement for no specific purpose (ie. as part of a multivitamin) then 150mg could be seen as a prudent upper limit.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	All-Cause Mortality	↓ ↑	★☆☆ Minor	7 studies	Minor increases in all cause mortality have been noted in mostly unhealthy cohorts with doses of vitamin E above 400IU (alpha-tocopherol) whereas lower doses exert a mild protective effect in the same cohorts. The magnitude is approximately 33-34 deaths per 10,000 subjects (both for the increase in mortality seen with vitamin E multnutrient supplements and the decrease seen with vitamin E alone), and it is unsure how this information applies to otherwise healthy persons.
B	General Oxidation	↓	★☆☆ Minor	6 studies	Supplementation of vitamin E appears to reduce oxidation in plasma, requiring over 500mg (if not more) α -tocopherol in

					states where there is abnormal elevations of oxidation. Vitamin E is without effect at lower doses or in persons without abnormal oxidation levels.
B	Lipid Peroxidation	↓ ↑	★☆☆ Minor	7 studies	Vitamin E tends to reduce lipid peroxidation in instances where there is elevated oxidation, and tends to have no effect in otherwise healthy persons. In instances where vitamin E is thought to greatly exceed the activity of co-antioxidants (vitamin C or ALA) it can exert a prooxidant effect.
B	Interleukin 4	↓ ↑	★☆☆ Minor	3 studies	IL-4 is increased when taken alongside a vaccination and decrease when supplemented in the elderly (alongside immune enhancement) with no significant influence in persons outside of both scenarios.
B	Interferon Gamma	↓ ↑	★☆☆ Minor	3 studies	IFN γ is increased when vitamin E is taken alongside a vaccination, and decrease in the elderly (alongside improvements in immunity) with no significant changes if neither of the above contexts are considered.
B	Immunity	↑	★☆☆ Minor	6 studies	There appears to be an increase in T-cell mediated immunity in older subjects when supplementing low dose (50-200mg) vitamin E; this immunity enhancement does not appear to occur in youth due to it alleviating an age-related immune suppression.
B	Weight	—	—	7 studies	There does not appear to be any influence of vitamin E supplementation at any tested dose in any subject on weight loss nor gain.
B	Subjective Well-being	—	—	4 studies	Studies assessing well being

					in otherwise healthy persons or those with disease states not associated with depression have failed to find any interaction with vitamin E supplementation.
B	White Blood Cell Count	—	—	6 studies	Supplementation of vitamin E does not appear to alter overall content of white blood cells relative to placebo.
B	Red Blood Cell Count	—	—	4 studies	The overall amount of red blood cells does not appear to be significantly altered with supplemental vitamin E.
B	Liver Enzymes	↓	★★★☆☆ Notable	9 studies	There appears to be a notable decrease in both ALT and γ-GPT in persons with non-alcoholic fatty liver (NAFLD) which may exceed 50% when vitamin E is supplemented above 300mg for half a year; there does not appear to be any influence whatsoever in healthy controls.
B	Blood Glucose	—	—	5 studies	Vitamin E does not appear to influence blood glucose in otherwise healthy persons nor in diabetics (type I or type II) relative to placebo.
B	Triglycerides	—	—	8 studies	No evidence to support changes in triglycerides associated with vitamin E supplementation in any tested person.
B	Total Cholesterol	—	—	10 studies	There does not appear to be a significant influence of vitamin E supplementation on cholesterol levels whether used by a healthy person or one with elevated cholesterol.
B	Serum T4	—	—	5 studies	Although one study noted a decrease with 600 IU, future studies in similar persons with

					multiple doses have failed to replicate these observations.
B	Serum T3	—	—	4 studies	The majority of evidence has failed to find any significant interaction with vitamin E supplementation and circulating levels of T3.
B	Bleeding Time	—	—	4 studies	When supplemented by itself, vitamin E does not appear to significantly influence bleeding time. This differs from a combination of vitamin E and coumarin based anticoagulants (such as warfarin) where an adverse interaction may occur.
B	HDL-C	—	—	4 studies	The majority of evidence has failed to find any influence of vitamin E supplementation on HDL total levels or particulates relative to placebo.
B	LDL-C	—	—	7 studies	Vitamin E supplementation does not appear to alter the overall levels of LDL cholesterol.
B	Blood Pressure	↓ ↑	★☆☆ Minor	3 studies	Blood pressure has been differentially affected by vitamin E supplementation, thought to be associated with whether it is an antioxidant or a prooxidant.
B	Blood Flow	↓ ↑	★☆☆ Minor	3 studies	Similar to blood pressure, blood flow is differentially affected by vitamin E supplementation thought to be due to whether it is acting as a prooxidant or an antioxidant.
B	C-Reactive Protein	—	—	3 studies	Most studies assessing C-reactive protein (an inflammatory biomarker) have failed to find a significant influence of vitamin E supplementation.

B	Cardiovascular Disease Mortality	↓	★☆☆ Minor	3 studies	A possible protective effect on overall cardiovascular disease mortality (not development of the disease states or incidences) has been reported with supplementation of 600 IU vitamin E every other day.
B	Risk of Stroke	—	—	3 studies	There does not appear to be a protective effect of vitamin E on the development of stroke relative to placebo.
B	Colon cancer risk	—	—	3 studies	600 IU vitamin E every other day for a decade does not appear to reduce the risk of developing colon cancer in otherwise healthy women.
B	Breast Cancer Risk	—	—	3 studies	No significant protective effect of 600 IU vitamin E every other day in otherwise healthy women for preventing the development of breast cancer.
B	Prostate Cancer Risk	↓ ↑	★☆☆ Minor	4 studies	Low doses of vitamin E (50mg) in smokers has been associated with significant decreases in prostate cancer risk, whereas moderate doses (400IU) of vitamin E in otherwise healthy older men is associated with a mild but significant increase in prostate cancer risk.
B	DNA damage	—	—	3 studies	While most evidence suggests no influence on DNA damage, it is possible based on some studies that when vitamin E turns prooxidative that it may damage DNA.
B	Cell Adhesion Factors	—	—	3 studies	While a decrease in P-selectin has been noted with low dose (100mg) γ-tocopherol, most studies have failed to find an influence of vitamin E supplementation on adhesion factors.

C	Prolactin	↓	★☆☆ Minor	1 study	May decrease prolactin in instances of uremia, but there is currently no evidence in otherwise healthy controls.
C	Follicle-Stimulating Hormone	—	—	1 study	FSH does not appear to be influenced following supplementation of vitamin E.
C	Luteinizing Hormone	—	—	1 study	Vitamin E supplementation does not appear to influence circulating levels of luteinizing hormone (LH).
C	Free Testosterone	—	—	1 study	Vitamin E does not appear to alter the concentrations of free testosterone in serum following supplementation.
C	Symptoms of Alzheimers	↓	★★★☆☆ Notable	2 studies	Very high dose Vitamin E supplementation in the form of α-tocopherol (2,000 IU) appears to reduce the rate of cognitive decline in persons with moderate to severe Alzheimer's Disease with a potency comparable to selegiline. Currently no research on lower (more standard) doses, and there appears to be no influence on minor AD or cognitive decline not characterized by AD.
C	Risk of Alzheimers Disease	—	—	1 study	Vitamin E supplementation taken by otherwise healthy older adults does not appear to reduce the risk of developing Alzheimer's relative to placebo.
C	Cognitive Decline	—	—	1 study	When supplemented by otherwise healthy elderly persons, the development of organic cognitive decline does not appear to be attenuated relative to placebo.
C	Memory	—	—	1 study	Supplementation of vitamin E

					by otherwise healthy women has failed to significantly improve memory formation.
C	Verbal Fluency	—	—	1 study	Verbal fluency does not appear to be significantly altered with vitamin E supplementation relative to placebo.
C	Risk of Cataracts	—	—	1 study	Vitamin E in isolation at tested doses of 500 IU has failed to show any protective effect on cataract formation or continued pathology, despite multinutrient formulations showing benefit (likely due to other compounds in the formulation).
C	Homocysteine	—	—	2 studies	There does not appear to be a significant influence of vitamin E supplementation on homocysteine concentrations.
C	Aerobic exercise	—	—	2 studies	Performance during aerobic exercise does not appear to be significantly altered with supplementation of vitamin E relative to placebo.
C	Cortisol	—	—	1 study	No significant reduction in cortisol seen with supplementation of vitamin E relative to placebo.
C	Muscle Damage	↓	★☆☆ Minor	1 study	In athletes who experienced a reduction in lipid peroxidation from vitamin E supplementation during exercise, there is also a reduction in biomarkers of muscle damage.
C	Heart Rate	—	—	1 study	Heart rate during exercise in elite athletes is unaltered by supplementation of vitamin E.
C	Lactate production	—	—	1 study	Lactate production during exercise does not appear to be influenced with

					supplementation of vitamin E.
C	Erythema	↑	★☆☆ Minor	2 studies	Topical application of vitamin E to scar tissue has, in some participants, caused significant increases in redness of the tissue associated with itching.
C	Scar Healing	—	—	2 studies	Topical application of vitamin E to scar tissue has failed to promote healing of scar tissue relative to placebo gels.
C	Interleukin 2	↑	★☆☆ Minor	2 studies	An increase in interleukin 2 (IL-2) concentrations has been noted in the elderly given supplementation of vitamin E alongside immunity enhancements.
C	Lymphocyte Count	—	—	2 studies	Vitamin E supplementation does not appear to influence overall lymphocyte count or its subdivisions.
C	Neutrophil count	—	—	1 study	The overall amount of neutrophils in the blood does not appear to be influenced with supplementation of vitamin E.
C	Serum Platelets	—	—	2 studies	The overall content of platelets is not affected by supplementation of vitamin E.
C	Sexual Function	—	—	1 study	Vitamin E does not appear to influence sexual function or satisfaction in otherwise healthy persons with no known sexuality disorders.
C	Bilirubin	—	—	2 studies	Serum bilirubin does not appear to be influenced with supplementation of vitamin E relative to placebo.
C	Anti-oxidant Enzyme Profile	—	—	2 studies	The levels of antioxidant enzymes in red blood cells

					(glutathione, superoxide dismutase, catalase) does not appear to be influenced with supplementation of vitamin E.
C	Hematocrit	—	—	1 study	Hematocrit does not appear to be significantly influenced with supplementation of vitamin E relative to placebo.
C	Neutrophil Activity	—	—	1 study	Similar to neutrophil count, there does not appear to be a significant influence of vitamin E on the activity of neutrophils.
C	Serum Folate	—	—	1 study	Serum folate does not appear to be modified with supplementation of vitamin E.
C	Serum Cobalamin	—	—	1 study	Serum levels of cobalamin (vitamin B12) do not appear to be influenced with supplementation of vitamin E.
C	Kidney function	—	—	2 studies	Biomarkers of kidney function are not significantly altered with supplementation of vitamin E relative to placebo.
C	Vaccine Augmentation	↑	★☆☆ Minor	2 studies	There appears to be an increased antibody response to vaccinations in otherwise healthy persons who supplement with a low dose of vitamin E relative to those receiving placebo with their vaccination; this applies to both youth and the elderly.
C	Prostaglandin E2	↓	★☆☆ Minor	1 study	There may be a minor reduction in PGE2 concentrations following supplementation of vitamin E.
C	Creatinine	—	—	1 study	In otherwise healthy elderly person, creatinine does not appear to be significantly altered relative to placebo.

C	Immunoglobulin A	—	—	1 study	Supplementation of vitamin E does not appear to significantly influence circulating concentrations of IgA relative to placebo in otherwise healthy elderly adults.
C	Immunoglobulin G	↑	★☆☆ Minor	2 studies	IgG has been noted to be increased when vitamin E is used as a vaccination adjuvant, but not in otherwise healthy persons not subject to a vaccination.
C	Immunoglobulin M	—	—	1 study	IgM concentrations in the blood of older persons do not appear to be influenced with supplementation of vitamin E.
C	Hair Regrowth	↑	★☆☆ Minor	1 study	One study noted that 100mg of mixed tocopherol was able to promote hair growth in persons with alopecia (androgen dependence not specified) relative to placebo.
C	Liver Fat	↓	★☆☆ Minor	3 studies	In persons with steatohepatitis, there may be a reduction in liver fat over time when taking vitamin E supplements; currently there is no evidence assessing otherwise healthy persons on this parameter
C	Liver Cirrhosis	↓	★☆☆ Minor	2 studies	Fibrotic scores may be slightly improved in persons with fatty liver associated with inflammation (steatohepatitis) although there may not be an effect in persons with NAFLD without evidence of inflammatory damage.
C	Insulin Sensitivity	—	—	2 studies	There does not appear to be improvements in insulin sensitivity associated with vitamin E supplementation relative to placebo, even in instances where NAFLD is being treated therapeutically.

C	CD4 Lymphocytes	—	—	1 study	No known influence of vitamin E supplementation on the overall count of CD4+ lymphocytes relative to placebo.
C	CD8 Lymphocytes	—	—	1 study	CD8+ Lymphocytes do not appear to be significantly influenced with supplementation of vitamin E relative to placebo.
C	Natural Killer Cell content	—	—	1 study	The overall amount of NK cells do not appear to be altered with supplementation of vitamin E.
C	B cell count	—	—	1 study	Vitamin E does not appear to influence B cell count relative to placebo.
C	Asthma	—	—	1 study	Supplementation of vitamin E in medicated asthmatics failed to exert any appreciable benefits to symptoms.
C	Immunoglobulin E	—	—	1 study	IgE concentrations in asthmatics has failed to be influenced with supplementation of vitamin E.
C	Hemoglobin	—	—	1 study	No significant influence of vitamin E supplementation on hemoglobin.
C	Upper Respiratory Tract Infection Risk	↓	★☆☆ Minor	1 study	Supplementation of 200 IU vitamin E in elderly persons has been noted to reduce overall occurrence of upper, but not lower, respiratory tract infections.
C	Arterial Stiffness	↓	★☆☆ Minor	2 studies	Mixed evidence, but vitamin E has been implicated in improving arterial stiffness (thought to underlie decreased cardiovascular mortality)

C	HbA1c	—	—	2 studies	HbA1c does not appear to be influenced in type II diabetics given supplementation of vitamin E.
C	Endothelin-1	—	—	1 study	Endothelin-1 has failed to be influenced with supplementation of vitamin E in diabetics.
C	Left Ventricular Ejection Fraction	—	—	2 studies	Supplementation of vitamin E has failed to influence the activity of the cardiac tissue itself.
C	Oxidation of LDL	↓	★☆☆ Minor	2 studies	While vitamin E appears to retain the potential to reduce LDL oxidation, it requires high doses as lower doses are not significantly effective.
C	Incidence of Type 2 Diabetes	—	—	1 study	Supplementation of vitamin E by otherwise healthy persons does not appear to influence the rates of developing type II diabetes.
C	Risk of Lung Cancer	—	—	2 studies	In otherwise healthy women, supplementation of vitamin E does not appear to reduce the rate of developing lung cancer.
C	Cancer Mortality	—	—	2 studies	Despite a small reduction in prostate cancer mortality seen in smokers with low dose (50mg) vitamin E, this does not appear to hold true as a general statement for all cancer types in most persons.
C	Insulin	—	—	1 study	Basal insulin concentrations (fasted state) do not appear to be influenced by supplementation of vitamin E.
C	Leukotriene B4	↓	★☆☆ Minor	2 studies	Mixed evidence as to whether leukotriene B4 can be reduced in diabetics with vitamin E

					supplementation.
C	Interleukin 6	—	—	1 study	IL-6 concentrations do not appear to be influenced relative to placebo.
C	TNF-Alpha	—	—	1 study	TNF-α does not appear to be influenced with supplementation of vitamin E relative to placebo.
C	Glomerular Filtration Rate	—	—	1 study	In type II diabetics, there is no influence of vitamin E supplementation on glomerular filtration rate.
C	Risk of Thromboembolism	↓	★★★☆☆ Notable	1 study	There appears to be a large (27%) reduction in thromboembolism associated with vitamin E supplementation at 600 IU every other day, more pronounced in those who reported such an event previously (44%).
C	Platelet Aggregation	—	—	2 studies	While 100mg of γ-tocopherol has been once implicated in reducing platelet aggregation, higher doses and all tested dose of α-tocopherol by themselves do not appear to have an effect (there is still an interaction with warfarin, however).
C	Thromboxane B2	—	—	1 study	The production of thromboxane B2 does not appear to be significantly altered in type II diabetic adults.
C	Risk of Rheumatoid Arthritis	—	—	1 study	Supplementation of vitamin E does not appear to reduce the risk of developing rheumatoid arthritis.
C	Risk of Myocardial Infarction	—	—	1 study	Vitamin E does not appear to reduce the incidence rates of myocardial infarctions despite a reduction in cardiovascular

					disease mortality.
C	Cardiovascular Disease Risk	—	—	1 study	In general, the development of various cardiovascular diseases is not prevented with supplementation of vitamin E.
C	Risk of Melanoma	—	—	1 study	Supplementation of 400IU vitamin E in older adults with preexisting medical conditions has failed to interact with the risk of developing melanoma.
C	Esophageal Cancer Risk	—	—	1 study	400IU of vitamin E does not appear to mitigate the risk of developing esophageal cancer relative to placebo.
C	Risk of Heart Failure	↑	★☆☆ Minor	1 study	Supplementation of 400 IU vitamin E, despite not increasing overall cardiovascular mortality, increased the risk of heart failure in older persons with preexisting medical conditions (from 443 instances in placebo over seven years to 519 in supplemental).
D	Serum TGF-β	↓	★☆☆ Minor	1 study	A decrease in serum TGF-β has been noted in persons with fatty liver given supplementation of 300mg vitamin E (as α-tocopherol)
D	Liver Damage	↓	★☆☆ Minor	1 study	In those with inflammatory liver damage, supplementation of vitamin E appears to be capable of reducing damage over a long period of time.
D	Symptoms of Ulcerative Colitis	↓	★★★ Notable	1 study	Rectal administration of high doses of vitamin E appears to be effective in reducing symptoms of ulcerative colitis, with preliminary research noting remission in the majority of patients.

Vitamin K

Also known as: Phylloquinone, Menaquinone, MK-4, MK-7, Menatetrenone, Phytonadione

Vitamin K is an essential vitamin found in plants or produced from intestinal bacteria. It plays an essential role in bone health and regulates blood clotting.

See [Vitamin K on Examine.com](#)

How to Take

Vitamin K comes in a variety of different forms, known as vitamers. Forms of vitamin K are either phylloquinones (vitamin K1) or menaquinones (vitamin K2). There are different vitamers within the vitamin K2 class, abbreviated as MK-x. The minimum effective dose for phylloquinone (vitamin K1) is 50mcg, which is enough to satisfy the Recommended Daily Intake (RDI) for vitamin K. The maximum dose for vitamin K1 is 1,000mcg. The minimum effective dose for short chain menaquinones (MK-4) is 1,500mcg. Doses of up to 45mg (45,000mcg) have been safely used in a superloading dosing protocol. The minimum effective dose for longer chain menaquinones (MK-7, MK-8, and MK-9) is between 90-360mcg. Further research is needed to determine the maximum effective dose for MK-7. A topical application of vitamin K should contain at least 5% phylloquinone. Vitamin K should be supplemented alongside fatty acids, even if the vitamin is coming from a plant-based source, so consider taking vitamin K at meal time. Microwaving plant-based sources of vitamin K will increase the absorption rate of the vitamin.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
A	Bone Mineral Density	↑	★★★☆☆ Notable	15 studies	There appears to be a <i>relative</i> increase in bone mineral density associated with vitamin K supplementation, due to attenuating the rate of bone loss in older individuals. Although it is significant overall in meta-analyses, it is quite unreliable and similar in potency to vitamin D when it occurs (less than estrogen replacement therapy)
B	Weight	—	—	3 studies	In studies that measure weight changes over time (usually as a secondary piece of data), there do not appear to be any significant alterations associated with vitamin K supplementation.

B	Bruising	—	—	3 studies	Although there may be a role for topical vitamin K in reducing the severity of bruising, currently the evidence is too unreliable to draw conclusions and is not looking promising. Menaquinones have not been tested yet
C	Food Intake	—	—	1 study	Studies that happen to measure dietary intake fail to note any influence of supplemental Vitamin K
C	Estrogen	—	—	1 study	No significant interactions with estrogen noted with vitamin K supplementation
C	Total Cholesterol	—	—	1 study	No significant interactions with total cholesterol concentrations in persons given vitamin K supplementation
C	Triglycerides	—	—	1 study	No significant influence on circulating triglycerides seen with MK-4 supplementation
C	LDL-C	—	—	1 study	LDL-C appears to be unaffected by supplemental vitamin K
C	HDL-C	—	—	1 study	Vitamin K does not appear capable of influencing HDL cholesterol
C	Bone Fracture Risk	↓	★★★☆☆ Notable	2 studies	The decrease in fracture risk seen with vitamin K supplementation in susceptible cohorts appears to be greater than seen with other supplements
C	Recurrence of Hepatocellular Carcinoma	↓	★★★☆☆ Notable	2 studies	Recurrence rates of hepatocellular carcinoma appears to be significantly less than placebo when using vitamin K in a superloading scheme (40mg or more daily)

C	Cancer Mortality	↓	★★★☆☆ Notable	2 studies	Although the studies have used superloading of vitamin K (40mg or more) and only in hepatic cancers, the reduction in mortality risk and prolongation of survival times appears to be quite notable
C	Interleukin 6	—	—	2 studies	No significant effect of vitamin K on circulating levels of IL-6, an inflammatory marker
C	C-Reactive Protein	—	—	2 studies	No significant influence on C-reactive protein (an inflammatory biomarker) seen with vitamin K supplementation
C	Osteoprotegerin	—	—	1 study	No significant alterations noted with vitamin K supplementation on osteoprotegerin
C	Reddening of the Skin	↓	★★☆☆☆ Minor	2 studies	It appears that for conditions with reddened skin (purpura or bags under the eyes) that vitamin K may have a role in removing the blood from the skin and reducing redness when 5% phyloquinone is applied to the skin. Mechanisms are not known, and study quality at the moment is lacklustre
C	Blood Glucose	—	—	1 study	Despite an improvement in insulin sensitivity, the lone study failed to note any significant changes in blood glucose concentrations in a fasted state
C	Insulin Sensitivity	↑	★★☆☆☆ Minor	1 study	An improvement of insulin sensitivity has been noted with 30mg of MK-4 supplementation over 4 weeks in otherwise healthy individuals, with the influence of lower doses of vitamin K not ascertained

C	Adiponectin	—	—	1 study	No significant alterations seen in adiponectin concentrations in serum with 4 weeks supplementation of 30mg MK-4
D	Insulin	↓	★☆☆ Minor	2 studies	A relative deficiency of vitamin K seems to be associated with higher post-meal insulin spikes (over 120 minutes), and this abnormal elevation is normalized upon supplementation of vitamin K

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Vitex agnus castus

Also known as: Chaste Tree

Vitex Agnus Castus (Chaste Tree) appears to be a reliable supplement for PMS, with possible benefits towards menopause not yet proven. Reduces prolactin by acting like dopamine in the body, and the opioid-like activity may also contribute to benefits. However, limited usage beyond controlling PMS.

See [Vitex agnus castus on Examine.com](#)

How to Take

Supplementation of Vitex Agnus Castus is usually based on the fruits dry weight, and dosing according to this uses 150-250mg of the fruit. Supplements of Vitex Agnus Castus are usually more concentrated than this, and the two major extractions are: BNO 1095, a 10:1 extraction which has shown benefits at doses as low as 4mg Ze 110, a 6-12:1 extraction which has shown benefits at doses of 20mg

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Symptoms of PMS	↓	★★★ Strong	6 studies	Vitex is the reference drug used for reductions in PMS symptoms, with about half of users experiencing a halving of menopausal symptoms with prolonged use (3+ cycles)
B	Breast Tenderness	↓	★★★☆ Notable	3 studies	The increase in breast tenderness during PMS is ameliorated with vitex supplementation; the degree of benefit correlating with general reductions in PMS symptoms. Notable as supplements catering to breast tenderness are rare.
C	Migraine	↓	★★★☆ Notable	1 study	Seems to reduce symptoms of migraines a bit more than other PMS related symptoms, but for the most part the reduction seen in migraines is solely a reduction of PMS symptoms.
C	Irritability	↓	★★☆☆ Minor	1 study	Can reduce irritability as a side

			Minor		effect of PMS, no evidence as to whether this reduction in irritability applies to other persons (males) or periods that are not PMS.
C	Depression	↓	★☆☆ Minor	2 studies	Can attenuate depressive symptoms that occur during PMS secondary to reducing PMS symptoms in general.
C	Cramps	↓	★☆☆ Minor	1 study	Efficacy against cramps appears to correlate both with how severe the cramps are during PMS and the response to Vitex supplementation; potency seems variable.
C	Insomnia	↓	★☆☆ Minor	1 study	Can reduce insomnia that is a side-effect of PMS, although the influence on insomnia in other scenarios is not known.
C	Anxiety	↓	★☆☆ Minor	1 study	Can reduce PMS related anxiety but may not have any inherent anxiolytic effects; the potency correlates to the severity of anxiety during a menstrual cycle.

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Watercress

Also known as: Nasturtium officinale

Watercress is a peppery herb in the same family as broccoli (Brassicaceae) and is a source of many glucosinolates, including PEITC. Consumption of watercress is thought to confer the benefits of cruciferous vegetables, mainly chemoprotection.

See [Watercress on Examine.com](#)

How to Take

Watercress is usually consumed as a food source, and benefits have been noted with the consumption of 85-100g of the vegetable daily (referring to the wet weight of the plant). The ideal supplemental dosage or the timing for supplementation are currently not known.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	DNA Damage	↓	★☆☆ Minor	1 study	DNA damage biomarkers have been reduced following watercress consumption
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	2 studies	There appears to be an influence on the enzymes superoxide dismutase and glutathione peroxidase, but this requires a certain genotype to occur

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Whey Protein

Also known as: whey, whey concentrate, whey isolate, whey hydrolysate, hydrolyzed whey

Whey is a component of Milk Protein, with the other being casein. Whey may be healthier than other forms of protein. The benefits of whey are due to the protein itself, while casein may be a better muscle builder.

See [Whey Protein on Examine.com](#)

How to Take

The amount of whey protein to supplement depends on individual daily protein goals. For example: If you are an athlete or highly active person attempting to lose body fat while preserving lean muscle mass, a daily intake of 1.5-2.2g/kg bodyweight (0.68-1g/lb bodyweight) is a good goal. If you are an athlete or highly active person, or you are attempting to lose body fat while preserving lean mass, then a daily intake of 1.0-1.5g/kg bodyweight (0.45-0.68g/lb bodyweight) is a good goal. If you are sedentary and not looking to change body composition, a daily target of 0.8g/kg bodyweight (0.36g/lb bodyweight) is a good goal. If daily protein targets are achieved through dietary protein alone, supplementation is unnecessary. Obese individuals should not follow the above recommendations, as bodyweight calculations would result in very high dosages. Obese people should calculate their protein targets based off of what their weight would be, assuming an overweight BMI.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Fat Mass	↓	★☆☆ Minor	6 studies	Inclusion of dietary protein in the diet above the recommended daily intake appears to aid the process of fat loss during hypocaloric diets (eating less than required to sustain body weight). There is currently no demonstrated benefit with whey protein over other protein sources.
B	Weight	—	—	8 studies	The influence of whey protein on weight <i>per se</i> is highly unreliable, and is subject to the overall context of the diet. Protein in general can aid weight loss attempts and is required to build lean mass, with whey not having any demonstrated benefit over other protein sources.

B	Insulin	↑	★☆☆ Minor	5 studies	Mixed effects on insulin, as there is an acute increase due to whey being a protein source (although whey increases insulin more than other proteins). Fasting insulin (chronically) tends to either be not affected or reduced, although the latter is usually confounded with weight loss.
B	Lean Mass	↑	★☆☆ Minor	4 studies	Protein in general increases lean mass, but there is not a significant body of evidence to support whey protein as being more effective than other protein sources
B	Power Output	—	—	3 studies	There doesn't seem to be an inherent effect of protein on power output, although it may augment training-induced power accural (an inherent effect of protein supplementation).
C	Muscle Protein Synthesis	↑	★★★☆☆ Notable	3 studies	Whey protein appears to increase muscle protein synthesis to a higher degree than other protein sources <i>acutely</i> , although over the prolonged supplementation it seems comparable in potency.
C	Ghrelin	↓	★☆☆ Minor	1 study	A decrease in Ghrelin has been observed with whey protein supplementation.
C	Blood Glucose	—	—	5 studies	No significant influence on fasted blood glucose levels, may decrease postprandial glucose levels (relative to no protein ingestion) due to the release of insulin
C	Bone Mineral Density	—	—	2 studies	Currently no demonstrated benefit to bone mineral density, although protein in general appears to have a protective effect

C	Blood Pressure	—	—	2 studies	Insufficient evidence to support the blood pressure reducing effects of whey protein
C	Blood Flow	—	—	1 study	Insufficient evidence to support a role of whey protein in improving blood flow
C	Inflammation	—	—	1 study	Insufficient evidence to support whey protein as interacting with inflammation and biomarkers of inflammation
C	C-Reactive Protein	—	—	1 study	No demonstrated effects on C-Reactive Protein
C	Insulin Sensitivity	↑	★☆☆ Minor	3 studies	Has been noted to increase insulin sensitivity to a larger degree than casein when consumed by obese persons in a part of a fat loss diet; has not yet demonstrated an insulin sensitizing effect in lean athletes
C	Triglycerides	↓	★☆☆ Minor	2 studies	Possible reductions in triglycerides, but it is not sure if this is exclusive to whey protein or due to protein in general.
C	LDL-C	↓	★☆☆ Minor	1 study	Possible LDL-C lowering effect, but has not yet been shown to be better than other protein sources.
C	HDL-C	—	—	2 studies	No significant evidence to support an increase in HDL-C with whey protein
C	Total Cholesterol	—	—	2 studies	No significant influence on circulating cholesterol has been demonstrated with whey protein
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	2 studies	Increased levels of glutathione are secondary to the Cysteine content and can be mimicked

					with all dietary sources of L-cysteine or supplemental N-acetylcysteine
C	IGF-1	—	—	1 study	Does not appear to inherently alter circulating IGF-1 levels
D	Appetite	↓	★☆☆ Minor	1 study	Appears to reduce appetite (common to all protein sources), but its superiority over other protein sources is not yet demonstrated.
D	Intestinal Permeability	↓	★☆☆ Minor	1 study	Appears to decrease intestinal permeability, which is due to the Glutamine content of whey protein.
D	Liver Enzymes	↓	★☆☆ Minor	1 study	Has been associated with a decrease in liver enzymes (in steatohepatitis) but not to a remarkable degree; may simply be due to the L-cysteine content.
D	Liver Fat	↓	★☆☆ Minor	2 studies	Reductions in liver fat have been noted with whey protein supplementation, which is thought to be more effective than other protein sources due to the high L-cysteine content.

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Yacon

Also known as: Smallanthus sonchifolius, Yacon Syrup, Aicama, Jicama, Diet potato, yacon potato, yacon strawberry

Yacon (*Smallanthus sonchifolius*) is a tuber, whose syrup contains a large amount of fructooligosaccharides (FOS), which are carbohydrates that are partially absorbed and prebiotic in nature. Yacon may have benefits for intestinal health and may reduce appetite, but studies on it are limited.

See [Yacon on Examine.com](#)

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Fecal Moisture	↑	★☆☆ Minor	1 study	A mild increase in fecal moisture and consistency has been reported with consumption of yacon syrup, thought to be related to prebiotic effects and a reduction in intestinal motility.
C	Intestinal Motility	↓	★★★☆☆ Notable	1 study	The one study to assess intestinal motility (speed of food transit from stomach to anus) has noted a near halving of time, suggesting a relatively notable anti-motility action.
C	Insulin	↓	★☆☆ Minor	1 study	A minor reduction in fasting insulin levels has been noted in obese women given supplementation, but this is confounded with weight loss.
C	Blood Glucose	—	—	1 study	No significant influence on fasting blood glucose in nondiabetic obese women who consume Yacon relative to placebo, despite weight loss.
C	Insulin Sensitivity	↑	★☆☆ Minor	1 study	A minor increase in insulin sensitivity has been noted in a lone study in obese women that is also confounded with weight loss (ie. the weight loss could explain the increase

					observed)
C	Weight	↓	★☆☆ Minor	1 study	A decrease in weight has been noted in obese women given Yacon, although this study could potentially be explained by a reduction in food intake (due to an increase in self-reported satiety and no tracking of calories noted).
C	Total Cholesterol	—	—	1 study	No significant influence on total cholesterol has been noted despite changes in LDL and accompanying weight loss.
C	Triglycerides	—	—	1 study	Despite a triglyceride reducing effect of fructooligosaccharides in rats, the limited evidence in humans (with mildly elevated triglycerides) failed to find any appreciable effect despite weight loss.
C	LDL-C	↓	★☆☆ Minor	1 study	A respectable decrease in LDL has been reported once, although this reduction in LDL is confounded with weight loss that occurred with yacon syrup.
C	HDL-C	—	—	1 study	No significant influence on HDL cholesterol has been noted with Yacon syrup, despite weight loss occurring.

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Yamabushitake

Also known as: *Hericium erinaceus*, Lion's Mane, Monkey's Head, Houtou (infrequent), Igelstachelbart, Pom Pom Blanc, Hedgehog Mushroom, Satyr's Beard

Yamabushitake, known as the Lion's Mane Mushroom, is a dietary mushroom that can be a supplement. It appears to be a promising cognitive enhancer and immunomodulator (thought to stimulate or suppress inflammation depending on context).

See [Yamabushitake on Examine.com](#)

How to Take

Currently, the only human study has used an oral dose of 1,000mg Yamabushitake (96% purity extract) thrice daily for a cumulative total of 3,000mg extract. While it is unknown if this is the optimal dose or not, it appeared to be effective.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Cognitive Decline	↓	★☆☆ Minor	1 study	The rate of cognitive decline seen with oral supplementation of yamabushitake appears to be significantly reduced in older persons, although there are no direct comparisons to reference drugs at this time to assess potency.
C	Anxiety	↓	★☆☆ Minor	1 study	Decreases in anxiety noted, this may be secondary to menopausal symptom reduction
C	Depression	↓	★☆☆ Minor	1 study	Decrease in depressive symptoms has been noted, which may be secondary to attenuating menopausal symptoms
C	Symptoms of Menopause	↓	★☆☆ Minor	1 study	Menopausal symptoms have been reduced, but this was mostly due to the reported antidepressant and anxiolytic properties of the mushroom.

C	Sleep Quality	-	-	1 study	No significant effects on sleep quality

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Yerba mate

Also known as: Ilex paraguariensis, Mate plant, St. Hilaire, Aquifoliaceae

Yerba Mate is a tea brewed in Southern America, and is a pretty good source of Caffeine alongside some other bioactive compounds like Quercetin and Ursolic Acid. It appears to just be a vessel for these compounds, and not significantly better or worse than other stimulant teas.

See [Yerba mate on Examine.com](#)

How to Take

It is thought that a good conversion dose from animal studies to humans is that 1g/kg bodyweight in rats equals about 1.5 liters of Yerba Mate tea Human studies that note benefit on lipid and glucose metabolism use 3 cups (each cup being 330mL) of Yerba Mate tea daily, for a period of up to 60 days. Tea up to 1.5 liters daily has been shown to be well tolerated in humans, although toxicity has not been seen in animals at higher dosages either. Isolated Yerba Mate in supplemental form tends to be around 1,000 to 1,500mg of Yerba Mate leaf.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Metabolic Rate	—	—	1 study	No significant influence on metabolic rate has been noted
C	Fat Oxidation	↑	★☆☆ Minor	1 study	An increase in fat oxidation assessed via a lower respiratory quotient has been noted
C	Heart Rate	↓	★☆☆ Minor	1 study	A decrease has been noted with Yerba Mate consumption, which is somewhat notable as stimulants tend to increase heart rate
C	Blood Pressure	—	—	1 study	No significant influences on blood pressure have been noted (although this may be due to it being underresearched; Mate may follow the same motifs as caffeine ingestion)
D	General Oxidation	↓	★☆☆	1 study	A decrease in serum oxidative

			Minor		Association in serum oxidative parameters tends to be noted following Mate consumption
D	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	2 studies	Appears to increase the primary three antioxidant enzymes (glutathione, catalase, and SOD) in both healthy and diseased persons
D	LDL-C	↓	★☆☆ Minor	3 studies	Decreases in LDL cholesterol have been noted in metabolically unwell persons following moderate Mate consumption (as brewed tea)
D	Apolipoprotein B	↓	★☆☆ Minor	1 study	Somewhat of a decrease in hyperlipidemic patients consuming Mate tea
D	HDL-C	↑	★☆☆ Minor	1 study	An increase in HDL-C has been noted with Mate consumption
D	Total Cholesterol	↓	★☆☆ Minor	1 study	A decrease of total cholesterol has been noted with Mate consumption
D	Lipid Peroxidation	↓	★☆☆ Minor	1 study	A decrease in lipid peroxidation has been noted with Mate consumption over 7 days
D	HbA1c	↓	★☆☆ Minor	1 study	A decrease in HbA1c levels has been detected in type II diabetics consuming Mate tea, although not to a remarkable degree
D	Blood Glucose	↓	★☆☆ Minor	1 study	A slight decrease in blood glucose has been noted with Mate consumption in type II diabetics; no evidence in otherwise healthy persons
D	Bone Mineral Density	↑	★☆☆ Minor	1 study	An <i>association</i> has been noted with increased bone mineral density and Mate consumption; insufficient evidence to

					suggest a causative role as no interventions exist
D	Esophageal Cancer Risk	—	—	1 study	Although associations exist between mate consumption and esophageal cancer risk, this appears to apply to any (scalding) hot beverage and is not associated with cooled mate. The increased risk is associated with the heat rather than the drink constituents.

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Yohimbine

Also known as: Yohimbe, Corynanthe Yohimbe, Yohimbe Bark

Yohimbine is a fat burning compound. Although effective, it may cause anxiety and adversely interact with pharmaceuticals.

See [Yohimbine on Examine.com](#)

How to Take

Dosages of 0.2mg/kg bodyweight have been successfully used to increase fat burning without significant implications on cardiovascular parameters like heart rate and blood pressure. This results in a dosage of: 14 mg for a 150lb person 18 mg for a 200lb person 22 mg for a 250lb person Supplementation is most effective between meals or during short term fasting. Caution should be exercised at higher body weight, since the cardiovascular system may not be prepared to handle a stimulatory agent such as yohimbine. When supplementing yohimbine for the first time, always start with a half-dose and assess tolerance before proceeding. When pairing yohimbine with other stimulatory agents, half-dose both supplements and work up to the recommended dose cautiously, as two supplements can interact negatively.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Erections	↑	★☆☆ Minor	1 study	Erections are increased following yohimbine ingestion which is thought to be a combination of alpha-2-adrenergic antagonism (enhancing relaxation of the penile tissue so engorgement of blood can ensure) and increasing blood pressure (which would increase the amount of force in an erection). However, may not be able to overcome organic erectile dysfunction associated with poor blood flow
C	Symptoms of Phobia	↓	★☆☆ Minor	2 studies	Thought to decrease symptoms of phobia via noradrenaline release (causing desensitization to the stress response) but studies looking at its efficacy are mixed.
C	Cortisol	↑	★☆☆	2 studies	

C		↑	☆☆☆ Minor		Appears to increase cortisol following ingestion
C	Anxiety	↑	☆☆☆ Minor	2 studies	Although unreliable, an increase in anxiety may occur following yohimbine ingestion
C	Heart Rate	↑	☆☆☆ Minor	2 studies	Due to stimulatory effects, an increase in heart rate follows yohimbine ingestion
C	Blood Pressure	↑	☆☆☆ Minor	2 studies	Appears to increase blood pressure, which may aid the proerectile effects (as it is an acute increase) but is a cardiovascular risk factor
C	Lean Mass	—	—	1 study	No significant influence on lean mass detected with yohimbine ingestion
C	Fat Mass	↓	☆☆☆ Notable	1 study	Fat mass is reduced with yohimbine ingestion and appears to affect both obese and lean individuals
C	Power Output	—	—	1 study	No significant influence on power output noted with yohimbine
C	Alcohol Dependence	↑	☆☆☆ Minor	1 study	Injections of yohimbine have been noted to increase cravings for alcohol, which although not demonstrated with oral intake is thought to be related to the reduction in inhibition
C	Rate of Gastric Emptying	—	—	1 study	No significant effect on gastric emptying rate
C	Diuresis	↑	☆☆☆ Minor	1 study	There appears to be an increased urge to urinate following supplementation of yohimbine
C	Plasma Melatonin	—	—	1 study	Despite increased rates of

					melatonin elimination from the body (via urination), there does not appear to be a significant influence on plasma melatonin concentrations.
D	Symptoms of Orthostatic Hypotension	↓	★☆☆ Minor	1 study	Orthostatic hypotension (light headedness upon rapidly standing up) appears to have reduced symptoms associated with yohimbine usage
D	Cerebral Blood Flow	↓	★☆☆ Minor	1 study	A decrease in cerebral blood flow has been noted to be independent of cognitive impairment
D	Testosterone	—	—	1 study	No significant influence on testosterone seen with yohimbine supplementation
D	Penile Girth	↑	★☆☆ Minor	1 study	An increase in penile girth has been noted (similar to L-DOPA) which was not to a large degree, only detectable when dividing the group into responders and nonresponders

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Zinc

Zinc is an essential mineral involved in regulating a large amount of enzymes in the body. It is known as an antioxidant and immune boosting supplement, and is most commonly supplemented to reduce the frequency of sickness and to support optimal testosterone levels.

See [Zinc on Examine.com](#)

How to Take

Note: The phrase 'elemental zinc' refers to the weight of just the zinc molecule by itself, and is what the following doses refer to. Different chelations and forms have different weights and dosing protocols Zinc is most commonly dosed in either the 'low dosage' range of 5-10mg or the 'high dosage' range of 25-45mg. The low dosage is a daily preventative that reduces the risk for deficiency, and the high dosage range is the one used to prevent deficiency in persons who have more than just a dietary deficiency working against them (athletes, diabetics, etc.). There is zinc 'superloading' protocol using up to 100mg zinc daily, and while this is confirmed to be safe for short term usage (2-4 months) it is well above the tolerable upper limit (TUL) of 40mg and thus not advisable for prolonged supplementation. Variants of Zinc Supplementation Zinc citrate is approximately 34% zinc by weight, and thus 50mg elemental zinc in this form is 146 mg zinc citrate. Zinc sulfate is approximately 22% zinc by weight, and thus 50mg elemental zinc in this form is 220 mg zinc sulfate. Zinc gluconate is approximately 13% zinc by weight, and thus 50mg elemental zinc in this form is 385 mg zinc gluconate.

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
B	Mucositis	↓	★☆☆ Minor	4 studies	Decreases in the severity but not occurrence of mucositis have been reported in cancer patients undergoing both radiotherapy and chemotherapy, although the benefits seem unreliable
B	Pneumonia	—	—	8 studies	In regards to pneumonia in particular, zinc does not appear to have any appreciable benefit either when superloaded by itself or taken as an adjuvant alongside antibiotics
B	IGF-1	↑	★☆☆ Minor	3 studies	There is an increase in IGF-1 concentrations if the subject is deficient in zinc, but no increase otherwise.

B	Insulin	↓	★☆☆ Minor	4 studies	Basal insulin concentrations appear to be reduced following supplementation of zinc.
B	Acne	↓	★☆☆ Minor	4 studies	Orally supplemented zinc (in the dosage range of 30-130mg elemental zinc) appears to be effective in reducing symptoms of acne, although the effects are modest at best.
B	Testosterone	↑	★☆☆ Minor	5 studies	Both chronic/excessive exercise as well as a zinc deficiency are associated with abnormally low testosterone concentrations, and in these states supplementation of zinc increases testosterone. There is no inherent increase in testosterone with zinc if either of those two conditions are not met
B	LDL-C	↓	★☆☆ Minor	3 studies	A decrease in LDL cholesterol may occur when a zinc deficiency in obese persons is being normalized.
B	C-Reactive Protein	↓	★☆☆ Minor	4 studies	Supplementation of zinc in persons who may be zinc deficient is able to reduce C-reactive protein
B	Blood Glucose	↓	★☆☆ Minor	3 studies	A reduction in blood glucose has been observed alongside improvements in insulin sensitivity in obese persons who may have been zinc deficient.
B	Lipid Peroxidation	↓	★☆☆ Minor	3 studies	A slight decrease in lipid peroxidation has been noted with supplementation of zinc in persons who may be deficient.
C	Dysgeusia	↓	★☆☆ Minor	3 studies	Although there may be an improvement in symptoms of persons who are specifically deficient in carbonic anhydrase

					VI (zinc dependent enzyme) which occurs with zinc deficiency, dysgeusia and hypogeusia associated with chemotherapy seem unaffected
C	Symptoms of OCD	↓	★☆☆ Minor	1 study	High dose zinc (220mg twice daily) may have a minor additive role to standard OCD therapy (fluoxetine), although the small magnitude of benefit and the high dose used suggest that it is not the best supplemental option.
C	Oxidation of LDL	↓	★☆☆ Minor	2 studies	Although there may not be an inherent protective effect and normalizing a deficiency does not <i>per se</i> reduce oxidation of LDL, if the body becomes more insulin sensitivity when restoring a deficiency then zinc may indirectly reduce oxidation.
C	Leptin	↓ ↑	★☆☆ Minor	2 studies	Normalizing a zinc deficiency increases leptin (which is suppressed during deficiency), but elsewhere the abnormal elevation of zinc seen in morbid obesity has been reduced alongside weight loss and insulin sensitization from zinc.
C	Symptoms of Pruritus	↓	★☆☆ Minor	1 study	High dose (440mg) zinc sulphate appears to be effective in hemodialysis patients in reducing pruritis.
C	Symptoms of Rosacea	—	—	2 studies	Although efficacy cannot yet be ruled out, the best evidence currently does not support a role for zinc supplementation in the treatment of rosacea
C	Subjective Well-being	↑	★☆☆ Minor	2 studies	Although the evidence is mixed currently, zinc has been previously associated with an improvement in mood state and has mechanisms by which

					it can work. It likely has a small but positive influence.
C	ADHD in Children	—	—	1 study	No significant influence of zinc supplementation on symptoms of ADHD in children.
C	Depression	↓	★★☆ Notable	2 studies	The reduction in depression is notable <i>only for</i> treatment resistant depression alongside a pharmaceutical antidepressant; there does not appear to be a benefit to persons who respond to antidepressants and the inherent anti-depressant effects without a pharmaceutical add-on are modest at best.
C	Aggression	↓	★★☆ Minor	1 study	Secondary to an improvement in overall mood, aggressive symptoms have been noted to be reduced with low dose zinc supplementation.
C	Stroke Recovery Rate	↑	★★☆ Minor	1 study	In zinc deficient persons who recently suffered a stroke, supplementation of zinc appears to accelerate the rate of recovery.
C	Cognition	↑	★★☆ Minor	2 studies	An improvement in cognition has been seen in stroke patients given zinc to complement their zinc insufficient diet.
C	Serum T3	↑	★★☆ Minor	2 studies	The decline in T3 hormone levels during prolonged exercise is abolished with supplementation of zinc.
C	Serum T4	↑	★★☆ Minor	2 studies	The decline in T4 hormone levels during prolonged exercise is abolished with supplementation of zin
C	Free Testosterone	↑	★★☆ Minor	2 studies	Free testosterone follows the

			Minor		same trends as testosterone, and may be increased following supplementation in persons who are deficient in zinc
C	Total Cholesterol	↓	★☆☆ Minor	2 studies	A decrease in cholesterol, due to LDL-C being reduced, seems to occur following oral supplementation of zinc in persons who are obese and likely zinc deficient
C	Weight	↓	★☆☆ Minor	2 studies	In children who are likely deficiency, zinc supplementation can reduce body weight.
C	HDL-C	—	—	2 studies	No significant influence on HDL-C, even when normalizing a zinc deficiency associated with weight loss.
C	Apolipoprotein B	↓	★☆☆ Minor	1 study	Apolipoprotein B may be abnormally elevated during zinc deficiency as it is reduced upon supplementation of zinc.
C	Apolipoprotein A	↑	★☆☆ Minor	1 study	A slight increase in apolipoprotein A has been reported in obese persons who may have been zinc deficient, but then supplemented to alleviate said deficiency.
C	Insulin Sensitivity	↑	★☆☆ Minor	2 studies	An increase in insulin sensitivity has been noted with supplementation of zinc in insulin resistant persons who were likely zinc deficient.
C	Interleukin 6	↓	★☆☆ Minor	1 study	Alongside other proinflammatory cytokines, IL-6 appears to be reduced following supplementation of zinc.
C	Cell Adhesion Factors	↓	★☆☆ Minor	1 study	In persons who were probably

					zinc deficient, supplementation of zinc is able to reduce cellular adhesion factors and the risk for atherosclerosis.
C	Rate of Sickness	↓	★☆☆ Minor	1 study	In regards to the common cold and infections, the rate of catching sickness with daily supplementation of zinc in persons who may be deficient is reduced.
C	Upper Respiratory Tract Infection Risk	—	—	1 study	Despite having lower sickness rates overall, the reduction seen in URTIs specifically does not appear to reach significance.
C	Functionality in Elderly or Injured	↑	★☆☆ Minor	1 study	An increase in functionality of elderly frail persons has been seen with zinc supplementation, thought to be related to the increase in IGF-1 also observed.
C	Anti-Oxidant Enzyme Profile	↑	★☆☆ Minor	1 study	There appears to be an increase in superoxide dismutase and glutathione peroxidase after supplementation of zinc in otherwise healthy persons.
C	Triglycerides	—	—	2 studies	No significant reduction in circulating triglycerides has been detected with zinc supplementation.
C	Symptoms of Tinnitus	↓	★☆☆ Minor	1 study	Zinc supplementation at higher levels (50mg) appears to be able to reduce subjective symptoms of tinnitus in most persons supplemented with zinc.
C	Iron Absorption	↓	★☆☆ Minor	5 studies	Iron absorption is decreased when both iron and zinc exceed 10mg in a supplement given on an empty stomach. The inhibition does not appear to be relevant if the same ratio is

					at lower doses (500mcg) or if the minerals are ingested via food products.
C	Viral Warts	↓	★★★☆☆ Notable	3 studies	Although the evidence is very preliminary right now, supplementation of high dose zinc (up to 132mg elemental zinc) is able to abolish viral warts by 50-60% while topical application (10% zinc sulphate solution) can abolish viral warts in 80% of persons. Nonviral warts have less of a response to treatment.
C	Reaction Time	↑	★★☆☆☆ Minor	1 study	A slight increase in reaction time has been noted in persons who are zinc deficient and then supplemented with zinc.
C	Psoriasis	↓	★★★☆☆ Notable	1 study	Topical application of a 0.25% zinc pyrithione cream is associated with highly significant reductions in psoriasis symptoms (twice daily application for three months reducing them by over 70%)
C	Plasma Nitrate	—	—	1 study	No significant influence of zinc supplementation on plasma nitrate or nitrite levels, suggesting no interaction with nitric oxide metabolism
C	General Oxidation	—	—	1 study	No significant interaction with biomarkers of general oxidation
C	Blood Pressure	—	—	1 study	Blood pressure does not appear to be modified with zinc supplementation.
C	Blood Flow	—	—	1 study	Blood flow does not appear to be modified with supplementation of zinc.
C	Liver Cirrhosis	↓	★☆☆☆☆	1 study	

			 Minor		Supplementation of zinc in persons with liver cirrhosis appears to be mildly therapeutic, possibly related to reducing hepatic copper concentrations.
C	Dental Health	↑	 Minor	1 study	Supplementation of zinc in children who were probably deficient is able to reduce the formation of plaque and is thought to then reduce risk of dental cavities; gingivitis risk was not affected.
C	Sperm Count	↑	 Minor	2 studies	An increase in sperm count has been noted in infertile men who also had low testosterone; it was ineffective in infertile men with normal testosterone
C	DHT	↑	 Minor	1 study	An increase in DHT has been noted in infertile men
C	Fertility	↑	 Minor	2 studies	Zinc can increase the fertility of men who are infertile <i>and</i> have low circulating testosterone, and appears ineffective in men who have normal testosterone levels with infertility. This is related to an increase in sperm count seen in the former group.
D	Serum DHEA	—	—	1 study	No significant influence on serum DHEA sulfate
D	Fat Mass	—	—	1 study	No known significant interactions with zinc supplementation on fat mass.
D	TNF-Alpha	↑	 Minor	1 study	A zinc deficiency is associated with reduced circulating TNF-α concentrations, which are normalized upon zinc sufficiency.
D	Interleukin 2	↑	 Minor	1 study	Interleukin 2 (IL-2) appears to be reduced during zinc deficiency, and this is

					normalized upon zinc sufficiency.
D	Follicle-Stimulating Hormone	—	—	1 study	No detectable influence of zinc supplementation of FSH concentrations in zinc deficient persons.
D	Prolactin	—	—	1 study	No detectable increase in prolactin in persons who are deficient in zinc and then supplemented to restore levels.
D	Luteinizing Hormone	↑	★☆☆ Minor	1 study	In persons who are deficient in zinc, an increase in LH occurs following zinc replenishment.

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Ziziphus jujuba

Also known as: Ziziphus Jujuba, Chinese Date, Da Zao, Jujube

Ziziphus Jujuba (Chinese/Korean Date, Jujube) is a plant which bears fruits and seeds that are used for medicinal purposes in Traditional Chinese Medicine. It may possess Anxiety-reducing and sedative properties.

See [Ziziphus jujuba on Examine.com](#)

How to Take

Traditional usage of Jujube is taking 50g of the fruits (20 individual 2-2.5cm diameter fruits) and doing a hot water extract, either a soup or a beverage. There currently is not enough evidence in humans to establish an effective oral dose of Zizyphus Jujube supplements but estimating from animal studies finding benefits with 500mg/kg for anxiety reduction, an estimated human dose would be: 5,500 mg for a 150lb person 7,300 mg for a 200lb person 9,000 mg for a 250lb person

LEVEL OF EVIDENCE	EFFECT	CHANGE	MAGNITUDE OF EFFECT SIZE	SCIENTIFIC STUDIES	COMMENTS
C	Constipation	↓	★☆☆ Minor	1 study	A decrease in the symptoms of constipation has been seen with the water extract of jujubes; which may apply to fruit consumption but may not apply to isolated supplements (due to the polysaccharides being the active ingredients)

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8-isoPGF2a

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Conjugated Linoleic Acid	↑	☆☆☆ Minor	3 studies	8-isoPGF(2)a is normally a biomarker of lipid peroxidation, but CLA may be causing a false positive (as fatty acids are known to interact with the enzymes in question and other markers of lipid peroxidation are unchanged).
C	Quercetin	—	—	1 study	Urinary 8-isoPGF2α is unchanged with prolonged quercetin supplementation.

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Acne

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Zinc	↓	☆☆☆ Minor	4 studies	Orally supplemented zinc (in the dosage range of 30-130mg elemental zinc) appears to be effective in reducing symptoms of acne, although the effects are modest at best.
D	Resveratrol	↓	☆☆☆ Notable	1 study	Topical application of resveratrol in a cream more than halved the rating scores of acne, and reductions in lesion count were also noted (but only to 10%)
D	Inositol	↓	☆☆☆ Notable	1 study	Although this may only apply to acne in women with PCOS, supplementation of normal doses of <i>myo</i> -inositol can abolish acne in over half of subjects within 3-6 months.

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ADHD in Children

Attention deficit hyperactive disorder (ADHD) in children is currently being investigated from a nutraceutical perspective, and these supplements are thought to confer similar (but perhaps lesser in magnitude) benefits as methylphenidate.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Fish Oil	↓	★☆☆ Minor	7 studies	Supplemental DHA above 300mg appears to be effective in reducing ADHD symptoms in children when supplemented
C	L-Carnitine	↓	★☆☆ Minor	2 studies	At least one study has noted reduction in ADHD symptoms in children
C	Phosphatidylserine	↓	★☆☆ Minor	2 studies	There appears to be reduced symptoms of both hyperactivity and attention deficit in children given PS, which may be more effective when the PS is complexed with fish oils
C	Modafinil	↓	★★★☆☆ Notable	1 study	Modafinil appears to be able to reduce symptoms of ADHD in children when taken as a daily preventative at the lowest active dose
C	Ginkgo biloba	↓	★☆☆ Minor	1 study	Ginkgo appears to reduce symptoms of ADHD, but 80-120mg of the EGb-761 extract has been confirmed to be less potent than 20-30mg Ritalin
C	Zinc	—	—	1 study	No significant influence of zinc supplementation on symptoms of ADHD in children.

Adiponectin

Adiponectin is an adipokine (signalling molecule secreted from fat cells, like leptin) which positively influences glucose metabolism and fat loss. Increasing adiponectin levels are thought to result in fat loss and improved health.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Conjugated Linoleic Acid	—	—	3 studies	No alterations in adiponectin has been noted with CLA supplementation
C	Coenzyme Q10	—	—	1 study	No detectable interaction of CoQ10 and adiponectin
C	L-Carnitine	↑	★☆☆ Minor	1 study	An increase in adiponectin has been noted
C	Licorice	—	—	1 study	No significant interaction between adiponectin and licorice
C	Green Tea Catechins	↑	★☆☆ Minor	1 study	Possible increase in adiponectin associated with green tea ingestion
C	Irvingia gabonensis	↑	★☆☆ Minor	1 study	An increase in adiponectin is noted with irvingia gabonensis, but this result is somewhat unreliable due to being confounded with both weight loss and industry influence
C	Melatonin	↑	★☆☆ Minor	1 study	An increase in adiponectin has been noted following acute ingestion of melatonin
C	Fish Oil	—	—	2 studies	No significant influence on Adiponectin concentrations
C	Arginine	↑	★☆☆ Minor	1 study	At least in persons with

					impaired glucose tolerance, an increase in adiponectin (and the adiponectin:leptin ratio) has been noted with supplemental L-arginine
C	Vitamin K	—	—	1 study	No significant alterations seen in adiponectin concentrations in serum with 4 weeks supplementation of 30mg MK-4
C	Curcumin	↑	★☆☆ Minor	1 study	Curcumin has been implicated in increasing adiponectin concentrations.
C	Inositol	↑	★☆☆ Minor	1 study	An increase in adiponectin has been noted in women with PCOS
C	Nigella sativa	—	—	1 study	No significant influence on adiponectin concentrations
C	Garlic	↑	★☆☆ Minor	1 study	There appears to be an increase in adiponectin associated with 1,200mg of aged garlic supplementation despite no other influence on the body of persons with metabolic syndrome.
C	Trimethylglycine	—	—	1 study	No significant influence on adiponectin concentrations in persons with fatty liver seen with betaine supplementation.
C	Astaxanthin			1 study	
C	Chromium	—	—	2 studies	No significant influences on adiponectin concentrations in the blood relative to placebo.
C	Rose Hip	—	—	1 study	No significant modifications in adiponectin concentrations when rose hip supplementation is given to humans.
D	Coffee	↑	★☆☆	1 study	

D		-	Minor		An increase in adiponectin has been associated with coffee consumption
D	Blueberry	-	-	1 study	No significant influence on adiponectin concentrations in obese individuals

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Adrenaline

Adrenaline is a catecholamine that mediates the 'fight or flight' response, and also possesses fat burning properties. Increases in serum adrenaline are known to improve focus and fat oxidation, and supplements that increase adrenaline are thought to retain these effects.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Caffeine	↑	★☆☆ Minor	3 studies	Serum catecholamines (adrenaline, noradrenaline) are increased in naive users of caffeine following acute ingestion
B	Melatonin	—	—	4 studies	There do not appear to be any influence of melatonin ingestion on plasma adrenaline, either inherently or from influencing the spike in adrenaline from stress
C	Alcohol	—	—	1 study	Serum adrenaline appears unaltered following alcohol ingestion
C	Ganoderma lucidum	—	—	1 study	No significant influence on serum adrenaline
C	Mucuna pruriens	↑	★☆☆ Minor	1 study	The decrease in adrenaline seen in infertility is normalized with mucuna
C	Branched Chain Amino Acids	—	—	1 study	No significant influence on adrenaline concentrations
C	Sodium Bicarbonate	—	—	2 studies	Mixed effects, but one intravenous study (not in the human effect matrix) that also noted no significant differences suggest that the increase in catecholamines during exercise is not associated with acidity and thus not

					suppressed by sodium bicarbonate
C	Creatine	—	—	1 study	No significant alterations in plasma adrenaline are seen with creatine supplementation during sleep deprivation.

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Aerobic Exercise

Aerobic exercise refers to cardiovascular exercise that does not fall under the anaerobic exercise category, and can be conducted for a prolonged period of time. Supplements that improve endurance significantly can benefit aerobic performance.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Creatine	—	—	7 studies	Does not appear to confer any apparent benefit to prolonged cardiovascular exercise.
B	L-Carnitine	—	—	5 studies	More evidence than not suggest no significant influence on low intensity and high duration cardiovascular exercise
B	Caffeine	↑	★☆☆ Minor	3 studies	An increase in aerobic exercise capacity is noted with caffeine, possibly secondary to increased free fatty acids and adrenaline
B	Vitamin C	—	—	4 studies	No significant influence on aerobic exercise performance
B	Branched Chain Amino Acids	↑	★☆☆ Minor	6 studies	An increase in time to exhaustion appears to exist in prolonged endurance exercise, but this benefit may only exist in untrained or lightly trained individuals. Several studies have noted that the anti-fatigue effects and increased time to exhaustion do not really occur in advanced athletes
B	Sodium Bicarbonate	↑	★☆☆ Minor	3 studies	For cardiovascular exercise that is prolonged in nature (45m or greater) and not exceeding the lactate threshold, there appears to be a small beneficial effect of

					sodium bicarbonate supplementation on improving time to fatigue or time to complete a test
B	Colostrum	—	—	5 studies	For the most part colostrum influenced aerobic exercise similar to whey protein (ie. not much benefit) although in specific instances of high endurance stressors in elite cyclists there may be a small ergogenic benefit thought to be due to reducing the rate of immunosuppression.
C	Pyruvate	—	—	1 study	No significant influence on aerobic exercise performance
C	Nitrate	↑	★☆☆ Minor	2 studies	The performance enhancing aspect of nitrate supplementation in prolonged aerobic exercise is less than that seen in shorter duration cardiovascular exercise, and is only somewhat effective for longer periods.
C	Cordyceps	—	—	1 study	No significant improvements in prolonged aerobic exercise have been noted with cordyceps supplementation
C	Velvet Antler	—	—	1 study	No benefit of velvet antler on aerobic cardiovascular exercise
C	Kaempferia parviflora	—	—	1 study	No significant influence on aerobic exercise when taken acutely before exercise in youth
C	Magnesium	↑	★★★☆☆ Notable	1 study	The one study to assess aerobic exercise capacity noted a significant improvement during extreme physical stress (triathletes), which is notable and needs replication
C	Citrulline	—	—	1 study	No significant influence on a

					treadmill test to exhaustion nor oxygen kinetics during this test
C	Pelargonium sidoides	—	—	1 study	There are no improvements in running performance in otherwise healthy athletes given this supplement for one month
C	Ashwagandha	↑	★☆☆ Minor	1 study	Appears to increase time to exhaustion on a treadmill test when given to athletes; the increase in endurance is mild but present
C	Astaxanthin			1 study	
C	Vitamin E	—	—	2 studies	Performance during aerobic exercise does not appear to be significantly altered with supplementation of vitamin E relative to placebo.
D	Blueberry	—	—	1 study	Chronic loading of blueberries with an acute dose prior to prolonged exercise (2.5 hours) in trained men does not improve physical performance.

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Aggression

Aggression (the opposite of calmness) is a confrontational behaviour that may be affected by supplementation or drugs.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Kava	↓	★☆☆ Minor	1 study	Aggressive symptoms of anxiety have been noted to be decreased following kava ingestion, an outright reduction of anxiety (without treating anxiety) is uncertain
C	Fish Oil	↓	★☆☆ Minor	1 study	A decrease in aggression has been noted, which is thought to be secondary to improvements in mood state and general well being
C	Piracetam	↓	★☆☆ Minor	1 study	In persons with cognitive decline, supplementation of Piracetam was able to reduce aggression and agitation symptoms.
C	Zinc	↓	★☆☆ Minor	1 study	Secondary to an improvement in overall mood, aggressive symptoms have been noted to be reduced with low dose zinc supplementation.
C	L-Carnitine	↓	★☆☆ Minor	1 study	Secondary to reducing symptoms of ADHD, L-carnitine may reduce aggression in children.
D	Melissa officinalis	↓	★☆☆ Minor	1 study	A reduction in agitation has been noted with lemon balm in stressed and anxious subjects, perhaps secondary to alleviating anxiety

Alertness

Alertness is an aspect of wakefulness with hints of attention, and is the ability to interpret and maintain attention on different targets. Supplements that increase alertness tend to be anti-sleep or stimulatory agents.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Melissa officinalis	↓	★★★☆☆ Notable	2 studies	A decrease in alertness appears to occur alongside lemon balm ingestion (with or without sedation)
C	Melatonin	↓	★☆☆☆☆ Minor	1 study	A decrease in alertness has been noted with melatonin supplementation
C	Modafinil	↑	★☆☆☆☆ Minor	1 study	An increase in alertness has been reported in persons using modafinil supplementation.
C	Centella asiatica	↑	★☆☆☆☆ Minor	1 study	An increase in the self-rated sensation of alertness is noted in older healthy adults supplementing with <i>centella asiatica</i>
C	Synephrine			1 study	
D	Creatine	↑	★☆☆☆☆ Minor	2 studies	Increases in alertness tend to be during sleep deprivation or stress, rather than outright increases in alertness. Not overly potent

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All-Cause Mortality

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Vitamin E	↓ ↑	★☆☆ Minor	9 studies	Minor increases in all cause mortality have been noted in mostly unhealthy cohorts with doses of vitamin E above 400IU (alpha-tocopherol) whereas lower doses exert a mild protective effect in the same cohorts. The magnitude is approximately 33-34 deaths per 10,000 subjects (both for the increase in mortality seen with vitamin E multnutrient supplements and the decrease seen with vitamin E alone), and it is unsure how this information applies to otherwise healthy persons.
C	Vitamin D	↓	★☆☆ Minor	2 studies	Cohorts of people with higher serum Vitamin D appear to die less frequently than cohorts with less serum Vitamin D; this may be heavily influenced by reducing falls in the elderly (reduction of falls and subsequent hospitalizations reducing death rates)

Allergies

Allergies refers to the ability of a stressor (antigen) to overstimulate the body's immune system and cause a reaction, and some supplements are able to generally suppress this response and then reduce the reaction to antigens.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Spirulina	↓	★★★ Strong	1 study	The lone study suggests that spirulina is strongly effective in controlling allergies, with the symptoms of nasal discharge, sneezing, nasal congestion and itching being time-dependently reduced and self-reported satisfaction doubling more than double that in spirulina relative to placebo.
C	Stinging Nettle	↓	★☆☆ Minor	1 study	A small decrease in allergic symptoms with oral stinging nettle consumption
C	Royal Jelly	—	—	1 study	No detectable benefit to hay fever or pollen allergies in youth
C	Rosmarinic Acid	↓	★☆☆ Minor	1 study	Rosmarinic acid appears to be effective in suppressing the response to pollen allergies in persons with seasonal rhinitis
C	Nigella sativa	↓	★★★ Notable	4 studies	Supplementation of the seed appears to beneficially influence most symptoms associated with allergies and most causes of the allergies (rhinitis, eczema, asthma, etc.), with the magnitude being somewhat notable among supplements.
C	Tinospora cordifolia	↓	★★★ Strong	1 study	At least in regards to allergic rhinitis, oral ingestion of

					<i>tinospora cordifolia</i> appears to abolish symptoms in 61-83% of persons (depending on symptom) extending to nasal blockage, mucus, pruritis, and sneezing.
C	Rubus suavissimus	—	—	1 study	Although this tea appears to be a popular tea for the purpose of treating allergic rhinitis, the currently available human evidence does not support this conclusion.
D	Methylsulfonylmethane	↓	★☆☆ Minor	1 study	A decrease in pollen-induced allergies has been noted with MSM supplementation, with efficacy within one week

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Ammonia

Ammonia is a metabolic byproduct of amino acids, with increases in serum ammonia being associated with some disease states (hepatic encephalopathy) or prolonged exercise; its reduction may improve endurance.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	L-Carnitine	↓	★★★☆☆ Notable	4 studies	A decrease in ammonia has been noted, and appears to influence both hepatic encephalopathy as well as persons with no significant liver damage
B	Glutamine	↓ ↑	★☆☆☆☆ Minor	3 studies	Differential effects on ammonia, with decreases being present when glutamine is taken as part of a daily supplement routine and measured during prolonged exercise with a possible increase with high acute doses (which fades with time)
C	Branched Chain Amino Acids	↓ ↑	★☆☆☆☆ Minor	1 study	Human studies suggest time-dependent influences on ammonia (increase after exercise up until 2 hours, a reduction the next day) while animal studies suggest that overdosing BCAAs can reverse a reduction into an increase
C	Sodium Bicarbonate	—	—	2 studies	No significant effects on plasma ammonia detected with supplemental bicarbonate
C	Ornithine	↓ ↑	★☆☆☆☆ Minor	2 studies	Although supplementation of Ornithine is recommended to reduce ammonia (which it appears to do in both models of hepatic encephalopathy and prolonged physical exercise) at least one study noted that for short term strenuous exercise

					ornithine caused an increase in ammonia
C	Arginine	—	—	1 study	Although it is plausible that arginine could decrease ammonia (secondary to ornithine), it does not appear to reliably occur

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Anaerobic Running Capacity

Anaerobic capacity refers to cardiovascular exercise that is short in duration and high in intensity, more prolonged than resistance training yet too intense to be maintained for more than a few minutes.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Creatine	↑	★☆☆ Minor	19 studies	Appears to increase anaerobic cardiovascular capacity, not to a remarkable degree however.
A	Sodium Bicarbonate	↑	★☆☆ Minor	34 studies	Cardiovascular exercise where failure is associated with metabolic acidosis (ie. 'the burn') appear to get benefit with bicarbonate supplementation to a small degree but reliably. For other exercises (rowing, sprinting, swimming) not characterized by the burn, the benefits are much less reliable
B	Caffeine	↑	★★★☆☆ Notable	7 studies	Appears to benefit anaerobic cardiovascular exercise, perhaps due to combination antifatigue effects and increasing power output
B	Beta-Alanine	↑	★☆☆ Minor	6 studies	Somewhat effective, may simply be secondary to enhancing muscular endurance and reducing fatigue rather than any cardiopulmonary interaction
B	Trimethylglycine	—	—	3 studies	Studies assessing distance, time, or other parameters of performance during cycling tests have failed to find any significant benefit with betaine supplementation (one positive study measuring power output is pooled in that parameter).
B	Colostrum	—	—	5 studies	There does not appear to be

					any benefit of dietary colostrum, relative to whey protein, in improving cardiovascular performance in anaerobic instances such as Wingate testing, resisted treadmill tests, or rowing.
C	L-Carnitine	↑	★☆☆ Minor	2 studies	An increase in anaerobic cardiovascular exercise has been noted with carnitine ingestion
C	Coenzyme Q10	—	—	1 study	No significant influence on anaerobic cardiovascular exercise has been detected with CoQ10 (although an anti-fatigue effect has been noted)
C	Maca	—	—	1 study	No significant influence on anaerobic running capacity associated with Maca
C	Nitrate	↑	★★★☆☆ Notable	1 study	The increase in performance on a sprint test appeared to be fairly significant, and pending more evidence nitrates may be a reference comparator.
C	Eleutherococcus senticosus	↑	★☆☆ Minor	1 study	Possibly effective at increasing cardiovascular exercise performance, likely secondary to fatigue reduction (although similarly unreliable)
C	Velvet Antler	—	—	1 study	No significant influence on anaerobic cardiovascular exercise capacity
C	Terminalia arjuna	↑	★☆☆ Minor	1 study	Able to increase intermittent sprint performance
C	Panax ginseng	—	—	1 study	Insufficient evidence to support a role of panax ginseng in improving exercise performance
C	Choline	—	—	2 studies	No significant influence on

					anaerobic cardiovascular capacity independent of choline depletion
C	Phosphatidylserine	↑	★★★☆☆ Notable	1 study	An increase in time to exhaustion has been noted in cycling at 85% of VO2 max with soy based phosphatidylserine (750mg) to the degree of 29+/- 8%, which is quite notable. This is independent of cortisol, and requires further investigation
C	Branched Chain Amino Acids	—	—	1 study	No significant performance enhancing effect on short-term cardiovascular exercise
C	Arachidonic acid			1 study	
C	HMB	—	—	1 study	No significant improvement in sprint capacity in trained persons supplementing HMB
C	Leucic Acid	—	—	1 study	No significant influence on anaerobic running capacity
C	Ornithine	—	—	1 study	Performance during short term cardiovascular exercise (assessed by time to exhaustion) does not appear to be significantly affected.
C	Arginine	↑	★★☆☆☆ Minor	1 study	May be able to increase anaerobic physical performance, but this is unreliable due to arginine not reliably increasing nitric oxide concentrations.
C	Taurine			1 study	
C	Ashwagandha	↑	★★☆☆☆ Minor	1 study	Supplementation of 500mg of the water extract has been noted to improve intermittent sprint performance in otherwise untrained persons then subject to a training protocol.

C	Quercetin	—	—	2 studies	No significant influence on anaerobic exercise capacity when preloaded
C	N-Acetylcysteine			1 study	
C	Chromium	—	—	1 study	No apparent influence of chromium supplementation on anaerobic cardiovascular exercise performance relative to placebo.

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Anti-Oxidant Enzyme Profile

Antioxidant enzymes (usually glutathione, superoxide dismutase, and catalase) are known to protect the body from oxidative damage, and increasing their levels or activity can confer protection from oxidative damage.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Alpha-Lipoic Acid	—	—	4 studies	Mixed effects on antioxidant enzymes, with decreases in glutathione peroxidase and increases in catalase with no effect on SOD
B	Watercress	↑	★☆☆ Minor	4 studies	There appears to be an influence on the enzymes superoxide dismutase and glutathione peroxidase, but this requires a certain genotype to occur
B	Curcumin	↑	★★★☆☆ Notable	4 studies	Although the exact enzyme that increases is not overly reliable (SOD, glutathione, and catalase), all three enzymes have individually been noted to be increased and they tend to do so to a large degree.
B	Chromium	—	—	4 studies	A lone study noted an increase in glutathione peroxidase, but the majority of the evidence finds no significant influence on antioxidant enzymes in the body (glutathione, SOD, or catalase).
C	Coenzyme Q10	↑	★☆☆ Minor	2 studies	May increase levels of antioxidant enzymes, does not appear to be reliable
C	L-Carnitine	↑	★☆☆ Minor	2 studies	An increase in all three main enzymes (SOD, glutathione peroxidase, catalase) has

					been detected following ingestion of carnitine
C	Vitamin C	↑	★☆☆ Minor	1 study	An increase in antioxidant enzymes have been noted in elderly persons
C	Panax ginseng	↑	★☆☆ Minor	2 studies	An increase in all three main antioxidant enzymes (SOD, glutathione peroxidase, and catalase) appear to occur to a small degree following ingestion of Panax ginseng
C	Whey Protein	↑	★☆☆ Minor	2 studies	Increased levels of glutathione are secondary to the Cysteine content and can be mimicked with all dietary sources of L-cysteine or supplemental N-acetylcysteine
C	Melatonin	↑	★☆☆ Minor	2 studies	Mixed effects on antioxidant enzymes, but there appears to be potential for melatonin to increase their content
C	Spirulina	↑	★☆☆ Minor	2 studies	Although increases have been noted in glutathione peroxidase and superoxide dismutase, it is difficult to assess potency thereof as there are no active controls and the two studies heterogenous.
C	Chlorella	↑	★☆☆ Minor	1 study	No remarkable effects following oral ingestion of chlorella, although some may be present
C	Olive leaf extract	↑	★☆☆ Minor	2 studies	Appears to induce the activity of the enzyme known as glutathione peroxidase
C	Stinging Nettle	↑	★☆☆ Minor	1 study	An increase in glutathione peroxidase has been detected
C	Shilajit	↑	★☆☆ Minor	1 study	An increase in superoxide dismutase has been noted

					with Shilajit consumption
C	Ganoderma lucidum	—	—	2 studies	No significant influences on superoxide dismutase or glutathione peroxidase are noted with ganoderma polysaccharide ingestion
C	Kaempferia parviflora	↑	★★★☆☆ Notable	1 study	The lone study to assess superoxide dismutase found a doubling after 8 weeks of supplementation (in older individuals); needs replication in youth
C	Arginine	↑	★☆☆☆☆ Minor	1 study	At least in persons with impaired glucose tolerance and/or type II diabetes, L-arginine appears to have an indirect antioxidant role and increase superoxide dismutase concentrations
C	Ginkgo biloba	↓ ↑	★☆☆☆☆ Minor	2 studies	Superoxide dismutase and glutathione have been noted to be increased with supplementation of ginkgo (240mg EGb-761) in persons with metabolic syndrome, while the abnormal elevation of these enzymes in schizophrenia is attenuated; essentially, a beneficial modulation appears to exist
C	Zinc	↑	★☆☆☆☆ Minor	1 study	There appears to be an increase in superoxide dismutase and glutathione peroxidase after supplementation of zinc in otherwise healthy persons.
C	N-Acetylcysteine	↑	★★★☆☆ Notable	1 study	NAC supplementation is able to reliably increase glutathione concentrations in cells specifically
C	Garlic	↑	★☆☆☆☆ Minor	3 studies	There appears to be an increase in glutathione related enzymes in red and white

					blood cells following ingestion of garlic supplements.
C	Creatine			1 study	
C	Astaxanthin			2 studies	
C	Vitamin E	—	—	2 studies	The levels of antioxidant enzymes in red blood cells (glutathione, superoxide dismutase, catalase) does not appear to be influenced with supplementation of vitamin E.
D	Yerba mate	↑	★☆☆ Minor	2 studies	Appears to increase the primary three antioxidant enzymes (glutathione, catalase, and SOD) in both healthy and diseased persons
D	Ginger	↑	★☆☆ Minor	1 study	An increase in seminal glutathione has been noted to reach 26.7% in otherwise infertile men.
D	Rubus coreanus	↑	★☆☆ Minor	1 study	There appears to be a mild increase in glutathione peroxidase with no significant influence on catalase nor SOD in otherwise healthy men.
D	Rose Hip	—	—	1 study	Limited evidence has failed to find any significant changes in antioxidant enzyme profiles in the red blood cells of those given rose hip extract

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Anxiety

Cognitive state of displeasing worry or concern with the feeling that bad events may arise; an impairment to well being, many supplements are anxiolytics (things that reduce anxiety).

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Kava	↓	★★★☆☆ Notable	8 studies	Appears to be quite reliable and effective in treating non-psychotic anxiety, with less reliability on the topic of generalized anxiety (which Lavender shows some promise for). It is possible that long-term usage of kava may have similar side-effects as long term usage of benzodiazepines (note demonstrated, but wholly logical) and most studies on kava are of a few weeks in duration without any problems.
B	Theanine	↓	★★☆☆☆ Minor	4 studies	Possible anxiety reducing effects, although anticipatory anxiety appears to be unaffected.
B	Ashwagandha	↓	★★★☆☆ Notable	3 studies	Preliminary evidence suggests potent anxiolytic effects <i>in the context of</i> chronic stress, with lesser potency in standard forms of anxiety not related to stress. There may be more benefit to social anxiety as well with Ashwagandha relative to other anxiolytics
B	Inositol	↓	★★★☆☆ Notable	4 studies	There appears to be a decrease in anxiety symptoms associated with high dose inositol, and it has been noted to be comparable to fluvoxamine in potency.
C	Fish Oil	↓	★★☆☆☆	2 studies	A decrease in anxiety has been

			Minor		A decrease in anxiety has been noted in medical students
C	Caffeine	↑	★☆☆ Minor	1 study	It is possible for caffeine to be anxiogenic, but requires genetic susceptibility to it
C	Yohimbine	↑	★☆☆ Minor	2 studies	Although unreliable, an increase in anxiety may occur following yohimbine ingestion
C	Black Cohosh	—	—	1 study	The trial to measure anxiety related to menopausal symptoms failed to find a benefit associated with black cohosh
C	Nicotine	↓ ↑	★☆☆ Minor	2 studies	Reduced anxiety symptoms have been noted in persons with cognitive decline, where anxiety was relieved as a symptoms of cognitive decline. In otherwise healthy persons prone to anxiety attacks, nicotine may be able to cause them.
C	Melissa officinalis	↓	★☆☆ Minor	2 studies	A decrease in anxiety has been noted with lemon balm extract, although not to a remarkable degree
C	Vitex agnus castus	↓	★☆☆ Minor	1 study	Can reduce PMS related anxiety but may not have any inherent anxiolytic effects; the potency correlates to the severity of anxiety during a menstrual cycle.
C	Bacopa monnieri	↓	★☆☆ Minor	2 studies	Appears to prevent rises in anxiety, and does not appear to unilaterally reduce anxiety. May be more of a modulator than anything, but doesn't appear overly potent
C	Ganoderma lucidum	↓	★☆☆ Minor	1 study	Some possible anti-anxiety effects secondary to reducing symptoms of cancer related fatigue

C	Lavender	↓	★★★☆☆ Notable	5 studies	There appears to be a notable decreased in symptoms of generalized anxiety disorder and with oral ingestion of lavender supplements; aromatherapy seems effective and implicated in reducing state anxiety (acute, situation based, anxiety), but has less robust evidence to support it. One study suggesting oral supplementation was comparable to lorazepam
C	Maca	↓	★★☆☆☆ Minor	2 studies	An anxiety reducing effect has been noted in postmenopausal women but not otherwise healthy young men
C	Melatonin	—	—	1 study	No significant influence on state anxiety during stress testing
C	Ginkgo biloba	↓	★★☆☆☆ Minor	1 study	Prolonged supplementation of ginkgo biloba appears to confer anxiolytic effects in persons with generalized anxiety disorder. Anxiety in dementia may also be reduced secondary to treating the symptoms of dementia
C	Yamabushitake	↓	★★☆☆☆ Minor	1 study	Decreases in anxiety noted, this may be secondary to menopausal symptom reduction
C	Centella asiatica	↓	★★☆☆☆ Minor	1 study	There appears to be a reduction in anxiety symptoms that build up over time (reaching a quarter reduction after two months) associated with twice daily ingestion of 500mg of the plant extract
C	N-Acetylcysteine			1 study	
C	Red Clover Extract	↓	★★★☆☆ Notable	2 studies	A minor reduction in anxiety

					(associated with menopause) has been noted in one independent trial while it was much more significant (near 80%) in a study with a potential conflict of interest; requires more research.
C	Synephrine			1 study	
C	Valeriana officinalis	—	—	1 study	Valerian does not appear to be effective for the treatment of generalized anxiety disorder in the one study assessing its effects.
C	Saffron	↓	★☆☆ Minor	1 study	The aroma of saffron has once been noted to cause a mild (approximately 10%) reduction in state anxiety following 20 minutes of exposure in otherwise healthy women.
D	Holy Basil	↓	★☆☆ Minor	1 study	A decrease has been noted, but the studies are not overly robust at this moment in time
D	Phenylpiracetam	↓	★☆☆ Minor	1 study	Anxiety as a symptom of stroke has been reduced with phenylpiracetam. No studies currently exist in otherwise healthy persons with anxiety symptoms

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Apolipoprotein A

Apolipoprotein A is the apolipoprotein for HDL cholesterol, and increasing its concentrations promotes flux of fatty acids and molecules that are carried on lipoproteins away from peripheral tissue and towards the liver.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Red Clover Extract	—	—	6 studies	A large decrease has been noted in one study in overweight postmenopausal women, although three other studies failed to replicate this decrease.
C	Fish Oil	—	—	2 studies	No significant influence on Apolipoprotein A concentrations
C	Zinc	↑	★☆☆ Minor	1 study	A slight increase in apolipoprotein A has been reported in obese persons who may have been zinc deficient, but then supplemented to alleviate said deficiency.
C	Ginkgo biloba	↓	★☆☆ Minor	1 study	In high risk individuals, the reduction has been noted to be 23.4+/-7.9%
C	Hesperidin	—	—	1 study	No significant influence on Apolipoprotein A seen with supplementation of hesperidin.
C	Trimethylglycine	↑	★☆☆ Minor	1 study	An increase in Apolipoprotein A1 has been noted with supplementation of betaine relative to placebo in otherwise healthy persons.
C	Astaxanthin			1 study	
C	Chromium	—	—	1 study	

					No known interactions with Apolipoprotein A.
D	Coconut Oil	—	—	1 study	No significant changes in apo-A levels with dietary inclusion of coconut oil
D	Hibiscus sabdariffa	—	—	1 study	No significant influence on apolipoprotein A levels in serum
D	Krill Oil	↓	★☆☆ Minor	1 study	A decrease in Apolipoprotein A has been noted with krill oil supplementation

Apolipoprotein B

Apolipoprotein B is the primary apolipoprotein (protein part of a lipoprotein) for LDL cholesterol, and increasing expression of apolipoprotein B is thought to help increase uptake of LDL from the blood into tissues.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	—	—	6 studies	Although at least one study has noted a decrease, usually there is no significant changes
C	Pueraria mirifica	↓	★☆☆ Minor	1 study	A slight decrease in Apolipoprotein B has been noted with Pueraria Mirifica
C	Garcinia cambogia	—	—	1 study	No significant influence on apolipoprotein B detected
C	Ginkgo biloba	—	—	1 study	No significant alterations are observed in apolipoprotein B concentrations
C	Zinc	↓	★☆☆ Minor	1 study	Apolipoprotein B may be abnormally elevated during zinc deficiency as it is reduced upon supplementation of zinc.
C	Hesperidin	↓	★☆☆ Minor	3 studies	There appear to be mild decreases of circulating Apolipoprotein B seen with supplementation of hesperidin in the populations with poor baseline cholesterol that actually see benefit from supplementation.
C	Astaxanthin			1 study	
C	Chromium	—	—	1 study	No known interactions with Apolipoprotein B.
D	Pueraria lobata	—	—	1 study	

D					No alterations in Apolipoprotein B have been noted
D	Coconut Oil	—	—	1 study	No significant alterations in Apolipoprotein B levels
D	Yerba mate	↓	★☆☆ Minor	1 study	Somewhat of a decrease in hyperlipidemic patients consuming Mate tea
D	Hibiscus sabdariffa	—	—	1 study	No significant influence on Apolipoprotein B levels in serum
D	Krill Oil	—	—	1 study	No significant influence on Apolipoprotein B noted
D	Red Clover Extract	↓	★☆☆ Minor	1 study	One preliminary study has noted a reduction in Apolipoprotein B concentrations with supplementation of a Formononetin rich red clover supplement.
D	Tetradecyl Thioacetic Acid			1 study	

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Appetite

The desire to eat food, independent of whether food is actually eaten or not. This pools together both physical hunger and subjective appetite, since studies measure this by self-report survey.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fenugreek	—	—	4 studies	Variable effects on appetite, but it seems the fenugreek fibers (not commonly in supplements) may reduce appetite similar to most dietary fibers while the saponins (commonly supplemented) have no significant effect or a possible increase
B	5-HTP	↓	★★★☆☆ Notable	3 studies	There does appear to be a fairly effective suppression in appetite noted with 5-HTP supplementation in the higher dosage range, which tends to reduce food intake.
B	Chromium	↓	★★★☆☆ Minor	3 studies	There may be a role in reducing appetite specifically in persons who self-report inappropriate eating patterns and carbohydrate cravings, with no known effect in persons who do not report such.
C	Caffeine	—	—	1 study	In elderly men, there does not appear to be a significant suppressive effect of caffeine on appetite.
C	Conjugated Linoleic Acid	—	—	2 studies	Mixed evidence, and even the promising evidence noted that the degree of appetite suppression was insufficient to suppress food intake.
C	Psyllium	↓	★★★☆☆	3 studies	Studies that report appetite

			Minor		Studies that report appetite note that there is a significant reduction after a meal containing psyllium (relative to no fiber ingestion) although it does not appear to be too remarkable in potency as overall food intake does not appear influenced.
C	Stevia	—	—	1 study	No significant influence on appetite have been detected with stevia (in isolation)
C	Caralluma fimbriata	↓	★☆☆ Minor	1 study	Might be more effective as the one study noted a time-dependent suppression of appetite (but was terminated at 2 months); requires more research and perhaps some comparators.
C	Salvia hispanica	↓	★☆☆ Minor	1 study	The decrease in appetite in one study was notable, but longer term studies do not note weight loss when diet is uncontrolled (which undermines the idea that chia is a potent appetite suppressant)
C	Garcinia cambogia	—	—	1 study	No significant influence of acute HCA supplementation on appetite when taken before a meal
C	Blueberry	—	—	1 study	No significant influence on appetite or satiety
C	Modafinil	↓	★☆☆ Minor	1 study	Modafinil appears to be able to reduce appetite, and 'loss of appetite' is a common side-effect of modafinil supplementation.
C	Nigella sativa	↓	★☆☆ Minor	1 study	The side-effect of 'high appetite' was effectively abolished in men with central obesity, which may underlie the observed weight loss; food intake was not reported in this

					study.
C	Hoodia gordonii	—	—	1 study	No significant reduction in appetite was seen with hoodia relative to placebo
C	Pelargonium sidoides	↑	★☆☆ Minor	2 studies	There appears to be an increase in appetite during sickness in those given this supplement, and surprisingly this may not be limited to acute bronchitis.
C	Synephrine			1 study	
C	Saffron	↓	★☆☆ Minor	1 study	High dose (176.5mg) saffron extract appears to be able to reduce snacking and increase self-reported satiety in otherwise healthy overweight women. It should be noted that with chronic supplementation of high doses (60mg) that have some minor toxic effects, that supplementation is associated with both increases and decreases in appetite.
D	Ephedrine	↓	★☆☆ Minor	1 study	A decrease in appetite following ephedrine intake is noted and thought to be secondary to its psychostimulatory effects
D	Ginger	↓	★☆☆ Minor	1 study	A decrease in appetite has been noted with ginger intake
D	Milk Protein	—	—	1 study	Despite the reduction in food intake, no significant influence on perceived appetite
D	Ascophyllum nodosum	—	—	1 study	The noted reduction in food intake was not associated with decreased appetite.
D	Whey Protein	↓	★☆☆ Minor	1 study	Appears to reduce appetite (common to all protein

					sources), but its superiority over other protein sources is not yet demonstrated.
D	CDP-choline	↓	★☆☆ Minor	1 study	There appear to be minor appetite suppressing effects at higher doses of oral CDP-choline ingestion (2,000mg daily), although on a 1-10 point Likert scale the reduction measured at 27% (6.8 to 5.92; 1 being the lowest possible ranking)

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Arterial Stiffness

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin E	↓	★☆☆ Minor	4 studies	Mixed evidence, but vitamin E has been implicated in improving arterial stiffness (thought to underlie decreased cardiovascular mortality)
C	Garlic	↓	★☆☆ Minor	2 studies	There appears to be a reduction in arterial stiffness seen with daily supplementation of garlic when measured over the course of a few years, relative to no garlic ingestion.
C	Red Clover Extract	↓	★☆☆ Minor	2 studies	Short term supplementation of red clover isoflavones appears to reduce arterial stiffness in a manner independent of changes in blood pressure or flow.

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Asthma

Asthma is an inflammatory breathing condition which can be aggravated by particular stimuli, and some supplements are currently being investigated as to whether the reactivity of a person to these stimuli can be reduced.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Magnesium	↓	★☆☆ Minor	4 studies	There appears to be a reduction in asthmatic symptoms associated with magnesium supplementation to a low degree, with the one study using corticosteroids alongside magnesium finding no effect. There may be a role for magnesium in aiding untreated asthma, but already medicated situations are not certain
C	Coleus forskohlii	↓	★★★☆☆ Notable	2 studies	Although more evidence is required, it appears to be more effective at suppressing asthmatic symptoms than other nutraceuticals. Mechanisms may be related to beta-adrenergic compounds (due to increasing cAMP and inducing bronchiol dilation)
C	Pycnogenol	↓	★☆☆ Minor	2 studies	A slight reduction in asthmatic symptoms has been noted with Pycnogenol supplementation
C	Boswellia serrata	↓	★★★☆☆ Notable	1 study	Preliminary evidence, but boswellia appeared to benefit much more people than did placebo in symptoms of asthma.
C	Vitamin D	↓	★☆☆ Minor	1 study	Appears to be somewhat effective at reducing the occurrence of asthma attacks in youth

C	Pelargonium sidoides	↓	★☆☆ Minor	1 study	In children with upper respiratory tract infections <i>and</i> asthma, the amount of asthmatic attacks during sickness appears to be slightly but significantly reduced relative to placebo.
C	Vitamin E	—	—	1 study	Supplementation of vitamin E in medicated asthmatics failed to exert any appreciable benefits to symptoms.
D	Conjugated Linoleic Acid	—	—	1 study	No significant interaction between CLA supplementation and asthmatic symptoms
D	Nigella sativa	↓	★☆☆ Minor	2 studies	Asthmatic symptoms appear to be reduced with supplementation of <i>nigella sativa</i> seeds, in part due to benefits to lung function and in part due to its anti-allergic properties. Potency has not been adequately assessed
D	Moringa oleifera	↓	★☆☆ Minor	1 study	Non-allergic asthmatic symptoms were reduced in a pilot study using the seeds of <i>moringa oleifera</i>

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Attention

The ability to keep focus on chosen targets, the clinical lack of attention is ADD (or ADHD if hyperactivity exists); Attention and/or Focus may be affected by supplements listed on this page.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Bacopa monnieri	—	—	3 studies	There is unlikely to be an inherent effect of bacopa on attention, although at least one study noted improvements in attention in persons with attention deficit (ADD).
B	Ginkgo biloba	—	—	5 studies	Attentional focus and similar parameters (task switching) do not appear to be significantly influenced by ginkgo supplementation.
C	L-Carnitine	↑	★☆☆ Minor	2 studies	An increase in attention has been noted to be secondary to reductions in the symptoms of chronic fatigue
C	S-Adenosyl Methionine	—	—	1 study	No significant alterations in attention in persons given SAME in conjunction with their SSRI antidepressant medication
C	Rhodiola Rosea	—	—	1 study	No significant influences on attention
C	Melissa officinalis	—	—	1 study	Despite the decrease in alertness seen with lemon balm, there does not appear to be any alterations in intentional attention
C	Melatonin	—	—	1 study	Despite the reduction in alertness, no significant influence on sustained

					attention tests
C	Pycnogenol	↑	★☆☆ Minor	1 study	An improvement in attention has been noted, possibly secondary to improvements in general cognition, in students during prolonged academic testing
C	Phosphatidylserine	↑	★☆☆ Minor	1 study	The improvement in attention is associated with reducing the symptoms of attention deficit, an increase in attention outright has not yet been demonstrated
C	Fish Oil	—	—	1 study	Fish oil supplementation in otherwise healthy adults has failed to significantly influence attention processing
C	Theanine			1 study	
C	CDP-choline	↑	★☆☆ Minor	1 study	There appear to be attention promoting effects of CDP-Choline, with the one study in adult women noting that 250-500mg was effective but 250mg was more effective.
C	Modafinil	↑	★☆☆ Minor	2 studies	There appears to be somewhat of an increase in subjective attention with modafinil secondary to its arousal promoting effects
C	Nigella sativa	↑	★☆☆ Minor	1 study	Attention processing on trail making tests appears to be increased.
C	Centella asiatica	↑	★☆☆ Minor	1 study	An increase in attention has been noted which may be secondary to the treatment of anxiety (or the reductions in stress and depression that also occurred due to treating anxiety).
C	Cocoa Extract			2 studies	

C	Creatine	—	—	1 study	Attention during sleep deprivation is not affected with creatine supplementation
C	Red Clover Extract	—	—	1 study	No significant influence on attention processing in older women in a postmenopausal state with supplementation of red clover isoflavones.
D	Nicotine	—	—	1 study	No significant influence on attention in otherwise healthy persons
D	Pueraria lobata	↑	★☆☆ Minor	1 study	Small boost in attention in menopausal women (independent of reductions in symptoms of menopause); needs to be reinvestigated
D	Peppermint	↑	★☆☆ Minor	2 studies	Although there is no influence acutely in cognitive testing, there appears to be improvements in sustained attention processing with prolonged testing (10-40 minutes) with the aroma of peppermint. Suggesting an anti-fatigue effect.

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B cell count

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	—	—	3 studies	The overall quantity of B lymphocytes does not appear to be altered with fish oil supplementation
C	Hesperidin	—	—	1 study	Overall B-cell count does not appear to be influenced with supplementation of hesperidin.
C	Vitamin E	—	—	1 study	Vitamin E does not appear to influence B cell count relative to placebo.
C	Colostrum	—	—	1 study	The overall count of B cells in response to supplementation does not differ between colostrum and whey protein, both seeming to be without any effect.

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Bilirubin

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	S-Adenosyl Methionine	—	—	1 study	No significant alterations in serum bilirubin seen with supplementation
C	Picrorhiza kurroa	↓	★☆☆ Minor	1 study	Supplemental <i>picrorhiza kurroa</i> can reduce bilirubin in a model of acute viral hepatitis, although no comparisons to reference drugs have yet been made.
C	Nigella sativa	—	—	2 studies	Despite treating the viral load of hepatitis C, no significant changes in serum bilirubin exist.
C	Hoodia gordonii	↑	★☆☆ Minor	1 study	The increase in bilirubin seen with hoodia is thought to be a biomarker of possible hepatotoxicity, although it was not met with hemolysis (usually accompanies)
C	Creatine			3 studies	
C	Astaxanthin			2 studies	
C	Chromium	—	—	1 study	No significant interactions with bilirubin concentrations in serum.
C	Vitamin E	—	—	2 studies	Serum bilirubin does not appear to be influenced with supplementation of vitamin E relative to placebo.
D	Tinospora cordifolia	—	—	1 study	The reduction in bilirubin seen with this herb failed to reach statistical significance when used in a clinical setting.

Bleeding Time

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin E	—	—	4 studies	When supplemented by itself, vitamin E does not appear to significantly influence bleeding time. This differs from a combination of vitamin E and coumarin based anticoagulants (such as warfarin) where an adverse interaction may occur.

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Blood Acidity

Blood Acidity is a way of referring to the pH of the blood, and while the blood tends to be resilient to large changes some supplements may slightly influence pH. Overly large deviations in pH are associated with metabolic abnormalities.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Sodium Bicarbonate	↓	★★★☆☆ Notable	46 studies	Although the magnitude of decrease is somewhat minor, this is due to blood pH being highly regulated in the body. pH appears to be reliably reduced following supplementation of 300mg/kg sodium bicarbonate
C	Colostrum	—	—	2 studies	While one study noted an increase in buffering capacity of the blood (reduction in acidity), this observation failed to be replicated in another study and both failed to find an ergogenic effect thought to occur after such an increase in buffer capacity.

Blood Flow

Blood flow is a measure of blood circulation, and is independent of blood pressure. It can be increased either by reducing artherosclerotic plaque, or producing nitric oxide.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Green Tea Catechins	↑	★☆☆ Minor	1 study	Appears to somewhat increase blood flow
B	Coenzyme Q10	↑	★☆☆ Minor	3 studies	Appears to increase blood flow in metabolic conditions characterized by both insufficient blood flow and an excess of oxidative stress.
B	Vitamin C	↑	★☆☆ Minor	4 studies	An increase in blood flow is seen in instances of impaired blood flow (smoking, obesity, etc.) which may be due to preservation of nitric oxide function (via reducing oxidation thereof); this is a phenomena general to antioxidants and not unique to Vitamin C
B	Pycnogenol	↑	★★★☆☆ Notable	3 studies	An improvement in nitric oxide dependent blood flow appears to occur following procyanidin supplementation which has been noted in both unhealthy persons as well as healthy controls; there does not appear to be a per se hypotensive effect either.
B	Fish Oil	—	—	5 studies	Although there is some counter evidence to suggest an improvement of small magnitude, most evidence suggest no significant changes in blood flow
B	Arginine	↑	★☆☆ Minor	6 studies	May increase blood flow secondary to activating nitric

					oxide, but due to the unreliability of increasing nitric oxide there is also unreliability in how arginine increases blood flow
B	Ginkgo biloba	↓ ↑	★☆☆ Minor	9 studies	Ginkgo biloba has shown both vasodilatory effects (via nitric oxide metabolism) and some possible constrictive effects, depending on the context of supplementation.
B	Centella asiatica	↑	★☆☆ Minor	4 studies	Blood flow appears to be increased alongside improvements in microcirculation seen in persons with impaired venous insufficiency being treated with <i>centella asiatica</i>
B	Vitamin E	↓ ↑	★☆☆ Minor	3 studies	Similar to blood pressure, blood flow is differentially affected by vitamin E supplementation thought to be due to whether it is acting as a prooxidant or an antioxidant.
C	L-Carnitine	↑	★☆☆ Minor	1 study	Increases in blood flow appear to occur following carnitine supplementation, which may be related to the increases in nitrate
C	Caffeine	↑	★☆☆ Minor	1 study	An increase in blood flow (Flow mediated vasodilation) has been noted with caffeine.
C	Curcumin	↑	★☆☆ Minor	2 studies	An increase in blood flow has been noted with curcumin supplementation
C	Dehydroepiandrosterone	↑	★☆☆ Minor	1 study	Possible increases in blood flow associated with DHEA supplementation
C	Ganoderma lucidum	—	—	1 study	No significant influence on blood flow noted with reishi ingestion

C	Panax ginseng	↑	★☆☆ Minor	2 studies	An increase in blood flow has been noted with panax ginseng supplementation
C	Conjugated Linoleic Acid	—	—	1 study	Insufficient evidence to support changes in blood flow.
C	Policosanol	—	—	1 study	No significant influence detected on blood flow
C	Whey Protein	—	—	1 study	Insufficient evidence to support a role of whey protein in improving blood flow
C	Alpha-Lipoic Acid	↑	★☆☆ Minor	2 studies	May increase blood flow, although not to a remarkable degree. Possibly secondary to antioxidative effects
C	Grape Seed Extract	↑	★★★ Notable	2 studies	An increase in blood flow appears to be reliable following ingestion of high dose procyanidins; this is likely the same increase seen with Pycnogenol due to the same molecules being bioactive
C	Grapefruit	—	—	1 study	No significant influence on blood flow noted
C	Nitrate	—	—	1 study	No significant influence on blood flow in studies that use flow-mediated vasodilation
C	Psyllium	↑	★☆☆ Minor	1 study	Study noted an improved augmentation index by 22% alongside a reduction in blood pressure, mechanisms unknown and no reference drug for comparison.
C	Melatonin	↑	★☆☆ Minor	1 study	Has been noted to increase blood flow at rest
C	Resveratrol	↑	★☆☆	1 study	An improvement in blood flow

			Minor		An improvement in blood flow (secondary to Nitric Oxide interactions) has been noted with low dose resveratrol, possibly relevant to high wine and grape product consumption
C	Taurine	↑	★★★☆☆ Notable	1 study	The improvement in blood flow seen in type 1 diabetics was sufficient to normalize to a non-diabetic control group
C	Citrulline	↑	★★☆☆☆ Minor	1 study	An increase in blood flow is noted with citrulline supplementation in persons with impaired blood flow
C	Cocoa Extract			1 study	
C	Zinc	—	—	1 study	Blood flow does not appear to be modified with supplementation of zinc.
C	Garlic	—	—	2 studies	Minimal studies have directly measured blood flow associated with garlic, and the best evidence currently suggests that basal flow mediated vasodilation is unaffected; there is likely an effect, although most studies indirectly measure blood pressure.
C	Hesperidin	↑	★★★☆☆ Notable	2 studies	An increase in blood flow has been noted in persons with metabolic impairments, and was fairly notable in the lone study due to reaching 24.5% over placebo.
C	Red Clover Extract	—	—	2 studies	The reduction in arterial stiffness (increase in arterial compliance) sometimes seen with supplementation of red clover extract does not necessarily coincide with improved blood flow.
C	Trimethylglycine			1 study	

C	Astaxanthin			1 study	
C	Chromium	—	—	1 study	In persons at risk for type II diabetics, chromium supplementation failed to improve blood flow relative to placebo.
D	Artichoke Extract	↑	★☆☆ Minor	1 study	The increase in blood flow was relatively minor in magnitude, possibly related to antioxidant effects.
D	Black Cohosh	—	—	1 study	No significant influences on blood flow and vasodilation
D	Creatine	↑	★☆☆ Minor	1 study	Lack of comparator prevents assessment of potency.

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Blood Glucose

How much glucose, or blood sugar, is floating around in your blood. Fasting blood glucose is measured during a fasted state and Postprandial blood glucose after a meal. Both used as indicators of diabetes risk.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Panax ginseng	↓	★☆☆ Minor	10 studies	A decrease in fasting blood glucose has been noted over time with standard supplemental doses of panax ginseng in diabetics, with this dose being ineffective in altering the blood glucose of non-diabetics; high (20g) doses may acutely reduce blood glucose in healthy persons
A	Fish Oil	—	—	21 studies	No significant alterations in fasting glucose are seen over time with fish oil supplementation
A	Chromium	↓	★☆☆ Minor	28 studies	In looking at the entirety of the data on type II diabetic persons, there does appear to be a mild reduction in fasting blood glucose despite no apparent changes in insulin sensitivity or HbA1c. No significant or reliable effect in non-diabetic persons.
B	L-Carnitine	↓	★☆☆ Minor	3 studies	A decrease in blood glucose has been noted with carnitine supplementation
B	Dehydroepiandrosterone	—	—	3 studies	Most evidence suggests no alterations to fasting blood glucose levels
B	Conjugated Linoleic Acid	—	—	9 studies	Insufficient evidence to support reliable increases in blood glucose

B	Berberine	↓	★★★ Strong	2 studies	The usage of berberine in reducing blood glucose, according to the most recent meta-analysis, is comparable to the oral hypoglycemic drugs Metformin or Glibenclamide; this suggests berberine is one of the more effective supplements for blood glucose reductions.
B	Psyllium	↓	★☆☆ Minor	4 studies	Reductions in blood glucose seen with psyllium seem to occur reliably in persons with high blood glucose, but are transient benefits and not of a remarkable magnitude.
B	Caffeine	↑	★☆☆ Minor	3 studies	There may be an acute increase in blood glucose when caffeine is paired with a carbohydrate containing meal, but long term ingestion of caffeine does not appear to adversely influence glucose (only acutely)
B	Stevia	↓	★☆☆ Minor	5 studies	There may be a very small glucose reducing effect of stevia consumption, but it does not appear to apply to everybody and is unreliable. Requires more evidence.
B	Magnesium	↓	★☆☆ Minor	8 studies	There appears to be some reduction in blood glucose in diabetics and persons with elevated glucose with magnesium supplementation, which may be secondary to better insulin functioning from the pancreas. The reduction in glucose is not overly impressive and is somewhat unreliable, and increases in glucose have been noted to occur during exercise when magnesium is supplemented in healthy persons
R	Salacia reticulata	↓	★★★☆☆	3 studies	

B			★ ★ ★ Notable		The decrease in blood glucose is acute due to blocking carbohydrate absorption (no studies on long-term glucose influence) and standard supplemental doses range between 20-25% inhibition of carbohydrate absorption, with is quite reliable and significant. This has been noted in both diabetics as well as lean/healthy persons.
B	Citrulline	—	—	3 studies	There do not appear to be any significant influences of supplemental citrulline on blood glucose concentrations
B	Blueberry	—	—	5 studies	Although the leaf extract has once been associated with a reduction in blood glucose, the fruits do not appear to inhibit carbohydrate absorption nor reduce fasting glucose concentrations.
B	Zinc	↓	★ ☆ ☆ Minor	3 studies	A reduction in blood glucose has been observed alongside improvements in insulin sensitivity in obese persons who may have been zinc deficient.
B	Inositol	↓	★ ☆ ☆ Minor	9 studies	Blood glucose can be reduced in women with PCOS secondary to treating that condition.
B	Creatine	↓	★ ☆ ☆ Minor	4 studies	The spike in blood glucose following a meal may be reduced in the range of 11-22% following creatine supplementation, with no apparent influence on fasting blood glucose.
B	Trimethylglycine	—	—	4 studies	No known alterations in fasting blood glucose concentrations or glucose concentrations during exercise seen with

					betaine supplementation.
B	Astaxanthin			3 studies	
B	Vitamin E	—	—	5 studies	Vitamin E does not appear to influence blood glucose in otherwise healthy persons nor in diabetics (type I or type II) relative to placebo.
C	Fenugreek	↓	★☆☆ Minor	3 studies	Appears to result in a decrease of blood glucose following ingestion of fenugreek
C	Curcumin	—	—	2 studies	No significant influence on blood glucose
C	ECA	—	—	1 study	No significant alterations in blood glucose noted with ECA supplementation
C	Chlorogenic Acid	↓	★☆☆ Minor	1 study	Not overly remarkable reductions in blood glucose
C	Glutamine	↑	★☆☆ Minor	2 studies	An increase in blood glucose may occur from direct conversion of glutamine into glucose following oral ingestion
C	Coenzyme Q10	—	—	2 studies	Insufficient evidence to support changes in blood glucose with CoQ10 supplementation
C	Tauroursodeoxycholic Acid	—	—	1 study	No significant influence on fasting glucose levels
C	Black Cohosh	—	—	1 study	No significant influence on blood glucose levels
C	Whey Protein	—	—	5 studies	No significant influence on fasted blood glucose levels, may decrease postprandial glucose levels (relative to no protein ingestion) due to the release of insulin

C	Alpha-Lipoic Acid	↓	—	1 study	A small decrease in blood glucose is noted with oral supplementation of ALA, related to the glucose disposal properties
C	Spirulina	↓	★☆☆ Minor	3 studies	Reductions in blood glucose seen are not overly remarkable or noteworthy
C	Nicotine	—	—	1 study	No significant influence on fasting glucose levels
C	Gynostemma pentaphyllum	↓	★★★☆☆ Notable	2 studies	Decrease in blood glucose in diabetics given gynostemma tea or root appears to be greater than other supplements; currently no studies in otherwise healthy persons.
C	Green Coffee Extract	—	—	1 study	No significant influence noted on fasting glucose levels (may reduce postprandial slightly)
C	7-Keto DHEA	—	—	1 study	Insufficient evidence to support changes in blood glucose
C	Artichoke Extract	—	—	2 studies	There is still a possibility that artichoke extract is able to aid the blood glucose of diabetics, but currently the best evidence does not support this conclusion
C	Bladderwrack	↓	★☆☆ Minor	1 study	Appears somewhat potent at acutely reducing blood glucose following a meal (possibly by inhibiting absorption) but no long term studies.
C	Ashwagandha	↓	★☆☆ Minor	4 studies	A decrease in blood glucose has been noted with ashwagandha, although the magnitude is fairly small (4.7%)

C	Olive leaf extract	↓	★☆☆ Minor	2 studies	There appears to be significant interactions with olive leaf and diabetes, and research is too preliminary to come to conclusions. Olive leaf may reduce blood glucose in diabetics only
C	Eleutherococcus senticosus	↓	★☆☆ Minor	1 study	A decrease in glucose consumption during exercise (without affecting metabolic rate and due to an increase in fat oxidation) has once caused an acute lowering of glucose. The magnitude is quite minor, and there is no evidence to assess the effects of eleuthero on fasting blood glucose or in diabetes management
C	Resveratrol	↓	★☆☆ Minor	1 study	A decrease in blood glucose has been noted, practical significance unknown
C	Ecklonia cava	↓	★☆☆ Minor	1 study	May reduce blood glucose levels, not overly potent in doing so
C	Salvia hispanica	↓	★☆☆ Minor	3 studies	Has been implicated in reducing postprandial glucose while having no significant influence on fasting glucose levels.
C	Green Tea Catechins	↓	★☆☆ Minor	1 study	A decrease in fasting blood glucose is noted with green tea catechin ingestion
C	Hibiscus sabdariffa	—	—	2 studies	No significant alterations in blood glucose noted
C	Japanese Knotweed	—	—	1 study	Blood glucose appears to be unaffected following ingestion of Japanese knotweed in otherwise healthy lean persons
C	Irvingia gabonensis	↓	★☆☆ Minor	1 study	May reduce fasting blood

					glucose following prolonged supplementation; confounded with both weight loss (seen in trials) and industry influence
C	Melatonin	—	—	1 study	No significant influence on blood glucose levels
C	Royal Jelly	↓	★☆☆ Minor	2 studies	May slightly reduce blood glucose in otherwise healthy older persons, but not to a remarkable degree
C	Capsaicin	↓	★☆☆ Minor	1 study	A possible reduction in blood glucose may occur secondary to pancreatic stimulation with high doses of capsaicin
C	Vitamin D	—	—	1 study	No significant influence on fasting blood glucose levels
C	Krill Oil	—	—	1 study	No significant influence on blood glucose levels
C	Branched Chain Amino Acids	—	—	2 studies	There does not appear to be a likely alteration in blood glucose concentrations <i>per se</i> with BCAA supplementation, but the increased fat oxidation may attenuate the decline in glucose seen during prolonged exercise (which would appear to be a relative increase at later time points)
C	Lactobacillus casei			1 study	
C	Sodium Bicarbonate	—	—	2 studies	No significant effect on blood glucose concentrations at rest or during exercise is seen with sodium bicarbonate supplementation
C	Arginine	—	—	2 studies	No significant influence on fasting blood glucose concentrations even in persons with impaired glucose tolerance

C	Cocoa Extract			1 study	
C	Sea Buckthorn	↑	★☆☆ Minor	1 study	An increase in glucose has been noted with sea buckthorn, but it was from one study which had the control group (coconut oil) also raise blood glucose; this may just be due to added calories.
C	Vitamin K	—	—	1 study	Despite an improvement in insulin sensitivity, the lone study failed to note any significant changes in blood glucose concentrations in a fasted state
C	Eucommia ulmoides			1 study	
C	Ginkgo biloba	—	—	1 study	In diabetics, ginkgo does not appear to significantly reduce blood glucose
C	Quercetin	—	—	1 study	No significant alterations in blood glucose are detected with quercetin supplementation.
C	Nigella sativa	—	—	5 studies	Although the best evidence to date shows no change in blood glucose, these studies were not structured to assess the influence on diabetics; in diabetics, there appears to be a significant reduction in glucose.
C	Rooibos	↓ ↑	★☆☆ Minor	2 studies	A decrease may occur in persons at risk of cardiovascular disease with daily ingestion of Rooibos tea, although at least one study noted an inexplicable acute increase in otherwise healthy persons (faded within an hour of ingestion).
C	Garlic	—	—	1 study	Supplementation of garlic does not appear to significantly reduce fasting blood glucose in persons with metabolic

					syndrome.
C	Anethum graveolens			1 study	
C	Hesperidin	—	—	2 studies	There are no known significant alterations in blood glucose seen with supplementation of hesperidin
C	Citrullus colocynthis	↓	★☆☆ Minor	1 study	May decrease blood glucose in diabetics at low doses, but the evidence at this moment in time is limited (due to differences between groups at the start of the study)
C	Red Clover Extract	—	—	2 studies	No significant influence on fasting blood glucose concentrations are known with supplementation of red clover extract.
C	Yacon	—	—	1 study	No significant influence on fasting blood glucose in nondiabetic obese women who consume Yacon relative to placebo, despite weight loss.
C	Rose Hip	—	—	1 study	Both fasting and postprandial glucose in persons given prolonged rose hip supplementation is not affected relative to placebo.
D	Holy Basil	↓	★☆☆ Minor	1 study	May reduce blood glucose, with the potency demonstrated (fairly good) limited by the quality of the evidence currently
D	Ginger	—	—	1 study	No significant alterations in blood glucose seen with ginger ingestion
D	Coconut Oil	—	—	1 study	Insufficient evidence to support alterations in blood glucose.
D	Aronia melanocarpa	↓	★☆☆ Minor	1 study	Requires more studies before conclusions can be made,

					appears to simply be exerting anti-oxidant effects.
D	Banaba Leaf	↓	★★★☆☆ Notable	1 study	The reduction in blood glucose appeared to range from 20-30%, which is more than usually seen with dietary supplements.
D	Yerba mate	↓	★☆☆☆☆ Minor	1 study	A slight decrease in blood glucose has been noted with Mate consumption in type II diabetics; no evidence in otherwise healthy persons
D	Sulbutiamine	—	—	1 study	No significant influence on blood glucose in diabetics detected
D	HMB	↓	★☆☆☆☆ Minor	1 study	A lone study that is underpowered suggest a decrease in blood glucose (measured by chance during a blood panel); not enough robust evidence supports a reduction in blood glucose but it cannot be ruled out
D	Vanadium	↓	★☆☆☆☆ Minor	1 study	A decrease in blood glucose has been noted in type II diabetics which is thought to be secondary to reducing hepatic synthesis of glucose
D	Safflower Oil	—	—	1 study	No significant influence on blood glucose in diabetics
D	Emblica officinalis	↓	★★★☆☆ Notable	1 study	Preliminary evidence suggested that 3g of the fruits (a fairly reasonable dosage) was as effective as 5mg glibenclamide twice daily
D	Moringa oleifera	↓	★☆☆☆☆ Minor	2 studies	There appears to be a decrease in postprandial blood glucose following a meal in type II diabetics (21%), and this hypoglycemia may apply to non-diabetics based

					on rodent research, and appears to increase with time.
D	Asteracantha longifolia	↓	★☆☆ Minor	1 study	Appears to reduce the spike and overall exposure to glucose following an oral glucose tolerance test in both healthy and diabetic adults
D	Rubus coreanus	—	—	1 study	No significant alterations in fasting blood glucose are noted with daily berry consumption in otherwise healthy persons.
D	Pyrroloquinoline quinone	—	—	1 study	Short term ingestion of PQQ supplementation in otherwise healthy adults has failed to significantly influence serum glucose concentrations.
D	Tetradecyl Thioacetic Acid			1 study	
D	Ruscus aculeatus	↓	★☆☆ Minor	1 study	A reduction reaching 10.2% blood glucose has been noted with continual supplementation of <i>ruscus aculeatus</i> in type II diabetic persons in this non-placebo controlled study; requires replication.
D	Colostrum	↓	★☆☆ Minor	1 study	Preliminary trial in type II diabetics noted a reduction in fasting glucose concentrations to 10-14% with four weeks of colostrum supplementation; no control was used for reference.

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Blood Pressure

A relation of how much blood is in your veins and how much diameter the vein is given to accomodate the blood, and measured in systolic over diastolic (average of 120/80). Many supplements interact, either acutely or chronically, with Blood Pressure.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Fish Oil	↓	★☆☆ Minor	8 studies	May decrease blood pressure in persons with high blood pressure, but does not appear to have efficacy in persons with normal blood pressure
B	Creatine	—	—	4 studies	Does not appear to significantly influence blood pressure.
B	Alpha-Lipoic Acid	—	—	6 studies	The majority of evidence using intravenous or oral supplements fail to find an influence, and the one study to suggest a reduction was also confounded with weight loss (known to reduce blood pressure). It can be assumed that ALA has no significant influence on blood pressure even in studies where blood flow is altered
B	Ephedrine	↑	★☆☆ Minor	5 studies	There may be an acute increase in blood pressure seen with ephedrine intake, although this does not appear to be overly reliable; long-term usage of ephedrine does not seem to alter blood pressure, and may reduce it secondary to weight loss
B	Caffeine	↑	★☆☆ Minor	6 studies	Tends to increase blood pressure more than it doesn't, which is in part due to caffeine tolerance (naive users experiencing increases in

					blood pressure at higher rates) or genetics; the increase in blood pressure tends to be transient and low in magnitude
B	Coenzyme Q10	↓	★☆☆ Minor	6 studies	There appears to be an interaction between CoQ10 and blood pressure, but it is not wholly reliable and uncertain whether this is at the level of the cardiac tissue or at the level of the endothelium (both plausible). Magnitude of reductions don't appear too remarkable.
B	Grape Seed Extract	↓	★☆☆ Minor	2 studies	The meta-analysis conducted noted a pooled reduction of 1.54mmHg systolic associated with standard doses of grape seed extract; something, but a small reduction.
B	Nicotine	—	—	4 studies	Mixed effects on blood pressure
B	Magnesium	↓	★★★☆☆ Notable	9 studies	There appears to be a significant reduction in blood pressure assuming one of two conditions is met, either the subject is low in magnesium levels in the body (deficient) or if the subject has elevated blood pressure (140/90 or above), with the latter not requiring a deficiency to precede the blood pressure reducing effects
B	Hibiscus sabdariffa	↓	★★★☆☆ Notable	6 studies	The decrease in blood pressure seen with roselle tea and supplements is notable and is greater than that seen with other supplements
B	Vitamin D	↓	★☆☆ Minor	2 studies	Both correlational and intervention studies note that higher cohorts of serum Vitamin D have less blood pressure than lower cohorts, establishing a role for Vitamin

					D in blood pressure reduction. The magnitude of reduction is small, around 5mmHg systolic, and likely not potent enough to be a reference therapy
B	Nitrate	↓	★★★☆☆ Notable	8 studies	Appears to be a fairly potent blood pressure reducing agent during periods of high blood pressure (at rest during disease states or during exercise in healthy persons) without having a reducing effect when blood pressure is normalized.
B	Psyllium	—	—	3 studies	No real significant effect of psyllium on blood pressure directly, although there may be an insignificant reduction seen with correcting other parameters of metabolic syndrome.
B	Olive leaf extract	↓	★★★☆☆ Notable	4 studies	One study assessing the potency in hypertensive persons noted it was comparable to Captopril, and olive leaf appears to be potent when it can reduce blood pressure. It does not appear to reduce blood pressure in normotensive persons, however
B	Stevia	↓	★★☆☆☆ Minor	4 studies	There appears to be a reduction in blood pressure associated with stevia only in persons with high blood pressure, this may be a transient effect that is normalized upon supplement cessation.
B	L-Tyrosine	—	—	3 studies	It is possible that Tyrosine can reduce blood pressure during stress, but the one study that noted this also noted a reduction in blood pressure in the stressed placebo; other studies have found no influence.

B	Curcumin	↓	★☆☆ Minor	3 studies	May decrease blood pressure, but more contextual evidence is required
B	Melatonin	↓	★☆☆ Minor	4 studies	An acute decrease in blood pressure occurs following melatonin ingestion, but this decrease is temporary and abolished upon standing; likely not practically relevant in an ambulatory population
B	Panax ginseng	—	—	4 studies	Although there may be a slight blood pressure reducing effect in persons with the highest blood pressure, overall there is not a significant reducing effect of panax ginseng
B	Quercetin	—	—	5 studies	No acute alterations in blood pressure following Quercetin supplementation
B	Arginine	↓	★☆☆ Minor	5 studies	Arginine has been implicated in reducing blood pressure, but the degree of reduction does not appear to be too remarkable and it is unreliable in doing so
B	Modafinil	↑	★☆☆ Minor	3 studies	There may be a slight increase in systolic blood pressure with acute usage of modafinil (when measured at its peak blood levels), although it does not appear to modify basal blood pressure values
B	Ginkgo biloba	—	—	7 studies	Despite the influence on blood flow and circulation, there does not appear to be a significant influence on blood pressure
B	Inositol	↓	★☆☆ Minor	8 studies	There may be a slight decrease in blood pressure in women with PCOS who are having it treated with inositol therapy.

B	Nigella sativa	↓	★☆☆ Minor	4 studies	The reduction in blood pressure is only seen in hypertensives and very mild (1-3mmHg), likely not practically relevant at all.
B	Garlic	↓	★★★☆☆ Notable	14 studies	Garlic supplementation appears to reduce blood pressure, and the magnitude is quite respectable in persons with hypertension (around 10 points systolic or 8-10%) whereas there is a smaller but present reduction in persons with normal blood pressure.
B	Red Clover Extract	—	—	7 studies	The one study in diabetics found a reduction in blood pressure, and due to no studies in hypertensives all other studies have failed to find an influence on blood pressure.
B	Chromium	—	—	8 studies	The majority of evidence does not support a role for chromium in reducing blood pressure any more than placebo.
B	Vitamin E	↓ ↑	★☆☆ Minor	5 studies	Blood pressure has been differentially affected by vitamin E supplementation, thought to be associated with whether it is an antioxidant or a prooxidant.
C	Green Tea Catechins	↓	★☆☆ Minor	1 study	Possible decrease in blood pressure noted with green tea catechin consumption
C	Coleus forskohlii	—	—	2 studies	No significant influence on blood pressure was noted with coleus supplementation
C	ECA	—	—	1 study	No significant alterations in long term blood pressure, although acute spikes are possible due to the ephedrine

					and caffeine components
C	L-Carnitine	↓	★☆☆ Minor	1 study	May reduce blood pressure
C	Yohimbine	↑	★☆☆ Minor	2 studies	Appears to increase blood pressure, which may aid the proerectile effects (as it is an acute increase) but is a cardiovascular risk factor
C	Conjugated Linoleic Acid	—	—	4 studies	No significant interaction between CLA and blood pressure
C	Policosanol	↓	★☆☆ Minor	1 study	Possibly a small effect in persons with high blood pressure.
C	Whey Protein	—	—	2 studies	Insufficient evidence to support the blood pressure reducing effects of whey protein
C	Spirulina	↓	★★★☆☆ Notable	3 studies	Insufficient evidence to fully evaluate the effects on blood pressure, but given how 6 weeks supplementation reduced both systolic and diastolic in <i>nonhypertensive</i> persons by about 11/6 points it is notable
C	Chlorella	↓	★☆☆ Minor	3 studies	Might reduce blood pressure in some instances but does not appear remarkably potent.
C	Green Coffee Extract	↓	★★★☆☆ Notable	1 study	Decrease in blood pressure noted with green coffee extract ingestion, due to the Chlorogenic Acid component. Degree of reduction reached 10mmHg (from just above 145mmHg to just above 135mmHg) and is quite notable.
C	1,3-Dimethylamylamine	↑	★★★☆☆ Notable	1 study	The increase in blood pressure with 1,3-DMAA was fairly notable and of concern,

					with 75mg paired with caffeine (common in preworkout supplements) increasing systolic by up to 20%.
C	7-Keto DHEA	—	—	1 study	Insufficient evidence to support changes in blood pressure following 7-keto supplementation.
C	Benfotiamine	—	—	1 study	No significant evidence to support alterations in blood pressure.
C	Chlorogenic Acid	↓	★★★☆☆ Notable	1 study	The decrease in systolic blood pressure with chlorogenic acid has reached 15 points systolic in hypertensives (150mmHg systolic initially) and appears to maintain at that level until supplement cessation.
C	Bacopa monnieri	—	—	1 study	No significant influence on blood pressure has been noted with chronic bacopa ingestion
C	Echinacea	—	—	1 study	No significant known effects on blood pressure
C	Rhodiola Rosea	—	—	1 study	No significant effects yet noted on blood pressure
C	Sesamin	↓	★★☆☆☆ Minor	1 study	A small decrease in blood pressure has been noted with sesamin supplementation
C	Yerba mate	—	—	1 study	No significant influences on blood pressure have been noted (although this may be due to it being underresearched; Mate may follow the same motifs as caffeine ingestion)
C	Resveratrol	↓	★★☆☆☆ Minor	1 study	Blood pressure has been reduced with resveratrol in persons with high blood

					pressure; influence on otherwise healthy persons unknown
C	Shilajit	—	—	1 study	No significant effect has been detected on blood pressure
C	Ecklonia cava	↓	★☆☆ Minor	2 studies	A possible reduction in blood pressure in overweight persons with supplementation of ecklonia cava
C	Salvia hispanica	—	—	2 studies	No significant influence on blood pressure noted with long term chia ingestion
C	Fucoxanthin	↓	★☆☆ Minor	1 study	In obese menopausal women, fucoxanthin may lower blood pressure; this is confounded with overall weight loss, however
C	Ganoderma lucidum	—	—	1 study	No significant influence on blood pressure noted with reishi
C	Irvingia gabonensis	↓	★☆☆ Minor	1 study	A decrease in blood pressure has been noted with weight loss associated with this supplement; no inherent blood pressure reduction has been demonstrated
C	Lavender	↓	★☆☆ Minor	1 study	A reduction in blood pressure is noted alongside reduced autonomic nervous system activation and increased relaxation; this is likely to not affect the body over the long term
C	Microlactin	↓	★☆☆ Minor	1 study	Has been noted to reduce blood pressure in persons with hyperlipidemia
C	Nattokinase	↓	★☆☆ Minor	1 study	A possible blood pressure reducing effect seen with nattokinase, notable but with

					high variability
C	Salvia sclarea	↓	★☆☆ Minor	1 study	A decrease in systolic blood pressure resulted in response to clary sage aromatherapy, to a small degree and likely not able to exert long-term benefit (probably more indicative of short-term CNS depression)
C	Royal Jelly	—	—	1 study	No significant alterations in blood pressure observed over long term supplementation with Royal Jelly
C	Rose Essential Oil	↓	★☆☆ Minor	1 study	A small reduction in blood pressure was noted, possibly secondary to reductions in CNS activity
C	Pyruvate	↓	★☆☆ Minor	1 study	May reduce blood pressure in hyperlipidemics, relation to weight loss not known
C	Pycnogenol	—	—	1 study	Despite the improvement in blood flow, no significant alterations noted in resting blood pressure
C	Taurine	—	—	2 studies	Despite the improvement in blood flow, no significant influence on blood pressure
C	Phosphatidylserine	—	—	1 study	No significant alterations in blood pressure noted with PS supplementation
C	Lactobacillus casei			1 study	
C	Sodium Bicarbonate	—	—	1 study	No significant influence on blood pressure
C	Ornithine	—	—	1 study	No significant interactions with blood pressure
C	Citrulline	↓	★☆☆ Minor	3 studies	A decrease in blood pressure is noted secondary to

					increasing plasma arginine (and thus increasing nitric oxide), but this blood pressure reduction may only occur in those with hypertension or prehypertension
C	Cocoa Extract			1 study	
C	CDP-choline	↓	★☆☆ Minor	1 study	One study in older adults noted, as a side-effect, that systolic blood pressure was slightly reduced
C	Eucommia ulmoides			1 study	
C	Blueberry	↓	★☆☆ Minor	2 studies	A decrease in blood pressure has been noted in persons at risk for cardiovascular disease (6% systolic and 4% diastolic), but this may be limited to high risk individuals only.
C	Ashwagandha	↓	★☆☆ Minor	2 studies	A small decrease in blood pressure (1.6% systolic and 5.6% diastolic) has been noted to occur alongside a reduction in pulse rate.
C	Zinc	—	—	1 study	Blood pressure does not appear to be modified with zinc supplementation.
C	Anatabine	—	—	1 study	6-12mg anatabine does not appear to significantly influence blood pressure in otherwise healthy persons.
C	Tribulus terrestris	↓	★☆☆ Minor	1 study	A decrease in blood pressure has been noted in hypertensive subjects; insufficient evidence to address efficacy in normotensive persons
C	Centella asiatica	—	—	1 study	No significant influence on blood pressure in otherwise healthy persons given an acute dosage.
C	Capsaicin			1 study	

C	Rooibos	—	—	1 study	Despite ACE inhibition, Rooibos tea does not appear to significantly reduce blood pressure
C	Anethum graveolens			1 study	
C	Hoodia gordonii	↑	★★★☆☆ Notable	1 study	The increase in blood pressure noted with <i>hoodia gordonii</i> in otherwise healthy persons reached 5.9-15.9mmHg systolic and 4.6-11.5mmHg diastolic; a worrying increase
C	Hesperidin	↓	★★☆☆☆ Minor	2 studies	There is a mild decrease in blood pressure seen with supplementation of Hesperidin; like blood flow, this is acute (within an hour with hesperitin and G-hesperidin; about 6-8 hours with hesperidin) and does not persist after supplementation ceases.
C	Citrullus colocynthis	—	—	1 study	No significant influence on blood pressure with up to 300mg of the fruit extract daily over two months
C	Trimethylglycine	—	—	1 study	No significant influence of betaine supplementation on blood pressure is currently known.
C	Synephrine			1 study	
C	Astaxanthin			2 studies	
C	Saffron	↓	★★☆☆☆ Minor	1 study	A decrease in blood pressure was noted in otherwise healthy (normotensive) men following 26 weeks of saffron supplementation at 60mg daily, although this was thought to possibly be related to chronic toxicity of the higher than normal dose.
C	Rose Hip	↓	★★☆☆☆	1 study	A mild (3.7%) decrease in

			Minor		Armlid (0.7%) decrease in systolic blood pressure has been noted in obese persons given supplementation of rose hip.
D	Kava	↓	★☆☆ Minor	1 study	One study has noted a reduction in blood pressure associated with kava, of minor magnitude
D	Black Cohosh	—	—	1 study	No significant influence on blood pressure
D	Eclipta alba	↓	★★★ Notable	1 study	Decreases of blood pressure in unhealthy persons using eclipta alba have occurred by 15% (mean arterial pressure)
D	Licorice	↑	★★★ Notable	2 studies	Has the potential to increase blood pressure secondary to increasing cortisol; this is notable as it seems hypertensives are at greater risk from an adverse reaction to high dose licorice and as such should exert caution when using this herb (related to the glycyrrhizin content, and deglycyrrhizinated supplements should not have the same risk)
D	Vanadium	—	—	1 study	No significant influence on blood pressure noted
D	Tetradecyl Thioacetic Acid	↓	★☆☆ Minor	2 studies	A slight reduction in blood pressure has been noted in dyslipidemic obese men with TTA supplementation
D	Cissus quadrangularis	—	—	1 study	In otherwise healthy athletic men, there is no significant influence of supplementation over eight weeks on blood pressure.

Bone Mineral Density

Bone mineral density (BMD) is the density of mineral in bone tissue (more mass in the same area causing an increase in density), and is thought to reflect structural integrity of bones. Improving BMD reduces the risk of osteoporosis and falls in the elderly.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Vitamin K	↑	★★★☆☆ Notable	15 studies	There appears to be a <i>relative</i> increase in bone mineral density associated with vitamin K supplementation, due to attenuating the rate of bone loss in older individuals. Although it is significant overall in meta-analyses, it is quite unreliable and similar in potency to vitamin D when it occurs (less than estrogen replacement therapy)
B	Creatine	↑	★☆☆☆☆ Minor	3 studies	Limited evidence in favor of improvements in bone mineral density with creatine supplementation
B	Dehydroepiandrosterone	—	—	9 studies	Most evidence suggests no increase in bone mineral density, but this may be due to short trials (6 months). Longer trials note a small but unreliable increase in bone mineral density, so there may be a role of DHEA in bone health
B	Red Clover Extract	—	—	6 studies	Beyond a small (less than 5%) attenuation in the rate of lumbar bone mineral density losses, standard supplementation does not appear to significantly influence bone mass or the rate of bone loss.
C	Vitamin C	↑	★★☆☆☆	2 studies	The rate of bone mineral

			Minor		the rate of bone mineral density loss over time in elder women appears to be reduced with dietary antioxidants, and as such applies to Vitamin C supplementation. The protective effect is not remarkably large
C	Conjugated Linoleic Acid	—	—	1 study	No evidence to support a link between CLA and alterations in bone mineral density
C	Whey Protein	—	—	2 studies	Currently no demonstrated benefit to bone mineral density, although protein in general appears to have a protective effect
C	Magnesium	↑	★☆☆ Minor	1 study	An increase in bone mineral density has been noted with magnesium supplementation
C	Coleus forskohlii	↑	★★★☆☆ Notable	1 study	Definitely requires more evidence, but a DXA confirmed increase in bone mass in men over 12 weeks makes this notable (rather than an increase in bone mass in osteoporotic women over 2 years)
C	Horny Goat Weed	↑	★☆☆ Minor	1 study	The rate of bone loss over 2 years has been noted to be reduced with icariin supplementation, although not to a remarkable degree
C	HMB	—	—	2 studies	Studies that assess bone mineral density via DEXA, albeit short in duration and in athletes rather than populations at risk for osteoporosis, fail to find significant alterations in bone mineral density.
C	Leucic Acid	—	—	1 study	No significant alterations in bone mineral density

C	Vitamin D			1 study	
D	Yerba mate	↑	★☆☆ Minor	1 study	An <i>association</i> has been noted with increased bone mineral density and Mate consumption; insufficient evidence to suggest a causative role as no interventions exist
D	Black Cohosh	—	—	1 study	No significant influence on bone mineral density
D	Fish Oil	—	—	1 study	No significant influence on bone mineral density noted with fish oil supplementation
D	Calcium			1 study	

Breast Cancer Risk

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin E	—	—	3 studies	No significant protective effect of 600 IU vitamin E every other day in otherwise healthy women for preventing the development of breast cancer.
C	Ginkgo biloba	↑	★☆☆ Minor	1 study	An increase in breast cancer risk has been noted to barely pass statistical significance in an analysis of cancer development in elderly persons (75 years or older) given EGb-761 daily for a median 6.1 years.
D	Vitamin D	↓	★☆☆ Minor	2 studies	There is less risk of breast cancer associated with Vitamin D supplementation
D	Melatonin	—	—	1 study	Too preliminary to conclude any relation to breast cancer, but urinary melatonin metabolites are positively correlated with breast cancer risk (not applied yet to supplementation)

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Breast Tenderness

Breast tenderness refers to the actual physical tenderness of breast tissue, usually associated with a small amount of pain. Breat tenderness tends to be a symptom of PMS or menopause, and supplements that reduce those symptoms help with breast tenderness.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitex agnus castus	↓	★★★☆☆ Notable	3 studies	The increase in breast tenderness during PMS is ameliorated with vitex supplementation; the degree of benefit correlating with general reductions in PMS symptoms. Notable as supplements catering to breast tenderness are rare.
C	Krill Oil	↓	★☆☆☆☆ Minor	1 study	Secondary to reducing symptoms of PMS, a reduction in breast tenderness has been reported
C	Serrapeptase	↓	★☆☆☆☆ Minor	1 study	A decrease in breast tenderness and soreness has been noted with serrapeptase treatment in one study.

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C-Reactive Protein

C-Reactive Protein is an inflammatory biomarker for cardiovascular disease and atherosclerosis (arterial plaque). Its reduction is thought to be protective and reduces the risk of cardiovascular incidents.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Fish Oil	—	—	16 studies	Although some decreases have been noted, the vast majority of the evidence suggests that there is no significant influence
B	Conjugated Linoleic Acid	—	—	8 studies	For the most part, CLA is seen as ineffective.
B	Curcumin	↓	★☆☆ Minor	3 studies	May decrease C-reactive protein if elevated
B	Zinc	↓	★☆☆ Minor	4 studies	Supplementation of zinc in persons who may be zinc deficient is able to reduce C-reactive protein
B	Hesperidin	↓	★☆☆ Minor	3 studies	There is a decrease in C-Reactive Protein (inflammatory biomarker) in those with higher baseline inflammation or inflammatory disease conditions, but not in healthy persons.
B	L-Carnitine			1 study	
B	Vitamin E	—	—	3 studies	Most studies assessing C-reactive protein (an inflammatory biomarker) have failed to find a significant influence of vitamin E supplementation.
C	Coenzyme Q10	—	—	2 studies	No significant influence on levels of C-reactive protein

C	Vitamin C	↓	★☆☆ Minor	1 study	A possible reduction in C-Reactive Protein exists with Vitamin C supplementation
C	Black Cohosh	—	—	1 study	No significant alterations seen in C-RP with black cohosh
C	Whey Protein	—	—	1 study	No demonstrated effects on C-Reactive Protein
C	Magnesium	↓	★☆☆ Minor	2 studies	Possible reduction in C-Reactive protein, but these changes are unreliable
C	S-Adenosyl Methionine	—	—	1 study	No significant influence on C-Reactive Protein
C	Alpha-Lipoic Acid	—	—	2 studies	Although there may be a reduction of C-Reactive protein in some populations, for the most part ALA does not seem significantly effective in reducing this inflammatory biomarker of cardiovascular disease
C	Feverfew	—	—	1 study	No significant effect on C-Reactive Protein
C	Rhodiola Rosea	↓	★☆☆ Minor	1 study	A decrease in C-reactive protein has been noted with rhodiola supplementation; practical significance of these results unknown
C	Stinging Nettle	↓	★☆☆ Minor	1 study	Minor decrease in C-reactive protein concentrations
C	Salvia hispanica	↓	★☆☆ Minor	2 studies	It is possible that a decrease in C-Reactive protein may exist but evidence is contradictory at this moment in time
C	Fucoxanthin	↓	★☆☆ Minor	1 study	A decrease in C-reactive protein is noted with

					fucoxanthin ingestion
C	Ganoderma lucidum	—	—	1 study	No significant interactions with C-reactive protein have been detected
C	Grape Seed Extract	↓	★☆☆ Minor	1 study	May reduce levels of C-reactive protein
C	Irvingia gabonensis	↓	★☆☆ Minor	1 study	A decrease in C-reactive protein has been noted, confounded with weight loss and industry influence
C	Melatonin	—	—	1 study	No significant influence on C-reactive protein
C	Resveratrol	—	—	1 study	No significant effect on C-reactive protein
C	Pycnogenol	—	—	1 study	No significant alterations in C-Reactive protein noted
C	Glutamine	—	—	1 study	No significant alterations in C-Reactive Protein levels
C	Panax ginseng	—	—	2 studies	No significant influence on C-reactive protein levels
C	Krill Oil	↓	★★★☆☆ Notable	2 studies	A decrease in C-Reactive protein has only been noted in rheumatoid arthritis (none in obese but healthy persons) but reached 30% within 30 days of 500mg krill oil, a very significant reduction
C	HMB	—	—	1 study	No significant influence on C-reactive protein
C	Lactobacillus casei			1 study	
C	Citrulline	—	—	1 study	No significant influence on C-reactive protein concentrations

C	Vitamin K	—	—	2 studies	No significant influence on C-reactive protein (an inflammatory biomarker) seen with vitamin K supplementation
C	Sea Buckthorn	—	—	1 study	2,000mg of the sea buckthorn supplement has failed to significantly influence C-reactive protein concentrations in serum
C	Cocoa Extract			1 study	
C	Blueberry	—	—	2 studies	C-reactive protein does not appear to be influenced with blueberry supplementation.
C	Ashwagandha	↓	★★★☆☆ Notable	1 study	The reduction seen in C-reactive protein over the course of 60 days has been noted to reach 31.6% with standard oral doses of ashwagandha supplementation.
C	Nigella sativa	—	—	1 study	The alterations in C-reactive protein failed to reach statistical significance, but are otherwise not very well explored.
C	Rooibos	—	—	1 study	No significant alteration in C-reactive protein
C	Garlic	—	—	2 studies	No significant influence on C-reactive protein is noted with supplementation of garlic.
C	Ginkgo biloba	↓	★★☆☆☆ Minor	1 study	A decrease in C-reactive protein is noted with supplementation of Ginkgo biloba
C	Creatine			1 study	
C	Chromium	—	—	1 study	No significant influence on C-reactive protein, a biomarker for inflammation.

C	Rose Hip	—	—	5 studies	Preliminary studies showed marked reductions in C-reactive protein concentrations in healthy persons, although more recently conducted blinded studies have failed to replicate such a large decrease.
C	Colostrum	—	—	2 studies	C-reactive protein does not appear to be significantly influenced with supplementation of colostrum relative to control or baseline values.
D	Boron	—	—	1 study	No significant effect on this inflammatory biomarker
D	Ecklonia cava	↓	★★★☆☆ Notable	1 study	Appears to reduce C-reactive protein, with the degree of reduction being noted almost a halving
D	Royal Jelly	—	—	1 study	No significant alterations in serum C-rp levels
D	Tetradecyl Thioacetic Acid	—	—	2 studies	No significant influence on C-Reactive Protein levels
D	Safflower Oil	↓	★★☆☆☆ Minor	1 study	A decrease in C-RP has been noted with safflower oil consumption
D	Inositol	—	—	1 study	No significant influence on C-reactive protein concentrations even in persons with metabolic syndrome.
D	Iodine	↓	★★☆☆☆ Minor	1 study	There may be a small decrease in C-reactive protein associated with moderate iodine supplementation in otherwise healthy persons, indicative of an antiinflammatory effect.
D	Rubus coreanus	—	—	1 study	

D					In otherwise healthy men, there are no changes in C-reactive protein levels seen with berry consumption.
D	Perilla Oil			1 study	
D	Pyrroloquinoline quinone	↓	★★★☆☆ Notable	1 study	The decrease in C-reactive protein seen in one study in otherwise healthy humans reached 45% after three weeks of supplementation.

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Calmness

Calmness is a similar parameter to relaxation, although they have different rating scales at time. Both calmness and relaxation are associated with slightly sedative and anxiolytic compounds.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Melissa officinalis	↑	★★★☆☆ Notable	2 studies	An increase in self-reported ratings of 'calmness' appears to exist following ingestion of lemon balm single doses
C	Lavender	—	—	1 study	Despite the increase in 'relaxation', there does not appear to be an increase in calmness
C	Rose Essential Oil	↑	★★☆☆☆ Minor	1 study	Self-reported ratings of calmness increase following application of rose oil topically
C	Panax ginseng	↑	★★☆☆☆ Minor	1 study	Has been noted to improve self-reported calmness
C	Modafinil	—	—	1 study	There do not appear to be any significant influences on self-reported ratings of calmness with supplementation of modafinil.
C	Ginkgo biloba	↑	★★☆☆☆ Minor	1 study	One study to assess the effects of ginkgo biloba in cognition, which failed to improve alertness, noted an increase in self-reported calmness with 120mg (EGb-761)
C	Centella asiatica	↑	★★☆☆☆ Minor	2 studies	A reduction in fear and anxiety responses to an acute startle response (indicative of less responsiveness to alerting stimuli and more calmness)

					has been noted with this plant extract
C	Cocoa Extract			1 study	
D	Peppermint	—	—	1 study	Subjective ratings of calmness during cognitive testing are not significantly influenced with the aroma of peppermint

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Cancer Mortality

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Melatonin	↓	★☆☆ Minor	1 study	There appears to be a significant protective effect on life in cancer patients with solid tumors, although the protective effect does not reach 'half risk' (RR of 0.50) and fluctuates in the range of quarter risk.
C	Vitamin K	↓	★★★☆☆ Notable	2 studies	Although the studies have used superloading of vitamin K (40mg or more) and only in hepatic cancers, the reduction in mortality risk and prolongation of survival times appears to be quite notable
C	Vitamin E	—	—	2 studies	Despite a small reduction in prostate cancer mortality seen in smokers with low dose (50mg) vitamin E, this does not appear to hold true as a general statement for all cancer types in most persons.
D	Garlic	—	—	1 study	The overall mortality rate from stomach cancer is not influence with garlic supplementation during 15 years of followup

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Canker Sores

Canker sore is the common phrase used to refer to small ulcers in the mouth (Aphthous stomatitis), and many anti-ulcer compounds have been tested for their usage against canker sores in reducing inflammation and pain.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Licorice	↓	★☆☆ Minor	1 study	Topical application of licorice is able to reduce canker sore size and pain associated with canker sores
C	Lavender	↓	★☆☆ Minor	1 study	A reduction in canker sore size and the pain associated with them are observed with topical lavender application
C	Aloe vera	↓	★☆☆ Minor	2 studies	Appears to be more effective than control, but less effective than the reference drug of 0.1% triamcinolone acetonide
C	Berberine	↓	★☆☆ Minor	1 study	Was able to reduce canker sores when topically applied, but was not compared to a reference compound.

Cardiovascular Disease Risk

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Vitamin D	↓	★☆☆ Minor	3 studies	There appears to be less risk of cardiovascular disease and related cardiovascular complications with supplementation of 1,000 IU of Vitamin D or higher serum levels of Vitamin D. The degree of prevention is borderline significant overall
C	Vitamin E	—	—	1 study	In general, the development of various cardiovascular diseases is not prevented with supplementation of vitamin E.

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CD4 Lymphocytes

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Colostrum	↑	★☆☆ Minor	4 studies	While there does not appear to be any influence in healthy controls or with low dose colostrum, higher doses of colostrum in persons with HIV (reduced CD4+ lymphocyte counts) may mildly increase CD4+ counts when compared to whey protein as control.
C	Andrographis paniculata	—	—	4 studies	Unclear effects on CD4+ lymphocytes at this moment in time
C	Tinospora cordifolia	—	—	1 study	Limited studies looking into CD4+ Lymphocytes have failed to find a stimulatory effect.
C	Ganoderma lucidum	↑	★☆☆ Minor	1 study	The decrease in the CD4:CD8 ratio seen with altitude training is attenuated with 2,500-5,000mg of the water soluble polysaccharides
C	Garlic	—	—	1 study	CD4+ Lymphocytes do not appear to be influence with supplementation of garlic
C	Vitamin E	—	—	1 study	No known influence of vitamin E supplementation on the overall count of CD4+ lymphocytes relative to placebo.

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CD8 Lymphocytes

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Garlic	—	—	1 study	CD8+ Lymphocytes do not appear to be influenced with supplementation of garlic.
C	Vitamin E	—	—	1 study	CD8+ Lymphocytes do not appear to be significantly influenced with supplementation of vitamin E relative to placebo.
C	Colostrum	↑	★☆☆ Minor	2 studies	At baseline CD8+ lymphocytes do not appear to be altered, although one study noted that the expected decrease in these lymphocytes during exercise was attenuated with colostrum (resulting in a relative increase to whey control).

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Cell Adhesion Factors

Cell Adhesion Factors are small targets expressed by blood vessels and organs to attract immune cells (and 'adhere' them to the cell) and draw them into tissue. Suppressing these factors is immunosuppressive, but may alleviate atherosclerosis.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	↓ ↑	★☆☆ Minor	8 studies	Appears to be able to reduce cellular adhesion factors (that draw immune cells into tissue to aid in inflammatory processes, reducing these is immunosuppressive) in elderly persons, while slightly increasing expression in youth
B	Vitamin E	—	—	3 studies	While a decrease in P-selectin has been noted with low dose (100mg) γ-tocopherol, most studies have failed to find an influence of vitamin E supplementation on adhesion factors.
C	Olive leaf extract	↓	★★★☆☆ Notable	1 study	A decrease was noted in CD40 and MCP1 adhesion factors, and this is notable as this downregulation was dose-dependently related to ingested tyrosol/hydroxytyrosol and may explain the reduced LDL oxidation
C	Tetradecyl Thioacetic Acid	↓	★☆☆☆☆ Minor	1 study	Expression of VCAM-1 has been noted to be decreased
C	Curcumin	↓	★☆☆☆☆ Minor	2 studies	Decreases in cell adhesion factors have been noted, which may underlie therapeutic benefits towards atherosclerosis of curcumin supplementation.
C	Zinc	↓	★☆☆☆☆	1 study	

C	Polypodium leucotomos	↓	★☆☆ Minor	1 study	In persons who were probably zinc deficient, supplementation of zinc is able to reduce cellular adhesion factors and the risk for atherosclerosis.
C	Hesperidin	↓	★☆☆ Minor	2 studies	Even in healthy persons, cell adhesion factor expression on immune cells appears to be reduced with supplementation of the herb at 720mg.
C	Red Clover Extract	↓	★☆☆ Minor	1 study	There is a mild decrease in E-selectin and perhaps sCAM-1 seen with oral supplementation of hesperidin, but not ICAM or VCAM; this is thought to be a mechanism underlying atherogenesis prevention.
C	Chromium	—	—	1 study	Isolated formononetin has been noted to reduce circulating VCAM-1 levels by approximately 11% in one study.
C	Colostrum	—	—	1 study	Cell adhesion factors (ICAM-1 and VCAM-1) are unaffected with chromium supplementation in nondiabetic obese adults.
D	Artichoke Extract	↓	★☆☆ Minor	1 study	Cellular adhesion factors on immune cells do not appear to be modified with colostrum relative to whey protein.
D	Royal Jelly	—	—	1 study	ICAM-1 and VCAM-1 decreased, not to a remarkable degree that would be indicative of immunosuppression.
D	Blueberry	—	—	1 study	No significant alterations in VCAM-1 levels in menopausal women, although a trend towards reduction was noted
D		—	—	1 study	No significant alterations in cell

					adhesion factors (sCAM-1 and vCAM-1)

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Cerebral Blood Flow

The amount of blood, and thus oxygen, that is delivered to the brain. Compounds can enhance cerebral blood flow by either fixing problems in unhealthy persons (fish oil) or outright increase flow (Resveratrol, Chocamine). Does not increase cognition per se, but may augment nootropics.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Green Tea Catechins	↓	★☆☆ Minor	1 study	A reduction in cerebral blood flow has been noted with green tea catechins; a simultaneous reduction in cognitive performance was not noted.
C	Resveratrol	↑	★☆☆ Minor	1 study	500mg of resveratrol (high dose) has been confirmed to increase cerebral blood flow
C	Melatonin	—	—	1 study	No significant influence on cerebral blood flow rates
C	Fish Oil	↑	★☆☆ Minor	1 study	Appears to improve cerebral blood flow and volume in persons with low dietary fish intake
C	Ginkgo biloba	↑	★☆☆ Minor	3 studies	There appears to be a significant improvement in blood flow to the middle and anterior cerebral arteries, although other arteries are unaffected.
C	Polypodium leucotomos	↑	★☆☆ Minor	1 study	In persons with senile dementia, supplementation of 360mg anapsos may increase blood flow in both hemispheres of the brain (720mg being less effective).
C	Cocoa Extract			1 study	
D	Yohimbine	↓	★☆☆ Minor	1 study	A decrease in cerebral blood

					flow has been noted to be independent of cognitive impairment

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Chronic Venous Insufficiency

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Horse Chestnut	↓	★★★☆☆ Notable	3 studies	Due to the venotrophic effects of aescin supplementation, disease states associated with blood pooling in extremities are significantly and fairly reliably treated with horse chestnut.
B	Centella asiatica	↓	★★★☆☆ Notable	8 studies	Symptoms of chronic venous insufficiency extending to poor circulation, venous reactivity, and adverse side-effects such as edema and leg pain are all reliably reduced with oral ingestion of centella asiatica
C	Ruscus aculeatus	↓	★★☆☆☆ Minor	1 study	<i>Ruscus aculeatus</i> appears to be more effective than placebo for treating chronic venous insufficiency, although the degree of benefit relative to other treatments is not established.
D	Pycnogenol	↓	★★★☆☆ Notable	1 study	Appears to reduce symptoms of chronic venous insufficiency, and preliminary evidence suggests a greater potency than the reference supplement of Horse Chestnut

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Cocaine Addiction

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	CDP-choline	↓	★☆☆ Minor	3 studies	CDP-Choline appears to be weakly anti-addictive against cocaine addiction, although the one study undertaken in persons with no intention to minimize cocaine usage can back negative.
D	N-Acetylcysteine	↓	★☆☆ Minor	1 study	Self-reported cravings for cocaine during one day of withdrawal appear to be significantly reduced following 12 hours (although acute cravings after 2 hours of supplementation are not affected); this lasts for 24 hours after cessation.

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Cognition

A general blanket statement referring to the abilities of the mind to pass tests put on it. Shares components of a lot of other cognitive phenomena, and not to be confused with Memory, Attention, or Anxiety.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Panax ginseng	↑	★☆☆ Minor	4 studies	An increase in cognition is seen acutely and thought to be due to anti-fatigue effects, with nonfatigued individuals not experiencing an increase in cognitive performance
B	Rhodiola Rosea	↑	★★★☆☆ Notable	4 studies	Notably effective assuming fatigue is being reduced. There is insufficient evidence to evaluate rhodiola's effects on cognition without the fatigue reduction aspect
B	L-Tyrosine	↑	★☆☆ Minor	3 studies	Tyrosine appears to effectively improve cognition during acute stressors (altitude and cold being tested most); this appears reliable if the acute stressor is present, but may not be an inherent increase in cognition and it is unsure if it applies to chronic stress and fatigue.
B	Phosphatidylserine	↑	★☆☆ Minor	3 studies	The interactions of supplemental PS with cognition in healthy persons is not fully researched, but there appears to be a positive influence; this may be secondary to a reduction in stress and excitation (the latter resulting in an increase in attention) but increased glucose utilization is an unexplored possibility
B	D-Serine	↑	★☆☆	3 studies	There may be an improvement

			Minor		There may be an improvement in cognitive performance secondary to reducing symptoms of schizophrenia, and while there is mechanistic plausibility that this can also work in normal controls it has not yet been demonstrated
B	Modafinil	↑	★☆☆ Minor	4 studies	Cognition is significantly improved in persons undergoing sleep deprivation or other conditions in which attention processing is highly impaired, while other conditions (cognitive decline or drug dependence) experience minor improvements in cognition that are lesser than those seen in sleep deprivation.
B	Ginkgo biloba	↑	★☆☆ Minor	7 studies	Other parameters of cognition are differentially influenced by ginkgo, as facial recognition in those with dementia has noted improvement yet trip planning in middle-aged persons is unaffected.
C	Green Tea Catechins	↑	★☆☆ Minor	2 studies	Mixed results, but may improve cognitive performance acutely in persons with poorer cognition at baseline
C	Resveratrol	—	—	1 study	No significant influence on cognition in otherwise healthy persons (despite an increase in cerebral blood flow)
C	L-Carnitine	↑	★☆☆ Minor	2 studies	Improvements in general cognitive capacity has been noted in elderly persons and in disease models (hepatic encephalopathy); lack of literature on otherwise healthy youth
C	Dehydroepiandrosterone	—	—	1 study	Overall cognition not affected by DHEA supplementation

C	Kava	↑	★☆☆ Minor	1 study	Possibly secondary to the anxiolytic effects, kava taken prior to a test is able to enhance cognition related to mood during the stressful test.
C	Nicotine	↑	★☆☆ Minor	1 study	An improvement in cognition has been noted in persons with mild cognitive impairment
C	Black Cohosh	—	—	1 study	No significant influences on cognition in menopausal women has been noted
C	Bacopa monnieri	—	—	1 study	No significant influences noted on acute cognitive performance with bacopa monnieri ingestion
C	Pycnogenol	↑	★☆☆ Minor	1 study	An improvement in cognitive function has been noted in students during academic testing
C	Choline	—	—	1 study	Acute ingestion of choline does not appear to per se influence cognitive capacity
C	Glycine	↑	★☆☆ Minor	2 studies	There are improvements in cognition due to glycine being able to treat schizophrenia and due to glycine being able to improve sleep; two states of impaired cognition.
C	Sarcosine			2 studies	
C	Phenylpiracetam	↑	★☆☆ Minor	3 studies	Cognition is improved in persons suffering from cognitive decline, organic brain lesions, and epilepsy. There are currently no studies conducted in otherwise healthy youth for the purpose of cognitive enhancement
C	Zinc	↑	★☆☆ Minor	2 studies	An improvement in cognition has been seen in stroke patients given zinc to

					complement their zinc insufficient diet.
C	Nigella sativa	↑	★☆☆ Minor	1 study	A slight improvement in cognition has been noted with supplementation of nigella seed extract in older persons
D	Piracetam	—	—	1 study	No significant influence on cognition and neural functioning has been noted in otherwise healthy persons following piracetam ingestion.
D	Pueraria lobata	↑	★☆☆ Minor	1 study	A small boost in cognition in menopausal women given the supplement; needs to be replicated and uncertain if it applies to otherwise healthy youth.
D	Pramiracetam	↑	★☆☆ Minor	1 study	Cognitive ability in youth who experienced brain trauma is improved with prolonged usage of pramiracetam, suggesting neuroprotective effects

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Cognitive Decline

Cognitive decline refers to a naturally occurring reduction in cognition and memory formation associated with aging, and may be benign or associated with some disease states (such as Alzheimer's). Some supplements that are not inherently nootropic may reduce cognitive decline.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Piracetam	↓	★★★☆☆ Notable	6 studies	There appears to be a notable reduction in the rate of cognitive decline (or rehabilitation of aged cognition) associated with high dose Piracetam over time and in a general manner. Piracetam is sometimes used as a comparator for cognitive decline.
A	Ginkgo biloba	↓	★★★☆☆ Notable	11 studies	For usage of EGb-761 at 240-360mg daily as a therapeutic option in people who already are experiencing cognitive decline, then it appears to be reliably effective and comparable to 10mg Donepezil. Usage of Ginkgo biloba for the purpose of reducing the risk of cognitive decline (as a preventative supplement) is currently not supported.
B	Phosphatidylserine	↓	★★☆☆☆ Minor	5 studies	There appears to be a protective effect against cognitive decline with PS supplementation above 300mg when using the bovine cortex form; usage of the soy based PS is not yet confirmed to have these effects, although it is possible
B	Oxiracetam	↓	★★☆☆☆ Minor	5 studies	Appears to reliably reduce the cognitive decline and related symptoms seen in dementia

					and other organic brain deterioration states, with particular efficacy towards verbal skill in doses above 1,200mg
C	Nitrate	—	—	1 study	Short-term supplementation failed to restore cognitive decline in older persons, no evidence as to whether nitrate exerts a preventative effect.
C	Eleutherococcus senticosus	↓	★☆☆ Minor	1 study	A positive influence on the cognitive state of elderly persons (reduction of cognitive decline) has once been noted
C	Curcumin	↓	★☆☆ Minor	1 study	Rate of cognitive decline may be lesser with dietary inclusion of curcumin, but requires more evidence
C	DMAE			1 study	
C	Fish Oil	↓	★☆☆ Minor	1 study	High dose (900mg) DHA appears to be somewhat beneficial in reducing the rate of cognitive decline in elderly but otherwise healthy persons
C	Alpha-GPC	↓	★★★☆☆ Notable	1 study	The rate of cognitive decline of either degenerative or vascular origin appears to be significantly reduced with Alpha-GPC supplementation
C	CDP-choline	↓	★☆☆ Minor	1 study	The rate of memory decline seen in older persons during the aging process appears to be attenuated with supplementation of CDP-Choline
C	Dehydroepiandrosterone	↓	★☆☆ Minor	2 studies	May attenuate the rate of cognitive decline in persons at higher risk, but this protective effect does not seem to be overly remarkable
C	Yamabushitake	↓	★☆☆	1 study	

C	Ginkgo biloba	↓	★☆☆ Minor	1 study	The rate of cognitive decline seen with oral supplementation of yamabushitake appears to be significantly reduced in older persons, although there are no direct comparisons to reference drugs at this time to assess potency.
C	Blueberry	↓	★☆☆ Minor	1 study	Supplementation of blueberry extract does appear effective in elderly persons with general cognitive decline, able to improve cognition and memory.
C	Polypodium leucotomos	↓	★☆☆ Minor	1 study	360mg anapsos daily appears to be somewhat benefit for persons with senile dementia.
C	Vitamin E	—	—	1 study	When supplemented by otherwise healthy elderly persons, the development of organic cognitive decline does not appear to be attenuated relative to placebo.
D	Vinpocetine	↓	★☆☆ Minor	2 studies	The rate of cognitive decline appears to be attenuated with vinpocetine administration, this may be related to blood flow
D	Panax ginseng	↓	★☆☆ Minor	1 study	A decrease in symptoms associated with cognitive decline has been noted
D	Phenylpiracetam	↓	★☆☆ Minor	1 study	The rate of cognitive decline appears to be significantly reduced following usage of phenylpiracetam

Colon cancer risk

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin E	—	—	3 studies	600 IU vitamin E every other day for a decade does not appear to reduce the risk of developing colon cancer in otherwise healthy women.
C	Ginger	↓	★☆☆ Minor	1 study	May reduce colon cancer risk as assessed by a beneficial influence in eicosanoids in the colon; requires more evidence

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Colorectal Cancer Risk

Some dietary supplements are thought to reduce the risk of colonic cancer, and this is assessed by either epidemiological research showing a relationship or studies that note how supplementation can reduce a known biomarker of colon cancer.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin D	↓	★★★☆☆ Notable	1 study	The association between serum Vitamin D at 37ng/mL and colorectal cancer is approximately a halving of risk according to one meta-analysis, which is a notable risk reduction
C	Curcumin	↓	★★☆☆☆ Minor	2 studies	Appears to be associated with a reduced risk for colon cancer
D	Panax ginseng	↓	★★★☆☆ Notable	1 study	More than a halving of the risk of colorectal cancer has been noted with panax ginseng daily ingestion

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Constipation

Constipation is the state where intestinal motility decreases to such a degree that the persons can no longer easily defecate and has intestinal pain. In this instance, some laxative compounds are recommended.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Senna alexandrina	↓	★★★ Strong	6 studies	Due to the strong laxative effect, constipation is greatly reduced with supplemental Senna Alexandria. Has been noted effective against regular, postpartum, and opioid-induced constipation and appears to not require a context-specific cause of constipation (ie. reliable) but appears to be associated with more cramping than placebo.
C	Ziziphus jujuba	↓	★☆☆ Minor	1 study	A decrease in the symptoms of constipation has been seen with the water extract of jujubes; which may apply to fruit consumption but may not apply to isolated supplements (due to the polysaccharides being the active ingredients)

Cortisol

Cortisol is the hormone that mediates waking up and a variety of catabolic (tissue breakdown) reactions; it isn't bad in any way, but many people with elevated cortisol could suffer pathology from it. In these scenarios, it is nice to lower cortisol and supplementation may be effective.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	↓	★☆☆ Minor	4 studies	A possible reducing effect of fish oil supplementation on cortisol
B	Caffeine	↑	★☆☆ Minor	4 studies	In general, cortisol appears to be increased at high doses of caffeine; lower doses may not have an effect.
B	Dehydroepiandrosterone	↓	★☆☆ Minor	5 studies	Highly unreliable influences on cortisol, with decreases seen in studies where androgens and estrogens are also increased (with no significant influence or possibly an increase in other studies)
B	Vitamin C	↓ ↑	★☆☆ Minor	6 studies	Vitamin C (500-1,500mg daily) appears to be associated with both increases and decreases in exercise-induced cortisol spikes, depending on whether it acts as a prooxidant or antioxidant (respectively). There is no influence on resting cortisol concentrations.
B	Phosphatidylserine	—	—	4 studies	A decrease in exercise-induced cortisol has been noted with the bovine cortex sourced PS only, soy based supplements (which are usually the only ones sold now due to fear of Creutzfeldt–Jakob disease) have been shown to have outright no effect at doses up to 750mg

B	HMB	—	—	3 studies	No significant influence on cortisol levels following acute ingestion
B	Creatine	—	—	4 studies	Cortisol changes associated with sleep deprivation are not affected with supplementation of creatine.
C	Yohimbine	↑	★☆☆ Minor	2 studies	Appears to increase cortisol following ingestion
C	Fenugreek	—	—	1 study	No significant influence on cortisol levels following fenugreek ingestion
C	Melatonin	↑	★☆☆ Minor	2 studies	Mixed results, a possible increase when measuring whole-day cortisol levels (when taken in the AM) with no augmentation of stress-induced cortisol increases; may reduce cortisol if taken prior to sleep, however
C	Alcohol	—	—	2 studies	No significant alterations in cortisol levels seen with alcohol ingestion in moderate levels
C	Beta-Alanine	—	—	1 study	
C	Nicotine	—	—	1 study	No significant influence on cortisol levels
C	Magnesium	—	—	1 study	No significant influence on cortisol seen with magnesium supplementation
C	5-HTP	↑	★☆☆ Minor	1 study	At least one study has noted increased in salivary cortisol following acute ingestion of 5-HTP supplementation.
C	Theaflavins	↓	★☆☆ Minor	1 study	A decrease in exercise-induced cortisol secretions has been noted with theaflavin

					consumption in high doses (above 1,800mg daily)
C	Ecdysteroids	—	—	1 study	No demonstrated changes in cortisol levels with ecdysterone consumption
C	Gamma Oryzanol	—	—	1 study	No significant influence on cortisol levels with prolonged supplementation
C	Licorice	↑	★☆☆ Minor	3 studies	Appears to increase cortisol at higher doses (500mg or more), with no significant influence at lower doses; this is related to the glycyrrhizin content, and would not occur in deglycyrrhizinated supplements
C	Mucuna pruriens	↓	★☆☆ Minor	1 study	In chronically stressed men, prolonged ingestion of mucuna pruriens appears to be able to reduce cortisol concentrations
C	Soy lecithin	↓	★☆☆ Minor	1 study	May reduce cortisol during a social stress test at 2g
C	Schisandra chinensis	↓ ↑	★☆☆ Minor	1 study	Conditional influences on cortisol, with an apparent increase in cortisol of beginner athletes at rest with decreases in exercise-induced cortisol in beginners and lower overall cortisol exposure in trained athletes
C	Salvia sclarea	↓	★☆☆ Minor	1 study	A decrease in cortisol may result following inhalation of clary sage, but the magnitude of reduction (2.5%) is very small
C	Rose Essential Oil	↓	★☆☆ Minor	1 study	A decrease in cortisol appears to result from the anti-stress response of rose oil inhalation
C	Glutamine	—	—	1 study	

C					No significant alterations in cortisol noted
C	Branched Chain Amino Acids	—	—	1 study	No significant interactions with BCAA supplementation and cortisol
C	Arachidonic acid			1 study	
C	Ornithine	↓ ↑	★☆☆ Minor	1 study	Increases have been noted with intravenous ornithine (not in human trials table) while decreases have been noted following treatment of hangovers. The most practical study of using ornithine as a preworkout supplement failed to find any effect
C	Arginine	—	—	1 study	No significant influence on circulating cortisol concentrations
C	Ashwagandha	↓	★★★☆☆ Notable	3 studies	The decrease in cortisol noted in humans has reached 14.5-27.9% in otherwise healthy but stressed humans, which is significantly larger than many other supplements.
C	Eurycoma Longifolia Jack	↓	★☆☆☆☆ Minor	1 study	In stressed persons, daily supplementation of eurycoma is associated with a 16% reduction in cortisol concentrations.
C	Ginkgo biloba	↓	★☆☆☆☆ Minor	1 study	The increase in cortisol seen before a stress test is attenuated with supplementation of ginkgo, secondary to its anti-stress effects
C	Garlic	—	—	1 study	No significant influence of garlic supplementation has been found on cortisol in cancer patients.
C	Trimethylglycine	↓	★☆☆☆☆ Minor	1 study	Cortisol appears to be

					minimally (6.1%) decreased with two weeks betaine supplementation when measured after exercise in a fasted state.
C	Saffron	↓	★☆☆ Minor	1 study	The aroma of saffron has been noted to reduce cortisol concentrations to a mild degree in otherwise healthy women, and this occurred alongside a reduction in state anxiety.
C	Vitamin E	—	—	1 study	No significant reduction in cortisol seen with supplementation of vitamin E relative to placebo.
C	Colostrum	—	—	3 studies	While one study noted an increase in morning cortisol during multiple day training in elite cyclists (a beneficial response), basal cortisol concentrations and those immediately after standard exercise do not appear to be influenced with colostrum supplementation.
D	Lavender	↓	★☆☆ Minor	1 study	A decrease in cortisol has been noted acutely with aromatherapy
D	Boron	—	—	1 study	No significant effect on cortisol has been noted with supplemental boron
D	Blueberry	—	—	1 study	Exercise-induced changes in cortisol are not influence by blueberry supplementation
D	Nigella sativa	—	—	1 study	No significant alterations in cortisol concentrations seen with supplementation of the seeds.

Cough

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Pelargonium sidoides	↓	★☆☆ Minor	12 studies	Symptoms of cough, <i>in the context of acute bronchitis</i> , are reduce in most subjects with around 50-60% of subjects reporting remission. There isn't an improvement in other lung disorders though, so this is more reflective of treatment of acute bronchitis.

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Creatinine

Creatinine is a metabolic byproduct of creatine, and is sometimes used as a biomarker for kidney damage as it can accumulate when kidneys are impaired (despite creatine supplementation giving a false positive).

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Creatine	↑	★★★☆☆ Notable	12 studies	Creatine supplementation usually increases serum creatinine levels during the loading phase (usually not maintenance) since creatinine is the breakdown product of creatine; this is <i>not</i> indicative of kidney damage.
B	Chromium	—	—	3 studies	No known influence on creatinine, a biomarker for kidney health.
C	Green Coffee Extract	—	—	1 study	No alterations noted in creatinine associated with green coffee extract intake
C	Cissus quadrangularis	↑	★☆☆☆☆ Minor	1 study	An increase in creatinine has been noted alongside weight loss; practical significance of this information is not known.
C	Glutamine	↑	★☆☆☆☆ Minor	1 study	An increase in serum creatinine has been noted, but thought to be due to a reduction in glomerular filtration rate acutely rather than due to alterations in muscle damage
C	Citrulline	↑	★☆☆☆☆ Minor	1 study	A slight increase in creatinine has been noted with citrulline supplementation, practical relevance unknown.
C	Eucommia ulmoides			1 study	

C	Ginkgo biloba	↓	★☆☆ Minor	1 study	A slight decrease in urinary creatinine has been noted with ginkgo supplementation in diabetics with nephropathy
C	Nigella sativa	—	—	2 studies	No significant influence on serum creatinine
C	Anethum graveolens			1 study	
C	Garlic	—	—	1 study	No significant influence of garlic supplement on creatinine concentrations in serum are present.
C	Citrullus colocynthis	—	—	1 study	No significant influence on creatinine concentrations with the lowest active dose of the supplement (300mg)
C	Trimethylglycine	—	—	1 study	No significant influence on circulating creatinine is seen with supplementation of betaine.
C	Astaxanthin			1 study	
C	Saffron	—	—	1 study	Creatinine does not appear to be influenced in serum following supplementation of saffron.
C	Vitamin E	—	—	1 study	In otherwise healthy elderly person, creatinine does not appear to be significantly altered relative to placebo.
D	Hibiscus sabdariffa	—	—	1 study	No significant influence on creatinine
D	Bulbine natalensis			1 study	
D	Rose Hip	↓	★☆☆ Minor	1 study	Creatinine, a biomarker of kidney damage and muscle damage, has been noted to be reduced with rose hip supplementation in one preliminary trial

Depression

Depression is a cognitive state associated with hopelessness and apathy. Clinical depression is a realm for medical doctors to address, but subclinical ennui might be counteracted with some supplements. Consider physical exercise as well, it might help a little.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Fish Oil	↓	★★★☆☆ Notable	22 studies	Fish oil supplementation has been noted to be comparable to pharmaceutical drugs (fluoxetine) in majorly depressed persons, but this may be the only cohort that experiences a reduction of depression. There is insufficient evidence to support a reduction of depressive symptoms in persons with minor depression (ie. not diagnosed major depressive disorder)
A	Saffron	↓	★★★☆☆ Notable	9 studies	30mg saffron daily (both petals and stigma) appear to be effective in reducing depressive symptoms in persons with major depressive disorder, and the potency has been noted to be comparable to reference drugs (fluoxetine and imipramine).
B	Inositol	↓	★★☆☆☆ Minor	8 studies	There appears to be a reduction in depressive symptoms associated with inositol supplementation, although it is less potent than the benefits of inositol on anxiety and panic attacks.
B	Chromium	↓	★★☆☆☆ Minor	5 studies	There is limited preliminary evidence for chromium having an adjuvant role in aiding depressive symptoms (betters overall outcomes when paired with a more effective 'reference'

					therapy), although the limited evidence for chromium in isolation is unconvincing.
C	Creatine	↓	★★★☆☆ Notable	3 studies	Notable due to seeming to be related to serotonin and augmenting SSRI therapy, and appears to have a gender difference (efficacy in females) which needs to be explored more.
C	Dehydroepiandrosterone	—	—	1 study	No significant interactions with depression noted
C	Panax ginseng	↓	★★☆☆☆ Minor	1 study	Anti-depressive effects may be secondary to reducing menopausal symptoms
C	Nicotine	—	—	1 study	No significant influence on depressive symptoms
C	S-Adenosyl Methionine	↓	★★★☆☆ Notable	2 studies	Has been noted to augment SSRI therapy (similar to Creatine) and monotherapy with SAME appears to be of similar potency to tricyclic antidepressants for some studies.
C	Vitex agnus castus	↓	★★☆☆☆ Minor	2 studies	Can attenuate depressive symptoms that occur during PMS secondary to reducing PMS symptoms in general.
C	Bacopa monnieri	↓	★★☆☆☆ Minor	2 studies	An anti-depressive effect has been noted, but to a relatively small magnitude. Requires more context-based evidence
C	Rhodiola Rosea	↓	★★★☆☆ Notable	1 study	Limited evidence, but up to a halving of symptoms has been noted with higher doses of Rhodiola
C	L-Tyrosine	—	—	1 study	Depressive symptoms that occur during acute stressors have not been affected by

					Tyrosine supplementation; chronic depression not yet researched
C	Ganoderma lucidum	↓	★☆☆ Minor	1 study	Depression as a symptom of cancer-related fatigue was reduced, may not hold inherent antidepressive effects
C	Kava	↓	★☆☆ Minor	2 studies	Depressive symptoms have been reduced vicariously through reductions in anxiety; <i>per se</i> antidepressant effects of kava uncertain
C	Maca	↓	★☆☆ Minor	2 studies	May reduce depression in postmenopausal women, unlikely to occur in otherwise healthy youth
C	Vitamin C			1 study	
C	Nefiracetam			1 study	
C	Ashwagandha	↓	★☆☆ Minor	2 studies	Antidepressive effects have been found with ashwagandha, although they are less notable than the anti-anxiety effects. They may be mediated by similar mechanisms.
C	Ginkgo biloba	—	—	1 study	Supplementation of ginkgo does not appear to significantly influence depressive symptoms in older individuals
C	Zinc	↓	★★★ Notable	2 studies	The reduction in depression is notable <i>only for</i> treatment resistant depression alongside a pharmaceutical antidepressant; there does not appear to be a benefit to persons who respond to antidepressants and the inherent anti-depressant effects without a pharmaceutical add-on are modest at best.
C	Yamabushitake	↓	★☆☆	1 study	Decrease in depressive

			Minor		Decrease in depressive symptoms has been noted, which may be secondary to attenuating menopausal symptoms
C	Centella asiatica	↓	★☆☆ Minor	1 study	A reduction in depressive effects may be secondary to the treatment of anxiety.
C	N-Acetylcysteine			1 study	
C	Red Clover Extract	↓	★★★☆☆ Notable	1 study	Depression as a side-effect of menopause has been noted to be decreased to quite a significant level (around 80%) which needs to be replicated due to possible funding issues.
D	Holy Basil	↓	★☆☆ Minor	1 study	A decrease in depressive symptoms during generalized anxiety disorder has been noted
D	Magnesium	↓	★☆☆ Minor	1 study	Reduced depressive symptoms have been found in elderly diabetics
D	Lavender	↓	★☆☆ Minor	1 study	Depression as a side effect of anxiety appears to be reduced
D	Royal Jelly	↓	★☆☆ Minor	1 study	Reduction in irritability noted with Royal Jelly may be secondary to reducing symptoms associated with menopause
D	Uridine	↓	★☆☆ Minor	1 study	Depressive symptoms in bipolar disorder have been noted to be reduced
D	Vitamin B12			1 study	
D	Phenylpiracetam	↓	★☆☆ Minor	1 study	Depressive symptoms following a stroke appear to be reduced following ingestion of phenylpiracetam. Currently, there are no studies on otherwise healthy persons with

					depressive symptoms
D	Curcumin	↓	★★☆ Notable	1 study	One study has noted improvements in major depressive disorder (1g curcumin) which were comparable to fluoxetine (20mg) as a reference, but no placebo group was available for comparison.

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DHT

Dihydrotestosterone (DHT) is a derivative of testosterone that is known as being more potent at signalling through the androgen receptor, and due to this it is involved to a larger degree in hair loss and prostate cancer.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Fenugreek	↓	★☆☆ Minor	2 studies	A decrease in DHT has been noted following consumption of fenugreek seeds in otherwise healthy men, but appears to be unreliable
C	Creatine	↑	★☆☆ Minor	1 study	An increase in DHT has been noted in one study independent of an increase in testosterone, requires replication due to some potential issues (location of study, lack of biological plausibility, etc.)
C	Dehydroepiandrosterone	↑	★☆☆ Minor	2 studies	May increase DHT levels alongside testosterone levels, but this has only been observed in postmenopausal women
C	Zinc	↑	★☆☆ Minor	1 study	An increase in DHT has been noted in infertile men
D	Boron	—	—	1 study	No significant influences on serum DHT noted

Diarrhea

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Colostrum	↓	★★★☆☆ Notable	10 studies	Diarrhea can be potentially reduced with colostrum under two conditions, either it is being used in persons with HIV-induced diarrhea from <i>cryptosporidium parvum</i> or when using colostrum (from cows immunized to E.coli) in response to food carrying E.coli (usually seen with traveler's diarrhea); despite being highly effective in those two scenarios it seems ineffective in other cases of diarrhea.

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Diuresis

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Astragalus membranaceus	↑	☆☆☆ Minor	1 study	Astragalus root appears to have diuretic properties with oral ingestion (0.3g/kg) in otherwise healthy persons.
C	Tribulus terrestris	↑	☆☆☆ Minor	1 study	3g of the fruits or a water extract thereof appears to increase overall urine volume after a month of supplementation by around 200mL daily.
C	Orthosiphon stamineus	—	—	1 study	Despite both traditional usage and rat studies, the lone study assessing the diuretic effects of 10g of the fresh leaves has failed to find any effect.
C	Yohimbine	↑	☆☆☆ Minor	1 study	There appears to be an increased urge to urinate following supplementation of yohimbine
D	Ashwagandha	↑	☆☆☆ Minor	1 study	May have diuretic effects, although not to a remarkable degree.
D	Eclipta alba	↑	☆☆☆ Notable	1 study	Urine volume has been noted to be increased by 34%, which is fairly notable as it outperforms other nutraceuticals

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DNA Damage

DNA damage refers to oxidative changes to DNA, which can be measured in the urine or in white blood cells. Reductions in DNA damage from antioxidant supplements are thought to reduce the risk of cancer development and mutations.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Blueberry	↓	★★★☆☆ Notable	4 studies	DNA damage appears to be acutely decreased following consumption of blueberries or its extracts (375mg anthocyanins or more) and tends to be in the range of a 20% reduction.
B	Vitamin E	—	—	5 studies	While most evidence suggests no influence on DNA damage, it is possible based on some studies that when vitamin E turns prooxidative that it may damage DNA.
C	Vitamin C	—	—	2 studies	No significant influences on DNA damage
C	Conjugated Linoleic Acid	—	—	2 studies	Insufficient evidence to suggest alterations in the rate of DNA damage with CLA ingestion.
C	Eleutherococcus senticosus	↓	★★★☆☆ Minor	1 study	A decrease in DNA damage biomarker has been noted, thought to be secondary to antioxidative effects
C	Chlorella	—	—	1 study	Has once failed to modify the DNA damage observed in male smokers
C	Creatine	↓	★★★☆☆ Minor	2 studies	Appears to reduce exercise-induced DNA damage; practical relevance unknown

					but potentially promising for cancer prevention.
C	Olive leaf extract	↓	★★★☆☆ Notable	1 study	The one study to measure DNA damage (via 8-oxo-dGF as a biomarker) noted up to 50% reductions in mitochondrial and urine measurements; a fairly significant reduction.
C	Watercress	↓	★☆☆☆☆ Minor	1 study	DNA damage biomarkers have been reduced following watercress consumption
C	Curcumin	↓	★☆☆☆☆ Minor	1 study	A decrease in DNA damage has been noted to be secondary to reducing arsenic toxicity
C	Ganoderma lucidum	—	—	1 study	DNA damage in lymphocytes of volunteers given the polysaccharides appear unchanged
C	Panax ginseng	↓	★☆☆☆☆ Minor	1 study	Can decrease the rates of DNA damage noted in lymphocytes, which may be related to the anticancer effects of panax ginseng
C	Fish Oil	—	—	2 studies	Does not appear to influence DNA damage
C	Citrulline	—	—	1 study	No significant influence of citrulline on DNA damage
C	Sea Buckthorn	—	—	1 study	DNA damage as measured in lymphocytes does not appear to be significantly affected by supplementation of sea buckthorn
D	Melissa officinalis	↓	★☆☆☆☆ Minor	1 study	A reduction in DNA damage has been noted with lemon balm tea in persons exposed to high levels of radiation

D	Garlic	↓	★☆☆ Minor	1 study	Urinary biomarkers of DNA damage are reduced in hypertensive persons following supplementation of garlic.
D	Chromium	—	—	1 study	One study assessing DNA damage following ingestion of chromium supplementation failed to find any harmful nor beneficial interactions.

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Dopamine

Dopamine is a catecholamine and neurotransmitter that can be measured in the blood, and changes in response to the diet or nutritional supplementation.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Ganoderma lucidum	—	—	1 study	No significant influence on serum dopamine
C	Melatonin	↓	★☆☆ Minor	1 study	Serum dopamine has been noted to be slightly reduced (37%) during waking at rest, but this decrease was eliminated upon walking
C	Mucuna pruriens	↑	★☆☆ Minor	1 study	The reduction in dopamine seen in infertility seems to be reversed with L-DOPA ingestion; theoretically L-DOPA ingestion should unilaterally increase dopamine
C	Branched Chain Amino Acids	—	—	1 study	Similar to the other catecholamines (adrenaline and noradrenaline), serum dopamine does not appear to be altered with supplemental BCAAs.
C	Creatine	—	—	1 study	No significant alterations in plasma dopamine are seen with creatine supplementation during sleep deprivation.

Dry Mouth

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Trimethylglycine	↓	★☆☆ Minor	4 studies	Symptoms of dry mouth either caused by a disease state (Sjögren's syndrome) or as a side-effect of pharmaceuticals appears to be significantly reduced when betaine is formulated into a toothpaste at 4%.

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Edema

Edema is the retention of water in tissue, resulting in weight gain and bloating, and the cause of leg swelling. Some conditions such as diabetics are characterized by edema, and treating the condition may reduce edema.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Centella asiatica	↓	★☆☆ Minor	5 studies	There appears to be a decrease in edema associated with chronic venous insufficiency (CVI), associated with the treatment of CVI by <i>centella asiatica</i>
C	Curcumin	↓	★☆☆ Minor	1 study	A decrease in edema has been noted with curcumin supplementation
C	Methylsulfonylmethane	↑	★☆☆ Minor	1 study	One study that used MSM as a placebo noted that there was an increase in edema relative to baseline; not known why.
C	Serrapeptase	↓	★☆☆ Minor	2 studies	Related to the antiinflammatory effects, swelling and edema post surgery appear to be reduced.

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Endothelial Function

Endothelial function (vasoreactivity) tends to refer to the reactivity of blood vessels to dilate or contract upon demand, and is associated with blood flow and arterial calcification. Improved vasoreactivity is associated with reduced risk for cardiovascular incidents.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Coenzyme Q10	↑	★☆☆ Minor	5 studies	The effective size does not appear to be overly large, but CoQ10 is associated with a protective effect on blood flow and endothelial function in persons with otherwise impaired function.
B	Fish Oil	↑	★☆☆ Minor	4 studies	There appears to be a slight increase in vascular reactivity and blood vessel responsiveness that may be independent of both blood flow alterations and blood pressure
C	Panax ginseng	↑	★☆☆ Minor	2 studies	A possible increase in endothelial reactivity is noted with panax ginseng supplementation
C	Vitamin D	—	—	1 study	No significant influence on endothelial function
C	Arginine	↑	★☆☆ Minor	2 studies	Unreliable improvements in endothelial function, notably in persons with impaired glucose tolerance/type II diabetes, associated with the supposed increase in nitric oxide

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Eosinophil count

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Tinospora cordifolia	↓	★★★☆☆ Notable	2 studies	There appears to be a reduction in eosinophils in the range of 30% or greater, somewhat notable
C	Chromium	—	—	1 study	No significant influence on baseline eosinophil count with supplementation of chromium relative to placebo in otherwise healthy women.
C	Saffron	—	—	1 study	Eosinophil concentrations are not affected by saffron supplementation in otherwise healthy persons.

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Erections

Erections refers to the ability to achieve and maintain an erection as well as its rigidity. Many supplements catering towards erectile dysfunction are said to possess these pro-erectile properties.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Yohimbine	↑	★☆☆ Minor	1 study	Erections are increased following yohimbine ingestion which is thought to be a combination of alpha-2-adrenergic antagonism (enhancing relaxation of the penile tissue so engorgement of blood can ensure) and increasing blood pressure (which would increase the amount of force in an erection). However, may not be able to overcome organic erectile dysfunction associated with poor blood flow
B	Panax ginseng	↑	★☆☆ Minor	4 studies	An improvement in erectile dysfunction is seen with 3g of Korean Red Ginseng (fermented panax ginseng, regular panax ginseng not as well tested) which is thought to be secondary to anti-fatigue effects and improved blood flow
C	Butea superba	—	—	2 studies	Currently assumed to be ineffective for erections or erectile dysfunction due to the poor quality of the evidence in existence.
C	Ashwagandha	—	—	1 study	Supplementation of 2,000mg of Ashwagandha thrice daily in men with psychogenic erectile dysfunction failed to exert any benefits more than placebo.
C	Coenzyme Q10	↑	★☆☆	1 study	Increased erectile function has

			Minor		increased erectile function has been noted with CoQ10, but this may be secondary to reductions in symptoms of Peyronie's Disease
C	Maca	↑	★☆☆ Minor	1 study	An increase in erection frequency has been noted in men, likely related to the libido enhancing properties
C	Dehydroepiandrosterone	—	—	1 study	No significant influence on erectile properties in persons with sexual dysfunction
C	Eurycoma Longifolia Jack	↑	★☆☆ Minor	1 study	There appears to be a slight proerectile effect of eurycoma supplements as assessed by self-report survey
C	Tribulus terrestris	↑	★☆☆ Minor	1 study	In infertile men, supplementation of 6g tribulus root appears to increase rigidity of erections and improve performance (reduce anxiety while delaying ejaculation and improving orgasm).
C	Saffron	—	—	3 studies	The best evidence to date does not support a pro-erectile effect of saffron supplementation <i>per se</i> , although it may have a particular role in combating SSRI related sexual dysfunction that results in erectile dysfunction.
D	L-Carnitine	↑	★☆☆ Minor	1 study	One study has noted an improvement in erections in persons thought to have impaired blood flow
D	Pycnogenol	↑	★☆☆ Minor	1 study	May be proerectile in persons with organic erectile dysfunction (due to poor blood flow)
D	Citrulline	↑	★☆☆	1 study	Hardness of erections in

			Minor		Hardness of erections in persons with mild erectile dysfunction appears to be increased following supplementation of citrulline supplementation.

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Erythema

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Feverfew	↓	★★★☆☆ Notable	1 study	The reduction in erythema with topical parthenolide-depleted feverfew was greater than that of the active control, Ibuprofen.
C	Fish Oil	↓	★★☆☆☆ Minor	2 studies	Ingestion of fish oil appears to prolong the time required for sunlight to induce reddening of the skin, and secondary to this fish oil ingestion above 1,800mg EPA is able to reduce the risk of sunburn.
C	Vitamin E	↑	★★☆☆☆ Minor	2 studies	Topical application of vitamin E to scar tissue has, in some participants, caused significant increases in redness of the tissue associated with itching.

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Estrogen

Known as the female hormone, 'Estrogen' is a group of compounds that tends to work in opposition to androgens (like testosterone) and mediate fat metabolism, cognition, blood flow, and female reproduction. Men sometimes wish to lower estrogen via aromatase inhibition.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Dehydroepiandrosterone	↑	★★★☆☆ Notable	14 studies	There appears to be a notable and unreliable increase in estrogen following DHEA supplementation, with most research being conducted in menopausal women. This increase in estrogen has been noted in men as well, although similarly unreliable.
B	Maca	—	—	3 studies	No significant influence on circulating estrogen noted
B	Red Clover Extract	—	—	6 studies	Regardless of any direct estrogenic effects (which also do not appear to occur) there are no changes in circulating estrogen seen with oral supplementation of red clover extract.
C	Horny Goat Weed	—	—	2 studies	No significant influence on serum estrogen levels
C	Fenugreek	—	—	2 studies	No significant influences detected on estrogen levels
C	Melatonin	—	—	1 study	No significant influence on circulating estrogen levels
C	Alcohol	—	—	3 studies	No significant influence on fasting estrogen levels in males
C	Garcinia cambogia	—	—	1 study	

C	7-Keto DHEA	—	—	1 study	No significant influence on circulating estrogen levels associated with garcinia
C	Black Cohosh	—	—	1 study	Insufficient evidence to claim changes in estrogen following 7-keto supplementation.
C	Gamma Oryzanol	—	—	1 study	No significant influences on circulating estrogen levels or biomarkers of estrogenicity (vaginal cytology)
C	Green Tea Catechins	—	—	1 study	No significant influence on circulating estrogen levels in healthy men given gamma-oryzanol over a few weeks
C	Royal Jelly	—	—	1 study	No significant alterations in estrogen seen with Royal Jelly
C	Panax ginseng	—	—	1 study	No significant influence on estrogen levels in women
C	Vitamin K	—	—	1 study	No significant interactions with estrogen noted with vitamin K supplementation
C	D-Aspartic Acid	—	—	1 study	Despite a possible induction of aromatase seen in some species, D-aspartic acid supplementation does not appear to increase serum estrogen.
C	Saffron	↑	★☆☆ Minor	1 study	The aroma of saffron appears to cause a mild increase in circulating estrogen concentrations in otherwise healthy women following 20 minutes of exposure.
D	Boron	↓ ↑	★☆☆ Minor	2 studies	Appears to influence estrogen, seems unreliable in its

					mechanisms and is likely context dependent. Both increases and decreases have been noted
D	Licorice	—	—	2 studies	No significant alterations in serum estrogen
D	Pueraria lobata	—	—	1 study	No significant influence of Pueraria lobata on circulating estrogen levels (although it itself may be a phytoestrogen; weak)
D	Punicalagins	—	—	1 study	No significant influence on estrogen

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Exercise Capacity (with Heart Conditions)

Cardiovascular exercise is known to be impaired in persons with heart disorder such as COPD, and supplements are being investigated to see whether the performance enhancing effects in healthy subjects can be extended to these persons.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Coenzyme Q10	↑	★☆☆ Minor	4 studies	Appears to aid exercise capacity in persons after myocardial infarction
B	Creatine	—	—	5 studies	Although there may be a small reduction of power output (typical of creatine), the main parameter of interest (cardiorespiratory output) is mostly unaffected by creatine supplementation.
C	Berberine	↑	★☆☆ Minor	1 study	A positive effect, but the potency thereof was not overly remarkable
C	Glutamine	↑	★☆☆ Minor	2 studies	Although a failure has been noted in persons with COPD, one study has noted acute benefits in chronic stable angina with 80mg/kg oral glutamine supplementation.
D	Taurine	↑	★☆☆ Minor	1 study	An improvement in walking distance has been noted
D	Citrulline	↑	★☆☆ Minor	1 study	Citrulline has been noted to increase physical exercise capacity in persons with heart failure.
D	Garlic	↑	★☆☆ Minor	1 study	In persons with coronary heart disease, supplementation of garlic appears to increase physical performance when

					ingested at a food dose (1g) daily over six weeks; the increase in performance is moderate.

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Exercise-Induced Immune Suppression

Intense exercise is known to be associated with an increased rate of sickness and reduced immune cell count, and supplementation is sometimes thought to reduce this rate of loss and thus preserve immunity. These effects are conditional on exercise being conducted.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin C	—	—	6 studies	More evidence suggests no significant effect than a possible protective effect, although the latter is possible
C	Echinacea	↓	★☆☆ Minor	1 study	Possible effects, but study assessed salivary IgA (biomarker of immunity) and not sickness rates; hard to assess potency.
C	Fish Oil	—	—	1 study	Does not appear to augment nor alleviate the immunosuppression that occurs during exercise in otherwise healthy persons
C	Pelargonium sidoides	↓	★☆☆ Minor	1 study	Although rates of sickness were not assessed, the alterations in the cytokine/immunoglobulin profile (increase in Immunoglobulin A, suppressing of IL-6 and IL-15) suggest less immunosuppression from exercise.
C	Colostrum	—	—	2 studies	The limited studies assessing sickness in athletes during exercise have not found a significant reduction in sickness rates relative to control protein sources (whey).
D	Blueberry	—	—	1 study	The alterations in most

					immune cells seen during exercise are wholly unaffected by blueberry supplementation.

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Exercise-Induced Oxidation

Physical exercise is associated with an increase in oxidation in the body (which contributes to fatigue, but also mediates beneficial adaptations to exercise), and ingestion of some antioxidant supplements may reduce oxidation and are thought to prolong endurance.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	L-Carnitine	↓	★☆☆ Minor	5 studies	A decrease in the exercise-induced increase in MDA levels is seen with carnitine supplementation, possibly secondary to reducing damage to muscle tissue. The degree of MDA reduction is not overly remarkable
B	Coenzyme Q10	↓	★☆☆ Minor	4 studies	Mixed effects on exercise-induced oxidation, but there appears to be some potential for CoQ10 supplementation to reduce oxidation.
C	Green Tea Catechins	↓	★☆☆ Minor	1 study	A decrease in the oxidation that occurs during exercise may occur following acute ingestion of green tea catechins
C	Melatonin	↓	★☆☆ Minor	2 studies	Related to the antioxidative effects, a reduction in exercise-induced oxidation has been noted
C	Vitamin C	—	—	2 studies	Highly mixed interactions with the exercise:oxidation axis with Vitamin C, with both increases and decreases being noted. Unlikely to have a reliable role
C	Methylsulfonylmethane	↓	★★★☆☆ Notable	1 study	A decrease in exercise induced oxidation is noted with MSM supplementation and thought to be the underlying reason for reductions in muscle damage

					and soreness. The degree of reduction seems to be notable, as the increase in MDA and protein carbonylation were fully abolished
C	Fish Oil	↑	★☆☆ Minor	1 study	Exercise induced oxidation has been noted to be increased in elite athletes with fish oil supplementation
C	Phosphatidylserine	—	—	1 study	No significant influence on oxidation biomarkers that are increased during exercise
C	Resveratrol	↓	★★★☆☆ Notable	1 study	The oxidation induced by exercise is effectively diminished with resveratrol, which is thought to underlie the inhibitory effects on exercise-induced adaptations.
C	Astaxanthin			1 study	
D	Blueberry	—	—	1 study	The lone study using a 2.5 hour running protocol at 72% VO2 max failed to find any significant differences between groups in oxidative status after exercise.

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Fat Mass

Fat Mass is a term for adipose tissue, the scientific name for any body fat you carry on you as a form of energy storage. Although not unhealthy per se, many people termed obese carry too much body fat and a reduction of fat mass is seen as healthy and desirable.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Green Tea Catechins	↓	★☆☆ Minor	6 studies	There appears to be a fat reducing effect associated with green tea, but it is minor and unreliable
A	Conjugated Linoleic Acid	—	—	21 studies	Evidence is too unreliable to conclude an inherent effect of CLA on fat mass. There may be a context-dependent reduction in body fat and explanation for the observed variability, but at this moment in time too much evidence concludes no effect
A	Chromium	—	—	11 studies	There doesn't appear to be a significant nor reliable reduction in fat mass even in diabetics given chromium supplementation according to the literature.
B	Ephedrine	↓	★★★☆☆ Notable	4 studies	It is thought that most weight lost with ephedrine administration is due to fat mass, due to a slight muscle preserving effect; studies that note reductions in fat mass support this hypothesis
B	L-Carnitine	↓	★☆☆ Minor	3 studies	There appears to be a fat reducing effect of L-Carnitine supplementation, but this may be limited to elderly persons; limited studies in otherwise healthy youth and adults fail to note an effect

B	Dehydroepiandrosterone	—	—	8 studies	No significant influence on fat mass appears to exist with DHEA supplementation in youth or in elderly persons
B	Whey Protein	↓	★☆☆ Minor	6 studies	Inclusion of dietary protein in the diet above the recommended daily intake appears to aid the process of fat loss during hypocaloric diets (eating less than required to sustain body weight). There is currently no demonstrated benefit with whey protein over other protein sources.
B	HMB	↓	★☆☆ Minor	7 studies	There may be a decrease in fat mass associated with HMB supplementation when combined with resistance training, but this reduction is not a large magnitude and usually does not occur; quite unreliable
B	Vitamin D	↓	★☆☆ Minor	3 studies	Mixed effects on overweight/obese persons, but it appears that normalizing a deficiency may aid fat loss in persons of higher body weight. Insufficient evidence to suggest the role of Vitamin D in lean persons
B	Pyruvate	—	—	5 studies	The majority of the evidence currently does not support a role for supplemental Pyruvate in weight loss. The limited evidence to suggest fat loss are in obese women under severe caloric restriction, of which pyruvate was twice linked to increase the already drastic weight loss
B	Creatine	—	—	9 studies	While creatine is reliable at increasing lean mass (acutely water, more prolonged supplementation is muscle), it does not appear to significantly

					modify fat mass at all.
B	Trimethylglycine	—	—	3 studies	Fat mass does not appear to be significantly influenced with either short term (2 week) or long term supplementation.
B	Colostrum	—	—	3 studies	Supplementation of colostrum has failed to increase fat mass in subjects relative to baseline, similar to the same doses of whey protein which usually also fail to influence fat mass.
C	Clenbuterol	↓	★★★☆☆ Notable	1 study	The reduction in fat mass under the influence of clenbuterol is greater than that observed with other fat burners such as Ephedrine or Yohimbine
C	Tauroursodeoxycholic Acid	—	—	1 study	No significant influence on fat mass in obese persons
C	Yohimbine	↓	★★★☆☆ Notable	1 study	Fat mass is reduced with yohimbine ingestion and appears to affect both obese and lean individuals
C	Vitamin C	—	—	1 study	Does not appear to significantly influence fat mass
C	Punicic Acid	—	—	1 study	No significant influence on fat mass by itself
C	Grapefruit	↓	★★☆☆☆ Minor	1 study	Fat mass appears to be reduced more in groups consuming grapefruit relative to placebo
C	Beta-Alanine	↓	★★☆☆☆ Minor	2 studies	Mechanisms unknown, but some studies suggest a fat loss effect (possibly secondary to extra workout volume)
C	Chlorella	—	—	1 study	No significant effects on fat mass

C	Licorice	—	—	1 study	No significant influence on fat mass
C	Green Coffee Extract	↓	★☆☆ Minor	1 study	Lone study to measure fat mass noted a decrease associated with green coffee extract consumption, but this is similarly confounded with industrial influence.
C	7-Keto DHEA	↓	★☆☆ Minor	1 study	The amount of fat lost appears to be more with 7-keto than with placebo when either of them are paired with a low calories weight loss regiment.
C	Coleus forskohlii	↓	★☆☆ Minor	1 study	Somewhat effective in reducing fat mass in obese and overweight persons.
C	Tribulus terrestris	—	—	2 studies	No significant influences on fat mass are noted with tribulus terrestris
C	Fenugreek	↓	★☆☆ Minor	1 study	A lone study measuring fat mass in athletes given fenugreek noted a reduction in fat mass, which was not to a remarkable degree
C	Irvingia gabonensis	↓	★☆☆ Minor	1 study	A decrease in fat mass has been detected, but may be due to industry influence; independent trials are needed. Mechanism appears to be from suppressing food intake
C	Fish Oil	—	—	3 studies	No significant influence on fat mass with routine supplemental fish oil
C	Leucine			1 study	
C	Arachidonic acid			1 study	
C	Leucic Acid	—	—	1 study	No significant interaction between leucic acid and body

					fat has yet to be detected
C	Arginine	↓	★☆☆ Minor	1 study	A slight reduction in fat mass has been noted with long-term usage in persons with impaired glucose tolerance. No evidence supports the usage of arginine as a fat burner in otherwise healthy persons
C	Glutamine	—	—	1 study	The addition of glutamine supplementation to an exercise regiment has failed to outperform placebo in reducing fat mass.
C	D-Aspartic Acid	—	—	1 study	Fat mass does not appear to be altered with D-aspartic acid supplementation alongside exercise.
C	Hoodia gordonii	—	—	1 study	No significant reductions in fat mass are noted, secondary to a lack of influence on appetite
D	Coconut Oil	↓	★☆☆ Minor	1 study	May decrease fat mass to a greater degree than an isocaloric amount of long chain fatty acids.
D	Eurycoma Longifolia Jack	—	—	1 study	No significant known influences on fat mass
D	Safflower Oil	—	—	1 study	No significant reduction in total fat mass, although in obese diabetic women a slight reduction in abdominal fat mass may exist.
D	Zinc	—	—	1 study	No known significant interactions with zinc supplementation on fat mass.
D	Ashwagandha	—	—	1 study	There was a trend to reduce fat mass over 30 days when supplemented to otherwise healthy persons, but this failed

					to reach statistical significance.

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Fat Oxidation

Fat Oxidation is the percentage of caloric expenditure that is derived from fatty acids (the alternative being mostly from glucose); it is independent of actual metabolic rate.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Green Tea Catechins	↑	★☆☆ Minor	8 studies	There appears to be a slight but unreliable increase in fat oxidation (percentage of overall calories used coming from fatty acids rather than glucose) associated with consumption of green tea catechins
B	L-Carnitine	—	—	3 studies	Rates of fat oxidation appear unaffected following carnitine supplementation
B	Caffeine	↑	★☆☆ Minor	3 studies	An increase in fat oxidation appears to be apparent (assessed via increased serum glycerol and free fatty acids) which is thought to be secondary to increases in adrenaline
B	Branched Chain Amino Acids	↑	★☆☆ Minor	3 studies	In prolonged exercise and somewhat related to the antifatigue effects, an increase in fat oxidation is noted with BCAA supplementation; this is thought to be related to the glycogen preserving effects of BCAAs.
B	Colostrum	—	—	3 studies	Colostrum does not influence fat oxidation rates or glucose expenditure during exercise any differently than other protein sources such as whey.
C	Conjugated Linoleic Acid	↑	★☆☆ Minor	1 study	May influence fat oxidation, but more evidence is required.

C	Vitamin C	—	—	1 study	No significant influence on fat oxidation
C	Spirulina	↑	★☆☆ Minor	1 study	Nothing remarkable in the one study on fat oxidation rates during exercise.
C	Alpha-GPC	↑	★☆☆ Minor	1 study	Some biomarkers of hepatic fat oxidation increased at rest, no indication as to the potency of this relative to reference drugs.
C	Eleutherococcus senticosus	↑	★☆☆ Minor	2 studies	Some studies have noted an increase in fat oxidation during exercise; no current studies conducted at rest
C	Yerba mate	↑	★☆☆ Minor	1 study	An increase in fat oxidation assessed via a lower respiratory quotient has been noted
C	Panax ginseng	—	—	1 study	Rates of fat oxidation during exercise appear unchanged
C	Quercetin	—	—	1 study	No significant alterations in fat oxidation noted with quercetin supplementation
C	Phosphatidylserine	—	—	1 study	No significant influence on fat oxidation during exercise
C	Sodium Bicarbonate	↑	★☆☆ Minor	2 studies	An increase in fat oxidation has been noted at rest with supplemental sodium bicarbonate which contributed solely to the increase in metabolic rate
C	Taurine			1 study	
C	Capsaicin			1 study	
C	Nicotine	—	—	1 study	When nicotine increases metabolic rate, there is no change in rates of fat or glucose oxidation.

C	Ashwagandha	—	—	1 study	Despite improvements seen in VO2 max and endurance capacities in this study, the respiratory exchange ratio (indicative of fat oxidation) was not significantly influenced.
C	Creatine			2 studies	
C	Astaxanthin			1 study	
C	Chromium	—	—	2 studies	Fat oxidation (percent of energy derived from fatty acids relative to glucose) does not appear to be influenced following supplementation of chromium.
D	Coconut Oil	↑	★☆☆ Minor	1 study	Appears to increase the percentage of calories derived from lipids in obese persons; no comparator.
D	Fish Oil	↑	★☆☆ Minor	1 study	An increase in fat oxidation (percentage of energy being taken from fat tissue) has been noted with fish oil supplementation

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Fatigue

A chronic lack of motivation and 'energy'/'vitality', Fatigue can be acutely countered by stimulants (not advisable for the long term) or may be slowly mended by other compounds like Reishi or CoQ10.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Branched Chain Amino Acids	↓	★☆☆ Minor	10 studies	A decrease in fatigue (mental fatigue when measured after the workout) results when BCAA supplementation is taken during exercise at a dose above 10g or so
A	Rhodiola Rosea	↓	★★★☆☆ Notable	7 studies	The decrease in fatigue appears to be quite strong and reliable, rhodiola may be an active control on this parameter
B	L-Carnitine	↓	★☆☆ Minor	7 studies	Carnitine appears to be somewhat effective in reducing fatigue in elderly persons with low muscular endurance and perhaps in chronic fatigue syndrome; there is insufficient evidence to support a role of carnitine in reducing exercise-induced fatigue
B	Coenzyme Q10	↓	★☆☆ Minor	3 studies	There may be an anti-fatigue effect of CoQ10 during exercise that may not extend to general fatigue.
B	Beta-Alanine	↓	★☆☆ Minor	9 studies	Seems somewhat effective in reducing fatigue and secondary to that, improving time to exhaustion.
B	Modafinil	↓	★★★☆☆ Notable	6 studies	Fatigue is notably reduced with modafinil supplementation, particularly during instances of sleep deprivation or hypersomnia.

B	Creatine	↓	★★★☆☆ Notable	7 studies	In the fatigue experienced by children subject to traumatic brain injury, frequency of fatigue is reduced from 90% down to 10% with 400mg/kg oral ingestion daily. Fatigue is also reduced to a lesser degree in sleep deprivation
B	Pelargonium sidoides	↓	★☆☆☆☆ Minor	7 studies	Fatigue as a side-effect of acute bronchitis is reduced quite respectably relative to placebo.
B	Trimethylglycine	—	—	5 studies	One study noted a reduced <i>rate of change</i> in fatigue (no overall differences in fatigue outright though) seen with betaine, whereas the other two studies have failed to find benefit with betaine.
C	Resveratrol	—	—	1 study	No significant influence on self-reported ratings of fatigue at rest
C	Coleus forskohlii	↓	★☆☆☆☆ Minor	1 study	Less fatigue reported as a side-effect, no comparator or ability to assess potency.
C	Vitamin C	↓	★☆☆☆☆ Minor	1 study	A decrease in fatigue has been noted in obese adults given Vitamin C in conjunction with exercise
C	7-Keto DHEA	—	—	1 study	Insufficient evidence to support changes in fatigue and energy following 7-keto supplementation.
C	Caffeine	↓	★☆☆☆☆ Minor	2 studies	Decrease in fatigue have been noted during exercise and during low strenuous physical exercise
C	Methylsulfonylmethane	—	—	1 study	No significant influence on exercise related fatigue

C	L-Tyrosine	—	—	1 study	No significant influence has been noted on fatigue from L-Tyrosine supplementation during acute stresses
C	Tribulus terrestris	—	—	2 studies	Exercise related fatigue and vigor is unaffected by tribulus supplementation in trained men
C	Ganoderma lucidum	↓	★☆☆ Minor	2 studies	A decrease in fatigue has been noted, but secondary to disease states characterized by fatigue. Usage of Reishi to reduce fatigue outright or to aid exercise is unexplored
C	Pyruvate	↓	★☆☆ Minor	1 study	May reduce fatigue during weight loss periods
C	Choline	—	—	2 studies	No significant influence on fatigue in exercise that is not associated with choline depletion (such as loaded carries) or in trained athletes, which do not appear to be depleted in choline
C	Quercetin	—	—	1 study	No significant influence on fatigue nor vitality in otherwise healthy persons
C	Phosphatidylserine	↓	★☆☆ Minor	2 studies	Unreliable effects, but a quite notable reduction in fatigue has been noted during intense exercise (85% VO2 max) which resulted in increased time to exhaustion. This was not present at lower intensities
C	Fish Oil	—	—	2 studies	No demonstrable benefit to fatigue
C	HMB	—	—	2 studies	No significant reduction in exercise-induced fatigue associated with HMB supplementation in athletes

C	Ornithine	↓	★☆☆ Minor	2 studies	A reduction in fatigue has been noted for both prolonged exercise, hepatic pathology, and for hangovers; all situations characterized by excessive ammonia concentrations in the blood.
C	Citrulline	↓	★★★☆☆ Notable	3 studies	The decrease in fatigue during exercise is thought to underlie most of the benefit seen with training capacity (work volume), although in men who self-report fatigue issues supplemental citrulline appears to help with that as well (independent of exercise)
C	Ashwagandha	↓	★☆☆ Minor	2 studies	Secondary to its adaptogenic effects, ashwagandha is able to reduce the perceptions of fatigue with prolonged daily usage.
C	Curcumin	↓	★☆☆ Minor	1 study	A decrease in postoperative fatigue has been noted with curcumin supplementation
C	Glycine	↓	★☆☆ Minor	2 studies	The reduction in fatigue may solely be secondary to how Glycine supplementation can improve sleep quality
C	Cocoa Extract			1 study	
C	Valeriana officinalis	↓	★☆☆ Minor	1 study	One study assessing valerian in persons with cancer on chemotherapy (of which insomnia may be a side effect of chemotherapy) found reductions in sleep disturbances which manifested as less fatigue during the day; no other evidence at this point in time.
C	Colostrum	↓	★★★☆☆ Notable	2 studies	Both studies on fatigue assessed persons with HIV-related diarrhea, but when diarrhea was successfully (and greatly) benefited with

					colostrum containing porridge fatigue was reduced by over 80% of baseline values. It is uncertain if this anti-fatigue effect influences other persons.
D	Spirulina	—	—	1 study	Currently no evidence to support an improvement in fatigue symptoms
D	Melissa officinalis	↓	★☆☆ Minor	1 study	A decrease in fatigue associated with anxiety has been noted, no research looking at the <i>per se</i> influence of lemon balm on fatigue
D	Pyrroloquinoline quinone	↓	★☆☆ Minor	1 study	A decrease in fatigue has been noted in older adults with self-reported energy problems
D	Vitamin B12			1 study	
D	Phenylpiracetam	—	—	1 study	Despite the usage of phenylpiracetam to treat asthenia, the lone study assessing this in persons with traumatic brain injuries failed to find a benefit (which may be a false negative if phenylpiracetam is inactive on brain injuries in the first place).

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Fatigue Resistance

Fatigue Resistance tends to refer to the resilience of the body towards developing fatigue (a sort of preeminative anti-fatigue effect), and supplements that enhance fatigue resistance are thought to be anti-stress and adaptogenic.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Creatine	↑	★☆☆ Minor	8 studies	Small degree of fatigue reduction during exercise, but appears unreliable.
C	Eleutherococcus senticosus	↑	★☆☆ Minor	2 studies	May increase physical performance, but is unreliable in doing so
C	Astaxanthin			1 study	

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Fecal Moisture

Fecal moisture is the measurement of water in feces, which contributes to the bulk thereof. This is an indicator of dietary soluble fiber (which resorbs water) and higher moisture eases the passing of stool.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Psyllium	↑	★★★ Strong	4 studies	Psyllium is the reference drug for increasing water content of stool.
C	Yacon	↑	★☆☆ Minor	1 study	A mild increase in fecal moisture and consistency has been reported with consumption of yacon syrup, thought to be related to prebiotic effects and a reduction in intestinal motility.

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Fecal Weight

Fecal weight refers to the overall weight of a bowel movement, and increases in fecal weight (independent of changes in food intake) tend to reflect water accumulation and retention by soluble fibers.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Psyllium	↑	★★★ Strong	4 studies	Psyllium tends to be the reference drug for increasing fecal weight, and due to that and the reliability of which this occurs it gets a strong rating
D	Colostrum	↓	★☆☆ Minor	1 study	A decrease in fecal weight has been noted in a trial assessing diarrhea, which was thought to be a consequence of successfully treating diarrhea.

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Fertility

Fertility refers to the capacity to create children, and in regards to supplementation this tends to refer to seminal parameters such as semen quality or semen motility.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Zinc	↑	★☆☆ Minor	4 studies	Zinc can increase the fertility of men who are infertile <i>and</i> have low circulating testosterone, and appears ineffective in men who have normal testosterone levels with infertility. This is related to an increase in sperm count seen in the former group.
B	Inositol	↑	★★★☆☆ Notable	9 studies	In women with PCOS, very low doses of inositol (200mg) and greater can reliably and significantly increase ovulation and fertility rates.
C	Dehydroepiandrosterone	↑	★☆☆ Minor	2 studies	An increase in fertility has been noted with DHEA supplementation
C	Astaxanthin			1 study	
D	D-Aspartic Acid	↑	★★★☆☆ Notable	2 studies	Limited evidence for D-aspartic acid suggest an increase in fertility of men, with one study noting that a group went from no conceptions to 26.6% of subjects reporting conception over 90 days.
D	Coenzyme Q10	↑	★☆☆ Minor	1 study	Insufficient evidence to support whether the increase in fertility is large or not, but preliminary evidence suggests that it exists.

Fever

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Pelargonium sidoides	↓	★★★☆☆ Notable	9 studies	Fever as a side effect of acute bronchitis is reduced quite potently (80-90% of persons reporting elimination of fever) due to the potent treatment of acute bronchitis, but there is no inherent anti-pyretic effect of this herb in other instances.

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Fibrinogen

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Melatonin	↑	★☆☆ Minor	1 study	An increase in fibrinogen has been noted
C	Hesperidin	—	—	1 study	No significant alterations in fibrinogen content have been noted with oral supplementation of hesperidin
C	Red Clover Extract	—	—	2 studies	No known changes to circulating fibrinogen concentrations.
C	Trimethylglycine	—	—	1 study	No significant alterations in fibrinogen concentrations seen with supplementation of betaine.
D	Nattokinase	↓	★☆☆ Minor	1 study	A decrease in fibrinogen appears to exist following nattokinase ingestion
D	Salvia hispanica	↓	★☆☆ Minor	1 study	A decrease in fibrinogen has been noted with chia seed ingestion according to one study

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Follicle-Stimulating Hormone

Follicle stimulating hormone (FSH) is a pituitary hormone similar to luteinizing hormone that positively regulates fertility and spermatogenesis.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Maca	—	—	3 studies	No significant influence on follicle stimulating hormone noted
B	Red Clover Extract	—	—	6 studies	No significant influence on FSH seen with oral supplementation of red clover to postmenopausal women
C	Ashwagandha	↓	★☆☆ Minor	2 studies	Not overly notable, but a decrease has reached statistical significance
C	Shilajit	↑	★☆☆ Minor	1 study	An increase in follicle-stimulating hormone has been detected with shilajit consumption
C	Coenzyme Q10	↓	★☆☆ Minor	1 study	A decrease in follicle stimulating hormone has been detected
C	Dehydroepiandrosterone	—	—	2 studies	No significant alterations in follicle-stimulating hormone levels
C	Vitamin E	—	—	1 study	FSH does not appear to be influenced following supplementation of vitamin E.
C	Velvet Antler	—	—	1 study	No alterations in FSH levels have been noted with velvet antler supplementation

C	Astaxanthin			1 study	
C	Chromium	—	—	1 study	No significant influence of chromium supplementation on follicle stimulating hormone (FSH) in women with PCOS relative to placebo.
C	Saffron	—	—	1 study	FSH is unaffected in infertile men given 60mg saffron daily over the course of 26 weeks.
D	Alcohol	↑	★☆☆ Minor	2 studies	Mixed effects on FSH, but although null effects have been reported an increase may be possible
D	Licorice	—	—	1 study	No significant alterations in follicle stimulating hormone seen with licorice consumption
D	Pueraria lobata	—	—	1 study	No significant alterations have been noted in follicle-stimulating hormone concentrations following pueraria lobata ingestion.
D	Zinc	—	—	1 study	No detectable influence of zinc supplementation of FSH concentrations in zinc deficient persons.
D	Ginger	↑	★☆☆ Minor	1 study	A 17.6% increase in follicle stimulating hormone has been noted in infertile men given ginger, which is thought to underlie the observed pro-seminal effects of supplementation.

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Food Intake

Food intake refers to the quantitative amount of food ingested over a designated period of time, and does not necessarily reflect hunger nor appetite. Appetite suppressants should result in a reduction in food intake.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	HMB	—	—	4 studies	Although there are sporadic alterations seen in food intake in studies using HMB supplementation, they are not reliable and the exact change observed changes. It is likely that there is no significant effect per se and this is due to the study population
B	Chromium	—	—	4 studies	No significant influence on food intake in standard diabetics, although limited evidence suggest a possible role specifically in persons who self-report elevated carbohydrate cravings and inappropriate eating patterns due to urges.
C	Stevia	↓	★☆☆ Minor	1 study	Stevia, in place of caloric sweeteners, has been associated with reducing whole-day food intake.
C	Garcinia cambogia	—	—	1 study	Food intake appears to be unaltered following ingestion of garcinia supplements, which is different than results seen in rats
C	Grape Seed Extract	↓	★☆☆ Minor	1 study	A decrease in voluntary food intake has been noted with grape seed extract ingestion, appetite <i>per se</i> not measured
C	Vitamin D	—	—	1 study	

C					No significant alterations in food intake noted with Vitamin D supplementation
C	Fish Oil	—	—	2 studies	There does not appear to be a significant influence of fish oil supplementation on food intake
C	Vitamin K	—	—	1 study	Studies that happen to measure dietary intake fail to note any influence of supplemental Vitamin K
C	Nigella sativa	—	—	1 study	No significant alterations in food intake associated with ingestion of nigella sativa.
C	Capsaicin			1 study	
C	Creatine	—	—	2 studies	Creatine supplementation does not appear to significantly alter food intake (unconsciously).
C	Garlic	—	—	1 study	No significant alterations in food intake are seen with garlic ingestion (assuming no taste aversion).
C	Saffron	↓	★☆☆ Minor	1 study	Secondary to reducing snacking (thought to be via increasing satiety from meals) saffron appears to reduce overall food intake.
D	Milk Protein	↓	★☆☆ Minor	1 study	Appears to reduce food intake, a phenomena common to all protein sources
D	Psyllium	—	—	1 study	Failed to significantly influence food intake
D	Ascophyllum nodosum	↓	★☆☆ Minor	1 study	The reduction in voluntary food intake noted was 16.4% of a test meal (which was 80kcal in this study) and is not likely to make significant effects during

					weight loss.

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Forgetting

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Bacopa monnieri	↓	★☆☆ Minor	1 study	A small reduction of acute forgetting (just during a task, not outright amnesia) has been noted, which may contribute better to long term memory (ie. grasping concepts better)
C	Pramiracetam	↓	★☆☆ Minor	1 study	Appears to decrease the influence of amnesiac drugs (scopolamine), and is effective when loaded over a few days rather than relying on acute administration
C	Inositol	—	—	1 study	Electroconvulsion therapy induced amnesia is not prevented with oral administration of 6g <i>myo</i> -inositol preloaded for five days
D	Phosphatidylserine	↓	★☆☆ Minor	1 study	A reduced rate of forgetting immediate information (results in 'grasping' information easier) has been noted during treatment of cognitive decline with PS; an inherent anti-amnesiac effect is not known

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Free Testosterone

Free testosterone is a measurement of testosterone that is not bound to SHBG, and is thought to be more reflective of the effects of testosterone than a basic blood measurement of testosterone.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Dehydroepiandrosterone	↑	★☆☆ Minor	2 studies	Increases in free testosterone have been noted to coincide with testosterone increases (which are unreliable)
C	Vitamin E	—	—	1 study	Vitamin E does not appear to alter the concentrations of free testosterone in serum following supplementation.
C	Zinc	↑	★☆☆ Minor	2 studies	Free testosterone follows the same trends as testosterone, and may be increased following supplementation in persons who are deficient in zinc
C	Velvet Antler	—	—	1 study	Free testosterone was unaltered with velvet antler relative to placebo
C	Nigella sativa	—	—	1 study	No significant influence on circulating free testosterone concentrations in men with central obesity
C	Chromium	—	—	1 study	No significant influence of chromium supplementation on free testosterone concentrations in women with PCOS.
D	Boron	↑	★☆☆ Minor	1 study	Appears to be quite effective, but requires some more robust trials

D	Calcium			1 study	

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Fructosamine

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Fish Oil	—	—	1 study	No evidence to support an increase in fructosamine, which alongside HbA1c is thought to indicate pathology from elevated blood glucose (fish oil appears to elevate glucose, but does not appear to be associated with higher diabetes risk)
C	Psyllium	↓	★☆☆ Minor	1 study	A decrease in fructosamine has been noted in diabetics supplementing psyllium husk.
C	Chromium	↓	★☆☆ Minor	2 studies	Both studies assessing fructosamine have found a mild decrease.
D	Ruscus aculeatus	↓	★☆☆ Minor	1 study	A 7.8% reduction in fructosamine has been noted with supplementation of <i>ruscus aculeatus</i> in diabetic persons.

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Functionality in Elderly or Injured

Supplements that improve symptoms of osteoarthritis, reduce the risk of falls, or improve muscle function in elderly persons tend to improve physical function and movement resulting in increased quality of life.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	S-Adenosyl Methionine	↑	★☆☆ Minor	3 studies	Somewhat of an increase in functionality of elderly persons, most likely secondary to the beneficial effects on joint health.
B	Dehydroepiandrosterone	—	—	3 studies	Most evidence measuring functionality in elderly persons have not found any improvement with DHEA supplementation, although it is possible that DHEA may play a role
C	Creatine	↑	★☆☆ Minor	2 studies	Possibly an effect, but the less reliable effects of creatine in the older population (which seem to respond less) seems to manifest here.
C	Nitrate	—	—	1 study	No significant influence has been noted on functional tests in elderly persons given nitrate supplementation
C	Kaempferia parviflora	↑	★☆☆ Minor	1 study	Grip strength has been found to be increased in elderly persons associated with supplementation at low doses
C	Vitamin D	↑	★★★☆☆ Notable	1 study	An improvement in muscular and neural functionality in the elderly is thought to underlie the reductions of fall risk and reduced bone fracture rate seen in elderly cohorts

C	Krill Oil	↑	★☆☆ Minor	1 study	The increase in functionality appears to be secondary to reductions in symptoms of rheumatoid arthritis
C	Oxiracetam	—	—	1 study	The one study to note functional capabilities in persons with dementia given oxiracetam failed to find a significant treatment effect
C	Phenylpiracetam	↑	★☆☆ Minor	1 study	Physical function and activities of daily living in elderly persons after a stroke appear to be benefitted with phenylpiracetam. While it should work in elderly persons without cognitive impairment, this has not been tested
C	Curcumin	↑	★★★ Notable	2 studies	In persons with osteoarthritis, the performance on a treadmill test after eight months was significantly increased (more than twice the distance covered with curcumin relative to control).
C	Zinc	↑	★☆☆ Minor	1 study	An increase in functionality of elderly frail persons has been seen with zinc supplementation, thought to be related to the increase in IGF-1 also observed.
D	Vinpocetine	↑	★☆☆ Minor	1 study	An improvement in balance has been noted with vinpocetine ingestion in the elderly, which may be related to the attenuation of cognitive decline
D	Cissus quadrangularis	↑	★★★ Notable	1 study	An increase in the function of the joint appears to occur alongside reductions in perceived pain and soreness when cissus treats athletic joint pain; one of the few options that sees to benefit athletes.

Gastrin

Gastrin is a peptide hormone that stimulates the production of stomach acid, and is required for proper digestion of protein-containing foods. Its overproduction is thought to contribute to heartburn at times.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Melatonin	↑	★★★☆☆ Notable	4 studies	There appears to be an increase in serum gastrin levels following ingestion of melatonin in persons with stomach ulceration, this increase is thought to be related to the ulcer healing effects of melatonin

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General Oxidation

General oxidation refers to a collection of biomarkers in the blood that are thought to reflect oxidative damage to the body. A reduction in these biomarkers is antioxidative, while an increase in prooxidative.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Vitamin E	↓	★☆☆ Minor	10 studies	Supplementation of vitamin E appears to reduce oxidation in plasma, requiring over 500mg (if not more) α-tocopherol in states where there is abnormal elevations of oxidation. Vitamin E is without effect at lower doses or in persons without abnormal oxidation levels.
B	Coenzyme Q10	↓	★☆☆ Minor	6 studies	Appears to generally reduce pro-oxidative biomarkers in the body
B	Vitamin C	↓	★☆☆ Minor	6 studies	Surprisingly mixed influences on biomarkers of oxidation, with either a decrease or no significant influence the majority of the time (with limited evidence to hint at an increase being possible)
B	Alpha-Lipoic Acid	↓	★☆☆ Minor	6 studies	Appears to reduce biomarkers of oxidation
B	Curcumin	↓	★☆☆ Minor	5 studies	Prooxidative biomarkers appear to be reduced following long term supplementation of curcumin
B	Rooibos	↓	★☆☆ Minor	3 studies	A decrease sometimes occurs, although this has not been noted in all instances. The decrease in healthy persons is minor and lasts for about 5 hours, whereas it may be more prominent in persons at risk for cardiovascular disease

B	Astaxanthin			3 studies	
B	Chromium	↓↑	★☆☆ Minor	4 studies	Mixed evidence leaning towards no effect, although a possible antioxidative effect remains possible in persons with high baseline HbA1c and a prooxidative effect in persons with normal HbA1c.
C	Quercetin	↓	★☆☆ Minor	2 studies	May reduce oxidative biomarkers in serum and urine, but is a tad unreliable in doing so.
C	Panax ginseng	↓	★☆☆ Minor	1 study	Oxidation in the body appears to be reduced, which is thought to be secondary to induction of antioxidant enzymes
C	Grape Seed Extract	↓	★☆☆ Minor	3 studies	A decrease in whole body oxidation appears to occur following ingestion of grape seed extract
C	Spirulina	↓	★★★☆☆ Notable	1 study	Notable due to mechanisms, but requires studies with reference drugs and more biomarkers measured.
C	Olive leaf extract	↓	★☆☆ Minor	1 study	Is able to reduce oxidative parameters in the blood when they are measured.
C	Resveratrol	↓	★☆☆ Minor	1 study	A decrease in oxidative biomarkers has been noted following resveratrol supplementation
C	Methylsulfonylmethane	↓	★☆☆ Minor	2 studies	A reduction in oxidative biomarkers has been noted following MSM ingestion
C	Ganoderma lucidum	—	—	2 studies	No significant alterations in whole-body oxidation are apparent

C	Japanese Knotweed	↓	★☆☆ Minor	1 study	Appears to reduce oxidative biomarkers, requires more evidence to gauge potency and reliability thereof
C	Melatonin	↓	★☆☆ Minor	1 study	May decrease biomarkers of oxidation in serum
C	Pycnogenol	↓	★☆☆ Minor	2 studies	A reduction in general oxidation is noted following prolonged Pycnogenol supplementation
C	Fish Oil	↑	★☆☆ Minor	2 studies	May increase general oxidation in the body, but seems unreliable in doing so
C	Arginine	↓	★☆☆ Minor	1 study	A decrease in oxidation has been noted in persons with impaired glucose tolerance, thought to be associated with the increase in superoxide dismutase activity
C	Blueberry	↓	★☆☆ Minor	3 studies	Oral ingestion of berries or their extracts tends to reduce oxidative biomarkers and improve antioxidant status either acutely or with daily supplementation
C	Ginkgo biloba	↓	★☆☆ Minor	1 study	There appears to be a reduction in general oxidation as assessed by biomarkers (reduced glutathione, etc.) associated with supplementation of ginkgo biloba
C	Zinc	—	—	1 study	No significant interaction with biomarkers of general oxidation
C	Inositol	↓	★☆☆ Minor	1 study	There may be a reduction in oxidation associated with PCOS when the condition is being treated by inositol
C	Hesperidin	—	—	1 study	

					General oxidative parameters do not appear to be significantly altered with supplementation of hesperidin under resting conditions.
C	Creatine			1 study	
C	Red Clover Extract	—	—	1 study	There does not appear to be a significant influence on oxidative parameters seen with supplementation of red clover isoflavones.
D	Green Tea Catechins	↓	★☆☆ Minor	1 study	Can decrease oxidation in the body (assessed via oxidative biomarkers)
D	L-Carnitine	↓	★☆☆ Minor	1 study	Reduction in general oxidation seems to be secondary to antioxidant enzyme induction
D	Aronia melanocarpa	↓	★★★☆☆ Notable	1 study	Requires more evidence, but it appears to reduce oxidative parameters more than other supplements.
D	Yerba mate	↓	★☆☆ Minor	1 study	A decrease in serum oxidative parameters tends to be noted following Mate consumption
D	Hibiscus sabdariffa	↓	★☆☆ Minor	1 study	Appears to reduce oxidative biomarkers in the body, surprisingly not the potency one would expect from <i>in vitro</i> evidence
D	Melissa officinalis	↓	★☆☆ Minor	1 study	A decrease in general oxidation occurs following lemon balm ingestion
D	Punicalagins	↓	★☆☆ Minor	1 study	A decrease in general oxidation has been noted with punicalagins
D	Garlic	↓	★☆☆ Minor	1 study	Oxidative biomarkers in the blood appear to be modestly reduced following

					supplementation of garlic in persons with high levels of oxidative damage indicative in serum.
D	Pyrroloquinoline quinone	—	—	1 study	Overall oxidation in serum as assessed by TRAP has failed to be significantly influenced by PQQ supplementation in otherwise healthy adults.

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Ghrelin

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Whey Protein	↓	★☆☆ Minor	1 study	A decrease in Ghrelin has been observed with whey protein supplementation.
C	Melatonin	↑	★☆☆ Minor	2 studies	An increase in Ghrelin appears to exist following acute supplementation of melatonin
C	Colostrum	—	—	1 study	Circulating ghrelin does not appear to be modified in response to colostrum supplementation.

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Glycemic Control

Glycemic controls refers to the ability to maintain somewhat controlled fluctuations in blood glucose following ingestion of carboydrates or fasting, which is important for persons who are insulin resistant or diabetic.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Creatine	↑	★☆☆ Minor	2 studies	Appears to be somewhat effective in diabetics for improving glycemic control.
C	Fenugreek	↑	★☆☆ Minor	1 study	May improve glycemic control secondary to reduction in blood glucose, although this may be more indicative of fenugreek fibers than the saponin content
C	Chlorogenic Acid	↓	★☆☆ Minor	1 study	Slight increase in glycemic control possibly secondary to reducing carbohydrate absorption
C	Vitamin C	—	—	1 study	No significant influence on glycemic control in diabetics with Vitamin C supplementation
D	Alpha-Lipoic Acid	—	—	1 study	No significant practical benefit on glycemic control noted

Glycogen Resynthesis

Glycogen resynthesis refers to the rate of glycogen replenishment following its depletion from exercise, and supplements that increase the rate of glycogen repletion are thought to be useful to athletes with a high workload and carbohydrate intake.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Fenugreek	↑	★☆☆ Minor	2 studies	Mixed influence on glycogen resynthesis rates, but may have a possible benefit
C	Creatine	↑	★★★☆☆ Notable	1 study	Degree of improvement is somewhat more potent than other supplemental options, and may be related to the improvements in glycemic control seen with creatine.
C	Chromium	—	—	1 study	When testing the addition of chromium to a glycogen repletion protocol (after exercise), chromium failed to augment the replenishment from carbohydrates any more than placebo.
D	Vanadium	↑	★☆☆ Minor	1 study	An increase in glycogen content has been noted in diabetic persons given vanadium, no studies in athletes currently

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Growth Hormone

Growth hormone (GH) is a peptide hormone that regulates growth in youth, and in adults is thought to promote fat loss and longevity. Increasing growth hormone should improve these goals, but supplements are currently lacklustre.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Arginine	↓ ↑	★☆☆ Minor	7 studies	Arginine has been implicated in increasing growth hormone (at rest) and suppressing an exercise-induced increase in growth hormone; both of these are short in duration, and it is unsure if there are any long lasting effects of such short a spike.
C	Melatonin	↑	★☆☆ Minor	2 studies	Appears to increase circulating levels of growth hormone
C	Beta-Alanine	—	—	1 study	
C	Nicotine	↓	★☆☆ Minor	1 study	An acute suppression of growth hormone has been noted with nicotine to a small degree
C	Alpha-GPC	↑	★☆☆ Minor	2 studies	Has noted an increase in circulating growth hormone, but measurements were acute (whole-day measurements of growth hormone are more reliable due to hourly fluctuations)
C	Velvet Antler	—	—	1 study	No significant influence on growth hormone levels
C	Gamma Oryzanol	—	—	1 study	No significant alterations in growth hormone following ingestion of gamma-oryzanol
C	HMB	—	—	1 study	

C					Serum growth hormone is not significantly altered with HMB supplementation in athletes
C	Citrulline	↑	★☆☆ Minor	2 studies	An increase in growth hormone has been noted with exercise, but not at rest. Practical significance of this information is unknown, since Arginine supplementation has unreliable effects itself
C	Creatine	↓ ↑	★★★☆☆ Notable	4 studies	Creatine is able to suppress growth hormone secretion during exercise when loaded (up to 35%) and to a lesser degree during maintenance (5% or less) while creatine at rest can spike growth hormone up to 83+/-45%. This bidirectional effect is similar to Arginine supplementation.
C	Trimethylglycine	—	—	1 study	The minor increase in growth hormone seen with betaine (6.1%), relative to placebo, failed to reach statistical significance and is too low of magnitude to consider it practically appreciable.
D	Alcohol	↓	★☆☆ Minor	1 study	An acute suppression of growth hormone is noted with alcohol ingestion
D	Phosphatidylserine	—	—	1 study	No significant influence on exercise-induced growth hormone
D	Dehydroepiandrosterone	↑	★☆☆ Minor	2 studies	May increase growth hormone concentrations, but this appears to be unreliable
D	Colostrum	—	—	1 study	There does not appear to be a significant influence of colostrum supplementation on circulating GH following oral supplementation relative to other protein sources.

Hair Regrowth

Hair regrowth refers to the rate of which hair grows, and may also refer to attenuating or reversing forms of alopecia (hair loss). These supplements can be both ingested or applied topically to the scalp.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Minoxidil	↑	★★★☆☆ Notable	8 studies	Topical application of Minoxidil (oral administration as well, but that is associated with more side-effects) appears to be highly effective in increasing the rate of hair regrowth and can reverse hair loss associated with non-androgenic hair loss (bald patch, rather than a receding hair line which is related to androgens)
C	Vitamin E	↑	★★☆☆☆ Minor	1 study	One study noted that 100mg of mixed tocopherol was able to promote hair growth in persons with alopecia (androgen dependence not specified) relative to placebo.
D	Raspberry Ketone	↑	★★☆☆☆ Minor	1 study	May induce hair growth when topically applied

HbA1c

HbA1c (Glycated hemoglobin) is a biomarker of glucose metabolism, and higher HbA1c is associated with more disease progression and comorbidities in states of insulin resistance or diabetes.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Fish Oil	—	—	10 studies	Although the majority of evidence suggests absolutely no influence on HbA1c, reductions have been reported and a lone case has noted a clinically irrelevant increase of HbA1c (secondary to the increase in glucose). Practically, there is unlikely to be any large changes
A	Chromium	—	—	17 studies	Although sporadic evidence suggest improvements in HbA1c in diabetics, the entirety of the evidence does not support a reliable and significant improvement in diabetic persons.
B	Coenzyme Q10	↓	★☆☆ Minor	3 studies	There may be an effect on HbA1c, but it appears unreliable and not overly potent.
B	Berberine	↓	★★★★ Strong	2 studies	The reduction of HbA1c associated with berberine, according to a meta-analysis of diabetics using 1,000-1,500mg berberine daily, was -0.72% (95% CI -0.97 to -0.47) more than placebo. This reduction appears to be one of the more significant reductions associated with dietary supplements.
B	Psyllium	↓	★☆☆ Minor	2 studies	Reduction seen in HbA1c was not overly remarkable

B	Conjugated Linoleic Acid	—	—	3 studies	No significant reduction (or increase) in HbA1c levels following CLA supplementation
B	Magnesium	↓	★☆☆ Minor	3 studies	More evidence than not suggest no significant effect on HbA1c levels, but one study suggests a decent decrease with the other two studies trending towards a decrease. There may be a role for magnesium in reducing HbA1c levels to a minor degree
C	Alpha-Lipoic Acid	↓	★☆☆ Minor	3 studies	There appears to be a slight reducing effect on HbA1c
C	Vitamin D	—	—	2 studies	The decrease in HbA1c is statistically insignificant and very small in magnitude, likely not a concern.
C	Vitamin C	—	—	1 study	No significant influence of Vitamin C supplementation on HbA1c levels
C	Panax ginseng	↓	★☆☆ Minor	2 studies	A possible reduction in HbA1c, but small in magnitude and unreliably seen
C	Spirulina	↓	★★★☆☆ Notable	2 studies	Lone study noted a decrease from 9% to 8% with 2g spirulina, which is somewhat notable but requires more evidence to establish this.
C	Gynostemma pentaphyllum	↓	★★★☆☆ Notable	2 studies	Preliminary evidence in diabetics suggest potent HbA1c reducing effects (6g of the root reducing HbA1c by 2% over a few months)
C	Benfotiamine	—	—	2 studies	Two studies in diabetics have failed to find an influence of benfotiamine on HbA1c
C	Olive leaf extract	↓	★☆☆	1 study	A minor decrease in HbA1c

			Minor		A minor decrease in HbA1c has been noted with olive leaf consumption
C	Stevia	—	—	1 study	No significant influence on HbA1c serum levels has been detected
C	Salacia reticulata	↓	★☆☆ Minor	1 study	A decrease in HbA1c has been noted in diabetics given a tea of Salacia for months, but the decrease was minor in magnitude and outperformed by Glibenclamide
C	Royal Jelly	—	—	1 study	No significant alterations in HbA1c levels following Royal Jelly ingestion for 6 months
C	Arginine	—	—	2 studies	No significant influence on HbA1c concentrations in persons with impaired glucose tolerance, even when endothelial function is improved
C	Hesperidin	—	—	1 study	Alongside a failure to improve insulin sensitivity or to reduce glucose was a failure to reduce HbA1c concentrations in the plasma of those with metabolic syndrome given 500mg hesperidin.
C	Citrullus colocynthis	↓	★☆☆ Minor	1 study	May be able to mildly decrease HbA1c, although the research supporting this claim is very preliminary at this time.
C	Red Clover Extract	—	—	1 study	No significant changes in HbA1c seen with supplementation of red clover in diabetics.
C	Astaxanthin			2 studies	
C	Rose Hip	—	—	1 study	No significant influence of rose hip on HbA1c concentrations in the blood of non-diabetic yet obese persons relative to

					placebo
C	Vitamin E	—	—	2 studies	HbA1c does not appear to be influenced in type II diabetics given supplementation of vitamin E.
D	Aronia melanocarpa	↓	★☆☆ Minor	1 study	Requires more studies before conclusions can be made, appears to simply be exerting anti-oxidant effects.
D	Yerba mate	↓	★☆☆ Minor	1 study	A decrease in HbA1c levels has been detected in type II diabetics consuming Mate tea, although not to a remarkable degree
D	Sulbutiamine	—	—	1 study	No significant influence of sulbutiamine on HbA1c
D	Salvia hispanica	—	—	1 study	No significant influence on HbA1c levels of diabetics given chia seeds
D	Vanadium	↓	★☆☆ Minor	2 studies	A decrease in HbA1c has been noted with vanadium supplementation
D	Tetradecyl Thioacetic Acid	—	—	2 studies	No significant alterations in HbA1c concentrations
D	Safflower Oil	↓	★☆☆ Minor	1 study	A slight decrease in HbA1c has been noted with safflower despite no alterations in any other diabetic biomarker
D	Blueberry	—	—	1 study	Currently no studies noting changes in HbA1c, as it appears to be unaffected by supplementation.
D	Nigella sativa	↓	★☆☆ Minor	1 study	A mild decrease in HbA1c has been noted in diabetics given the seeds as an adjuvant to standard therapy

D	Moringa oleifera	↓	★☆☆ Minor	1 study	The reduction of HbA1c noted is minor, from 7.8% down to 7.4% with 90 days supplementation of the leaf extracts
D	Ruscus aculeatus	↓	★★☆☆ Notable	1 study	The decrease in HbA1c noted in this pilot study (15.6%) was fairly marked and requires replication.

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HDL-C

High Density Lipoprotein Cholesterol (HDL-C) is seen as the 'good' cholesterol (relative to LDL-C). Its job is to bring circulating cholesterol and fatty acids back to the liver tissue and clear them from the blood; high levels are desired to protect the heart.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Conjugated Linoleic Acid	—	—	15 studies	Insufficient evidence to support significant influences on HDL-C
A	Policosanol	↑	★☆☆ Minor	12 studies	Unlikely to be potent, either small or no increases in HDL-C are likely to occur after policosanol ingestion. A good deal of the literature is based upon some highly suspicious past research from Cuba
A	Fish Oil	↑	★☆☆ Minor	27 studies	Mixed evidence, but a possible increase in HDL-C is seen with fish oil supplementation in unhealthy persons
A	Garlic	↑	★★★☆☆ Notable	14 studies	Garlic supplementation tends to increase HDL cholesterol in persons with cardiovascular disease risk reliably and in the range of 10-15% when looking at individual trials and by 1.49mg/dL (95% CI of 0.19-2.79mg/dL) as assessed by meta-analysis.
A	Red Clover Extract	—	—	13 studies	Similar to other lipid parameters, despite an increase (10-20%) being noted in a few studies the best evidence to date does not support this conclusions and the benefits, when they occur, are unreliable.
A	Chromium	—	—	16 studies	

A					Although an increase in insulin sensitivity in diabetics should increase HDL cholesterol, the best evidence to date does not support a role for chromium supplementation in improving HDL cholesterol in diabetics.
B	Green Tea Catechins	↑	★☆☆ Minor	3 studies	Mixed effects with somewhat of an increase, not to a remarkable magnitude
B	Curcumin	↑	★☆☆ Minor	3 studies	Possible increases in HDL-C
B	Dehydroepiandrosterone	—	—	5 studies	Most of the evidence leans towards no significant influence of DHEA on HDL-C levels
B	Spirulina	↑	★☆☆ Minor	7 studies	A positive influence of spirulina on HDL-C appears to be present, but the magnitude of benefit is not overly remarkable and varies depending on the disease state (with states associated with fatty liver having a much greater increase in HDL-C seen with spirulina)
B	Berberine	↑	★☆☆ Minor	1 study	Degree of improvement was 0.07mmol/L (95% CI 0.04 to 0.10) according to the meta-analysis, not remarkably effective
B	Psyllium	↓	★☆☆ Minor	3 studies	Similar to the reductions in LDL-C and total cholesterol, the reduction in HDL-C is seemingly small in magnitude and likely not much to be concerned about
B	Olive leaf extract	↑	★☆☆ Minor	7 studies	The increase in HDL seen with olive phenolics is somewhat inconsistent and not to a large magnitude when it occurs
B	Grape Seed Extract	—	—	3 studies	No significant influence on

					HDL-C even at up to 600mg GSE daily in a high risk population
B	L-Carnitine	—	—	2 studies	No significant changes in HDL cholesterol seen with supplementation
B	Magnesium	—	—	4 studies	For the most part, there is no significant direct influence of magnesium on HDL-C levels. Some counter evidence suggests it may occur vicariously through betterment of glycemic control in diabetics, but that is not always seen
B	Inositol	↑	★☆☆ Minor	5 studies	An increase in circulating HDL-C is seen in women with PCOS getting inositol therapy
B	Nigella sativa	—	—	8 studies	Mild increases have been reported in some cases, but for the most part <i>nigella sativa</i> does not influence HDL cholesterol in the active dosage range.
B	Hesperidin	—	—	5 studies	There is no significant or long lasting effect on HDL cholesterol seen with hesperidin, except maybe a very small (less than 5%) increase in those with the lowest levels of HDL which fades after cessation of supplementation.
B	Trimethylglycine	—	—	3 studies	No significant alterations in circulating HDL-C are seen with prolonged supplementation of betaine in persons with metabolic impairment.
B	Astaxanthin			4 studies	
B	Vitamin E	—	—	4 studies	The majority of evidence has failed to find any influence of vitamin E supplementation on

					HDL total levels or particulates relative to placebo.
C	Fenugreek	↑	★☆☆ Minor	1 study	An increase in HDL-C has been associated with fenugreek ingestion
C	Pyruvate	—	—	2 studies	No significant influence on HDL-C levels
C	Ephedrine	↑	★☆☆ Minor	2 studies	An increase in HDL-C has been noted with ingestion of ephedrine, may be confounded with weight loss also seen in the trials
C	Ginger	↑	★☆☆ Minor	1 study	May increase HDL-C levels
C	Quercetin	↑	★☆☆ Minor	2 studies	An increase in HDL-C has been noted following quercetin supplementation
C	Black Cohosh	—	—	1 study	No significant influence on HDL-C
C	Punicic Acid	↑	★☆☆ Minor	2 studies	Although there are possible increases in HDL-C with punicic acid, this has not been noted all the time and may be unreliable
C	Whey Protein	—	—	2 studies	No significant evidence to support an increase in HDL-C with whey protein
C	Vanadium	—	—	2 studies	No significant influence on HDL-C levels in serum of obese subjects
C	Artichoke Extract	—	—	3 studies	There does not appear to be an inherent effect of Artichoke on HDL-C, although the one study in diabetics suggest that HDL-C might increase when glucose is decreased.

C	Licorice	—	—	1 study	No significant influence of licorice on HDL
C	Gynostemma pentaphyllum	—	—	1 study	HDL appears unaffected
C	Green Coffee Extract	—	—	1 study	No significant alterations in HDL cholesterol noted following consumption of GCE
C	Pueraria mirifica	↑	★☆☆ Minor	1 study	Not overly potent, only testing in menopausal women has been conducted
C	Hemp Protein	—	—	2 studies	No detectable differences in HDL-C levels
C	Nattokinase	—	—	1 study	No significant influence on HDL-C levels
C	Eleutherococcus senticosus	—	—	1 study	No significant influences yet known for HDL cholesterol
C	Benfotiamine	—	—	2 studies	No significant influences on HDL-C observed.
C	Caffeine	—	—	1 study	No significant influences on HDL cholesterol noted
C	Stevia	—	—	1 study	No significant influence on HDL-C has been detected with stevia
C	Shilajit	↑	★☆☆ Minor	1 study	Minor increase in HDL-C has been detected in persons after shilajit consumption
C	Theaflavins	—	—	1 study	No significant influence of theaflavins on HDL-C
C	Salvia hispanica	—	—	2 studies	HDL-C appears to be unaffected with chia ingestion when compared to similar macronutrient sources

C	Gamma Oryzanol	—	—	2 studies	No detectable influences on HDL cholesterol, although rice bran oil (a source of gamma oryzanol) may have a slight positive effect
C	Garcinia cambogia	—	—	1 study	No significant influence on HDL-C levels
C	Ganoderma lucidum	↑	★★☆ Notable	2 studies	There may be an increase in HDL-C in persons with hyperlipidemia that doesn't occur in otherwise healthy adults, but this is not certain due to lack of evidence. The degree of increase was fairly strong (24%).
C	Hibiscus sabdariffa	—	—	3 studies	HDL cholesterol appears to be unaffected following roselle ingestion
C	HMB	—	—	2 studies	No significant influence on HDL cholesterol levels
C	Japanese Knotweed	—	—	1 study	No significant influence on HDL-C in otherwise healthy lean persons
C	Irvingia gabonensis	↑	★☆☆ Minor	2 studies	An increase has been noted, but not to a remarkable degree. Independent trials need to be conducted to confirm.
C	Melatonin	—	—	1 study	No significant influences on HDL-C are noted with melatonin supplementation
C	Microlactin	—	—	1 study	Despite reductions in LDL and total cholesterol, there do not appear to be significant influences on HDL-C levels
C	Vitamin C	—	—	1 study	No significant influence on HDL cholesterol

C	Soy lecithin	—	—	1 study	No significant influence on HDL-C levels
C	Royal Jelly	—	—	3 studies	No significant influences on HDL-C detectable
C	Resveratrol	—	—	1 study	No significant influence on HDL cholesterol
C	Guggul	↓	★☆☆ Minor	2 studies	Either no significant change associated with Guggul supplementation or a small decrease is observed
C	Panax ginseng	↑	★☆☆ Minor	2 studies	May increase HDL-C levels, seems unreliable in doing so
C	Phosphatidylserine	—	—	1 study	No significant influence on HDL-C with PS supplementation
C	Krill Oil	↑	★★★☆☆ Notable	2 studies	Although one study suggest no such increase (healthy persons), the increase seen in hyperlipidemics exceeded 50% and was remarkable; requires replication
C	Citrulline	—	—	1 study	No significant influence on HDL-C concentrations
C	Vitamin K	—	—	1 study	Vitamin K does not appear capable of influencing HDL cholesterol
C	Sea Buckthorn	—	—	1 study	No significant influence on circulating HDL-C levels
C	Blueberry	—	—	2 studies	No significant influence on HDL-C
C	Ashwagandha	↑	★☆☆ Minor	3 studies	A fairly notable increase in HDL-C has been reported with ashwagandha

					supplementation (17.3% over 60 days)
C	Zinc	—	—	2 studies	No significant influence on HDL-C, even when normalizing a zinc deficiency associated with weight loss.
C	Rooibos	↑	★☆☆ Minor	2 studies	Increases HDL-C in persons at risk for cardiovascular disease to a small amount, does not appear effective in otherwise healthy persons
C	Anethum graveolens			2 studies	
C	Citrullus colocynthis	—	—	2 studies	A possible benefit in hyperlipidemics only has failed to reach statistical significance.
C	Creatine			2 studies	
C	Phosphatidylcholine			1 study	
C	Yacon	—	—	1 study	No significant influence on HDL cholesterol has been noted with Yacon syrup, despite weight loss occurring.
C	Rose Hip	—	—	1 study	No significant alteration of HDL-C concentrations has been noted with limited evidence investigating rose hip supplementation.
D	Coleus forskohlii	↑	★★★☆☆ Notable	1 study	Needs to be replicated in larger trials, but the degree of increase was quite remarkable.
D	Coffee	↑	★☆☆ Minor	1 study	An increase in HDL-C is noted with coffee ingestion
D	Tauroursodeoxycholic Acid	↓	★☆☆ Minor	1 study	A decrease in HDL-C has been noted to be secondary to treating cholestasis
D	Pueraria lobata	—	—	1 study	

D					No detectable influence on HDL-C levels
D	Coconut Oil	↓	★☆☆ Minor	1 study	Decrease in HDL-C is minor and likely not practically relevant.
D	Yerba mate	↑	★☆☆ Minor	1 study	An increase in HDL-C has been noted with Mate consumption
D	Ecklonia cava	—	—	1 study	No significant influence on HDL-C detected
D	Eclipta alba	—	—	1 study	No detectable influence on HDL-C cholesterol
D	Pycnogenol	↑	★☆☆ Minor	2 studies	May increase HDL cholesterol, but has mixed evidence to support it and may be unreliable
D	Tetradecyl Thioacetic Acid	↑	★☆☆ Minor	3 studies	An increase in HDL cholesterol has been noted with TTA consumption
D	Safflower Oil	↑	★☆☆ Minor	1 study	A slight increase in HDL-C has been noted with safflower oil
D	Emblica officinalis	↑	★☆☆ Minor	1 study	Higher doses of the fruits (3g) appear to be able to increase circulating HDL cholesterol in otherwise healthy persons and diabetics
D	Horse Chestnut	—	—	1 study	No significant influence on HDL-C levels associated with horse chestnut extract supplementation.
D	Rubus coreanus	—	—	1 study	No significant influence of the berries on HDL cholesterol levels in men who are otherwise healthy.
D	Perilla Oil			1 study	

D	Pyrroloquinoline quinone	—	—	1 study	Three weeks supplementation of PQQ has failed to significantly influence HDL cholesterol levels in otherwise healthy adults.
D	Ruscus aculeatus	↑	★★☆ Notable	1 study	A fairly notable increase in HDL-C (23%) in the lone (but not placebo controlled) study with <i>ruscus aculeatus</i> , requires replication

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Heart Rate

Heart Rate is a term used to refer to the amount of beats a heart gives in X amount of time, usually a minute. Heart rate is variable, and should be constant; arrhythmia (irregular beats) are a cause for concern, and some supplements (usually stimulants) influence Heart Rate.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Ephedrine	↑	★☆☆ Minor	5 studies	An increase in heart rate is present following ephedrine administration which correlates well with its psychostimulatory properties; this is not 100% reliable, and heart rate increases may not occur
B	Caffeine	↑	★☆☆ Minor	6 studies	An increase in heart rate is noted, but not wholly consistent. It appears to affect those with lower caffeine tolerance or high overdoses of caffeine
B	Vitamin C	↓	★☆☆ Minor	3 studies	A decrease in heart rate has been noted in exercising obese adults, a per se effect of Vitamin C on heart rate (rather than secondary to the rate of perceived exertion) seems unlikely.
B	Grape Seed Extract	↓	★☆☆ Minor	1 study	A small decrease in heart rate may occur following grape seed extract, although the studies are currently in persons with metabolic syndrome and not healthy persons
B	Arginine	—	—	4 studies	No significant influence on heart rate seen with supplemental L-Arginine
B	Sodium Bicarbonate	—	—	5 studies	

B					There is no significant effect of sodium bicarbonate on heart rate at rest or during exercise
B	Ornithine	—	—	5 studies	For the most part there is no significant effect, although one trial did not that after exercise during a recovery period ornithine had a higher heart rate. The reason for this is not known
B	Modafinil	—	—	3 studies	Heart rate and pulse do not appear to be influenced from modafinil supplementation, despite a small increase in systolic blood pressure.
B	Ginkgo biloba	—	—	6 studies	No significant influence of ginkgo biloba supplementation on heart rate.
B	Creatine	—	—	3 studies	There is no known influence of creatine supplementation on heart rate.
B	Colostrum	—	—	4 studies	Heart rate during exercise, either submaximal or at lactate threshold, is not modified with dietary supplementation of colostrum.
C	Green Tea Catechins	↓	★☆☆ Minor	2 studies	Mixed influence on heart rate, a possible decrease secondary to weight loss and blood pressure reduction but no apparent alteration <i>per se</i> (possible increases with overdoses of green tea catechins)
C	L-Carnitine	↓	★☆☆ Minor	2 studies	A decrease in heart rate has been noted associated with supplementation
C	ECA	—	—	1 study	Heart rate at rest is not affected by ECA supplementation and may indirectly be lowered secondary to weight loss.

					However, an acute increase in heart rate is possible from the stimulatory effects of ephedrine
C	Yohimbine	↑	★☆☆ Minor	2 studies	Due to stimulatory effects, an increase in heart rate follows yohimbine ingestion
C	Maca	—	—	1 study	No significant influence on heart rate noted with Maca ingestion
C	Chlorella	—	—	1 study	No significant influence on heart rate has been detected
C	Green Coffee Extract	↓	★☆☆ Minor	1 study	A decrease has been noted in hypertensives alongside a reduction in blood pressure; no studies in otherwise healthy persons
C	Nitrate	—	—	2 studies	Does not appear to significantly influence heart rate
C	1,3-Dimethylamylamine	—	—	1 study	No significant effect on heart rate noted with DMAA supplementation despite the increase in blood pressure.
C	Alpha-Lipoic Acid	—	—	1 study	No significant interaction between ALA and heart rate has been noted
C	Rhodiola Rosea	—	—	2 studies	No significant influences on heart rate found so far
C	Stevia	—	—	2 studies	No significant influence on heart rate detected with stevia consumption
C	Yerba mate	↓	★☆☆ Minor	1 study	A decrease has been noted with Yerba Mate consumption, which is somewhat notable as stimulants tend to increase heart rate

C	L-Tyrosine	—	—	1 study	No significant influences of Tyrosine on heart rate has been noted
C	Lavender	↓	★☆☆ Minor	2 studies	A decrease in heart rate has been noted at rest over a long period of time (12 weeks in insomniacs) and acutely; both studies have used aromatherapy
C	Melatonin	—	—	2 studies	No significant influence of melatonin on heart rate during waking either at rest or ambulation
C	Soy lecithin	—	—	1 study	Despite the reduction in perceived stress, heart rate does not appear to be affected by supplemental soy lecithin
C	Salvia sclarea	↓	★☆☆ Minor	1 study	A decrease in heart rate has been noted acutely in response to the aroma of clary sage
C	Pyruvate	↓	★☆☆ Minor	1 study	May decrease heart rate alongside blood pressure in hyperlipidemics according to one trial
C	Pycnogenol	—	—	1 study	No significant alterations in heart rate noted
C	Taurine	—	—	3 studies	No significant influence on heart rate following Taurine supplementation
C	Panax ginseng	—	—	1 study	No significant influence on heart rate
C	Phosphatidylserine	—	—	2 studies	No significant influence on heart rate with PS supplementation
C	Nicotine	↑	★☆☆	2 studies	An increase in heart rate is

			Minor		An increase in heart rate is present after nicotine ingestion due to the stimulatory properties
C	Fish Oil	—	—	1 study	No significant acute effect on heart rate seen with fish oil supplementation
C	Branched Chain Amino Acids	—	—	2 studies	No significant alterations in heart rate noted with BCAA supplementation at rest or during exercise
C	Citrulline	—	—	2 studies	No significant influence on heart rate seems likely, although at least one study noted a random but significant reduction post-exercise
C	Theanine			2 studies	
C	Cocoa Extract			2 studies	
C	Eucommia ulmoides			1 study	
C	Blueberry	—	—	1 study	No known interactions with heart rate and blueberry supplementation.
C	Ashwagandha	↓	★☆☆ Minor	1 study	A slight reduction in pulse rate has been noted in otherwise healthy but anxious persons.
C	Curcumin	—	—	1 study	No significant influence on heart rate seen with curcumin supplementation
C	Quercetin	—	—	1 study	No significant influence on heart rate either acutely or with prolonged supplementation.
C	Anatabine	—	—	1 study	There is no significant influence on heart rate seen with 6-12mg anatabine in otherwise healthy persons
C	Nigella sativa	—	—	1 study	No significant influence on heart rate or pulse rate.

C	Tribulus terrestris	↓	★☆☆ Minor	1 study	A decrease in heart rate has been observed in hypertensive persons given tribulus supplementation
C	Centella asiatica	—	—	1 study	No significant influence on heart rate with acute ingestion of the herb in healthy persons.
C	Capsaicin			2 studies	
C	Rooibos	—	—	1 study	No significant alterations in heart rate are seen with Rooibos ingestion
C	Anethum graveolens			1 study	
C	Garlic	—	—	6 studies	There is no inherent influence of garlic on heart rate, although when garlic aids cardiovascular performance in persons with heart problems it is associated with a reduced heart rate relative to control (due to less stress on the tissue).
C	Hoodia gordonii	↑	★☆☆ Minor	1 study	Both heart rate and pulse rate are increased with hoodia ingestion, which are thought to be related to toxic effects of the herb
C	Red Clover Extract	—	—	1 study	No significant influence on resting heart rate is seen with supplementation of red clover extract.
C	Trimethylglycine	—	—	2 studies	No significant influence on heart rate in subjects who are rehydrated and then subject to exercise.
C	Synephrine			1 study	
C	Astaxanthin			1 study	
C	Chromium	—	—	2 studies	No significant influence on heart rate is known with

					chromium supplementation.
C	Vitamin E	—	—	1 study	Heart rate during exercise in elite athletes is unaltered by supplementation of vitamin E.
D	Conjugated Linoleic Acid	—	—	1 study	No significant interaction between heart rate and CLA supplementation
D	Grapefruit	—	—	1 study	No significant alterations in heart rate associated with grapefruit ingestion
D	Eleutherococcus senticosus	—	—	1 study	No significant influences on heart rate are yet known
D	Cissus quadrangularis	—	—	1 study	No significant influence on heart rate when taken over the course of eight weeks.
D	Tetradecyl Thioacetic Acid			1 study	

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Hematocrit

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	L-Carnitine			2 studies	
C	Glutamine	—	—	1 study	No significant alterations in hematocrit noted
C	Trimethylglycine	—	—	2 studies	No significant influence on hematocrit is noted with supplementation of betaine.
C	Astaxanthin			2 studies	
C	Vitamin E	—	—	1 study	Hematocrit does not appear to be significantly influenced with supplementation of vitamin E relative to placebo.

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Hemoglobin

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	L-Carnitine			1 study	
C	Ashwagandha	↑	★☆☆ Minor	1 study	A slight but significant 6.3% increase in hemoglobin has been detected in otherwise healthy persons given ashwagandha daily for a period of 60 days.
C	Saffron	↓	★☆☆ Minor	1 study	Hemoglobin has been noted to be decreased in one study and thought to be related to possible toxic effects of moderately high dose saffron (60mg for more than 8 weeks).
C	Vitamin E	—	—	1 study	No significant influence of vitamin E supplementation on hemoglobin.
C	Colostrum	—	—	2 studies	There does not appear to be an <i>inherent</i> increase in hemoglobin with colostrum, although when it successfully treated HIV-associated diarrhea an increase in hemoglobin was noted once (thought to partially underlie the reduction in fatigue).

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Homocysteine

Homocysteine is a biomarker of cardiovascular disease, and it is thought that higher circulating levels of homocysteine are indicative of a higher risk for cardiovascular incidents.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Trimethylglycine	↓	★★★ Strong	9 studies	Betaine (3g or more) appears to potently and reliably reduce homocysteine concentrations following a single dose and maintaining this reduction for as long as supplementation is continued. The magnitude is around 10% in persons with normal homocysteine levels, and greater (20-40%) in those with high homocysteine, and (unlike folate) works in instances of methionine loading tests. 500mg betaine can reduce homocysteine after a methionine load, but it too low to influence fasting homocysteine.
C	Creatine	↓	★☆☆ Minor	1 study	Decrease in homocysteine (biomarker of inflammatory cardiovascular disease) was present, but not to a remarkable magnitude
C	Fish Oil	↓	★☆☆ Minor	2 studies	May decrease homocysteine content
C	Chlorogenic Acid	↑	★☆☆ Minor	1 study	Somewhat high acute spike of homocysteine, which is normally a negative thing. Practical significance of this unknown
C	S-Adenosyl Methionine	—	—	3 studies	No significant alterations in plasma homocysteine occur following supplemental SAMe ingestion

C	Green Coffee Extract	↓	★☆☆ Minor	1 study	Decrease in homocysteine noted, thought to be indicative of cardioprotection
C	Vitamin B12			1 study	
C	Garlic	—	—	2 studies	No significant alterations in homocysteine concentrations are seen with garlic supplementation.
C	Hesperidin	—	—	1 study	There was no influence on homocysteine seen with supplementation of hesperidin relative to placebo, despite subjects being in an inflammatory state.
C	Red Clover Extract	—	—	1 study	There do not appear to be changes to circulating homocysteine in premenopausal women given supplementation of red clover extract.
C	Vitamin E	—	—	2 studies	There does not appear to be a significant influence of vitamin E supplementation on homocysteine concentrations.

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Hydration

Hydration is an approximately measurement of reserves of water on the human body, and a severe reduction in hydration from either no water intake or diuretic usage is known as dehydration. Some supplements are either diuretic or may promote water retention.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Creatine	↑	★★★☆☆ Notable	9 studies	Appears to be quite notable due to the increase in water weight in skeletal muscle tissue following creatine supplementation.
C	Sodium Bicarbonate	—	—	1 study	The addition of sodium bicarbonate to a pre-testing rehydration protocol does not enhance hydration more than the protocol itself (mostly water and carbohydrates)
C	Quercetin	—	—	1 study	Hydration during exercise in the heat is unaffected by quercetin supplementation.
C	Trimethylglycine	—	—	2 studies	Betaine supplementation does not appear to be significantly beneficial in improving hydration status of users either outright or after prior dehydration relative to water alone.
D	Rooibos	—	—	1 study	Rooibos tea does not appear to be significantly better than the water it is brewed in at restoring hydration in athletes

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IGF Binding Protein

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Red Clover Extract	—	—	3 studies	No influence of supplementation on circulating concentrations of any measured IGF binding protein (IGFBP-1, IGFBP-2, IGFBP-3) in any tested population.
C	Olive leaf extract	↑	★☆☆ Minor	1 study	An increase in IGF binding proteins has been noted in one study (which would sequester and reduce the activity of IGF hormones); potency of this interaction unable to be determined (no reference drug)
C	L-Carnitine	↑	★☆☆ Minor	1 study	An increase in IGF binding protein (3) has been noted following carnitine supplementation in otherwise healthy youth
C	Dehydroepiandrosterone	—	—	1 study	There may be an influence (study noted both increases and decreases with high variability) but this does not appear to be a clinical concern

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IGF-1

Insulin-like growth factor-1 (IGF-1) is an anabolic derivative of growth hormone that is thought to mediate cell growth and muscle protein synthesis. Supplements that increase IGF-1 are thought to promote muscle hypertrophy.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Creatine	—	—	5 studies	Insufficient evidence to support a role of creatine in increasing IGF-1
B	Dehydroepiandrosterone	↑	★☆☆ Minor	6 studies	An increase in IGF-1 hormone levels may exist following DHEA supplementation, although this has only been investigated in older persons.
B	Zinc	↑	★☆☆ Minor	5 studies	There is an increase in IGF-1 concentrations if the subject is deficient in zinc, but no increase otherwise.
B	Red Clover Extract	—	—	3 studies	Supplementation does not appear to significantly influence circulating IGF-1 concentrations, although equol (a possible metabolite of formononetin) has been associated with a reduction not observed to a significant degree in most trials on red clover extract.
B	Colostrum	—	—	5 studies	While any protein sources has the potential to increase IGF-1 when included in the diet, colostrum is no different than whey protein at doing so. The IGF-1 that is present in colostrum naturally appears to be fully digested in the intestinal tract and does not reach the blood.

C	Melatonin	—	—	1 study	No significant influence on IGF-1 levels
C	Olive leaf extract	—	—	1 study	No significant influence on circulating IGF-1 nor IGF-2 levels
C	Whey Protein	—	—	1 study	Does not appear to inherently alter circulating IGF-1 levels
C	Velvet Antler	—	—	1 study	No significant influence of velvet antler on IGF-1
C	L-Carnitine	—	—	1 study	No significant changes in IGF-1 seen with carnitine supplementation; IGF-2 also appears unaffected
C	HMB	—	—	1 study	No significant alterations in circulating IGF-1 concentrations
C	Citrulline	—	—	1 study	No demonstrated effects on IGF-1 concentrations following the usage of citrulline supplementation
C	Eurycoma Longifolia Jack	—	—	1 study	No detectable alterations in IGF-1 for eurycoma extract
C	Trimethylglycine	↑	★☆☆ Minor	1 study	IGF-1 appears to be minimally increased relative to placebo (7.8%) following two weeks supplementation of betaine and when tested after exercise in a fasted state.

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Immunity

Immunity tends to refer to the capacity of the body to ward off infections, and tends to be measured acutely by seeing the count or activity of immune cells that can help ward off sickness. Enhanced immunity results in less sickness.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin E	↑	★☆☆ Minor	8 studies	There appears to be an increase in T-cell mediated immunity in older subjects when supplementing low dose (50-200mg) vitamin E; this immunity enhancement does not appear to occur in youth due to it alleviating an age-related immune suppression.
C	Astragalus membranaceus	↑	★★★☆☆ Notable	1 study	Appears to activate T-cells to a degree higher than the reference drug echinacea
C	Glutamine	—	—	1 study	No significant influence on immunity per se
C	Ganoderma lucidum	↑	★☆☆ Minor	4 studies	There appears to be proliferative effects on T-lymphocytes and natural killer cells and no significant alteration in a CD4:CD8 lymphocytic ratio following ingestion of Ganoderma polysaccharides.
C	Chlorella	↑	★☆☆ Minor	1 study	Increase in salivary IgA suggests an immune enhancing effect; no comparison to an active control.
C	Feverfew	—	—	1 study	No significant influence detected on immunity
C	Eleutherococcus	↑	★☆☆ Minor	2 studies	

C	Lactobacillus ruminantium sensu lato	↑	★☆☆ Minor	1 study	Appears to have a stimulating effect on T-cell proliferation and NK cell activity, but requires more evidence.
C	Holy Basil	↑	★☆☆ Minor	1 study	Appears to induce proliferation of T cytokines and T lymphocytes
C	Lactobacillus casei			1 study	
C	Citrulline	↑	★☆☆ Minor	1 study	Neutrophil oxidative burst post-workout appears to be enhanced when the exercise is preloaded with citrulline supplementation
C	Chromium	↑	★☆☆ Minor	1 study	At least one study has noted an increase rate of lymphocyte proliferation when they were stimulated with a mitogen (proliferation inducing factor) with chromium supplementation relative to placebo.
C	Colostrum	—	—	1 study	DTH responsiveness (indicative of T-cell mediated immunity) was not affected with colostrum in adults overall or in the elderly cohort which are normally more responsive to therapeutic interventions on DTH responsiveness.
D	Ashwagandha	↑	★☆☆ Minor	1 study	Minor T-cell activation following ingestion of Ashwagandha tinctures, needs to be replicated.
D	Nigella sativa	↑	★☆☆ Minor	1 study	Macrophage phagocytic activity and killing potential is increased following oral ingestion of the seed extract.

Immunoglobulin A

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Colostrum	—	—	8 studies	IgA concentrations in saliva and serum do not appear to be reliably increased although a few studies have noted spikes, which do not appear to be consistent in their magnitude nor incidence. The only incidence where IgA appears to be reliably increased is when it is taken as a vaccine adjuvant.
C	Pelargonium sidoides	↑	★★★☆☆ Notable	1 study	The decrease in Immunoglobulin A noted with exercise in one study in marathon runners (60% relative to baseline) was reversed to a large increase (194% relative to baseline) when measured after exercise.
C	Saffron	—	—	1 study	No significant influence on circulating IgA concentrations following saffron ingestion.
C	Vitamin E	—	—	1 study	Supplementation of vitamin E does not appear to significantly influence circulating concentrations of IgA relative to placebo in otherwise healthy elderly adults.

Immunoglobulin G

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Colostrum	—	—	4 studies	IgG has been noted to be increased once when colostrum was used as a vaccine adjuvant (relative to skim milk with whey as control), but in general there is no influence without coadministered vaccination.
C	Saffron	↑	★☆☆ Minor	1 study	An increase in IgG concentrations has been noted to occur with saffron supplementation alongside a decrease in IgM and no influence on IgA.
C	Vitamin E	↑	★☆☆ Minor	2 studies	IgG has been noted to be increased when vitamin E is used as a vaccination adjuvant, but not in otherwise healthy persons not subject to a vaccination.

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Immunoglobulin M

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Colostrum	—	—	3 studies	IgM does not appear to <i>per se</i> be modified in serum relative to control protein, and unlike the other immunoglobulins there is no augmentation of a vaccine-induced IgM spike.
C	Saffron	↓	★☆☆ Minor	1 study	A decrease in IgM concentrations has been noted to occur following supplementation of saffron.
C	Vitamin E	—	—	1 study	IgM concentrations in the blood of older persons do not appear to be influenced with supplementation of vitamin E.

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Inflammation

Not inherently good or bad, Inflammation is the process recruiting immune cells to tissues in the body for their actions; good for immunity and cell defense, excessive levels can cause joint pain and accelerate signs of aging and disease pathology such as cancer or obesity.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Fish Oil	↓	★☆☆ Minor	17 studies	Highly mixed and unreliable influences on circulating inflammatory cytokines (although, due to immunosuppression on cellular adhesion factors, the overall effect may still be antiinflammatory)
B	Coenzyme Q10	—	—	3 studies	Classical inflammatory cytokines do not appear to be altered much following CoQ10 supplementation, although there may still be a minor antiinflammatory effect
B	Ginger	↓	★☆☆ Minor	4 studies	Inflammatory parameters seem to be reduced following ginger consumption
B	Vitamin C	—	—	4 studies	No significant alterations seen in inflammatory cytokines associated with Vitamin C supplementation
B	Conjugated Linoleic Acid	—	—	4 studies	Insufficient evidence to support significant changes in inflammatory status.
B	Curcumin	↓	★★★☆☆ Notable	5 studies	There appears to be a decrease in disease states or conditions characterized by inflammation associated with curcumin ingestion, does not appear to be too discriminatory in which inflammatory states it

					benefits
B	Serrapeptase	↓	★☆☆ Minor	4 studies	Appears to reduce swelling and inflammation following surgery or trauma, although to a lesser degree than corticosteroids. There is a lack of practical evidence for the claims behind serrapeptase (instead, studies tend to only look at post-surgery inflammation)
C	L-Carnitine	↓	★☆☆ Minor	1 study	Possible antiinflammatory effect on exercise-induced inflammatory biomarkers
C	Quercetin	—	—	1 study	Mixed influence on inflammation, but does not appear to at all be practically significant
C	Whey Protein	—	—	1 study	Insufficient evidence to support whey protein as interacting with inflammation and biomarkers of inflammation
C	Melatonin	↓	★☆☆ Minor	1 study	A reduction in inflammatory cytokines is noted with melatonin supplementation
C	Spirulina	↓	★☆☆ Minor	2 studies	Some various and uncertain changes in cytokines that are seen as indicators of inflammation; not enough human interventions to draw conclusions.
C	Alpha-Lipoic Acid	↓	★☆☆ Minor	2 studies	Mixed effects depending on what inflammatory biomarker or cytokine is measured; practical significance unknown
C	Benfotiamine	—	—	1 study	Insufficient evidence with the preliminary evidence failing to any influence on circulating cytokines.
C	Olive leaf extract	—	—	1 study	

					No significant effects on biomarkers of inflammation when measured
C	Stinging Nettle	↓	★☆☆ Minor	2 studies	Appears to reduce LPS-stimulated proinflammatory cytokine release, and thus is likely to have anti-inflammatory effects. The potency of this is not overly remarkable
C	Theaflavins	—	—	1 study	No significant influence on inflammatory cytokines noted with theaflavins supplementation
C	Salvia hispanica	—	—	1 study	No significant alteration in serum biomarkers noted with chia seeds
C	Japanese Knotweed	↓	★★★☆☆ Notable	1 study	The study in question measured nF-kB activity and noted a 25% decrease, which is somewhat novel (not a common measurement) and to quite a large degree; may be related to the Resveratrol or stilbene content
C	Pycnogenol	—	—	2 studies	No significant influence on standard inflammatory cytokines
C	Glutamine	—	—	1 study	No significant influence on inflammatory cytokines except perhaps IL-6 seen with glutamine supplementation
C	Panax ginseng	↓	★☆☆ Minor	1 study	A decrease in IL-6 concentrations has been noted
C	Phosphatidylserine	—	—	1 study	No significant influence on inflammatory cytokines
C	Vitamin D	—	—	1 study	No significant influence on select inflammatory cytokines

C	Sea Buckthorn	—	—	1 study	Supplementation of sea buckthorn in persons on hemodialysis has failed to significantly influence any inflammatory biomarker measured at the standard supplemental dosage.
D	Coffee	↓	★☆☆ Minor	1 study	A decrease in some inflammatory cytokines has been noted with coffee ingestion
D	Boron	↓	★☆☆ Minor	1 study	Some influence on typically inflammatory cytokines, practical relevance of these changes unknown
D	Bromelain	↓	★☆☆ Minor	1 study	Requires more evidence, but at the moment appears somewhat effective
D	Hibiscus sabdariffa	↓	★☆☆ Minor	1 study	Possible decreases in MCP-1 with mixed or no influence on other inflammatory cytokines

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Insomnia

Insomnia is the inability to sleep or an excessive awakening during night that significantly impairs daily functioning. Supplements that improve sleep quality may also improve symptoms of insomnia.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Melatonin	↓	★★★ Strong	4 studies	Melatonin is the reference drug for insomnia related purposes, and appears to be highly effective at 3mg (time release formulation) or lower concentrations when taken before sleep.
C	Vitex agnus castus	↓	★☆☆ Minor	1 study	Can reduce insomnia that is a side-effect of PMS, although the influence on insomnia in other scenarios is not known.
C	Valeriana officinalis	↓	★☆☆ Minor	2 studies	Mixed evidence, with benefit to insomnia in menopausal women yet no apparent benefit in those with restless leg syndrome. Overall, a lack of evidence to conclude efficacy for this particular disorder.
D	Lavender	↓	★☆☆ Minor	1 study	May be effective in reducing insomnia when measured
D	Melissa officinalis	↓	★☆☆ Minor	1 study	A decrease in insomnia has been noted to be to quite a large degree in one open-label trial, but may be secondary to anxiety reduction
D	Ashwagandha	↓	★☆☆ Minor	1 study	Self-reports of insomnia have been reduced with supplementation of ashwagandha in women undergoing chemotherapy.

Insulin

Insulin is a hormone that increases when blood glucose rises, and acts to reduce blood glucose by putting it into cells and increasing its usage. It temporarily shifts energy metabolism from fats to carbs, and does not inherently make somebody fat. Its potency is seen as Insulin Sensitivity.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Chromium	—	—	18 studies	Somewhat similar to the influence on insulin sensitivity, the reductions in fasting insulin concentrations in diabetics appear to exist in some studies but are highly unreliable.
B	Fenugreek	—	—	3 studies	No consensus as to the influence of fenugreek on insulin levels
B	Conjugated Linoleic Acid	—	—	5 studies	No significant influence on fasting insulin levels
B	Whey Protein	↑	★☆☆ Minor	5 studies	Mixed effects on insulin, as there is an acute increase due to whey being a protein source (although whey increases insulin more than other proteins). Fasting insulin (chronically) tends to either be not affected or reduced, although the latter is usually confounded with weight loss.
B	Berberine	↓	★☆☆ Minor	2 studies	Degree of reduction of fasting insulin according to meta-analysis was SMD -0.50mU/L (95% CI -0.96 to -0.03) which is not overly remarkable.
B	Magnesium	↓	★☆☆ Minor	6 studies	Decreases in fasting insulin appear to occur over long term supplementation with magnesium in persons at risk

					for diabetes or already with the disease state; decreases in insulin may not occur in normoglycemic persons
B	Salacia reticulata	↓	★★☆ Notable	3 studies	A decrease in postprandial insulin has been noted with acute supplementation, which is thought to be secondary to the reduction in glucose absorption (as the two correlate highly). There are currently no studies assessing long term changes in fasting insulin
B	Fish Oil	—	—	10 studies	No significant influence on fasting insulin levels
B	Citrulline	—	—	4 studies	Most studies note that there is no significant change in insulin concentrations, although a lone study (not replicated) suggested that the exercise-induced increase in insulin was suppressed with citrulline. As this study also noted performance degradation, it may be a flaw
B	Zinc	↓	★☆☆ Minor	4 studies	Basal insulin concentrations appear to be reduced following supplementation of zinc.
B	Inositol	↓	★☆☆ Minor	7 studies	Secondary to treating symptoms of PCOS, fasting insulin concentrations are fairly reliably reduced.
B	Creatine	—	—	3 studies	Fasting insulin concentrations are not affected with creatine supplementation.
C	Green Tea Catechins	—	—	2 studies	No significant influence on fasting insulin levels
C	ECA	—	—	1 study	No significant alterations in fasting insulin reported

C	L-Carnitine	↓	★☆☆ Minor	1 study	Fasting insulin has been noted to be decreased in diabetics given carnitine
C	Chlorogenic Acid	↓	★☆☆ Minor	1 study	Spike in insulin was attenuated a bit, secondary to attenuating the rate of glucose absorption. Not overly remarkable
C	Glutamine	↑	★☆☆ Minor	2 studies	An increase in insulin occurs following ingestion of glutamine supplementation, which is thought to be secondary to the increase in blood glucose seen with glutamine ingestion
C	Tauroursodeoxycholic Acid	—	—	1 study	No significant influence on fasting insulin levels
C	Black Cohosh	—	—	1 study	No significant influence on fasting insulin
C	Panax ginseng	—	—	2 studies	No significant influence on fasting insulin levels seen with panax ginseng
C	Punicic Acid	—	—	1 study	No significant influence on fasting insulin levels
C	Nicotine	—	—	1 study	No significant influence on fasting insulin levels
C	Licorice	—	—	1 study	No significant changes in fasting insulin levels
C	Bladderwrack	↓	★☆☆ Minor	1 study	Appears to reduce insulin AUC after a carbohydrate containing meal
C	Coenzyme Q10	—	—	1 study	Insufficient evidence to support changes in insulin associated with CoQ10 supplementation.

C	Olive leaf extract	↓	★☆☆ Minor	2 studies	A decrease of fasted and postprandial insulin with olive leaf consumption has been noted, not to a remarkable degree
C	Caffeine	—	—	2 studies	No significant influences on fasting insulin (not postprandial) are noted with caffeine
C	Resveratrol	↓	★☆☆ Minor	1 study	A decrease in insulin (fasting) has been noted in persons with metabolic syndrome
C	Dehydroepiandrosterone	—	—	1 study	No significant alterations in fasting glucose levels
C	Gamma Oryzanol	—	—	1 study	No significant alterations noted in fasting insulin levels following prolonged ingestion of gamma-oryzanol in healthy persons
C	Gynostemma pentaphyllum	↓	★☆☆ Minor	1 study	A decrease in fasting insulin has been noted with supplementation in diabetics
C	Japanese Knotweed	—	—	1 study	No significant alterations in fasting insulin levels seen with treatment
C	Melatonin	—	—	1 study	No significant influence on fasting insulin levels noted with melatonin
C	Capsaicin	↑	★☆☆ Minor	1 study	High doses of capsaicin may induce insulin release from the pancreas
C	Vitamin D	—	—	1 study	No significant influence on fasting insulin levels
C	Krill Oil	—	—	1 study	No significant influence on fasting insulin levels

C	Branched Chain Amino Acids	—	—	1 study	No significant influence of BCAA supplementation on fasting insulin levels
C	Sodium Bicarbonate	—	—	1 study	Fasting insulin concentrations are not affected with sodium bicarbonate supplementation
C	Vitamin K	↓	★☆☆ Minor	4 studies	A relative deficiency of vitamin K seems to be associated with higher post-meal insulin spikes (over 120 minutes), and this abnormal elevation is normalized upon supplementation of vitamin K
C	Cocoa Extract			1 study	
C	Blueberry	↓	★☆☆ Minor	1 study	Insulin has once been noted to be decreased in elderly persons with blueberry ingestion.
C	Garlic	—	—	1 study	In persons with metabolic syndrome, there is no significant influence on fasting insulin concentrations relative to placebo after supplementation of garlic.
C	Psyllium	↓	★☆☆ Minor	2 studies	A minor decrease in diabetics following supplementation, although it is small in magnitude and does not carry over to nondiabetics.
C	Hesperidin	—	—	2 studies	Similar to blood glucose, there is no significant influence on basal insulin concentrations in otherwise healthy persons or those with metabolic diseases.
C	Red Clover Extract	—	—	2 studies	Fasting blood insulin concentrations do not appear to be significantly influenced with supplementation of red clover extract.

C	Trimethylglycine	—	—	1 study	Similar to blood glucose, there is currently no known influence of betaine supplementation on fasting insulin concentrations.
C	Yacon	↓	★☆☆ Minor	1 study	A minor reduction in fasting insulin levels has been noted in obese women given supplementation, but this is confounded with weight loss.
C	Rose Hip	—	—	1 study	No significant influence on circulating (basal) insulin has been noted with rosehip supplementation.
C	Vitamin E	—	—	1 study	Basal insulin concentrations (fasted state) do not appear to be influenced by supplementation of vitamin E.
D	Curcumin	↑	★☆☆ Minor	1 study	May increase postprandial insulin concentrations
D	Ginger	—	—	1 study	No significant alterations in insulin levels (fasting) seen with ginger
D	Coconut Oil	—	—	1 study	No significant influence detected on fasting insulin levels following coconut oil consumption
D	Salvia hispanica	—	—	1 study	No significant influence on fasting insulin levels following chronic consumption of chia seeds in the diet
D	Safflower Oil	—	—	1 study	No significant influence on fasting insulin levels in diabetics
D	Arginine	—	—	1 study	No significant influence on <i>fasting</i> insulin concentrations associated with arginine supplementation

Insulin Secretion

Insulin secretion refers to the amount of insulin released from the pancreas either inherently or from a carbohydrate containing test meal. Supplements that increase insulin release are known to be hypoglycemic when taken with a meal.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	—	—	5 studies	There does not appear to be an augmented insulin release from dietary carbohydrate nor an inherent insulin release from the pancreas associated with fish oil supplementation
C	Green Tea Catechins	↓	★☆☆ Minor	1 study	A minor decrease in insulin secretion has been noted associated with green tea catechin ingestion
C	Vitamin D	↑	★☆☆ Minor	3 studies	An improvement in insulin secretion is noted in diabetics (type II mostly) and in persons at risk for diabetes, which is thought to be secondary to protective effects at the level of the pancreas.
C	Arginine	↑	★☆☆ Minor	1 study	An increase in insulin secretion has been noted with arginine supplementation. This is both due to arginine being a secretagogue (when used acutely), and prolonged usage in those with impaired glucose tolerance may regenerate pancreatic beta-cells
C	Curcumin	↑	★☆☆ Minor	1 study	Curcumin has been found to increase insulin secretion in insulin resistant persons, suggesting benefits to pancreatic tissue.
C	Inositol	↓	★☆☆	3 studies	

C			 Minor		The amount of insulin secreted in response to orally ingested glucose is attenuated after supplementation of inositol to insulin resistant persons
C	Creatine	—	—	1 study	The insulin secretion in response to a test meal does not appear to be altered with creatine supplementation.
C	Chromium	↑	 Minor	2 studies	Mixed evidence, but it is possible that chromium causes an increased insulin response to dietary glucose (leading to a greater release of insulin acutely, possibly preceding a reduction in blood glucose).
D	Sodium Bicarbonate	—	—	1 study	No significant influence of supplementaion sodium bicarbonate on insulin secretion
D	Sea Buckthorn	↓	 Minor	1 study	Secondary to reducing the absorption of carbohydrates from a test meal, insulin secretion is attenuated
D	Moringa oleifera	—	—	1 study	The hypoglycemic properties of this supplement do not appear to be related to an increase in insulin secretion from the pancreas following a meal

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Insulin Sensitivity

A relation of how well Insulin in the body is able to affect cells by inducing insulin-like effects. Insulin resistance is poor efficacy in affecting cells, and insulin sensitivity is good efficacy. Chronic Insulin resistance is one of the pathological signs of type II diabetes.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Fish Oil	—	—	14 studies	No significant influence on insulin sensitivity seems to be the consensus, although there are isolated reports of both an increase and decrease (in response to a glucose tolerance test and fasting, respectively)
A	Conjugated Linoleic Acid	—	—	14 studies	For the most part, ineffective; too unreliable to reach any conclusions in regards to the efficacy of CLA. There appears to be some manner of interaction, but both sensitization and resistance has been noted
A	Chromium	—	—	16 studies	There appears to be highly unreliable evidence for this property for unknown reasons, but chromium <i>may</i> have a role in increasing insulin sensitivity in diabetic persons to a mild degree despite the majority of evidence showing no effects.
B	Green Tea Catechins	↑	★☆☆ Minor	3 studies	Mixed effects on insulin sensitivity, possible improvements seen in unhealthy persons
B	L-Carnitine	↑	★☆☆ Minor	4 studies	An increase in insulin sensitivity appears to exist with carnitine supplementation, and at least once has been noted in otherwise healthy lean males. This may be secondary

					to glucose disposition into tissues
B	Panax ginseng	—	—	3 studies	More evidence than not suggests no significant improvement in insulin sensitivity, although it is still a minor possibility
B	Nicotine	—	—	5 studies	Long term insulin sensitivity does not appear to be highly affected, but acutely nicotine exposure can reduce insulin sensitivity
B	Caffeine	↓	★☆☆ Minor	4 studies	A decrease in insulin sensitivity is noted acutely when caffeine is taken alongside carbohydrates, thought to be secondary to reducing glucose deposition.
B	Magnesium	↑	★☆☆ Minor	4 studies	There appears to be increases in insulin sensitivity as assessed by HOMA-IR, which is thought to be secondary to aiding pancreatic function
B	Inositol	↑	★☆☆ Minor	12 studies	Insulin sensitivity appears to be reliably improved following the treatment of PCOS in women.
C	Vitamin D	↑	★☆☆ Minor	4 studies	Improvements in insulin sensitivity can occur secondary to increasing pancreatic insulin secretion
C	Fenugreek	↑	★☆☆ Minor	1 study	An increase in insulin sensitivity has been noted with fenugreek ingestion
C	Alpha-Lipoic Acid	—	—	1 study	No significant influence on insulin sensitivity has been noted
C	Tauroursodeoxycholic Acid	↑	★★★☆☆ Notable	1 study	Notable due to reaching near 30% improvement in obese

					persons and only being localized to muscle tissue and the liver, but not adipose tissue
C	Vitamin C	—	—	1 study	No significant influence on insulin sensitivity
C	Punicic Acid	—	—	1 study	No significant alterations in insulin sensitivity noted
C	Whey Protein	↑	★☆☆ Minor	3 studies	Has been noted to increase insulin sensitivity to a larger degree than casein when consumed by obese persons in a part of a fat loss diet; has not yet demonstrated an insulin sensitizing effect in lean athletes
C	Spirulina	↑	★☆☆ Minor	1 study	Requires more evidence to establish its potency
C	Vanadium	—	—	7 studies	Although an insulin sensitizing effect cannot be fully ruled out at this point in time, the more robust evidence currently does not support this insulin sensitizing effect in obese persons with impaired glucose tolerance. It may be only in diabetics
C	Licorice	—	—	1 study	No significant changes in insulin sensitivity following licorice ingestion
C	Nitrate	—	—	1 study	No significant observed effects on insulin sensitivity.
C	Berberine	—	—	1 study	Currently no evidence to support efficacy, although it may increase insulin sensitivity (requires more research)
C	Bladderwrack	↑	★☆☆ Minor	1 study	Appears to be pretty effective at increasing insulin sensitivity acutely after a meal, which may be due to reduced insulin in

					serum.
C	Olive leaf extract	↑	☆☆☆ Minor	1 study	An increase in insulin sensitivity has been noted in otherwise healthy persons (Matsuda Index and oral glucose tolerance test) and thought secondary to the pancreas; may be relevant to otherwise healthy persons
C	Resveratrol	↑	☆☆☆ Minor	3 studies	There appears to be an increase in insulin sensitivity seen with resveratrol at doses low enough to be achieved via wine consumption, all tests currently in obese and unhealthy persons
C	Stinging Nettle	—	—	1 study	No significant interactions between insulin sensitivity and stinging nettle yet detected
C	Dehydroepiandrosterone	—	—	3 studies	No significant influences on insulin sensitivity seem apparent with DHEA supplementation
C	Grapefruit	↑	☆☆☆ Minor	1 study	Improvement in insulin sensitivity may be secondary to weight loss
C	Gynostemma pentaphyllum	↑	★★☆ Notable	2 studies	An improvement in insulin sensitivity is noted in diabetics which is fairly notable; no studies in otherwise healthy persons at this time
C	Japanese Knotweed	—	—	1 study	Insulin sensitivity is unaffected in otherwise healthy lean persons given this supplement
C	Melatonin	↑	☆☆☆ Minor	1 study	An increase in insulin sensitivity has been noted to be secondary to reducing liver fat; an inherent influence on insulin sensitivity is uncertain
C	Roval Jelly	—	—	1 study	

C	Sodium Bicarbonate	↑	★☆☆ Minor	2 studies	Despite a slight reduction in blood glucose, no significant influence on insulin sensitivity noted
C	Arginine	↑	★☆☆ Minor	1 study	Mixed effects on insulin sensitivity in persons who may be suffering from metabolic acidosis, with one positive and one null result
C	Vitamin K	↑	★☆☆ Minor	1 study	An increase in insulin sensitivity has been noted in persons with impaired glucose tolerance using arginine for long periods of time; this is thought to be secondary to increased pancreatic function
C	Blueberry	↑	★☆☆ Minor	2 studies	An improvement of insulin sensitivity has been noted with 30mg of MK-4 supplementation over 4 weeks in otherwise healthy individuals, with the influence of lower doses of vitamin K not ascertained
C	Curcumin	↑	★☆☆ Minor	1 study	An improvement of insulin sensitivity has been noted in persons with insulin resistance, but this may only affect high risk individuals.
C	Zinc	↑	★☆☆ Minor	2 studies	In insulin resistant persons, curcumin can increase insulin sensitivity.
C	Garlic	—	—	1 study	An increase in insulin sensitivity has been noted with supplementation of zinc in insulin resistant persons who were likely zinc deficient.
C	Psyllium	—	—	1 study	There is no significant influence on insulin sensitivity when garlic is given to persons with metabolic syndrome.

C	Cinnamon	—	—	1 study	No significant alterations of insulin sensitivity in those who are not insulin resistant at baseline
C	Creatine	—	—	1 study	There do not appear to be any alterations in insulin sensitivity associated with creatine supplementation.
C	Hesperidin	—	—	1 study	There is no significant change in insulin sensitivity in persons with metabolic syndrome given 500mg of hesperidin daily.
C	Red Clover Extract	↓	★☆☆ Minor	2 studies	While one study has noted no significant effect, another has noted a minor reduction in sensitivity as assessed by QUICKI; reasons underlying this are unknown.
C	Yacon	↑	★☆☆ Minor	1 study	A minor increase in insulin sensitivity has been noted in a lone study in obese women that is also confounded with weight loss (ie. the weight loss could explain the increase observed)
C	Rose Hip	—	—	1 study	No significant influence on insulin sensitivity has been noted in obese humans relative to placebo.
C	Vitamin E	—	—	2 studies	There does not appear to be improvements in insulin sensitivity associated with vitamin E supplementation relative to placebo, even in instances where NAFLD is being treated therapeutically.
D	Coffee	—	—	1 study	No significant influences on insulin sensitivity with caffeinated coffee
D	Coconut Oil	↑	★☆☆ Minor	1 study	May improve insulin sensitivity in diabetics, requires more

					evidence though as the one study was confounded with fat loss.
D	Safflower Oil	—	—	1 study	No significant influence on insulin sensitivity in diabetics
D	Tetradecyl Thioacetic Acid			1 study	

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Interferon Gamma

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin E	↓ ↑	★☆☆ Minor	3 studies	IFN γ is increased when vitamin E is taken alongside a vaccination, and decrease in the elderly (alongside improvements in immunity) with no significant changes if neither of the above contexts are considered.
C	Garlic	↑	★☆☆ Minor	1 study	Alongside the increase in immune cell activity in otherwise healthy persons is an increase in IFN- γ concentrations
C	Colostrum	—	—	1 study	IFN- γ does not appear to be influenced with supplementation of colostrum relative to control proteins (whey).

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Interleukin 2

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Fish Oil	↑	★☆☆ Minor	2 studies	Mixed effects on IL-2 concentrations, with an increase noted when supplemented around exercise and no change noted at rest.
C	Vitamin E	↑	★☆☆ Minor	2 studies	An increase in interleukin 2 (IL-2) concentrations has been noted in the elderly given supplementation of vitamin E alongside immunity enhancements.
D	Conjugated Linoleic Acid			1 study	
D	Zinc	↑	★☆☆ Minor	1 study	Interleukin 2 (IL-2) appears to be reduced during zinc deficiency, and this is normalized upon zinc sufficiency.

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Interleukin 6

Interleukin 6 (IL-6) is a proinflammatory cytokine that is thought to reflect a more inflammatory state in the body.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Fish Oil	↓	★☆☆ Minor	1 study	A decrease in circulating IL-6 has been noted with fish oil supplementation
C	HMB	—	—	1 study	No significant alterations in circulating IL-6 concentrations
C	Vitamin K	—	—	2 studies	No significant effect of vitamin K on circulating levels of IL-6, an inflammatory marker
C	Blueberry	—	—	2 studies	No significant influence on IL-6 concentrations in serum
C	Curcumin	↓	★☆☆ Minor	1 study	A slight decrease in IL-6 concentrations has been noted, practical relevance unknown.
C	Zinc	↓	★☆☆ Minor	1 study	Alongside other proinflammatory cytokines, IL-6 appears to be reduced following supplementation of zinc.
C	Quercetin	—	—	1 study	The alterations in IL-6 concentrations seen with exercise are unchanged with quercetin supplementation.
C	Garlic	—	—	2 studies	Supplementation of garlic to persons in chronic pro-inflammatory states does not seem to significantly influence circulating IL-6 concentrations

C	Ginkgo biloba	↓	★☆☆ Minor	1 study	A slight reduction in IL-6 has been reported in persons who are diagnosed with metabolic syndrome
C	Hesperidin	—	—	1 study	No significant influence on interleukin 6 (IL-6) is seen with oral supplementation of hesperidin.
C	Vitamin E	—	—	1 study	IL-6 concentrations do not appear to be influenced relative to placebo.
C	Colostrum	—	—	2 studies	IL-6 does not appear to be influenced with supplementation of colostrum.
D	Conjugated Linoleic Acid			1 study	
D	Vitamin C			1 study	
D	Iodine	↓	★☆☆ Minor	1 study	There is a minor decrease in circulating IL-6 associated with iodine supplementation, thought to be indicative of a minor antiinflammatory effect.
D	Pyrroloquinoline quinone	↓	★☆☆ Minor	1 study	IL-6 appeared to be significantly reduced in the serum of adults given PQQ supplementation relative to baseline.

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Intestinal Motility

Intestinal motility refers to the speed of which food particulate passes through the intesines, with an increase in motility causing faster evacuation and a prolonged motility time being the opposite.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Senna alexandrina	↑	★★★ Strong	10 studies	Senna Alexandria is a reference drug for its laxative effects , with comparable efficacy to oral polyethylene glycol (PEG; used before colonoscopies) and lactulose, but more cost-effective than the latter
C	Curcumin	↑	★☆☆ Minor	1 study	May increase intestinal motility
C	Yacon	↓	★★★ Notable	1 study	The one study to assess intestinal motility (speed of food transit from stomach to anus) has noted a near halving of time, suggesting a relatively notable anti-motility action.
D	Psyllium	↑	★☆☆ Minor	1 study	Increases intestinal motility due to being a bulk laxative, but is unlikely to have a strong laxative effect.

Intestinal Parasites

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Colostrum	—	—	3 studies	Even in cases where traveler's diarrhea (from E.coli) is successfully treated, the overall amount of bacteria found in the stool is not modified suggesting no actual antibacterial properties.
D	Origanum vulgare	↓	★★★☆☆ Notable	1 study	One lone study (potential financial influence) has noted ablation of parasites in infected humans (77% of study group) and a reduction otherwise as assessed by stool samples.

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Intestinal Permeability

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Colostrum	↓ ↑	★☆☆ Minor	3 studies	Evidence is preliminary, and there are studies suggesting both an increase in permeability and a decrease seen with endurance exercise (increase) or with high heat stress exercise or NSAID coingestion (decrease).
C	Quercetin	↑	★☆☆ Minor	1 study	An increase in the amount of intestinal permeability induced by training in the heat has been noted with quercetin supplementation, which is an adverse event; the influence of quercetin at rest is uncertain
C	Lactobacillus casei			1 study	
D	Whey Protein	↓	★☆☆ Minor	1 study	Appears to decrease intestinal permeability, which is due to the Glutamine content of whey protein.

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Intraocular Pressure

Intraocular pressure (IOP) is the pressure within an eye that is elevated in instances of retinal disorders such as glaucoma, and contributes to the pathology. Supplements that reduce IOP are known to reduce pain and possibly improve vision in these conditions.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Ginkgo biloba	—	—	3 studies	Despite the increase in ocular blood flow associated with repeated dosing of ginkgo biloba, there does not appear to be a significant modification of intraocular blood pressure in persons with normal IOP.
C	Coleus forskohlii	↓	★☆☆ Minor	2 studies	Somewhat effective as ocular eyedrops in reducing ocular pressure.
C	Melatonin	↓	★☆☆ Minor	1 study	Oral supplementation of melatonin (500mcg) is able to reduce intraocular pressure in otherwise healthy persons
C	Astaxanthin			1 study	
D	CDP-choline	—	—	1 study	Despite the improvements seen in visual acuity and eye health with supplementation of CDP-Choline, intraocular pressure does not appear to be affected.

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Iron Absorption

Iron Absorption is the percentage of iron that is absorbed from a meal, also known as its bioavailability. Many supplements appear to interact with iron absorption in a meal, either in an additive or hindering fashion.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Green Tea Catechins	↓	★☆☆ Minor	1 study	A decrease in iron absorption associated with green tea catechins has been noted
C	Psyllium	—	—	2 studies	No significant influence on iron absorption; it is possible the inhibitory effect of phytates in the small intestine are negated by the reduced pH in the colon that enhances mineral reuptake
C	Zinc	↓	★☆☆ Minor	7 studies	Iron absorption is decreased when both iron and zinc exceed 10mg in a supplement given on an empty stomach. The inhibition does not appear to be relevant if the same ratio is at lower doses (500mcg) or if the minerals are ingested via food products.
D	Curcumin	—	—	1 study	No significant influence on iron absorption
D	Alpha-GPC	↑	★☆☆ Minor	2 studies	It is possible that Alpha-GPC increases iron absorption from non-meat sources (nonheme iron), but the evidence is currently mixed and a very low dose of 46mg may be required (which would render supplementation irrelevant).

Irritability

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Vitex agnus castus	↓	★☆☆ Minor	1 study	Can reduce irritability as a side effect of PMS, no evidence as to whether this reduction in irritability applies to other persons (males) or periods that are not PMS.
C	Krill Oil	↓	★☆☆ Minor	1 study	Irritability as a side-effect of PMS has been reduced with supplemental krill oil
C	Peppermint	↓	★☆☆ Minor	1 study	Irritability as a side-effect of tension headaches is reduced secondary to the treatment of tension headaches
C	N-Acetylcysteine			2 studies	
D	Royal Jelly	↓	★☆☆ Minor	1 study	Decrease in irritability seen with Royal Jelly may be secondary to reducing the symptoms of menopause

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Ketone Bodies

Ketone bodies are small molecules that are produced in higher amounts during states of carbohydrate depletion, and are known to contribute to energy metabolism and may influence other aspects of the body.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Fish Oil	↑	★☆☆ Minor	1 study	An increase in ketone bodies has been noted when fish oil is paired with a weight loss diet (relative to placebo)
C	Branched Chain Amino Acids	—	—	1 study	No significant alterations in formation of ketone bodies, which may be due to the ketogenic BCAA (leucine) being offset by the other two glucogenic ones
D	Coconut Oil	↑	★☆☆ Minor	1 study	Has been implicated in increasing serum ketones more than other fatty acids.
D	Sodium Bicarbonate	↑	★☆☆ Minor	2 studies	During fasting or ketogenic diets, sodium bicarbonate supplementation may be able to increase ketone body production. This appears to be of somewhat small magnitude and was not associated with additional fat loss
D	Colostrum	↓	★☆☆ Minor	1 study	A decrease in ketone bodies in type II diabetics was noted with supplementation of colostrum daily for four weeks; the decrease was mild, and there was no protein containing placebo for comparison.

Kidney Function

Kidney function tends to refer to a series of urinary or serum biomarkers that are thought to accurately assess kidney health, and supplements that change these biomarkers in a positive direction are thought to aid in kidney function.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Creatine	—	—	13 studies	In otherwise healthy persons given creatine supplementation, there is no significant beneficial nor negative influence on kidney function.
C	Benfotiamine	—	—	1 study	Insufficient evidence to support enhanced kidney function.
C	Curcumin	↑	★☆☆ Minor	2 studies	Appears to promote kidney function in instances where function is normally hindered
C	Trimethylglycine	—	—	1 study	No significant alterations of kidney function in healthy persons given betaine (4g) for six months.
C	Astaxanthin			1 study	
C	Chromium	—	—	1 study	No apparent influence on kidney function (negative nor positive) with chromium supplementation in older sedentary adults.
C	Vitamin E	—	—	2 studies	Biomarkers of kidney function are not significantly altered with supplementation of vitamin E relative to placebo.
D	Astragalus membranaceus	↑	★★★☆☆ Notable	1 study	Despite statistically weak evidence, case studies suggest <i>curative</i> effects.

					Potential of astragalus for aiding kidney function.
D	Conjugated Linoleic Acid	—	—	1 study	No significant influence of CLA supplementation on renal functioning
D	Tetradecyl Thioacetic Acid			2 studies	

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Lactate Production

Lactate can be produced during prolonged exercise, and while it is not thought to contribute to muscular failure it seems to be a good biomarker of it. Reductions in lactate production tend to be associated with prolonged physical endurance.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Sodium Bicarbonate	↓ ↑	★★★☆☆ Notable	37 studies	Increases of lactate production are noted in short intense exercises (due to allowing more work to be conducted, and the work produces more lactate) while prolonged exercise is associated with a decrease in lactate concentrations relative to placebo
B	L-Carnitine	↓	★☆☆☆☆ Minor	5 studies	Lactate production appears to be decreased in studies that note an increase in muscular carnitine stores, although the decrease is not overly notable
B	Caffeine	↑	★☆☆☆☆ Minor	6 studies	Seems to increase lactate production during exercise when caffeine is acutely preloaded
B	Branched Chain Amino Acids	—	—	3 studies	There does not appear to be any reliable or significant changes in blood lactate concentrations following exercise with BCAA supplementation
B	Creatine	—	—	6 studies	On studies in swimmers, there is no apparent reduction or increase in lactate after sprinting exercises.
B	Trimethylglycine	—	—	3 studies	An attenuation in the rise of lactate seen in more

					endurance based exercise may need to be replicated, since two other studies (majority of evidence) have failed to find an interaction with betaine ingestion and lactate.
B	Colostrum	—	—	4 studies	Lactate production during physical exercise does not appear to be any different with dietary colostrum when compared to whey protein.
C	Rhodiola Rosea	↓	★☆☆ Minor	1 study	A decrease in lactate production has been noted with rhodiola supplementation; practical significance unknown
C	Panax ginseng	↓	★☆☆ Minor	1 study	A decrease in lactate has been noted one hour into training in heat, with no significant influence prior to one hour
C	Citrulline	—	—	1 study	No significant influence on lactate production seen with citrulline supplementation before exercise
C	Arginine	—	—	1 study	No significant influence on lactate production associated with L-arginine supplementation
C	Astaxanthin			1 study	
C	Chromium	↑	★☆☆ Minor	2 studies	Mixed evidence, but at least one study has noted that lactate production during exercise was greater with 600mcg chromium than it was with placebo; no known mechanism for this observation.
C	Vitamin E	—	—	1 study	Lactate production during exercise does not appear to be influenced with supplementation of vitamin E.
D	Phosphatidylserine	—	—	1 study	

					No significant influence on exercise-induced lactate production

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LDL-C

Low Density Lipoprotein (LDL) cholesterol is (sometimes falsely) seen as the 'bad' cholesterol and is the ying to HDL-C's yang. LDL serves to bring fatty acids and cholesterol from the liver and circulate them to tissues, oxidized LDL (oLDL) can contribute to heart disease.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Policosanol	↓	★☆☆ Minor	13 studies	It is possible that policosanol is either effective or totally ineffective due to older Cuban studies being remarkably different than more recent replications; high probability of publicity bias
A	Psyllium	↓	★☆☆ Minor	6 studies	Not overly potent reductions of LDL-C, although they seem to reliably occur in persons with high cholesterol
A	Fish Oil	↓ ↑	★☆☆ Minor	32 studies	A decrease has been noted in persons without high cholesterol in the first place, and the decreasing effect of statins appears to be augmented with fish oil. However, in persons at higher risk for cardiovascular disease due to high triglycerides and cholesterol (who more frequently use fish oil as therapy) it is possible LDL-C may actually be increased. The magnitude tends to be in the 5-10% range.
A	Garlic	↓	★★★☆☆ Notable	14 studies	There appears to be a reliable and significant reduction in circulating LDL cholesterol in hypercholesterolemic persons with garlic supplementation, and the magnitude of this change tends to be in the range of 10-20% (more potency in those with worse profiles at baseline)

A	Red Clover Extract	—	—	13 studies	Although a minor effect may occur in those with high blood cholesterol concentrations, the majority of evidence does not support a role of Red Clover Extract in reducing LDL-C when supplemented.
A	Chromium	—	—	13 studies	The best evidence to date does not support a role for chromium in the reduction of LDL cholesterol, even when assessing type II diabetic individuals.
B	Curcumin	—	—	3 studies	Possible reducing effects that need to be further demonstrated
B	Conjugated Linoleic Acid	—	—	11 studies	Insufficient evidence to support decreases of LDL-C and evidence to support no influence whatsoever.
B	Spirulina	↓	★☆☆ Minor	6 studies	Degree of efficacy seems variable and correlated with disease state (more drastic improvements when LDL-C is much higher) but currently does not appear to be overly remarkable unless fatty liver exists.
B	Berberine	↓	★☆☆ Minor	1 study	The reduction of LDL-C when berberine was paired with lifestyle changes was -0.58mmol/L (95% CI -0.78 to -0.39) in diabetics, suggesting a significant benefit but not remarkably potent.
B	Olive leaf extract	↓	★☆☆ Minor	5 studies	A decrease in LDL-C seems to be somewhat consistent, but the magnitude of decrease is not overly impressive relative to other agents
B	Dehydroepiandrosterone	—	—	4 studies	Although there is some

					counter evidence, usually DHEA supplementation does not alter LDL-C concentrations
B	Green Tea Catechins	↓	★☆☆ Minor	4 studies	There appears to be somewhat of a reduction in LDL-C associated with consumption of green tea polyphenolics (5% or so with 500mg catechin intake)
B	L-Carnitine	—	—	2 studies	No detectable influence on LDL-C levels
B	Zinc	↓	★☆☆ Minor	3 studies	A decrease in LDL cholesterol may occur when a zinc deficiency in obese persons is being normalized.
B	Nigella sativa	↓	★☆☆ Minor	8 studies	Reductions in LDL-C are mild at best and only occur in persons with impaired lipid profiles (high cholesterol or dyslipidemia), but they do appear to occur with ingestion of the seed extract
B	Hesperidin	—	—	5 studies	Similar to total cholesterol, while there may be a minor reduction in those at the worst levels of LDL cholesterol those with minor increases fail to find benefit.
B	Trimethylglycine	↑	★☆☆ Minor	3 studies	Similar to total cholesterol, one study noted a stasis in LDL when placebo decreased (a relative increase). Reasons for this unknown and the data needs to be replicated, and HDL was unaffected.
B	Astaxanthin			3 studies	
B	Vitamin E	—	—	9 studies	Vitamin E supplementation does not appear to alter the overall levels of LDL cholesterol.
C	Pruvate	↓	★☆☆	2 studies	

C	Ginger	↓	★☆☆ Minor	1 study	A reducing effect on LDL-C has been noted once during caloric surplus; practical relevance of this information unknown
C	Quercetin	↓	★☆☆ Minor	2 studies	A decrease in LDL-C has been noted in persons with high blood lipids, although this decrease is not observed in persons who do not have high LDL-C concentrations.
C	Black Cohosh	—	—	1 study	No significant effects on LDL-C
C	Punicic Acid	—	—	2 studies	No significant influences on LDL-C levels
C	Whey Protein	↓	★☆☆ Minor	1 study	Possible LDL-C lowering effect, but has not yet been shown to be better than other protein sources.
C	Grapefruit	↓	★☆☆ Minor	1 study	A decrease in LDL cholesterol has been noted, but may be due to weight loss
C	Vanadium	—	—	3 studies	Mixed effects on LDL-C, likely no direct influence on LDL but may reduce overall LDL levels secondary to improving the diabetic state (which normally increases LDL)
C	Artichoke Extract	↓	★☆☆ Minor	4 studies	Nothing remarkable about the reductions in LDL-C, seem to occur somewhat reliably and are minor in magnitude
C	Licorice	—	—	1 study	No significant influence on LDL cholesterol seems apparent
C	Gynostemma pentaphyllum	—	—	1 study	LDL cholesterol appears unaffected

C	Green Coffee Extract	—	—	1 study	LDL cholesterol appears unaffected
C	Pueraria mirifica	↓	★☆☆ Minor	1 study	Somewhat effective in menopausal women.
C	Hemp Protein	—	—	2 studies	No significant modifications in LDL-C levels
C	Nattokinase	—	—	1 study	No significant influence on LDL cholesterol
C	Eleutherococcus senticosus	↓	★☆☆ Minor	1 study	A decrease in LDL-C has once been noted
C	Benfotiamine	—	—	1 study	Although not a primary research end-point, no significant influence on LDL-C is seen.
C	Ashwagandha	↓	★☆☆ Minor	3 studies	A slight decrease in LDL-C has been noted following ashwagandha supplementation.
C	Caffeine	—	—	1 study	No significant influences on LDL cholesterol noted
C	Shilajit	↓	★☆☆ Minor	1 study	Minor decrease in LDL has been noted with shilajit
C	Theaflavins	—	—	1 study	No detectable influence on LDL-C levels following theaflavin consumption
C	Ecklonia cava	↓	★☆☆ Minor	2 studies	Possible reductions in LDL-C
C	Salvia hispanica	—	—	2 studies	LDL-C appears to be unaffected with chia ingestion when compared to similar macronutrient sources
C	Gamma Oryzanol	—	—	1 study	Although rice bran oil may

					reduce LDL cholesterol, there is insufficient evidence to support the role of gamma-oryzanol in this role
C	Garcinia cambogia	—	—	1 study	Garcinia appears unable to influence LDL-C levels based on preliminary evidence
C	Ganoderma lucidum	—	—	1 study	No significant reducing effects on LDL cholesterol have been noted with ganoderma supplementation
C	Grape Seed Extract	—	—	2 studies	No significant interactions with LDL-C even in high risk persons
C	Hibiscus sabdariffa	—	—	3 studies	LDL cholesterol appears to be unaffected following Roselle ingestion
C	HMB	—	—	2 studies	No significant influence on LDL cholesterol levels
C	Japanese Knotweed	—	—	1 study	LDL-C appears to be unaffected, but testing has not been conducted in metabolically unwell persons
C	Irvingia gabonensis	↓	★☆☆ Minor	2 studies	A decrease in LDL-C has been noted, confounded with both weight loss and industry influence.
C	Magnesium	—	—	2 studies	No significant influence on LDL cholesterol levels seen with magnesium supplementation
C	Melatonin	—	—	1 study	No significant influence on LDL cholesterol is noted with melatonin
C	Microlactin	↓	★☆☆ Minor	1 study	A reduction in LDL-C is seen in hyperlipidemics associated with hyperimmune milk

					consumption
C	Vitamin C	—	—	1 study	No significant alterations in LDL cholesterol seen with Vitamin C supplementation
C	Vitamin D	↑	★☆☆ Minor	1 study	Either no significant influence on LDL cholesterol or a slight increase (around 5%) has been noted; practical significance of this information unknown
C	Soy lecithin	↓	★★★☆☆ Notable	1 study	A decrease in LDL-C has been noted with soy lecithin ingestion to the degree of 42.05-56.15% in hypercholesterolemics, which is a remarkable decrease. Requires replication.
C	Royal Jelly	—	—	3 studies	Although a reduction in LDL-C cannot be ruled out (due to the reduction in total cholesterol), the best evidence currently suggest no effect while uncontrolled studies confirm a reduction of minor magnitude
C	Resveratrol	↓	★☆☆ Minor	1 study	Possible decreases in LDL-C in persons at risk for heart disease, but it does not appear to be of large magnitude
C	Guggul	↑	★☆☆ Minor	2 studies	Although unreliable, there is a possible increase in LDL cholesterol from Guggul supplementation
C	Panax ginseng	↓	★☆☆ Minor	2 studies	May reduce LDL-C levels to a very small degree, seems unreliable in doing so
C	Phosphatidylserine	—	—	1 study	No significant influence on LDL-C with PS supplementation
C	Krill Oil	↓	★★★☆☆ Notable	2 studies	A decrease in LDL-C has been

			Notable		noted with krill oil, which appears to be to quite a significant degree
C	Ephedrine	↓	★☆☆ Minor	1 study	A decrease in LDL-C has been noted to be associated with ephedrine, although this may be confounded with weight loss (also seen in the trials)
C	Citrulline	—	—	1 study	No significant influence on LDL-C concentrations in serum following citrulline supplementation
C	Vitamin K	—	—	1 study	LDL-C appears to be unaffected by supplemental vitamin K
C	Sea Buckthorn	—	—	1 study	No significant influence on LDL-C levels in otherwise healthy men
C	Blueberry	—	—	2 studies	No significant changes in LDL-C concentrations in serum with blueberries.
C	Inositol	↓	★☆☆ Minor	5 studies	A decrease in LDL-C has been noted alongside other improvements in lipid parameters.
C	Rooibos	↓	★☆☆ Minor	2 studies	A decrease in LDL-C has been noted to a minor degree in persons at risk for cardiovascular disease, but there is no inherent reduction in LDL-C in otherwise healthy persons.
C	Anethum graveolens			2 studies	
C	Citrullus colocynthis	—	—	2 studies	A possible reduction seen in persons with high blood triglycerides and cholesterol failed to reach statistical significance due to large variance.

C	Creatine			2 studies	
C	Phosphatidylcholine			1 study	
C	Yacon	↓	★☆☆ Minor	1 study	A respectable decrease in LDL has been reported once, although this reduction in LDL is confounded with weight loss that occurred with yacon syrup.
C	Rose Hip	↓	★☆☆ Minor	1 study	A mild reduction in LDL cholesterol levels seen in obese persons with rose hip supplementation explains the reduction in total cholesterol, as HDL-C appears to be unaffected.
D	Pueraria lobata	—	—	1 study	No significant influence on circulating LDL-C has been noted with supplementation
D	Coconut Oil	↓	★☆☆ Minor	1 study	Not an overly significant reduction of LDL-C, but it does appear to be present relative to longer chain fatty acids
D	Yerba mate	↓	★☆☆ Minor	3 studies	Decreases in LDL cholesterol have been noted in metabolically unwell persons following moderate Mate consumption (as brewed tea)
D	Eclipta alba	↓	★★★☆☆ Notable	1 study	Decreases in LDL-C have been noted with eclipta alba in hypertensive persons to 24%, which is quite a significant reduction.
D	Pycnogenol	↓	★☆☆ Minor	2 studies	May reduce LDL cholesterol for as long as pycnogenol is taken (some evidence to suggest a normalization after supplement cessation)
D	Tetradecyl Thioacetic Acid	↓	★☆☆ Minor	3 studies	Possible reductions in LDL cholesterol seen with TTA consumption

D	Safflower Oil	—	—	1 study	No significant alterations in LDL-C concentrations
D	Emblica officinalis	↓	★☆☆ Minor	1 study	A decrease in LDL-C has been noted with consumption of the fruits over 21 days, affecting both healthy controls and diabetics
D	Horse Chestnut	—	—	1 study	No detectable influence on LDL cholesterol concentrations associated with horse chestnut extract.
D	Rubus coreanus	—	—	1 study	No significant influence of <i>rubus coreanus</i> on LDL cholesterol levels in otherwise healthy persons.
D	Perilla Oil			1 study	
D	Pyrroloquinoline quinone	—	—	1 study	No apparent changes to LDL cholesterol exist in otherwise healthy adults given PQQ supplementation daily for up to three weeks.

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Lean Mass

Lean Mass is overall body mass after Fat Mass has been subtracted. It consists of organs, bone, the brain, water and contractile muscle; since changes in the first three do not occur often, changes in lean mass are assumed to either be muscle tissue, glycogen (energy storage) or water.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Creatine	↑	★☆☆ Minor	19 studies	Does appear to have inherent lean mass building properties, but a large amount of research is confounded with water weight gains (difficult to assess potency).
A	Conjugated Linoleic Acid	↑	★☆☆ Minor	15 studies	Some evidence that CLA can preserve lean mass during fat loss in an obese cohort of patients, but even in this subgroup the results are highly unreliable.
B	Dehydroepiandrosterone	—	—	8 studies	Perhaps due to a lack of studies pairing DHEA with a prolonged resistance training program, there is no evidence to support DHEA supplementation to increase muscular or lean mass
B	Whey Protein	↑	★☆☆ Minor	4 studies	Protein in general increases lean mass, but there is not a significant body of evidence to support whey protein as being more effective than other protein sources
B	HMB	—	—	8 studies	No significant influences on lean body mass associated with HMB supplementation
B	Chromium	—	—	8 studies	Studies in trained and untrained persons, with or without physical exercise, have

					failed to find an increase in the rate of lean mass accrual relative to placebo.
B	Colostrum	↑	★☆☆ Minor	5 studies	Colostrum, inherently due to being a dietary protein, appears to promote lean mass accrual. This is comparable to a similar dose of whey protein as the growth factors in colostrum do not appear to provide an additional benefit.
C	L-Carnitine	↑	★☆☆ Minor	2 studies	An increase in lean mass has been noted in elderly persons. This may not apply to lean healthy individuals, and no research assesses youth
C	Yohimbine	—	—	1 study	No significant influence on lean mass detected with yohimbine ingestion
C	Punicic Acid	—	—	1 study	No significant influence on lean mass has been noted with puniceic acid supplementation
C	Beta-Alanine	↑	★☆☆ Minor	3 studies	Doesn't appear overly potent, but either inherently or through greater workload there appears to be a hypertrophic effect associated with beta-alanine.
C	Licorice	—	—	1 study	No significant alterations in lean mass associated with licorice
C	Coleus forskohlii	↑	★☆☆ Minor	1 study	Somewhat effective (2lbs over 12 weeks relative to placebo) although somewhat confounded with the increase in bone mass, as lean mass is inclusive of bone and skeletal muscle.
C	Velvet Antler	—	—	1 study	No interaction between velvet antler and lean mass accrual

C	Tribulus terrestris	—	—	2 studies	Insufficient evidence to support an increase of lean mass associated with tribulus relative to placebo during a training program.
C	Ecdysteroids	—	—	1 study	No differences between ecdysteroids and placebo in improving lean mass accrual during a weight lifting program
C	Fenugreek	—	—	1 study	No demonstrated benefit to lean mass accrual in otherwise healthy trained men given a workout program
C	Vitamin D	↓↑	★☆☆ Minor	2 studies	An increase in lean mass has been noted in dieting obese women relative to control (2,000IU) and a trend to reduce lean mass relative to control has been noted in exercising healthy persons (4,000IU); there appears to be potential for both effects with Vitamin D supplementation, but there is insufficient evidence to draw conclusions
C	Fish Oil	—	—	3 studies	No significant influence on lean mass associated with fish oil supplementation
C	Leucine			1 study	
C	Arachidonic acid			1 study	
C	Leucic Acid	↑	★☆☆ Minor	1 study	An increase in lean mass has been noted in the legs of soccer players to the degree of 0.4kg over 4 weeks; this study currently stands alone
C	Arginine	↑	★☆☆ Minor	1 study	An increase in lean mass has been noted in persons with impaired glucose tolerance using L-arginine over a long period of time, where placebo experienced a decrease. It is unsure how this applies to

					otherwise healthy persons
C	Glutamine	—	—	1 study	Supplemental glutamine does not appear capable of increasing lean mass when paired with a weightlifting routine.
C	D-Aspartic Acid	—	—	1 study	No significant influence on lean mass in otherwise healthy trained men.
C	Hoodia gordonii	—	—	1 study	No significant modifications in lean mass during weight loss with hoodia relative to placebo
C	Trimethylglycine	—	—	2 studies	In studies assessing lean mass, there are no apparent changes with supplementation of betaine.
D	Eurycoma Longifolia Jack	↑	★☆☆ Minor	1 study	One pilot study has noted an increase more than control when both eurycoma and control were paired with exercise
D	Safflower Oil	↑	★☆☆ Minor	1 study	An increase in lean mass relative to control (CLA) has been noted in obese menopausal women
D	Ashwagandha	—	—	1 study	There was a slight trend to increase lean mass in otherwise sedentary persons over 30 days, but it failed to reach statistical significance.

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Left Ventricular Ejection Fraction

Left ventricular ejection fraction (LVEF) is the capacity of the heart to 'pulse' blood out of cardiac tissue and into circulation, and is a biomarker of cardiac health. The reduction in LVEF seen during cardiac ailments tends to be a focus of rehabilitation.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Terminalia arjuna	↑	★☆☆ Minor	2 studies	Appears to increase LVEF in person suffering from cardiovascular ailments; preliminary evidence suggests that this is not limited to myocardial infarction
C	Resveratrol	↑	★☆☆ Minor	1 study	10mg resveratrol appears to improve left ventricle function slightly
C	Vitamin E	—	—	2 studies	Supplementation of vitamin E has failed to influence the activity of the cardiac tissue itself.
D	Coenzyme Q10	↑	★☆☆ Minor	1 study	Has been noted to increase LVEF in persons with myocardial impairment

Leg Swelling

Leg swelling is a transient state of edema caused by prolonged sitting, and may occur even during walking in persons with poor circulation or during the later months of pregnancy. Some supplements that improve blood circulation may help with leg swelling.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Horse Chestnut	↓	★★★☆☆ Notable	3 studies	Symptoms of leg swelling and varicose veins appear to be fairly reliably reduced with the recommended oral doses of horse chestnut supplementation.
B	Centella asiatica	↓	★☆☆☆☆ Minor	5 studies	The leg swelling associated with chronic venous insufficiency appears to be significantly reduced secondary to treating the state of chronic venous insufficiency.
C	Grape Seed Extract	↓	★☆☆☆☆ Minor	1 study	A reduction in leg swelling has been noted in sedentary women (sitting for a day or so), thought to be indicative of better blood flow with grape seed extract
C	Pycnogenol	↓	★★★☆☆ Notable	2 studies	Appears to reduce leg swelling secondary to the enhancement of blood flow. While the evidence is not overly robust, it is comparable if not better than the reference supplement of Horse Chestnut
C	Ruscus aculeatus	↓	★☆☆☆☆ Minor	1 study	Secondary to its venotropic actions in persons with chronic venous insufficiency, supplementation of <i>ruscus aculeatus</i> appears to reduce leg swelling and edema (thigh and ankle).

D	Boswellia serrata	↓	★☆☆ Minor	1 study	Lack of reference drugs limits conclusions that can be made in regards to the potency
D	Chlorella	↓	★☆☆ Minor	1 study	Study in pregnant women, it did have efficacy but more studies are required to assess chlorella overall.

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Length of Sickness

Length of sickness is the duration of which symptoms of a cold or infection persist, and reducing the duration of sickness is said to be a pro-immunity effect. Supplements may either be a daily supplement or taken on an as-needed basis.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Echinacea	↓	★★★☆☆ Notable	6 studies	Although a high variability exists, the meta-analysis has concluded a 1.4-day reduction in sickness when it occurs relative to placebo. As echinacea is also a comparator for sickness, this reduction is notable
B	Vitamin C	—	—	4 studies	Mixed influences on the length one is sick for, with possibly no effect
B	Colostrum	—	—	4 studies	Despite tenuous evidence suggesting a reduction in the frequency of sickness with colostrum, when sickness does occur there is no benefit of colostrum in reducing how long it occurs for.
C	Andrographis paniculata	↓	★★★☆☆ Notable	1 study	Seems to be one of the few compounds able to reduce the length of sickness when taken at the first signs of sickness. The lack of a reference drug to compare Andrographis limits the strength of the evidence
C	Garlic	↓	★★☆☆☆ Minor	1 study	The length that one is sick for is only modestly reduced with garlic supplementation even at higher doses.

Leptin

Leptin is a well-known 'adipokine' (signalling molecule made in body fat) that acts as a nutrient sensor, and increases metabolic rate during periods of overfeeding; its secretion is sensitive to carbohydrate ingestion, and its elevation during dieting desired.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Melatonin	↑	★☆☆ Minor	3 studies	Mixed influences on leptin, but melatonin may be able to increase leptin levels following acute administration
C	Conjugated Linoleic Acid	—	—	2 studies	Not enough evidence to support alterations in circulating leptin due to CLA ingestion.
C	Fenugreek	—	—	1 study	No significant influences detected on circulating leptin levels with fenugreek
C	Japanese Knotweed	—	—	1 study	No significant influence on leptin in otherwise healthy and lean individuals
C	Irvingia gabonensis	↓	★☆☆ Minor	1 study	May decrease leptin, but is confounded with weight loss
C	Fish Oil	—	—	2 studies	No significant influence on Leptin in serum
C	Zinc	↓ ↑	★☆☆ Minor	2 studies	Normalizing a zinc deficiency increases leptin (which is suppressed during deficiency), but elsewhere the abnormal elevation of zinc seen in morbid obesity has been reduced alongside weight loss and insulin sensitization from zinc.
C	Garlic	—	—	1 study	

					In a study that noted an increase in adiponectin in persons with metabolic syndrome, there was no influence on circulating leptin concentrations.

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Leukotriene B4

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin E	↓	★☆☆ Minor	4 studies	Mixed evidence as to whether leukotriene B4 can be reduced in diabetics with vitamin E supplementation.
C	Fish Oil	—	—	2 studies	No significant influence on LKB4 concentrations

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Libido

Libido is the spontaneity, frequency, and magnitude of sexual desire. Some supplements (falsely referred to as aphrodisiacs) are known to enhance libido or normalize a reduced libido seen in instances of sexual dysfunction.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Dehydroepiandrosterone	—	—	3 studies	Insufficient evidence to support an increase in libido despite increases in androgen status
B	Maca	↑	★★☆ Notable	3 studies	An increase in libido appears to occur following Maca ingestion, which is notable as it appears to influence all demographics and is not associated with systemic hormones
B	Ginkgo biloba	—	—	4 studies	Although a potential benefit cannot be ruled out at this moment in time (the first pilot study showed promise and there are some responders), overall ginkgo does not appear to influence SSRI-induced sexual dysfunction in more well conducted trials.
C	L-DOPA	—	—	1 study	No significant influence on libido
C	Fenugreek	↑	★★☆ Notable	1 study	Increases in libido have been noted before, which is notable due to the lack of significant influence on testosterone and possible suppression of DHT (theoretically should reduce libido, yet a large increase is seen with fenugreek)
C	Panax ginseng	↑	★★☆ Minor	1 study	May increase libido as a side-effect of reducing the

					symptoms associated with menopause, may not work inherently in youth or men
C	Nicotine	—	—	2 studies	There do not appear to be any significant interactions with nicotine and libido
C	Eurycoma Longifolia Jack	↑	★☆☆ Minor	1 study	An increase in libido is seen with prolonged daily ingestion of eurycoma supplements in the range of 8.4-10.8%
C	Velvet Antler	—	—	1 study	There does not appear to be a significant influence of velvet antler supplementation on the libido
C	Tribulus terrestris	↑	★☆☆ Minor	1 study	There appears to be an increase in frequency of coitus and improvement in sexual well being associated with supplementation of 6g of the basic root extract of tribulus.
C	Chromium	↑	★☆☆ Minor	1 study	Perhaps secondary to causing an antidepressive effect, supplementation of chromium was able to alleviate a suppressed libido resulting in an increase relative to control; no studies in nondepressed persons.

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Lipid Peroxidation

A form of oxidation that influences lipids. In the body, it tends to reflect damage to cell membranes and is assessed by biomarkers thought to represent lipid peroxidation (MDA and TBARS).

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Creatine	↓	★☆☆ Minor	3 studies	A minor reduction, nothing to a remarkable degree.
B	L-Carnitine	↓	★☆☆ Minor	3 studies	The reduction in MDA that occurs during exercise may also occur at rest, suggesting a per se effect
B	Coenzyme Q10	↓	★★★☆☆ Notable	4 studies	Appears to reduce biomarkers of lipid peroxidation. CoQ10 tends to be a reference drug for lipid peroxidation, and although it is more potent than other nutraceuticals it is not astounding.
B	Vitamin C	↓	★☆☆ Minor	6 studies	Mixed and weak influences on lipid peroxidation, but a possible reduction exists
B	Spirulina	↓	★★★☆☆ Notable	3 studies	Although there is no reference drug to compare the effects of Spirulina against, the decrease in lipid peroxidation as assessed by serum MDA is quite notable and is likely stronger than other supplements. A comparative study would be needed
B	Curcumin	↓	★☆☆ Minor	3 studies	A decrease in lipid peroxidation results following curcumin ingestion chronically
B	Fish Oil	↓ ↑	★☆☆ Minor	5 studies	Both increases and decreases in lipid peroxidation have been

					noted with fish oil supplementation, with the increases in peroxidation usually seen with high doses of fish oil paired with other oxidative stressors (such as marathon running)
B	Zinc	↓	★☆☆ Minor	3 studies	A slight decrease in lipid peroxidation has been noted with supplementation of zinc in persons who may be deficient.
B	Astaxanthin			4 studies	
B	Chromium	↓ ↑	★☆☆ Minor	7 studies	While minor, increases in lipid peroxidation have been noted in nondiabetic controls while decreases have occurred in those with a high baseline HbA1c. A possible modulatory effect exists.
B	Vitamin E	↓ ↑	★☆☆ Minor	9 studies	Vitamin E tends to reduce lipid peroxidation in instances where there is elevated oxidation, and tends to have no effect in otherwise healthy persons. In instances where vitamin E is thought to greatly exceed the activity of co-antioxidants (vitamin C or ALA) it can exert a prooxidant effect.
C	Melatonin	↓	★☆☆ Minor	1 study	A reduction in lipid peroxidation has been noted with melatonin
C	Eleutherococcus senticosus	—	—	1 study	Insufficient evidence to evaluate lipid peroxidation reducing effects
C	Alpha-Lipoic Acid	↓	★☆☆ Minor	2 studies	Appears to reduce biomarkers of lipid peroxidation (MDA mostly)
C	Cissus quadrangularis	↓	★☆☆ Minor	1 study	A minor reduction in lipid peroxidation has been seen in serum associated with weight loss; uncertain significance.

C	Rhodiola Rosea	—	—	2 studies	No significant influences on lipid peroxidation biomarkers in serum
C	Olive leaf extract	↓	★☆☆ Minor	2 studies	Appears to reduce biomarkers of lipid peroxidation.
C	Shilajit	↓	★☆☆ Minor	1 study	A decrease in lipid peroxidation (assessed by MDA) has been noted in serum and semen following oral ingestion of shilajit
C	Stinging Nettle	—	—	1 study	No significant effect on lipid peroxidation has been noted.
C	Ganoderma lucidum	—	—	2 studies	No significant changes in lipid peroxidation biomarkers (such as MDA) are present following ingestion of Reishi
C	Kaempferia parviflora	↓	★☆☆ Minor	1 study	A minor decrease in lipid peroxidation has been noted with supplementation of low doses
C	Licorice	↓	★☆☆ Minor	2 studies	A decrease in lipid peroxidation is noted with licorice consumption, not to a remarkable degree
C	Methylsulfonylmethane	↓	★☆☆ Minor	1 study	A decrease in exercise-induced lipid peroxidation is noted as assessed by serum MDA
C	Citrulline	—	—	1 study	No significant influence of citrulline on lipid peroxidation has been noted
C	Rooibos	↓	★☆☆ Minor	1 study	A decrease in lipid peroxidation has been noted following oral ingestion of Rooibos tea
C	Garlic	↓	★☆☆ Minor	3 studies	A reduction in lipid peroxidation in the blood and in red blood

					cells has been noted in some states of metabolic ailment (aging and hypertension). Not 100% reliable as it wasn't seen in one study on hypercholesterolemia, and no studies in healthy controls.
C	Red Clover Extract	—	—	1 study	No known interactions with serum MDA concentrations, a biomarker of lipid peroxidation.
C	Trimethylglycine	—	—	1 study	No significant alterations have been noted in circulating biomarkers of lipid peroxidation.
D	Green Tea Catechins	↓	★☆☆ Minor	1 study	Can decrease biomarkers of lipid peroxidation
D	Aronia melanocarpa	↓	★★★☆☆ Notable	1 study	Definitely requires more evidence, but appears to be fairly effective at reducing lipid peroxidation and other oxidative parameters (lone study noting a 40% reduction with aronia)
D	Yerba mate	↓	★☆☆ Minor	1 study	A decrease in lipid peroxidation has been noted with Mate consumption over 7 days
D	Eclipta alba	↓	★☆☆ Minor	1 study	A decrease in biomarkers of lipid peroxidation has been noted, possible related to an increase in serum Vitamin E concentrations
D	Hibiscus sabdariffa	↓	★☆☆ Minor	1 study	Has been noted to reduce lipid peroxidation
D	Melissa officinalis	↓	★☆☆ Minor	1 study	A slight decrease in biomarkers of lipid peroxidation occurs following ingestion of lemon balm
D	Punicalagins	↓	★☆☆ Minor	1 study	A decrease in lipid peroxidation has been noted

D	Krill Oil	—	—	1 study	Despite containing PUFAs, no significant changes in lipid peroxidation
D	Blueberry	↓	★☆☆ Minor	1 study	Alongside the reduction in serum oxidation comes a reduction in lipid peroxidation biomarkers such as MDA
D	Ginger	↓	★★★☆☆ Notable	1 study	In the semen of infertile men, the reduction in lipid peroxidation has reached 53.7% with supplementation of ginger over three months.
D	Stephania tetrandra	↓	★☆☆ Minor	1 study	A minor decrease in levels of lipid peroxidation in serum were noted, to the tune of 17%.
D	Rubus coreanus	↓	★☆☆ Minor	1 study	In otherwise healthy men with no apparent health problems, there is a mild decrease in lipid peroxidation associated with consumption of the berries (12% reduction in MDA)
D	Pyrroloquinoline quinone	↓	★☆☆ Minor	1 study	Although a decrease technically exists as assessed by TBARS, the decrease was measured at around 0.2% and is practically irrelevant.

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Liver Damage

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	S-Adenosyl Methionine	—	—	1 study	Supplemental SAME in a study of persons with liver damage failed to confer rehabilitative effects
C	Trimethylglycine	↓	★☆☆ Minor	3 studies	Preliminary evidence showed a large decrease in fibrotic area and inflammation in the livers of persons with NAFLD given high dose (20g) betaine, but the best evidence failed to find a significant influence. An interaction is apparent, but the exact role is not known as this time.
D	Vitamin E	↓	★☆☆ Minor	1 study	In those with inflammatory liver damage, supplementation of vitamin E appears to be capable of reducing damage over a long period of time.

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Liver Enzymes

Liver enzymes are a commonly used biomarker to test the toxicity of a supplement, and are elevated in instances of fatty or cirrhotic livers. Their reduction in the blood is thought to reflect less damage to liver cells.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Tauroursodeoxycholic Acid	↓	★★★☆☆ Notable	5 studies	The decrease in liver enzymes associated with cholestasis is quite strong, and TUDCA is a reference drug for these effects
B	Conjugated Linoleic Acid	—	—	10 studies	Inconsistent and unreliable effects on liver enzymes, no significant influence is thought to exist.
B	Nigella sativa	—	—	5 studies	There may be a reducing effect in instances of liver damage (this curative effect needs to be explored more), and there are no alterations in liver enzymes that would be indicative of liver damage.
B	Creatine	—	—	7 studies	No known influence on circulating liver enzymes, suggesting no liver toxicity in humans.
B	Trimethylglycine	↓	★★☆☆☆ Minor	5 studies	Similar to liver fat and damage, the levels of liver enzymes in serum appears to be reduced potentially in preliminary evidence with the currently largest trial showing no significant influence; there may be a role, but it needs to be further elucidated.
B	Chromium	—	—	3 studies	No known influence on liver enzymes or other markers of hepatic health.

B	Vitamin E	↓	★★★☆☆ Notable	9 studies	There appears to be a notable decrease in both ALT and γ-GPT in persons with non-alcoholic fatty liver (NAFLD) which may exceed 50% when vitamin E is supplemented above 300mg for half a year; there does not appear to be any influence whatsoever in healthy controls.
C	L-Carnitine	↓	★★☆☆☆ Minor	1 study	A decrease in liver enzymes has been noted in a model of hepatic encephalopathy, a per se reducing effect is uncertain
C	S-Adenosyl Methionine	—	—	3 studies	No significant rehabilitative effects on liver function in persons with impaired liver function, and no significant alterations in serum liver enzymes in otherwise healthy persons
C	Green Coffee Extract	—	—	1 study	No significant influence noted for liver enzymes when tested in part of a safety assay
C	Nattokinase	—	—	1 study	No significant influence on liver enzymes noted
C	Eleutherococcus senticosus	—	—	2 studies	No significant influence on liver enzymes when measured as a part of a safety test battery
C	Artichoke Extract	↓	★★☆☆☆ Minor	1 study	More evidence is required to establish the potency of the hepatoprotective effects (with liver enzymes as a biomarker)
C	Olive leaf extract	—	—	2 studies	No significant influences on liver enzymes have been noted in trials that assess them (safety reasons)
C	Resveratrol	↓	★★☆☆☆ Minor	1 study	In persons with elevated liver enzymes (not pathological, just metabolic syndrome) there

					appeared to be a protective effect on the liver from resveratrol supplementation
C	Curcumin	—	—	2 studies	No significant influence on liver enzymes associated with curcumin supplementation
C	Ecdysteroids	—	—	1 study	No significant alterations in any measured liver enzymes (ALT, AST, GGT)
C	Fucoxanthin	↓	★★★☆☆ Notable	1 study	In a model of liver fat in obese premenopausal women, fucoxanthin was fairly effective at reducing liver enzymes after prolonged usage
C	Ganoderma lucidum	—	—	1 study	No significant influence on liver enzymes has been noted in toxicological testing with ganoderma
C	Gynostemma pentaphyllum	↓	★★☆☆☆ Minor	1 study	Liver enzymes in a model of fatty liver are decreased with gynostemma ingestion
C	Kava	—	—	2 studies	No significant influence on liver enzymes assuming the water extract (WS1490) is being used
C	Melatonin	↓	★★☆☆☆ Minor	1 study	A decrease in liver enzymes has been noted in persons with fatty liver given melatonin supplementation, although not to a remarkable degree
C	Glutamine	—	—	1 study	In safety testing, there does not appear to be an adverse effect of glutamine supplementation on liver enzymes in serum
C	Fish Oil	—	—	1 study	No significant influence on liver enzymes noted
C	Phosphatidylserine	—	—	1 study	No significant influence on liver

					enzymes seen with PS supplementation
C	Leucine			1 study	
C	HMB	—	—	2 studies	No significant alterations in serum liver enzymes are noted with HMB supplementation
C	Citrulline	—	—	1 study	Plasma concentrations of LDH are unaffected following citrulline supplementation
C	Dehydroepiandrosterone	—	—	1 study	No detectable alteration in serum liver enzymes (biomarker of liver damage) seen with DHEA supplementation
C	Inositol	—	—	1 study	No adverse effects to the liver during human toxicology testing.
C	Picrorhiza kurroa	↓	★☆☆ Minor	1 study	Supplementation of <i>picrorhiza kurroa</i> is able to reduce circulating liver enzymes in acute viral hepatitis. While animal research suggests it is more potent than Milk Thistle , the human evidence is not yet able to directly compare the two.
C	Garlic	↓	★☆☆ Minor	2 studies	One study has noted a 20% decrease in the ALT enzyme following garlic supplementation to otherwise healthy controls.
C	Anethum graveolens			1 study	
C	Hoodia gordonii	↑	★☆☆ Minor	1 study	ALP was noted to be increased in otherwise healthy women given the standard dose of hoodia, although the other liver enzymes were not affected significantly
C	Citrullus colocynthis	—	—	2 studies	Both studies using 300mg of

					either the fruit or seed extract have failed to find alterations in liver enzymes associated with supplementation.
C	Hesperidin	↓	★☆☆ Minor	1 study	In men with high triglycerides and cholesterol, the serum liver enzymes appear to be reduced suggesting protective effects at the level of the liver.
C	Red Clover Extract	—	—	1 study	Liver function does not appear to be significantly altered with supplementation of red clover.
C	Astaxanthin			2 studies	
C	Saffron	—	—	1 study	Supplementation of 100mg saffron extract for six weeks failed to increase liver enzymes in otherwise healthy persons.
C	Rose Hip	—	—	2 studies	No significant influence on the liver enzymes of otherwise healthy persons subject to rose hip supplementation
D	Whey Protein	↓	★☆☆ Minor	1 study	Has been associated with a decrease in liver enzymes (in steatohepatitis) but not to a remarkable degree; may simply be due to the L-cysteine content.
D	Spirulina	↓	★★★☆☆ Notable	2 studies	Preliminary evidence suggests the reduction of liver enzymes correlates with the degree of liver damage somewhat, and this is notable since the reduction of liver fat seen is strongly effective at this moment in time.
D	Black Cohosh	—	—	1 study	No significant influence on liver enzymes
D	Andrographis paniculata	↑	★☆☆ Minor	1 study	Study was in persons with HIV, although the magnitude was of

					concern it needs to be replicated.
D	Terminalia arjuna	—	—	1 study	No significant influence on liver enzymes during standard testing of safety
D	Hibiscus sabdariffa	↓	★☆☆ Minor	1 study	A decrease in liver enzymes has been reported
D	Royal Jelly	—	—	1 study	In safety testing, supplemental Royal Jelly does not appear to increase liver enzymes
D	Tetradecyl Thioacetic Acid	—	—	3 studies	No significant influence on liver enzymes in preliminary testing for possible toxicity
D	Bulbine natalensis			1 study	
D	Rubus coreanus	↓	★☆☆ Minor	1 study	In otherwise healthy men with no health problems, the mild reduction in lipid peroxidation seen was associated with a mild reduction in circulating ALP levels (6%) although AST and GST were unaffected.
D	Ashwagandha	—	—	1 study	In otherwise healthy persons, there is no significant influence on liver enzymes seen with supplementation.
D	Perilla Oil			1 study	
D	Pyrroloquinoline quinone	—	—	1 study	Serum ALT is not affected by supplementation of PQQ for up to three weeks.

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Liver Fat

Liver fat refers to the triglycerides that can be stored in the liver, of which their excess accumulations results in fatty liver (alcohol or non-alcoholic) and possibly later cirrhosis. Some supplements may be able to reduce liver fat stores.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Fucoxanthin	↓	★★★☆☆ Notable	1 study	The decrease in liver fat seen with fucoxanthin tends to be greater than that seen with other supplements, although insufficient evidence exists to suggest reliability of results
C	Fish Oil	↓	★☆☆☆☆ Minor	1 study	A possible decreasing effect of liver fat seen in persons with NAFLD
C	Trimethylglycine	↓	★☆☆☆☆ Minor	3 studies	Preliminary evidence showed a major decrease in liver fat (normalization in over half of persons with fatty liver) but currently the best evidence suggests that this does not occur as potently; there may still be a role, but this requires more research.
C	Vitamin E	↓	★☆☆☆☆ Minor	3 studies	In persons with steatohepatitis, there may be a reduction in liver fat over time when taking vitamin E supplements; currently there is no evidence assessing otherwise healthy persons on this parameter
D	Whey Protein	↓	★☆☆☆☆ Minor	2 studies	Reductions in liver fat have been noted with whey protein supplementation, which is thought to be more effective than other protein sources due to the high L-cysteine content.
D	Spirulina	↓	★★★★★	1 study	

			Strong		Although only based on a series of case studies at this moment in time, the reduction of liver fat seen after 3 months was remarkably effective

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Lung Function

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Pelargonium sidoides	↑	★☆☆ Minor	10 studies	Secondary to treating sickness (bronchitis, URTIs, common cold) there is improvement in sputum content, rhonchi, breathing, coughing, and chest pain while coughing relative to placebo; while the improvements are marked, they only occur secondary to treating illness.
B	Creatine	—	—	7 studies	Either in healthy persons or in disease states characterized by impaired lung function, creatine supplementation does not modify the strength of exhalations or lung power.
C	N-Acetylcysteine			1 study	
D	Moringa oleifera	↑	★☆☆ Minor	1 study	Respiratory capacity (as assessed by breath testing) in persons with nonallergic asthma (most of whom were smokers) appears to be enhanced following supplementation of the seeds of Moringa

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Luteinizing Hormone

Luteinizing hormone (LH) is a hormone that is secreted from the pituitary and is known to regulate fertility and stimulate testosterone production from the testicles. Its increase is thought to promote testosterone (somewhat unreliably).

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Maca	—	—	3 studies	No significant influence on luteinizing hormone noted with maca ingestion
B	Red Clover Extract	—	—	3 studies	Luteinizing hormone does not appear to be significantly influenced with oral supplementation of red clover extract in postmenopausal women.
C	Alcohol	—	—	5 studies	No significant influence of alcohol on luteinizing hormone levels when consumed moderately
C	Nicotine	↑	★☆☆ Minor	1 study	An increase in luteinizing hormone has been noted
C	Ashwagandha	↑	★☆☆ Minor	2 studies	An increase in luteinizing hormone has been detected with ashwagandha supplementation.
C	Shilajit	—	—	1 study	No significant influence on luteinizing hormone
C	Coenzyme Q10	↓	★☆☆ Minor	1 study	A decrease in luteinizing hormone has been detected with CoQ10 supplementation
C	Tribulus terrestris	—	—	1 study	No influence on luteinizing hormone has been detected with supplemental tribulus

C	Dehydroepiandrosterone	—	—	2 studies	No significant alterations detected in luteinizing hormone levels
C	Vitamin E	—	—	1 study	Vitamin E supplementation does not appear to influence circulating levels of luteinizing hormone (LH).
C	Velvet Antler	—	—	1 study	No significant influence on luteinizing hormone levels
C	Chromium	—	—	1 study	No significant influence of chromium supplementation on luteinizing hormone (LH) in women with PCOS relative to placebo.
C	Saffron	—	—	1 study	LH concentrations are unaffected by saffron supplementation at 60mg in infertile men.
D	Licorice	—	—	3 studies	More evidence than not suggests no significant changes in lutenizing hormone, although limited evidence suggests an increase of minor magnitude.
D	Pueraria lobata	—	—	1 study	No significant alterations in luteinizing hormone has been detected with pueraria lobata ingestion.
D	Zinc	↑	★☆☆ Minor	1 study	In persons who are deficient in zinc, an increase in LH occurs following zinc replenishment.
D	Ginger	↑	★★★ Notable	1 study	Although the study is limited by lack of placebo control and disclosure of dosage, ginger is associated with a 43.2% increase in serum luteinizing hormone over three months in infertile men.

D	D-Aspartic Acid	↑	★☆☆ Minor	1 study	An increase in LH concentrations has been noted to 30-60% in infertile men, correlating well with the testosterone increases seen in this study.

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Lymphocyte Count

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Tinospora cordifolia	↓↑	☆☆☆ Minor	4 studies	Variable effects on Lymphocytes, with both increases and decreases being noted in persons with allergic rhinitis and no effect being observed in those with HIV.
C	Fish Oil	↓	☆☆☆ Minor	1 study	A decrease in lymphocytic count has been noted in obese persons
C	Chromium	—	—	1 study	No significant alterations in baseline lymphocyte count with chromium supplementation relative to placebo.
C	Vitamin E	—	—	2 studies	Vitamin E supplementation does not appear to influence overall lymphocyte count or its subdivisions.
C	Colostrum	—	—	1 study	Overall lymphocyte count does not appear to be significantly influenced with supplementation of dietary colostrum.
D	Trametes versicolor	↑	☆☆☆ Notable	1 study	In women with breast cancer, a very large preservation of lymphocytes is noted with polysaccharide K
D	Stephania tetrandra	—	—	1 study	Lymphocytes (both B and T cells) are unchanged in their overall quantity with 12 weeks of supplementation.
D	Moringa oleifera	—	—	1 study	No significant alterations in Lymphocyte count following

					continued supplementation of the seeds of <i>Moringa oleifera</i>

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Memory

The ability to remember things currently being done (working memory) recently learned (short term) and possible for life (long term memory); some compounds enhance memory by reversing states of neural malaise (Fish Oil, Curcumin) whereas some can increase memory unilaterally (Bacopa Monnieri).

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Ginkgo biloba	↑	★☆☆ Minor	12 studies	There appears to be a fairly reliable increase in short term memory and free recall associated with ginkgo supplementation in older individuals (55yrs or above) either with or without diagnosed neurodegenerative disease states.
B	Bacopa monnieri	↑	★★★☆☆ Notable	8 studies	Although general and requiring a long time to take effect (4-6 weeks), bacopa appears to reliably and effectively improve memory in both healthy persons and during cognitive decline
B	Caffeine	—	—	7 studies	Overall, highly mixed effects effects of caffeine on memory. It appears to increase spatial/perceptual memory and reduce working memory (perhaps secondary to overstimulation)
B	Melissa officinalis	↑	★☆☆ Minor	5 studies	Mixed influences on memory, with one study noting a decrease in 'total' memory formation and two studies noting improvements in 'quality' of memories formed. There is likely a modulatory effect associated with lemon balm.
C	Nicotine	↑	★☆☆ Minor	1 study	An increase in memory has been noted with ingestion of nicotine in persons with mild

					cognitive impairment
C	Fish Oil	↑	★☆☆ Minor	2 studies	Possible improvements in memory
C	S-Adenosyl Methionine	↑	★☆☆ Minor	1 study	In persons with SSRIs, adding SAME confers a cognitive promoting effect; it is unsure if this persists in persons without SSRIs, and this augmenting effect with SSRIs is only seen in limited other instances (ie. with Creatine)
C	Piracetam	↑	★☆☆ Minor	2 studies	Small increase in backwards recall with piracetam; nothing remarkable and overall very limited evidence in otherwise healthy individuals to draw from.
C	Ginger	↑	★☆☆ Minor	1 study	An increase in memory has been noted in older women, no current studies in youth
C	Black Cohosh	—	—	1 study	No significant effect on memory function
C	Melatonin	↑	★☆☆ Minor	1 study	An increase in memory retention under periods of stress has been noted
C	Choline	—	—	1 study	No acute effect on spatial memory formation
C	Phosphatidylserine	↑	★☆☆ Minor	3 studies	Increases in memory have been noted in persons with cognitive decline. A memory improving effect in otherwise healthy people is theoretical (secondary to reducing stress, has been noted in rodents), but not demonstrated in humans yet
C	Vinpocetine	↑	★☆☆ Minor	1 study	An increase in acute memory formation has been noted in female volunteers given 40mg

					Vinpocetine
C	CDP-choline	↑	★☆☆ Minor	2 studies	Appears to promote cognition in otherwise healthy older adults. Although animal studies suggest this may apply to youthful subjects as well, no human currently exists for youth
C	Oxiracetam	↑	★☆☆ Minor	2 studies	Although it has mechanisms and animal evidence to support improvements in memory in healthy youth, all human studies are currently in those with cognitive decline
C	Modafinil	↑	★☆☆ Minor	2 studies	Memory (usually studies investigate short term) appears to be beneficially influenced with modafinil supplementation, possible secondary to the improvements in working memory and attention.
C	Blueberry	↑	★☆☆ Minor	1 study	Memory formation in elderly subjects can be improved with daily supplementation of blueberries or their extract
C	Nigella sativa	↑	★☆☆ Minor	1 study	There appears to be a small but respectable (15-20% higher than baseline) improvement in logical memory and 30 minute recall in older subjects supplementing the seeds in their daily lifestyle.
C	Cocoa Extract			1 study	
C	Creatine	—	—	2 studies	Supplementation of creatine does not influence short term recall during sleep deprivation
C	Red Clover Extract	↓ ↑	★☆☆ Minor	1 study	The lone study to assess cognition in older women in menopause has noted an increase in visuospatial

					processing yet a reduction in digit span and verbal memory tests; uncertain implications.
C	Chromium	—	—	1 study	No evidence for chromium reducing memory decline seen with aging.
C	Vitamin E	—	—	1 study	Supplementation of vitamin E by otherwise healthy women has failed to significantly improve memory formation.
C	PRL-8-53	↑	★★★☆☆ Notable	1 study	The lone study noted mild increases in memory (14%) bordering on statistical significance in high performers on a word recollection test, with higher performances in subjects over the age of 30 regardless of initial performance (108-152% increase over placebo performance) and in poor performers (87.5-105%).
D	Pramiracetam	↑	★★☆☆☆ Minor	2 studies	While it appears effective in promoting memory formation in elderly persons and cognitively injured youth, there is currently no evidence in otherwise healthy use for nootropic purposes
D	Peppermint	—	—	1 study	The aroma of peppermint has been unable to influence memory processing (quantity or quality of memory formation) relative to control

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Metabolic Rate

Metabolic Rate is a term used to refer to how many calories one 'uses' per day, and dietary intake per day is usually measured in accordance to Metabolic Rate. Some supplements may increase or decrease Metabolic Rate, and influence weight gain or loss.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Ephedrine	↑	★★★☆☆ Notable	6 studies	Ephedrine, secondary to the stimulatory properties, appears to reliably increased metabolic rate
B	Green Tea Catechins	—	—	3 studies	No significant influences on metabolic rate overall
B	Conjugated Linoleic Acid	—	—	5 studies	Currently thought to be somewhat ineffective as the evidence supporting an increase are confounded with food intake whereas the evidence supporting no increase is more statistically robust.
C	L-Carnitine	—	—	1 study	No significant influence on metabolic rate noted with carnitine supplementation
C	ECA	↑	★★★☆☆ Notable	2 studies	The increase in metabolic rate seen with ephedrine is augmented with the inclusion of both aspirin and caffeine, hence its notable efficacy
C	Coconut Oil	↑	★★☆☆☆ Minor	8 studies	Appears to be a short lived and of small magnitude increase in metabolic rate.
C	7-Keto DHEA	↑	★★★☆☆ Notable	1 study	Somewhat notable as the decrease seen with dieting was effectively abolished and reversed with 7-keto

					supplementation over 7 days of low caloric intake, but more evidence is required to establish the reliability of this and how strong it actually is.
C	Aframomum melegueta	↑	★☆☆ Minor	1 study	Requires more evidence, and the increase in metabolic rate was wholly conditional on cold therapy also being used (where supplementation with aframomum melegueta increased cold therapy's efficacy rather than <i>per se</i> increasing metabolic rate)
C	Caffeine	↑	★☆☆ Minor	2 studies	Mixed effects on metabolic rate following acute doses of caffeine
C	Yerba mate	—	—	1 study	No significant influence on metabolic rate has been noted
C	Resveratrol	↓	★☆☆ Minor	1 study	A decrease in the metabolic rate has been noted in humans, thought to be related to the caloric restriction mimetic aspect
C	Fucoxanthin	↑	★★★☆☆ Notable	1 study	The lone study in obese premenopausal women noted a fairly remarkable increase in metabolic rate (the highest estimate being around 450kcal daily); this study requires replication to see if the effect size persists
C	Vitamin D	—	—	1 study	No detectable influence on metabolic rate over time
C	Quercetin	—	—	1 study	No significant influence on metabolic rate following acute Quercetin supplementation
C	Nicotine	↑	★☆☆ Minor	1 study	Chewing gum containing nicotine can increase the metabolic rate in a dose-dependent manner (3.7-4.9%

					with 1-2mg nicotine) when measured for the 180 minutes following 20 minutes of chewing.
C	Trimethylglycine	—	—	1 study	No significant influence of betaine on the metabolic rate of obese persons subject to chronic supplementation.
C	Synephrine			1 study	
D	Ginger	—	—	1 study	Despite an increase in the thermic effect of food, overall metabolic rate does not appear affected
D	Fish Oil	—	—	1 study	No significant influence on metabolic rate seen with fish oil supplementation
D	Sodium Bicarbonate	↑	★☆☆ Minor	1 study	An increase in metabolic rate has been noted and calculated (extrapolated) to be approximately 0.5% extra over the course of 24 hours, associated with a low dose of sodium bicarbonate (17mg/kg)
D	Chromium	—	—	1 study	Six months supplementation of chromium has failed to alter the metabolic rate relative to baseline.

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Microcirculation

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Centella asiatica	↑	★★★☆☆ Notable	8 studies	There appears to be a notable improvement in microcirculation associated with oral ingestion of <i>centella asiatica</i> in the treatment of chronic venous insufficiency; this may extend to otherwise healthy persons, albeit at a lesser magnitude
C	Vitamin C	↑	★☆☆☆☆ Minor	1 study	An increase in microcirculation has been noted secondary to increased blood flow, thought to be a general property of antioxidants
C	Ginkgo biloba	↑	★☆☆☆☆ Minor	1 study	There is a small increase in microcirculation seen in elderly persons given ginkgo biloba, extending to both periphery and the liver. Benefits seem to be time dependent and greater at day 30 relative to day 10
C	Hesperidin	↑	★☆☆☆☆ Minor	1 study	While hesperidin does not influence basal (fasting) microcirculation, there is an acute increase in circulation seen with supplementation of hesperidin at the time of peak blood concentrations.

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Migraine

A migraine is an intense and prolonged headache that may or may not be preceded by an aura. Supplementation for migraines either reduces the severity of a migraine or, when taken daily, reduces the monthly frequency of migraines.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Feverfew	↓	★★★ Strong	7 studies	Feverfew appears to be strongly effective in reducing migraines when the population in question are people with high frequency migraines possibly accompanied by auras. Feverfew is not as effective, although still somewhat effective, in persons with less frequent migraines.
C	Melatonin	—	—	1 study	No detectable influence of melatonin on migraines that exceeds placebo
C	Magnesium	↓	★★☆ Minor	1 study	One study has noted a reduction in symptoms of migraines associated with oral magnesium supplementation
C	Vitex agnus castus	↓	★★★ Notable	1 study	Seems to reduce symptoms of migraines a bit more than other PMS related symptoms, but for the most part the reduction seen in migraines is solely a reduction of PMS symptoms.
C	Coenzyme Q10	↓	★★☆ Minor	1 study	Degree of improvement is not overly remarkable, with portions of the trial not outperforming placebo.
C	Lavender	↓	★★☆ Minor	1 study	Acute inhalation of lavender at the onset of a migraine is associated with less pain

					symptoms than placebo scent

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Mucositis

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Zinc	↓	★☆☆ Minor	4 studies	Decreases in the severity but not occurrence of mucositis have been reported in cancer patients undergoing both radiotherapy and chemotherapy, although the benefits seem unreliable
C	Curcumin	↓	★☆☆ Minor	1 study	Symptoms of mucositis have been noted to be decreased with curcumin supplementation

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Mucus Production

Some nasal congestion is due to excessive mucus production in the sinus cavity, which then narrows the breathable space. Supplements that reduce mucus production may be beneficial for nasal congestion related to allergies or sickness.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Serrapeptase	↓	★★★☆☆ Notable	4 studies	A somewhat notable decrease in mostly the viscosity of mucus (elasticity is somewhat unreliably decreased), due to the mucolytic properties of serrapeptase. This may be of use for both nasal discharge and lung sputum (cystic fibrosis)

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Muscle Creatine Content

Muscle creatine content refers to how much creatine (total creatine plus creatine phosphate) is bioaccumulated in muscle tissue, and supplements that enhance muscular creatine concentrations are thought to confer the effects of creatine supplementation.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Creatine	↑	★★★ Strong	18 studies	Creatine supplementation is the reference compound for increasing muscular creatine levels; there is variability in this increase, however, with some nonresponders.
C	Trimethylglycine	—	—	1 study	Betaine (2g) has failed to increase phosphocreatine levels in skeletal muscle and failed to augment the increase caused by 20g of creatine.
D	Alpha-Lipoic Acid	↑	★☆☆ Minor	1 study	Has been associated with augmenting Creatine uptake into muscle cells acutely; long term influence unknown

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Muscle Damage

Muscle damage refers to the breaking of muscle tissue during exercise, and is approximately by measuring some biomarkers in the blood released by damaged muscle (such as creatine kinase). Reducing muscle damage may alleviate soreness from exercise.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Creatine	↓	★☆☆ Minor	8 studies	Not overly protective, but there appears to be a degree of protection.
B	Vitamin C	↓	★☆☆ Minor	4 studies	Although not acute, a possible reduction in biomarkers of muscle damage is sometimes noted with antioxidative supplementation which applies to Vitamin C; results are unreliable
B	L-Carnitine	↓	★☆☆ Minor	4 studies	Biomarkers of muscle damage including creatine kinase and muscle soreness are both fairly reliably reduced following ingestion of carnitine and pairing with exercise
B	HMB	↓	★★★☆☆ Notable	3 studies	Decrease creatine kinase exists following acute supplementation (15-30 minutes before a workout) of HMB free acid to about a third of control, and is effective in trained individuals
C	Coenzyme Q10	↓	★☆☆ Minor	1 study	A slight decrease in biomarkers of muscle damage has been noted with CoQ10 supplementation.
C	Melatonin	↓	★☆☆ Minor	1 study	A decrease in muscle damage biomarkers (creatine kinase) has been noted with melatonin supplementation

C	Rhodiola Rosea	↓	★☆☆ Minor	2 studies	Able to reduce circulating levels of creatine kinase following exercise
C	Methylsulfonylmethane	↓	★☆☆ Minor	1 study	Biomarkers of muscle damage such as creatinine and bilirubin are decreased following exercise with an MSM preload
C	Glutamine	—	—	1 study	Serum creatinine (increased during exercise and thought to be indicative of muscle damage) does not appear to be significantly altered with glutamine supplementation
C	Panax ginseng	↓	★☆☆ Minor	1 study	A decrease in biomarkers of muscle damage (creatine kinase) has been noted 72 hours after exercise in which panax ginseng was preloaded
C	Phosphatidylserine	—	—	1 study	No significant influence on serum biomarkers of muscle damage such as creatinine
C	Fish Oil	—	—	1 study	No significant influence on biomarkers of muscle damage seen with fish oil supplementation
C	Taurine			1 study	
C	Blueberry	↓	★☆☆ Minor	1 study	Appears to reduce biomarkers of muscle damage such as creatine kinase
C	Anatabine	—	—	1 study	The progression of recovery after a novel workout (when measured over three days) was unaffected by 6-12mg anatabine
C	Astaxanthin			1 study	
C	Vitamin E	↓	★☆☆ Minor	1 study	In athletes who experienced a reduction in lipid peroxidation

					from vitamin E supplementation during exercise, there is also a reduction in biomarkers of muscle damage.

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Muscle Oxygenation

Muscle oxygenation is the rate of oxygen usage and supply to a working muscle tissue. This is usually tied in with nitric oxide metabolism, and increased muscle oxygenation should lead to increased anaerobic muscle performance.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Rhodiola Rosea	—	—	1 study	No significant effects on oxygenation during exercise or simulated altitude tests
C	L-Carnitine	↓	★☆☆ Minor	1 study	A decrease in muscle oxygenation has been noted during occlusion, but not during squat exercise; practical significance of these results unknown
C	Magnesium	↑	★★★☆☆ Notable	1 study	The one study to measure muscle oxygenation in high intensity exercise noted quite a remarkable increase in oxygenation in healthy athletes; this needs to be replicated
C	Sodium Bicarbonate	↑	★☆☆ Minor	1 study	The rate of muscle deoxygenation is reduced with attenuation of acidosis (which can be achieved with sodium bicarbonate), and in later stretches of exercise this can be manifest as a relative increase in oxygenation
C	Creatine			1 study	
C	Trimethylglycine	↑	★☆☆ Minor	1 study	There appears to be a minor increase in overall oxygen consumption during physical training (anaerobic) to fatigue associated with betaine supplementation, although this was alongside increased work volume (which may be the causative factor).

D	Citrulline	↑	★☆☆ Minor	1 study	An increase in muscle ATP production via aerobic means was noted in men given 6g citrulline daily, but this appeared to be attenuated with time.

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Muscle Protein Synthesis

Muscle protein synthesis refers to the rate of protein synthesis of the actual muscle fibers, and is a short-term marker of muscle hypertrophy as daily muscle protein synthesis results in visible muscle growth.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Whey Protein	↑	★★★☆☆ Notable	3 studies	Whey protein appears to increase muscle protein synthesis to a higher degree than other protein sources <i>acutely</i> , although over the prolonged supplementation it seems comparable in potency.
C	Citrulline	—	—	1 study	Currently no human evidence to support a practically significant increase in muscle protein synthesis at rest with citrulline supplementation
C	Colostrum	↑	★★★☆☆ Minor	1 study	There is an increase in protein synthesis with colostrum relative to maltodextrin due to colostrum being a dietary protein, but there is also an increase in protein breakdown seen; efficacy of colostrum relative to other protein sources in MPS is currently not well investigated.

Muscle Soreness

Muscle soreness refers to the perceived soreness or tender state of muscle tissue following physical exercise, usually manifesting after a short delay (and hence its common name of 'delayed onset muscle soreness' or DOMS).

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	—	—	3 studies	Although one study suggests a decrease, most evidence suggest no significant influence
C	Green Tea Catechins	↓	★☆☆ Minor	1 study	A decrease in muscle soreness has been noted with catechin ingestion
C	Ginger	↓	★☆☆ Minor	2 studies	A possible reduction of delayed onset muscle soreness, but this topic is a bit contested
C	Bromelain	↓	★☆☆ Minor	2 studies	It is possible bromelain might reduce muscle soreness, but currently the evidence does not support this claim (although the trial to note a failure of bromelain also noted a failure with Ibuprofen, a known active drug)
C	Vitamin C	↓	★☆☆ Minor	1 study	A possible reduction in muscle soreness the day after exercise may result when preloading exercise with Vitamin C
C	Branched Chain Amino Acids	—	—	2 studies	No significant influence on muscle soreness when assessed 2-3 days after exercise that is preloaded with BCAA supplementation
C	HMB	—	—	2 studies	No significant influence on perceived muscle soreness

					following exercise with HMB supplementation
C	Methylsulfonylmethane	↓	★☆☆ Minor	1 study	A decrease in muscle soreness has been noted with MSM preloads before exercise
C	Theaflavins	↓	★☆☆ Minor	1 study	May decrease muscle soreness at high doses, with the efficacy of lower doses uncertain.
C	L-Carnitine	↓	★☆☆ Minor	2 studies	The decrease in muscle soreness appears to correlate with the reduced muscle damage
C	Phosphatidylserine	—	—	1 study	No significant influence on perceived muscle soreness
C	Leucic Acid	↓	★☆☆ Minor	1 study	A decrease in muscle soreness has been noted in the one study conducted in athletes (when measured at week 4 only) to the degree of around 23%, but muscle soreness was not overly high in the study to begin with
C	Citrulline	↓	★★★☆☆ Notable	1 study	The lone study using citrulline acutely pre-workout noted a 40% reduction in muscle soreness the following two days after the workout.
C	Taurine			1 study	
C	Blueberry	—	—	1 study	Despite the reduction in muscle damage and increased rate of recovery, there are no significant changes in subjective muscle soreness
C	Anatabine	—	—	1 study	Perceived muscle soreness and pain from a workout was unaffected by anatabine supplementation.

C	Trimethylglycine	-	-	1 study	No significant influence of betaine supplementation of subjective ratings of muscular soreness nor the pump relative to placebo.

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Muscular Endurance

Muscular endurance tends to refer to the capacities of a muscle tissue to continuously exert itself during one 'set' of exercises, and improvements in muscular endurance are thought to reflect antifatigue effects.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Beta-Alanine	↑	★☆☆ Minor	8 studies	The data from the lone meta-analysis suggesting a 2.5% increase in muscular endurance during exercises between 60-240s (usually measured by time to exhaustion) seems to be a good summation. The benefit is present, but is pretty small in magnitude.
B	Creatine	↑	★☆☆ Minor	3 studies	Somewhat effective.
B	Spirulina	↑	★☆☆ Minor	3 studies	Studies currently assessing the effects of spirulina on muscular endurance are too heterogeneous to properly assess potency thereof. However, a positive effect does appear to exist
B	Trimethylglycine	—	—	3 studies	There may be a small benefit in prolonged and exhaustive resistance training with betaine relative to placebo, but at this moment in time most evidence assessing muscular endurance has failed to find a statistically significant increase (trends to improve do seem apparent).
C	Chromium	—	—	1 study	Low dose chromium supplementation failed to promote muscular endurance in trained athletes relative to placebo.

C	Colostrum	—	—	1 study	Supplementation of colostrum, relative to whey protein, does not appear to promote greater increases in muscular endurance (as assessed by bench press repetitions) when taken alongside a training regimen.

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Nasal Congestion

Nasal congestion refers to conditions such as allergic rhinitis or sickness where an excess of mucus is able to clog the nasal passages and impair breathing. Some supplements are said to reduce this congestion.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Pelargonium sidoides	↓	★★★☆☆ Notable	4 studies	Nasal congestion appears to be decreased with supplementation of this herb, and while this is noted in acute bronchitis (most potently) it also affects other bacterial or viral instances such as the common cold and acute rhinosinitus.
C	Ephedrine	↓	★★★☆☆ Notable	2 studies	Ephedrine appears to result in notable nasal decongestion
C	ECA	↓	★★☆☆☆ Minor	1 study	Due to the ephedrine component, ECA may also reduce nasal congestion
C	Astragalus membranaceus	↓	★★☆☆☆ Minor	1 study	Not an overly potent reduction of nasal congestion and other rhinitis symptoms, but more than placebo.
C	Spirulina	↓	★★★★★ Strong	1 study	The decrease in nasal congestion seen in the one study was remarkably strong relative to placebo in a model of allergic rhinitis; it is not sure if this applies to other causes of nasal congestion.
C	Stinging Nettle	↓	★★☆☆☆ Minor	1 study	A slight decrease in nasal congestion seen with stinging nettle
C	Rosmarinic Acid	↓	★★☆☆☆ Minor	1 study	Nasal congestion is reduced

					secondary to reducing pollen allergies
C	Nigella sativa	↓	★☆☆ Minor	1 study	Nasal congestion as a side-effect of allergic rhinitis is slightly reduced following the treatment of rhinitis with <i>nigella sativa</i> seeds
C	Tinospora cordifolia	↓	★★★★ Strong	1 study	In persons suffering from allergic rhinitis, nasal congestion is completely resolved in around two-thirds of persons. Currently no studies in nasal congestion for persons without allergies.
C	Rubus suavissimus	—	—	1 study	Due to the lone study failing to find benefit to allergic symptoms with 400mg of the leaf extract, there are no reported benefits to allergic rhinitis
D	Bromelain	↓	★☆☆ Minor	1 study	The potency at this moment in time does not appear remarkable.
D	Methylsulfonylmethane	↓	★☆☆ Minor	1 study	Decreases upper respiratory symptoms have been noted with MSM supplementation, although not to a remarkable degree.

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Natural Killer Cell Activity

Natural Killer Cell Activity refers to the ability of natural killer cells to do their actions in the body, and this activity can be increased either by increasing cell count of promoting activity in a direct stimulatory manner.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	↓	☆☆☆ Minor	3 studies	Although there do not appear to be changes in the amounts of NK cells in the body following fish oil, their activity appears to be a tad reduced
C	Garlic	↑	☆☆☆ Minor	2 studies	There is an increase in NK cell activity alongside the increase in NK cell content, although it is not sure if there is an inherent increase in NK cell activity if you control for the increase in cell content.
C	Hesperidin	—	—	1 study	Natural Killer (NK) cell activity does not appear to be influenced with supplementation of hesperidin, with the count also remaining unchanged.
C	Colostrum	—	—	1 study	The phagocytic activity of natural killer cells does not appear to be modified with supplementation of colostrum relative to whey control.
D	Spirulina	↑	☆☆☆ Notable	1 study	NK cell activity against a tumor cell line (K562) increased 40% following a week ingestion of fairly reasonable oral dosing, suggesting that this is a notable increase of possible interest.
D	Ashwagandha	↑	☆☆☆ Minor	1 study	A slight increase in natural killer cell activity has been noted with ashwagandha

					supplementation.
D	Ganoderma lucidum	↑	★★★☆☆ Notable	1 study	Up to a 50% increase in NK cell activity relative to control has been noted with reishi, and this may be independent of a basic stimulatory action (which would lead into possible supplement combinations)
D	Trametes versicolor	—	—	1 study	No significant alterations in NK cell activity

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Natural Killer Cell Content

Natural killer cells can have their population increased by nutritional supplements, which usually (but not always) results in an increase in activity.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	—	—	3 studies	Although one increase in NK cell content has been noted after exercise, the two studies using similar doses at rest have failed to find a significant influence on NK cell content
C	Eleutherococcus senticosus	↑	★☆☆ Minor	1 study	An increase has been noted, but there is insufficient evidence to assess the magnitude of increase or the reliability
C	Holy Basil	↑	★☆☆ Minor	1 study	An increased level of NK cell count has been noted following ingestion of Tulsi leaves
C	Polypodium leucotomos	—	—	1 study	Although it cannot yet be ruled out, the best evidence currently suggests that the increase in NK cell activation seen with this herb does not apply after oral supplementation.
C	Garlic	↑	★☆☆ Minor	2 studies	There is an increase in NK cell levels seen in both healthy controls as well as cancer patients, and this is thought to be due in part to both immunostimulatory and anti-immunosuppressive effects.
C	Hesperidin	—	—	1 study	The overall cell population of Natural Killer (NK) cells does not appear to be influenced with supplementation of Hesperidin

C	Vitamin E	—	—	1 study	The overall amount of NK cells do not appear to be altered with supplementation of vitamin E.
C	Colostrum	—	—	2 studies	There does not appear to be a sustained influence on NK cell content relative to controls, although one study noted very transient decreases (which were shortly normalized).
D	Spirulina	↑	★★★☆☆ Notable	1 study	The increases in mRNA content of natural killer cell content increased 37-55% (NKG2D) and 75% (perforin) which appeared to be dose-dependent, a possibly potent immunostimulatory effect.
D	Trametes versicolor	—	—	1 study	No significant influence on NK cell count
D	Blueberry	↑	★★★☆☆ Minor	1 study	An increase in natural killer cells has been noted in the range of 76-122% following physical exercise.

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Nausea

Nausea is the feeling of acute sickness that may result in vomiting and loss of appetite. Some supplements are known as antiemetics, and are used to reduce the sensation of nausea when taken.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Ginger	↓	★★★☆☆ Notable	11 studies	There appears to be a reliable and fairly notable decrease in nausea symptoms with 1-3g of ginger related to pregnancy and seasickness (not as much consensus for post-operative nausea)
B	Peppermint	↓	★★☆☆☆ Minor	5 studies	There appears to be interactions with peppermint as aromatherapy and reducing nausea, but the best evidence at this point in time is mixed and with some faults. More research is needed to see the potential role of peppermint aromatherapy in nausea reduction
C	Pelargonium sidoides	↓	★★☆☆☆ Minor	2 studies	Nausea as a side-effect of acute bronchitis may be reduced, although studies assessing nausea/vomiting outside of acute bronchitis have failed to find an effect despite the subjects being sick.
D	Ephedrine	↑	—	1 study	Ephedrine has been noted to reduce postoperative nausea, but is also linked to inducing nausea secondary to its psychostimulatory and appetite suppressing effects. The latter is more practical for supplementation

Neutrophil count

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Tinospora cordifolia	—	—	3 studies	Although there was a reduction in neutrophils in the nasal mucosa, the two studies measuring neutrophils in serum failed to find any benefit.
C	Hesperidin	—	—	1 study	There are no significant alterations in the amount of neutrophils seen in subjects consuming hesperidin.
C	Chromium	—	—	1 study	No significant influence of chromium supplementation relative to placebo on neutrophil count.
C	Saffron	—	—	1 study	Neutrophil concentrations in serum are unaffected by supplementation of saffron.
C	Vitamin E	—	—	1 study	The overall amount of neutrophils in the blood does not appear to be influenced with supplementation of vitamin E.
C	Colostrum	—	—	2 studies	The overall amount of neutrophils in serum does not appear to be modified with supplementation of colostrum relative to placebo.

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Nitric Oxide

Nitric Oxide is a signalling molecule formed from Nitrogen (N) and Oxygen (O) and simply called NO. It induces pro-oxidative changes, and is mostly implicated (positively) in blood pressure, erections, muscle, and Immunology.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Arginine	↑	★☆☆ Minor	7 studies	Has been implicated in increasing nitric oxide formation in the body, but this does not appear to be a reliably occurring phenomena (despite arginine being required to make nitric oxide, it is not a good inducer thereof)
C	Dehydroepiandrosterone	↑	★☆☆ Minor	1 study	Has been detected to increase nitric oxide concentrations in serum, needs to be replicated to investigate mechanisms
C	L-Carnitine	↑	★☆☆ Minor	1 study	An increase in nitric oxide has been noted, thought to be secondary to increases in plasma nitrate
C	Schisandra chinensis	↑	★☆☆ Minor	1 study	An increase in serum nitric oxide has been detected in one study in elite athletes
C	Pycnogenol	—	—	1 study	Despite one study establishing the blood flow effects are dependent on nitric oxide, there do not appear to be any significant differences in nitric oxide quantities in saliva
C	Fish Oil	↑	★☆☆ Minor	1 study	An increase in exercise-induced nitric oxide production has been noted
C	Citrulline	↑	★★★☆☆ Notable	2 studies	Nitric oxide derivatives (nitrate

			Notable		and urinary cGMP, since nitric oxide itself is hard to measure these biomarkers are indicative of nitric oxide production) appear to be reliably increased following oral consumption of citrulline supplementation
C	Blueberry	—	—	1 study	Blueberries do not appear to significantly influence nitric oxide metabolism
C	Curcumin	↑	★★☆ Notable	1 study	80mg of a bioavailability enhanced curcumin supplement has been reported to increase nitric oxide in serum by 40% or so, which is significantly larger than many other dietary supplements.
C	Ginkgo biloba	↑	★☆☆ Minor	2 studies	An increase in cGMP (downstream mediator of nitric oxide signalling) has been noted in high risk individuals alongside an increase in superoxide dismutase, to the degree of 27.7+/-8.3% and nitric oxide itself has been increased by up to 40% in persons with poor circulation.
C	Rooibos	—	—	1 study	No significant alterations in nitric oxide levels with acute ingestion of Rooibos tea to otherwise healthy persons.
C	Hesperidin	—	—	1 study	The increase in nitric oxide (and nitrate) seen with supplementation of hesperidin failed to reach statistical significance.
C	Trimethylglycine	—	—	2 studies	A potent increase in nitric oxide seen in a pilot study has failed to be replicated in a controlled intervention.
D	Punicalagins	↑	★☆☆ Minor	1 study	An increase in metabolites of nitric oxide metabolism have

					been noted and thought to be indicative of increased nitric oxide production
D	Garlic	↑	★★★☆☆ Notable	1 study	The lone study assessing nitric oxide and garlic noted that a raw garlic clove (2g) could increase nitric oxide by 224% in otherwise healthy persons within 2-4 hours of ingestion; potency did not decrease after seven days

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Noradrenaline

Noradrenaline is a catecholamine involved in the flight or fight response, and has a fairly important role as a neurotransmitter in the body. Elevations of serum noradrenaline are thought to reflect increases in cerebral noradrenaline.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Melatonin	↓	★☆☆ Minor	4 studies	A decrease in noradrenaline appears to reliably occur after melatonin ingestion, but only at rest; this reduction is abolished upon moving
C	L-Tyrosine	—	—	1 study	No significant influence on plasma noradrenaline levels (despite increased plasma tyrosine) during rest or during a cold stress test (which increases noradrenaline)
C	Mucuna pruriens	↑	★☆☆ Minor	1 study	The reduction in noradrenaline levels seen in infertility is normalized following mucuna ingestion
C	Branched Chain Amino Acids	—	—	1 study	BCAA supplementation does not appear to significantly influence noradrenaline concentrations in serum
C	Sodium Bicarbonate	↓	★☆☆ Minor	1 study	A decrease in exercise-induced noradrenaline has been noted before, but it is unsure if this is correct information (as this was the lone study to measure noradrenaline, three studies have measured adrenaline and are split with the only one noting a decrease in adrenaline also being this study)
C	Cocoa Extract			1 study	

C	Creatine	-	-	1 study	No significant alterations in plasma noradrenaline are seen with creatine supplementation during sleep deprivation.

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Ocular Blood Flow

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Ginkgo biloba	↑	★☆☆ Minor	3 studies	An increase in ocular blood flow has been noted in instances of normal tension glaucoma as well as healthy controls, although a one-time oral dose is ineffective (at least two days supplementation is required)
C	Astaxanthin			1 study	

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Oxidation of LDL

LDL oxidation is known to contribute to atherosclerosis (plaque buildup in arteries), and reducing the rate of LDL oxidation reduces atherosclerosis. Antioxidants that are potent enough and stay in serum can reduce this oxidation.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Olive leaf extract	↓	★★★☆☆ Notable	8 studies	The decrease in LDL oxidation seen with olive oil phenolics appears to be of notable potency due to its reliability (occurring in both healthy persons and diseased persons, chronically and acutely) and a reduction in LDL oxidation rates can exceed 25% in some studies with low intakes of olive phenolics (enough from virgin olive oil consumption)
C	Policosanol	↓	★☆☆☆☆ Minor	2 studies	Mixed evidence, possibly an effect but needs to be replicated
C	Conjugated Linoleic Acid	—	—	1 study	No significant protective or augmenting effects on the oxidation rates of LDL-C.
C	Dehydroepiandrosterone	↓	★☆☆☆☆ Minor	1 study	One study has noted less small particles of LDL, indicative of less LDL oxidation; possibly protective effects
C	Grape Seed Extract	—	—	1 study	Does not appear to influence oxidation rates of LDL cholesterol
C	Licorice	↓	★★★☆☆ Notable	2 studies	The decrease in oxidation of LDL seen with either licorice or isolated Glabridin appears to exceed 20% and is more than

					other supplements
C	Vitamin C	—	—	2 studies	No significant influence on the oxidation rates of LDL cholesterol
C	Panax ginseng	↓	★☆☆ Minor	2 studies	A possible reducing effect on the oxidation of LDL, secondary to reduction of oxidation in general; however, this appears to be unreliable
C	Fish Oil	—	—	2 studies	No significant influence detected
C	Cocoa Extract			1 study	
C	Blueberry	↓	★☆☆ Minor	2 studies	There appears to be a reduction in LDL oxidation, with the one chronic study suggesting a 27% reduction (the acute study noting less of a protective effect).
C	Ginkgo biloba	↓	★★★☆☆ Notable	2 studies	In high risk individuals, the reduction has been noted to be 17.0+/-5.5%
C	Zinc	↓	★☆☆ Minor	2 studies	Although there may not be an inherent protective effect and normalizing a deficiency does not <i>per se</i> reduce oxidation of LDL, if the body becomes more insulin sensitivity when restoring a deficiency then zinc may indirectly reduce oxidation.
C	Garlic	↓	★☆☆ Minor	2 studies	A possible decrease in LDL oxidation rates, although this does not appear to be overly reliable.
C	Hesperidin	↓	★☆☆ Minor	1 study	There is a mild increase in particulate size of LDL cholesterol, indicative of less oxidation of these particulates and less atherogenicity, with hesperidin supplementation.

C	Trimethylglycine	—	—	1 study	No significant alterations in the overall oxidation of LDL cholesterol associated with supplementation of betaine.
C	Chromium	—	—	1 study	No significant influence on the rates of LDL oxidation when compared to placebo supplementation.
C	Vitamin E	↓	★☆☆ Minor	2 studies	While vitamin E appears to retain the potential to reduce LDL oxidation, it requires high doses as lower doses are not significantly effective.
D	Magnesium	—	—	1 study	No significant influence on oxidation rates of LDL cholesterol
D	Alpha-Lipoic Acid	↑	★☆☆ Minor	1 study	Appeared to increase oxidation of LDL according to one study, which was abolished by exercise but noted to be a concern during rest.
D	Saffron	↓	★☆☆ Minor	1 study	Supplementation of saffron appears to be capable of reducing LDL oxidation when tested <i>ex vivo</i> in both healthy controls and persons with cardiovascular disease, although to a mild degree.

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Oxygen Uptake

Oxygen uptake (not to be confused with VO2 max) is the amount of oxygen taken up during exercise, and is known to reflect overall energy expenditure during exercise.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Trimethylglycine	—	—	4 studies	A minor increase in oxygen uptake was noted in selective testing (final sprint of one, but not both, betaine conditions) which did not manifest over the whole study period and is likely practically insignificant.
C	Coenzyme Q10	—	—	1 study	No detectable influence on oxygen uptake during exercise
C	Eleutherococcus senticosus	↑	★☆☆ Minor	1 study	Limited evidence, but it is in support of an increase in oxygen consumption
C	Caffeine	↑	★☆☆ Minor	1 study	Appears to be an increase in oxygen uptake with caffeine consumption, may be related to the increase in metabolic rate
C	Green Tea Catechins	↑	★☆☆ Minor	1 study	An increase in oxygen uptake has been noted with green tea catechin ingestion
C	Branched Chain Amino Acids	—	—	1 study	Oxygen uptake during anaerobic cardiovascular exercise does not appear to be modified with BCAA supplementation
C	Sodium Bicarbonate			1 study	
C	Ornithine	—	—	1 study	Oxygen uptake during exercise does not appear to be significantly altered

C	Ginkgo biloba	↑	★☆☆ Minor	1 study	In persons undergoing high altitude climbing, the reduced risk of AMD is associated with increased functional capacity of blood to carry oxygen.
D	Garlic	—	—	1 study	In otherwise healthy athletes given 4.5g of garlic cloves daily before a performance test, the lack of increased performance is met by a lack of changes in oxygen uptake.

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Oxygenation Cost of Exercise

The oxygenation cost of exercise refers to how much oxygen is required to metabolize energy efficiently, and a reduction in this cost signifies more efficiency and improved physical performance. Improved oxygen efficiency tends to result from increasing nitric oxide.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Nitrate	↓	★★★☆☆ Notable	2 studies	A notable reduction in the oxygenation cost of exercise associated with nitrate supplementation.
C	Echinacea	↓	★☆☆☆☆ Minor	1 study	Effective, but to a small degree based on one trial.
C	Panax ginseng	—	—	1 study	No significant influence on oxygen uptake during exercise
C	Phosphatidylserine	—	—	1 study	No significant influence on oxygenation cost of exercise
C	Arginine	↓	★☆☆☆☆ Minor	2 studies	When nitric oxide is increased, the oxygenation cost of exercise appears to be decreased. This is unreliable with supplemental L-arginine as arginine is unreliable in increasing nitric oxide
C	Vitamin C			1 study	

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Pain

Pain is the adverse sensation associated with injury, arthritis, and various forms of nerve injury that impairs well being and day-to-day living. Supplements may either universally reduce pain, or may alleviate the pain associated with a disease state.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Glucosamine	↓	★☆☆ Minor	8 studies	There appears to be a decrease in pain, with one meta-analysis noting that over the long term it account for "a 13 point reduction on a scale of 0-100". Although present, it is not as effective as most painkillers and may be exclusive to osteoarthritis
B	Serrapeptase	↓	★☆☆ Minor	5 studies	When a decrease in inflammation occurs post surgery, there appears to be a concomitant reduction in pain; it tends to hover around a 1 point reduction on a VAS scale (scale of 1-10).
B	Curcumin	↓	★★★☆☆ Notable	4 studies	There appear to be decreases in pain associated with curcumin at higher doses (400-500mg) which extend to post-operative, arthritic, and general pain symptoms. This does seems comparable to 2g acetaminophen in potency.
B	Horse Chestnut	↓	★☆☆ Minor	1 study	The pain associated with chronic venous insufficiency may be alleviated when that condition is treated by horse chestnut extract.
C	ECA	↓	★☆☆ Minor	1 study	At least in persons with upper respiratory tract infections, a possible analgesic effect of ephedrine with aspirin exists

C	Agmatine	↓	★★★☆☆ Notable	1 study	In the trial on lumbar disc-associated radiculopathy, the degree of pain alleviation was fairly notable relative to placebo and persisted for two months after supplementation was ceased. No reference drug comparisons, unfortunately
C	Microlactin	↓	★☆☆☆☆ Minor	2 studies	Possible pain reduction associated with reducing symptoms of osteoarthritis, with one study suggesting comparable efficacy to Glucosamine sulfate
C	Methylsulfonylmethane	—	—	1 study	No significant influence on pain symptoms in osteoarthritis
C	S-Adenosyl Methionine	↓	★★★☆☆ Notable	2 studies	The decrease in pain associated with osteoarthritis appears to be similar to the reference drugs Aleve (Naproxen) and Celecoxib, but requires more time to act (up to one month)
C	Rose Essential Oil	↓	★☆☆☆☆ Minor	1 study	Inhalation of rose may confer pain relieving properties in emergency situations, although potency relative to other agents is not assessed
C	Pycnogenol	↓	★☆☆☆☆ Minor	1 study	A reduction in pain secondary to improvements in symptoms of osteoarthritis has been noted, and while notable in this certain instance it is not certain if there are inherent analgesic effects
C	Nigella sativa	↓	★☆☆☆☆ Minor	1 study	Pain as a side-effect of rheumatoid arthritis is modestly reduced.
C	Peppermint	↓	★☆☆☆☆ Minor	1 study	Pain has been noted to be reduced in instances where pain is associated with

					tightened intestinal tissue (ie. during a colonoscopy) or during tension headaches. No inherent analgesic effect is known
C	Vitamin D			1 study	
C	Valeriana officinalis	↓	★☆☆ Minor	1 study	Menstrual pain appears to be reduced with supplementation of low dose valerian extracts.
C	Rose Hip	↓	★☆☆ Minor	4 studies	Pain is reduced alongside improvements in osteoarthritic and rheumatoid arthritis, and at least one study (cohort) noted benefits in persons without these diseases yet with high labour jobs. No studies in athletes to assess the analgesic properties yet.
D	Pyrroloquinoline quinone	↓	★☆☆ Minor	1 study	In persons with sleep disorders taking PQQ (which improved sleep) there were reductions in pain ratings at the end of the trial
D	Ashwagandha	↓	★☆☆ Minor	1 study	A decrease in pain has been noted with supplementation of ashwagandha root during chemotherapy relative to control.
D	Cissus quadrangularis	↓	★★★☆☆ Notable	1 study	Joint pain appears to be reduced following supplementation of cissus, and while the magnitude is not remarkable (respectable, but comparable to other supplements) it seems to be one of the few validated in athletes with nonpathological joint pain.

Parathyroid Hormone

Parathyroid hormone (PTH) is a hormone secreted from the parathyroid that negatively influences the actions of Vitamin D and promotes bone loss when in excessive concentrations.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin D	↓	★★★ Strong	4 studies	Vitamin D supplementation is the reference drug for reductions in parathyroid hormone due to directly negatively regulating its secretion
C	7-Keto DHEA	—	—	1 study	Insufficient evidence to support changes in parathyroid hormone from 7-keto supplementation.
D	Licorice	↑	★☆☆ Minor	1 study	An increase in parathyroid hormone has been noted with consumption of licorice

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Penile Girth

Penile girth refers to the (usually flaccid) thickness of penile tissue, and appears to be positively modulated by agents that interact with dopamine or blood flow. It is somewhat related to the supplementations that promote erections.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	L-DOPA	↑	★☆☆ Minor	2 studies	An increase in penile girth has been noted in the flaccid state at rest, which is no longer present during sexual stimulation.
C	Nicotine	↓	★☆☆ Minor	1 study	A decrease in penile girth in the flaccid state is noted, which is thought to be secondary to reduced blood flow
D	Yohimbine	↑	★☆☆ Minor	1 study	An increase in penile girth has been noted (similar to L-DOPA) which was not to a large degree, only detectable when dividing the group into responders and nonresponders
D	Saffron	↑	★☆☆ Minor	1 study	In men with erectile dysfunction, saffron appeared to increase nighttime tumescence at both the tip and base.

Photoprotection

Photoprotection refers to the ability of an agent to protect the skin from radiation damage, which practically tends to refer to solar waves. Although protective, they may also reduce photosynthesis of molecules (like Vitamin D).

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	↑	★☆☆ Minor	3 studies	There appears to be reduced risk of DNA damage, immunosuppression, and erythema in response to sunlight associated with fish oil consumption. Studies have only investigated higher doses (1,800mg EPA minimum) and it is unsure if these protective effects apply to lower doses
C	Green Tea Catechins	↑	★☆☆ Minor	1 study	An increase in photoprotection (protection of the skin from the sun) has been found with green tea catechin ingestion

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Plasma Arginine

Plasma arginine refers to blood concentrations of arginine, and can be increased following oral ingestion of mixed protein meals or any amino acid in the urea cycle.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Arginine	↑	☆☆☆ Minor	6 studies	Supplemental L-Arginine increases plasma L-Arginine. The spike in plasma L-arginine concentrations may be slightly more than that seen with L-citrulline, but the latter lasts longer and is thus more effective
C	Citrulline	↑	☆☆☆ Notable	2 studies	Citrulline can increase plasma arginine concentrations, and due to acting as a resevoir of arginine it is actually more effective overall at increasing plasma arginine than arginine itself (acute peaks are still observed to a higher level with arginine supplementation).

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Plasma Melatonin

Plasma melatonin refers to serum concentrations of melatonin, which are quite significantly spiked following consumption of melatonin supplementation. Other stimuli, such as dark therapy, may encourage production of melatonin and increase serum levels.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Melatonin	↑	★★★ Strong	6 studies	Plasma melatonin is increased at both night and daylight following supplementation of melatonin. Although the degree of increase is a tad unreliable, it seems to always occur and to a fairly large magnitude
C	Yohimbine	—	—	1 study	Despite increased rates of melatonin elimination from the body (via urination), there does not appear to be a significant influence on plasma melatonin concentrations.

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Plasma Nitrate

Oral ingestion of nitrate can increase plasma nitrate and nitrite, although they can also be used as biomarkers of nitric oxide metabolism by being able to be preserved and increased relative to their lower rate of decay. Higher plasma nitrate is associated with better blood flow.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Nitrate	↑	★★★ Strong	1 study	Nitrate ingestion strongly and fairly reliably increases plasma nitrate and nitrite.
C	L-Carnitine	↑	★☆☆ Minor	2 studies	Plasma Nitrate appears to be increased following carnitine ingestion, although not to the same degree as nitrate supplementation itself
C	Citrulline	↑	★☆☆ Minor	1 study	An increase in plasma nitrate has been noted with citrulline supplementation, but not to the degree of supplemental Nitrate itself
C	Arginine	—	—	1 study	There does not appear to be a reliable increase in plasma nitrate seen with arginine supplementation
C	Zinc	—	—	1 study	No significant influence of zinc supplementation on plasma nitrate or nitrite levels, suggesting no interaction with nitric oxide metabolism

Plasminogen Inhibitor 1

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Fish Oil	↑	★☆☆ Minor	1 study	An increase in PAI-1 is noted with fish oil supplementation
C	Red Clover Extract	—	—	1 study	Circulating levels of PAI-1 (plasminogen activation inhibitor 1) have not been altered with supplementation of red clover isoflavones.
C	Trimethylglycine	↑	★☆☆ Minor	1 study	An increase in PAI-1 concentrations has been noted with 4g of betaine supplementation daily over the course of six months in otherwise healthy adults.
D	Perilla Oil			1 study	

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Platelet Aggregation

Platelet aggregation is the rate of which platelets in the blood can form clots to stop bleeding. While it serves a vital role in preventing excessive bleeding, abnormally active aggregation can be a risk factor for cardiovascular diseases.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	↓	★☆☆ Minor	4 studies	Possible decreases in platelet aggregation
C	Sea Buckthorn	↓	★☆☆ Minor	1 study	5g of the oil daily is able to reduce platelet aggregation in otherwise healthy persons.
C	Garlic	↓	★☆☆ Minor	4 studies	Garlic appears to reduce platelet aggregation at the supplemental dose, but not a moderate dietary dose of garlic cloves. The potency is less than Ginkgo biloba as a reference.
C	Vitamin E	—	—	2 studies	While 100mg of γ-tocopherol has been once implicated in reducing platelet aggregation, higher doses and all tested dose of α-tocopherol by themselves do not appear to have an effect (there is still an interaction with warfarin, however).

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Pneumonia

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Zinc	—	—	8 studies	In regards to pneumonia in particular, zinc does not appear to have any appreciable benefit either when superloaded by itself or taken as an adjuvant alongside antibiotics

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Postpartum Depression

Postpartum depression is a transient depressive state that occurs after the birth of a child, and is a target for anti-depressive compounds that have been confirmed to be safe to both mother and child.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	—	—	5 studies	There does not appear to be any unique effect of supplemental fish oil on postpartum depression. Fish oil in postpartum and perinatal periods follows the same motifs as other depressive states, with EPA being the active molecule but likely only of benefit in major depressive disorder

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Power Output

Power Output is the ability to procure a large amount of strength in a rapid manner, and considered both muscular and neural factors. Supplements that increase power output are of interest to athletes and strength enthusiasts.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Creatine	↑	★★★ Strong	65 studies	Creatine is the reference compound for power improvement, with numbers from one meta-analysis to assess potency being "Able to increase a 12% improvement in strength to 20% and able to increase a 12% increase in power to 26% following a training regiment using creatine monohydrate". There does appear to be a high degree of variability, which is correlated with the amount of creatine reaching muscle tissue. There does not appear to be much difference between trained and untrained persons. An acute study noted an increase in peak torque by 33.4% and reduction in the time to reach peak torque by 54.7%; perhaps useful as comparator.
A	HMB	—	—	16 studies	Limited evidence supports the increase in power output, which may be due to chance; more often than not, there is no significant influence
A	Sodium Bicarbonate	—	—	28 studies	Although <i>technically</i> an increase in average power output may occur during exercise associated with the 'burn' (metabolic acidosis) to the degree of 1-2%, saying this is an inherent or reliable

					increase in power would be misleading; it is an attenuation of the decrease in power that acidosis is able to induce
B	L-Carnitine	—	—	7 studies	Highly mixed effects on power output, with mostly no significant influence but a possible increase in mean power output occurring in short-term anaerobic endurance exercise secondary to reducing the rate of perceived exertion
B	Dehydroepiandrosterone	—	—	3 studies	No significant improvement in power output has been noted with DHEA supplementation (studies mostly in older individuals)
B	Beta-Alanine	—	—	5 studies	No significant effects on acute power output
B	Caffeine	↑	★★★☆☆ Notable	11 studies	There appears to be a reliable and significant increase in power output (both weight lifting as well as cycle ergometer measurements) in both trained and sedentary persons with doses of caffeine exceeding 5mg/kg, assuming the subject is not caffeine tolerant. Tolerance, or lower doses of caffeine, are not as effective.
B	Whey Protein	—	—	3 studies	There doesn't seem to be an inherent effect of protein on power output, although it may augment training-induced power accural (an inherent effect of protein supplementation).
B	Arachidonic acid			4 studies	
B	Trimethylglycine	—	—	9 studies	There appear to be isolated cases of power output being increased which fail to be replicated elsewhere under similar experimental

					conditions, and the majority of evidence suggests that the power output increase seen is no greater than placebo; a potential ergogenic effect is either due to a currently unknown prerequisite (ie. parameter of the study population) or is not present.
B	Chromium	—	—	5 studies	No interaction between chromium and strength gain in naive nor trained athletes.
B	Colostrum	—	—	9 studies	For the most part and aside from one pilot study, there is no consistent or remarkable increase in power output seen with colostrum that is not replicated by whey. Protein, inherently, may increase power output when combined in the diet over longer periods though.
C	Clenbuterol	↑	★☆☆ Minor	1 study	An increase in power output is noted with clenbuterol usage
C	Pyruvate	—	—	1 study	No significant influence on power output noted with pyruvate supplementation in healthy athletes
C	Ephedrine	—	—	1 study	No significant influence on power output with standard oral doses of ephedrine (higher doses may influence power output, but this is not well researched)
C	Yohimbine	—	—	1 study	No significant influence on power output noted with yohimbine
C	Alcohol	↓	★☆☆ Minor	1 study	Acute ingestion of alcohol may be able to reduce subsequent power output
C	Nitrate	—	—	1 study	No significant effect on acute

					power output
C	Spirulina	↑	★★★☆☆ Notable	1 study	Notable as acute power output (leg extension measurement) increased by 20-30% (more efficacy in untrained persons, some efficacy in trained persons) after 8 weeks whereas placebo failed to have an increase. Needs more research to fine-tune the efficacy.
C	Rhodiola Rosea	—	—	1 study	No significant influences on power output
C	Velvet Antler	↑	★☆☆☆☆ Minor	2 studies	A lone study noted an increase in muscle torque associated with Velvet Antler supplementation, which needs to be replicated to see if it is a true effect.
C	Tribulus terrestris	—	—	2 studies	No significant alterations in power output associated with tribulus supplementation.
C	Theaflavins	↑	★☆☆☆☆ Minor	1 study	An increase in power output on a Wingate test has been noted with theaflavins supplementation above 1,800mg daily; efficacy of lower doses is uncertain
C	Terminalia arjuna	↑	★☆☆☆☆ Minor	1 study	Power output has been noted to be increased in sprint tests, which is thought to be secondary to pulmonary effects of terminalia
C	Ecdysteroids	—	—	1 study	No difference between improvements in power output between ecdysteroids and placebo
C	Gamma Oryzanol	—	—	1 study	No interactions with power output have been noted with gamma-oryzanol ingestion

C	Kaempferia parviflora	—	—	1 study	No significant influence on power output when taken acutely before exercise
C	Arginine	—	—	2 studies	No significant influence on power output
C	Vitamin D	—	—	1 study	Although a trend to increase power output has been noted, most research suggest no such benefit
C	Branched Chain Amino Acids	—	—	2 studies	Mixed effects on power output, but when it does occur it is not a <i>per se</i> increase in power output but secondary to reduced muscular soreness after repeated exercise. This may be more indicative of anti-fatigue effects than of genuine power output improvement
C	Leucine			1 study	
C	Leucic Acid	—	—	1 study	Power output as assessed by jumping tasks and weightlifting is unaffected
C	Alpha-GPC	↑	★☆☆ Minor	1 study	The lone pilot study noted a 14% increase in power output as assessed by bench throws, requires replication
C	Ashwagandha	↑	★☆☆ Minor	2 studies	Improvements in power output have been noted in trained persons subject to a sprint test and in sedentary persons who simply took the supplement for 30 days and assessed quadricep strength.
C	Glutamine	—	—	1 study	No significant influence on power output and strength associated with glutamine supplementation over placebo.
C	Anatabine	—	—	1 study	Strength recovery over the course of three days recovery

					was not significantly improved by 6-12mg anatabine
C	D-Aspartic Acid	—	—	1 study	Otherwise healthy trained men do not experience a further increase in power output relative to placebo when D-aspartic acid is taken alongside resistance training.
C	N-Acetylcysteine			1 study	
C	Astaxanthin			1 study	
D	Eurycoma Longifolia Jack	↑	★☆☆ Minor	1 study	A slight increase in power output has been noted, which may be secondary to increased training adaptations

Pre-Eclampsia Risk

Pre-Eclampsia refers to a spike in blood pressure and proteinuria that some pregnant women experience, and due to the severity of this condition some supplements are sought after for reducing the risk of it ever developing.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	—	—	2 studies	There does not appear to be a significant protective effect against pre-eclampsia in women who supplement fish oil during pregnancy
C	Coenzyme Q10	↓	★☆☆ Minor	1 study	A reduction in risk has been noted, but not to an overly amazing degree
C	Vitamin C	—	—	1 study	No significant influence on pre-eclampsia risk

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Processing Accuracy

Processing accuracy refers to the ability to not make errors during information processing and testing. Attempts to increase processing speed and reaction time should make note of processing accuracy to maximize efficiency.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Rhodiola Rosea	↑	★☆☆ Minor	1 study	Increases in processing accuracy are likely secondary to reductions in fatigue
C	Phosphatidylserine	↑	★☆☆ Minor	1 study	Increased processing accuracy has been noted in otherwise healthy persons at 400mg PS daily when testing was conducted in a fatigued state (post exercise)
C	Fish Oil	↑	★☆☆ Minor	1 study	An improvement in processing accuracy (assessed by amount of errors in a cognitive test) has been noted with fish oil in otherwise healthy adults that do not frequently consume fish products
C	Branched Chain Amino Acids	↑	★☆☆ Minor	1 study	The increased processing accuracy appears to be secondary to reducing exercise-related fatigue, and occurs when testing is after exercise.
C	Vinpocetine			1 study	
C	Modafinil	↑	★☆☆ Minor	1 study	There is a possible improvement in processing accuracy with supplementation of modafinil.
C	Ginkgo biloba	↑	★☆☆ Minor	2 studies	The number of errors seen in serial threes and serial sevens tasks appears to be reduced with acute supplementation of

					EGB-761
C	Nigella sativa	—	—	1 study	No significant improvements in the accuracy of cognitive processing appears to occur with supplementation of nigella sativa seeds.
C	Centella asiatica	—	—	1 study	No significant influence on processing accuracy is seen with <i>centella asiatica</i> supplementation
D	Peppermint	—	—	1 study	Processing accuracy does not appear to be significantly influenced with acute inhalation of peppermint extract during cognitive testing

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Processing Speed

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Coconut Oil	↑	★☆☆ Minor	1 study	Study was unable to properly assess coconut oil as it was used as an active control; some benefit appears apparent relative to fish oil.
C	Melissa officinalis	↓	★☆☆ Minor	1 study	A decrease in processing speed appears to occur following lemon balm ingestion, which may be related to the sedation effects
C	Phosphatidylserine	↑	★☆☆ Minor	1 study	Increased processing speed has been noted in otherwise healthy persons at 400mg PS daily when testing was conducted in a fatigued state (post exercise) which coincided with increase accuracy as well.
C	Modafinil	—	—	1 study	There does not appear to be a significant influence on processing speed, with some evidence suggesting a possible reduction thereof.
C	Ginkgo biloba	↑	★☆☆ Minor	2 studies	In older individuals, there appears to be an increase in processing speed without a sacrifice in accuracy
C	Nigella sativa	↑	★☆☆ Minor	1 study	Trail making test time in older adult men appears to be reduced modestly with daily supplementation of nigella seed extract
D	Peppermint	—	—	1 study	Processing speed is not significantly influenced with the aroma of peppermint during

					cognitive testing

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Prolactin

Prolactin is a peptide hormone that is known to regulate lactation in females and are a negative regulator of steroid hormones (estrogen and testosterone) when it is highly elevated.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Melatonin	—	—	1 study	No significant influence on prolactin concentrations
C	Nicotine	↑	★☆☆ Minor	1 study	An increase in prolactin has been noted with nicotine ingestion
C	Maca	—	—	2 studies	No significant influence on prolactin levels
C	Fenugreek	—	—	1 study	No detectable interactions with fenugreek and prolactin levels
C	Mucuna pruriens	↓	★☆☆ Minor	2 studies	A decrease in prolactin appears to occur following Mucuna or L-DOPA ingestion
C	Panax ginseng	—	—	1 study	No significant influence on prolactin in men
C	Vitamin E	↓	★☆☆ Minor	1 study	May decrease prolactin in instances of uremia, but there is currently no evidence in otherwise healthy controls.
C	Velvet Antler	—	—	1 study	No significant interactions with prolactin and velvet antler noted
C	Saffron	—	—	1 study	Supplementation of 60mg saffron for 26 weeks does not significantly influence prolactin in infertile men.

D	Alcohol	↑	★☆☆ Minor	1 study	An increase in prolactin has been noted following acute ingestion of alcohol
D	Licorice	—	—	1 study	Prolactin appears unaffected following licorice consumption
D	Phosphatidylserine	—	—	1 study	No significant influence on exercise-induced prolactin
D	Zinc	—	—	1 study	No detectable increase in prolactin in persons who are deficient in zinc and then supplemented to restore levels.

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Prostate Cancer Risk

Prostate cancer risk is thought to be reduce with some supplements or foods, and is usually measured either with survey data or by measuring prostate specific antigen doubling time and looking for a reduction.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Selenium	↓	★☆☆ Minor	1 study	A small decrease in prostate cancer risk is seen when comparing areas with high soil selenium (indicative of dietary intake of selenium) against areas with low soil selenium.
B	Vitamin E	↓ ↑	★☆☆ Minor	4 studies	Low doses of vitamin E (50mg) in smokers has been associated with significant decreases in prostate cancer risk, whereas moderate doses (400IU) of vitamin E in otherwise healthy older men is associated with a mild but significant increase in prostate cancer risk.
C	Curcumin	↓	★☆☆ Minor	1 study	Appears to be associated with a reduced risk of prostate cancer
D	Punicalagins	↓	★★★☆☆ Notable	2 studies	Notable as consumption of pomegranate juice is associated with a prolongation in the time require for PSA (biomarker of prostate cancer) to double, from 15 months to 54 months

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Prostate Hypertrophy

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Stinging Nettle	—	—	1 study	No significant influence on prostatic hypertrophy despite reducing symptoms
C	Ganoderma lucidum	—	—	2 studies	At an oral dose that can reduce symptoms of prostatic hyperplasia, there is no apparent effect on prostatic hypertrophy
D	Garlic	↓	★★★☆☆ Notable	1 study	The lone pilot study has noted a 32% reduction in prostatic size after a month of eating 200mg/kg garlic (as a water soluble liquid extract)

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Prostate Specific Antigen

Prostate specific antigen (PSA) is a biomarker that is known to be reflective of prostate cancer risk. An elevated PSA is associated with greater risk of prostate cancer, and reducing the rate that PSA increases is seen as protective.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Curcumin	↓	★☆☆ Minor	1 study	Has been noted to decrease prostate specific antigen levels following supplementation
C	Fenugreek	—	—	1 study	No significant influence on prostate specific antigen levels
C	Ganoderma lucidum	—	—	2 studies	The ethanolic extract has failed to alter serum levels of PSA
C	Dehydroepiandrosterone	—	—	2 studies	No significant influence on PSA levels
D	Punicalagins	↓	★☆☆ Minor	2 studies	Does not appear to be able to reduce PSA levels outright, although it can attenuate the rate of which PSA increases over time (relative to untreated control, this is a reduction)
D	Garlic	↓	★★★☆☆ Notable	1 study	The lone study (no placebo control) noted a 60% reduction in both total and free PSA in a small group of men with prostate cancer; requires more evidence to evaluate the therapeutic potential

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Protection from Smoking

Smoking a cigarette is associated with some acute adverse changes in blood flow and oxidative biomarkers, and due to these thought to be risk factors for heart health some supplements are being investigated for negating the effects of smoking.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin C	—	—	3 studies	There do not appear to be any inherent protective effects of Vitamin C against the oxidative and inflammatory changes associated with cigarette smoking, although the reduction in blood flow may be attenuated somewhat with antioxidants and this applies to Vitamin C
C	Benfotiamine	↑	★☆☆ Minor	1 study	There appears to be an attenuation in how much a cigarette constricts peripheral blood flow by about half, with other biomarkers not changed overly to an overly potent degree.

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Protein Carbonyl Content

Similar to how lipid peroxidation measures oxidation as it applies to lipids, protein carbonyls measure the oxidation rates of protein structures. The accumulation of protein carbonyls is highly associated with cellular aging.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Eleutherococcus senticosus	↓	★☆☆ Minor	1 study	A decrease in protein carbonylation has been noted, which is thought to be secondary to antioxidative effects
C	Alpha-Lipoic Acid	↓	★☆☆ Minor	1 study	Appears to reduce protein carbonylation, which may be related to the antioxidative effects
C	Curcumin	—	—	1 study	No significant influence on protein carbonylation has been noted with curcumin ingestion
C	Methylsulfonylmethane	↓	★☆☆ Minor	1 study	A decrease in protein carbonylation is noted with MSM supplementation

Proteinuria

Proteinuria is losses of large protein structures in the urine, which normally does not occur and signifies structural damage to the kidneys. A higher rate of proteinuria correlates with worsened kidney damage, and reductions in proteinuria reflect improved renal function.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Benfotiamine	—	—	2 studies	No evidence to support a reduction in the amount of protein lost in the urine of persons with diabetic nephropathy (UAE between 15-300mg/24 hours). Whether there is a preventative effect or not, there does not appear to be a rehabilitative effect.
C	Creatine	—	—	1 study	No significant influence on protein losses in the urine (proteinuria)
C	Curcumin	↓	★☆☆ Minor	1 study	A reduction in proteinuria has been noted in persons with kidney impairment given curcumin
C	Fish Oil	—	—	1 study	Although a trend to reduce protein losses in the urine was noted (which would be kidney protective), this was a statistically insignificant and secondary to lupus treatment
C	Ginkgo biloba	↓	★★★☆☆ Notable	1 study	The study in diabetics noting a reduction in urinary albumin noted a near halving over 8 weeks with a low dose of ginkgo.
C	Nigella sativa	—	—	1 study	No significant influence on the rate of proteinuria, suggesting no kidney damage associated with supplementation.

C	Chromium	—	—	1 study	Chromium supplementation does not appear to cause proteinuria (protein losses in the urine) suggesting no kidney toxicity, as proteinuria is a biomarker of such damage.
D	Ganoderma lucidum	↓	★☆☆ Minor	1 study	A decrease in urinary protein has been noted, indicative of kidney protective effects
D	Chlorella	↓	★☆☆ Minor	1 study	Reduced proteinuria in pregnant women (possibly indicative of kidney protective effects); more studies would be prudent as to include comparators or use in other contexts.

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Quality of Life

Quality of life (QOL) refers to a general, all encompassing, response as to how tolerance and enjoyable one's living conditions are. QOL is impaired in various disease states that reduce functionality or cause pain, and treating these symptoms causes an increase in QOL.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Coenzyme Q10	↑	★☆☆ Minor	3 studies	An increase in QOL has been noted in persons who either have heart ailments or are at risk for them, but this may not be a universal increase (perhaps dependent on reducing disease state symptoms)
C	Berberine	↑	★☆☆ Minor	1 study	Minor effect in persons with cardiomyopathy, but it is unsure if berberine has a per se benefit on quality of life.
C	Oxiracetam	↑	★☆☆ Minor	1 study	The one study to measure subjective quality of life in persons with dementia found a significant improvement with supplementation
C	Garlic	—	—	1 study	Quality of life in cancer patients is unaffected despite an increase in NK cell activity, thought to be indicative of a therapeutic effect of supplementation.

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Rate of Gastric Emptying

The rate of gastric emptying is how fast food leaves the stomach, and a delayed rate of emptying is able to reduce hunger due to the physical presence in the stomach causing release of appetite suppressing hormones.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Ginger	↑	★☆☆ Minor	4 studies	Ginger appears to increase the rate of gastric digestion, although the potency thereof is not too reliable
C	Yohimbine	—	—	1 study	No significant effect on gastric emptying rate
C	Psyllium	↓	★☆☆ Minor	1 study	No reference drug to compare it to, and thus the potency in psyllium delaying gastric emptying is not certain.
C	Peppermint	↑	★☆☆ Minor	1 study	A slight increase in the rate of gastric emptying is noted with peppermint oil, which is thought to be of benefit to persons with GERD

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Rate of Perceived Exertion

The rate of perceived exertion (RPE) is a subjective measurement of how difficult it is to conduct an exercise, usually used during cardiovascular exercise. Reducing the RPE may help with performance by allowing one to push harder (due to less difficulty and pain).

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Caffeine	↓	★☆☆ Minor	5 studies	Although the effects are somewhat unreliable, there appears to be a reduction in the rate of perceived exertion associated with caffeine ingestion
B	Nitrate	↓	★☆☆ Minor	4 studies	May reduce the rate of perceived exertion in some instances (prolonged cardiovascular exercise), but is not highly reliable.
B	Sodium Bicarbonate	—	—	10 studies	Although there is some limited evidence that sodium bicarbonate can increase 'perceived readiness' for a task and ample evidence that it can reduce the rate of neuromuscular decline (seen with fatigue), the actual rate of perceived exertion (how hard an exercise feels) is wholly unaffected.
C	Ginger	—	—	1 study	No significant influence on the rate of perceived exertion
C	Coenzyme Q10	↓	★☆☆ Minor	1 study	A decrease in the rate of perceived exertion has been noted with CoQ10 supplementation
C	Vitamin C	↓	★☆☆ Minor	2 studies	The rate of perceived exertion in obese adults appears to be attenuated with Vitamin C

					supplementation
C	Maca	—	—	1 study	No significant influence on the rate of perceived exertion associated with Maca root
C	Rhodiola Rosea	↓	★☆☆ Minor	1 study	Possibly effective if confounded with fatigue (the antifatigue effects may reduce the rate of perceived exertion during submaximal exercise) but there does not appear to be strong effects in maximal effort trials
C	Eleutherococcus senticosus	—	—	1 study	Despite possible influences on fatigue production, there is currently no demonstrated reduction in the rate of perceived exertion during exercise
C	Kaempferia parviflora	—	—	1 study	No significant influence on the rate of perceived exertion when a single dose is taken acutely
C	L-Carnitine	↓	★☆☆ Minor	1 study	A reduction in the rate of perceived exertion appears to exist following carnitine supplementation
C	Panax ginseng	—	—	1 study	No significant influence on the rate of perceived exertion during exercise
C	Choline	—	—	1 study	No significant alterations in the rate of perceived exertion during loaded carrying exercises
C	Branched Chain Amino Acids	↓	★☆☆ Minor	1 study	There is some evidence to support a reduction in the rate of perceived exertion during exercise under the influence of BCAA supplementation, but this appears to unreliably improve performance and is of low magnitude

C	Leucine			1 study	
C	Taurine			1 study	
C	Trimethylglycine	—	—	2 studies	No significant influence of betaine (acute or two weeks of supplementation) on the rate of perceived exertion.
D	Ashwagandha	—	—	1 study	Despite alterations in power output seen, the rate of perceived exertion in otherwise sedentary persons is not affected.

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Rate of Percieved Exertion

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Quercetin	—	—	2 studies	There is no significant influence of quercetin supplementation on the rate of percieved exertion (RPE)
C	Trimethylglycine	—	—	1 study	No significant influence on the rate of perceived exertion is seen with supplementation of betaine in rehydrated athletes.
C	Colostrum	—	—	1 study	Colostrum does not appear to reduce (benefit) the rate of perceived exertion during physical exercise.

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Reaction Time

Reaction time refers to one's reflexes and the speed of which a task can be done, and is a cognitive parameter that is of interest to athletes or persons in need of more rapid coordination.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Caffeine	↑	★☆☆ Minor	5 studies	Although the overall effect is unreliable and context dependent, caffeine appears to increase reaction time and attention (possibly at the cost of accuracy)
B	Modafinil	↓	★☆☆ Minor	3 studies	An improvement in reaction time (decrease) is noted in both healthy and normal persons as well as those undergoing either drug addiction or sleep deprivation. This may be related to the alertness promoting effects of the compound.
B	Centella asiatica	↓	★☆☆ Minor	4 studies	There are decreased in reaction time when otherwise healthy older adults take this supplement (youth not tested) which span to choice recognition, and spatial memory reaction time but <i>not</i> digit vigilance and simple reaction time.
C	Kava	↓	★★★☆☆ Notable	1 study	The one study to measure reaction time noted an astounding decreased (approximately 40% reduction), which needs to be replicated
C	Policosanol	↓	★☆☆ Minor	1 study	Reductions in reaction time were not overly significant.
C	Panax ginseng	↓	★☆☆ Minor	2 studies	Mixed effects on reaction time, with a possible decrease

					occurring
C	Nicotine	↓	★☆☆ Minor	1 study	A decrease in reaction time is noted with acute nicotine ingestion
C	Ginger	↓	★☆☆ Minor	1 study	A decrease in reaction time has been noted to be secondary to improvements in cognition in older women; no studies in youth at this moment in time.
C	Rhodiola Rosea	—	—	1 study	No significant influences on reaction time
C	Choline	—	—	1 study	No significant alterations in reaction time noted with choline
C	Phosphatidylserine	—	—	1 study	No significant alterations in reaction time during treatment of cognitive decline
C	Fish Oil	↓	★☆☆ Minor	1 study	A reduction in reaction time has been noted with fish oil supplementation in persons who consume low levels of fish in the diet
C	Branched Chain Amino Acids	↓	★☆☆ Minor	1 study	A (beneficial) decrease in reaction time has been noted during a stimulated soccer test, which was thought to be secondary to the antifatigue effects. Hypothesized to be useful for prolonged sports
C	Theanine			1 study	
C	Vinpocetine	↓	★☆☆ Minor	1 study	High doses (40mg) may reduce reaction time during tested, with lower doses not being potent enough to influence reaction time
C	Ginkgo biloba	↑	★☆☆ Minor	2 studies	Alongside improvements in general cognition in older

					individuals, an increase in reaction time has been noted.
C	Zinc	↑	★☆☆ Minor	1 study	A slight increase in reaction time has been noted in persons who are zinc deficient and then supplemented with zinc.
C	PRL-8-53	—	—	1 study	The dose of PRL-8-53 that improves memory formation does not appear to have any significant influence on reaction time.

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Red Blood Cell Count

Red blood cell count refers to total erythrocytes in serum, and is usually measured in toxicology testing or some instances of anemia. Although higher than average levels of red blood cells can needlessly increase blood pressure, it supports aerobic exercise and oxygen delivery.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin E	—	—	4 studies	The overall amount of red blood cells does not appear to be significantly altered with supplemental vitamin E.
C	Spirulina	—	—	1 study	Currently insufficient evidence to support a change in RBC count.
C	Echinacea	—	—	1 study	Oddly ineffective despite an increase in erythropoetin seen
C	Velvet Antler	—	—	1 study	No influence of this supplement on red blood cell count following prolonged supplementation
C	Royal Jelly	↑	★☆☆ Minor	1 study	At least one study has noted an increase in red blood cell count following ingestion of Royal Jelly
C	Garlic	—	—	1 study	There are no alterations in red blood cell count with normal doses of garlic (although there does appear to be a decrease when a <i>toxic</i> dose of garlic oil is ingested)
C	Astaxanthin			1 study	
C	Saffron	↓	★☆☆ Minor	2 studies	A decrease in RBCs has been noted in one study suggesting saffron toxicity with prolonged supplementation of a double

					dose (60mg).
D	Nigella sativa	↑	★☆☆ Minor	1 study	A normalization of RBC count has been noted in the treatment of hepatitis C with the seed oil of <i>nigella sativa</i>
D	Ashwagandha	—	—	1 study	Supplementation with the water extract of the roots for 30 days in otherwise healthy persons does not significantly influence red blood cell count.
D	Tetradecyl Thioacetic Acid			1 study	

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Relaxation

Relaxation refers to a self-reported peace of mind and calmness, and may be influenced by light sedative or relaxing compounds. Relaxing compounds are said to be anti-stress.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Theanine	↑	★★★☆☆ Notable	3 studies	A notable increase in relaxation (usually without sedation) appears to occur, as assessed by neural measurements (such as alpha-waves) or self-report surveys. Occurs within 30 minutes to an hour
C	Lavender	↑	★★★☆☆ Minor	3 studies	An increase in the magnitude of self-reported 'relaxation' is noted with lavender aromatherapy more than placebo
D	Melissa officinalis	↑	★★★☆☆ Minor	1 study	An increase in self-reports of relaxation occur, which may be related to the increased calmness and sedation ratings also seen

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Rhonchi

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Pelargonium sidoides	↓	★★★☆☆ Notable	5 studies	Rhonchi (coarse rattling sound associated with mucus in the airway, similar to wheezing and crackles) appears to be eliminated in more than 90% of persons (with bronchitis) using the standard dose of this supplement within a week.

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Risk of Falls

Risk of falling refers to elderly individuals with funtional impairment, and interventions to improve muscular function or bone integrity tend to reduce falls and thus reduce both fracture and mortality risk.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Vitamin D	↓	★★★☆☆ Notable	6 studies	The risk of falls in the elderly (and subsequently, rate of bone fractures) appears to be significantly reduced with Vitamin D supplementation at 700 IU or greater, with most research in the 700-1000 IU range. Lower doses do not appear effective, and a greater protective effect appears to exist alongside calcium supplementation (and possibly Vitamin K supplementation)

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Risk of Stroke

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitamin E	—	—	3 studies	There does not appear to be a protective effect of vitamin E on the development of stroke relative to placebo.
C	Ginkgo biloba	—	—	1 study	The risk of stroke does not appear to be reduced with supplementation of 240mg EGb-761 in older individuals.

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Sedation

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Lavender	↑	☆☆☆ Minor	1 study	An increase in sedation has been noted with aromatherapy, but not with oral usage of lavender supplements
C	Theanine			1 study	
C	Modafinil	↓	★★★ Strong	2 studies	Modafinil (300mg) taken prior to sleep is as potent as 20mg D-amphetamine in reducing the need to sleep and improving cognitive performance during intentional sleep deprivation. Occasionally, this potency manifests itself as the 'side-effect' of insomnia in some persons who take it in the AM
C	Synephrine			1 study	
C	Valeriana officinalis	↑	☆☆☆ Minor	2 studies	Doses above 750mg may be associated with the 'morning hangover' side effect (sleepiness upon waking) whereas lower doses of 400mg have not been associated with such.
D	Peppermint	—	—	1 study	Peppermint aromatherapy does not appear to significantly influence the state of wakefulness

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Seminal Motility

Seminal motility is an aspect of fertility, and refers to the ability of sperm cells to move in medium (and in the womb). Increasing sperm motility can improve fertility in men who are otherwise infertile.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Coenzyme Q10	↑	★☆☆ Minor	2 studies	Requires more evidence to assess potency, but it does appear to reliably increase seminal motility
C	Mucuna pruriens	↑	★☆☆ Minor	2 studies	An increase in seminal motility is observed following mucuna ingestion
C	Vitamin C			1 study	
C	Ashwagandha	↑	★☆☆ Minor	2 studies	Alongside improvements in all seminal parameters, ashwagandha is able to increase seminal motility as well; both are thought to underlie pro-fertility effects.
C	Eurycoma Longifolia Jack	↑	★☆☆ Minor	1 study	Sperm motility appears to be increased, with more efficacy in those with lower baseline motility and improvements averaging 44.4%
C	Astaxanthin			1 study	
C	Saffron	—	—	2 studies	The best evidence to date does not support a role for saffron supplementation in increasing seminal motility.
D	Ginger	↑	★★★☆☆ Notable	1 study	Preliminary evidence suggests a 47.3% increase in seminal motility seen with three months supplementation of ginger to infertile men.

D	D-Aspartic Acid	↑	★☆☆ Minor	1 study	Seminal motility is increased 50-100% in infertile men supplementing with D-aspartic acid

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Serum Albumin

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	L-Carnitine			1 study	
C	Nigella sativa	↑	★☆☆ Minor	3 studies	An increase in serum albumin has been noted, and the reason for this currently unknown.
C	Astaxanthin			1 study	

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Serum Bicarbonate

Serum bicarbonate is a way to indirectly measure the pH of the blood, as a higher bicarbonate concentration tends to reflect a more alkaline (buffered) pH. Bicarbonate is reliably increased in oral sodium bicarbonate.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Sodium Bicarbonate	↑	★★★ Strong	47 studies	For the purpose of increasing serum bicarbonate concentrations, orally ingested bicarbonate is the reference compound for it. The increases tend to be around a 30% increase from baseline values (as there is always a circulating bicarbonate concentration)

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Serum Cobalamin

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Trimethylglycine	—	—	3 studies	Mixed evidence as to whether B12 is influenced with supplementation of betaine, but the higher quality study appears to show no effect (since the other study noted a decline in B12 in placebo).
C	Vitamin E	—	—	1 study	Serum levels of cobalamin (vitamin B12) do not appear to be influenced with supplementation of vitamin E.

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Serum DHEA

Serum DHEA refers to the concentration of DHEA in the blood, a steroid hormone precursor. Increasing DHEA concentrations is thought to reduce some side-effects of aging and promote longevity.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Dehydroepiandrosterone	↑	★★★ Strong	13 studies	Supplemental DHEA results in a reliable and significant increase in DHEA concentrations in the blood (both sulfated DHEAS and unsulfated DHEA)
C	Ashwagandha	↑	★☆☆ Minor	1 study	A slight increase has been detected in serum DHEA sulfate (13.2%) with 60 days of ashwagandha supplementation.
C	Eurycoma Longifolia Jack	—	—	1 study	No significant changes in the sulfate form of DHEA (DHEA-S) is noted after twelve continual weeks of supplementation
C	Chromium	—	—	1 study	Chromium supplementation does not appear to alter serum concentrations of DHEA or sulfated DHEA.
D	Zinc	—	—	1 study	No significant influence on serum DHEA sulfate

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Serum Folate

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Trimethylglycine	—	—	4 studies	<i>Chronically</i> there are no changes to serum folate due to the body normalizing folate levels, but acute supplementation can reduce folate concentrations in serum sharply for a short time.
C	Red Clover Extract	—	—	1 study	There do not appear to be any significant changes to circulating folate seen with supplementation of red clover extract.
C	Vitamin E	—	—	1 study	Serum folate does not appear to be modified with supplementation of vitamin E.

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Serum Magnesium

Serum magnesium is the blood levels of magnesium. While an acute spike results after magnesium supplementation, blood levels tend to be a poor predictor of magnesium status (erythrocytes are better) but are associated with the ability of magnesium to reduce blood pressure.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Magnesium	↑	★★★☆☆ Notable	8 studies	Has the capacity to increase serum magnesium stores, but this is somewhat unreliable and maybe dependent on the person being deficient in magnesium prior to supplementation

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Serum Platelets

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Anethum graveolens	↓	★☆☆ Minor	1 study	12 week supplementation of dill, yet not 8 weeks for some reason, was able to reduce blood platelet concentrations in obese persons with metabolic syndrome (600mg dill)
C	Garlic	—	—	1 study	Despite any possible interactions with the platelets (in regards to preventing their clotting), there are no alterations in the overall amount of platelets.
C	Astaxanthin			2 studies	
C	Saffron	↓	★☆☆ Minor	1 study	Supplementation of 60mg saffron was able to reduce platelet counts in serum following eight weeks of exposure (increasing in magnitude until study cessation at 26 weeks) thought to be related to toxicity.
C	Vitamin E	—	—	2 studies	The overall content of platelets is not affected by supplementation of vitamin E.
D	Ashwagandha	—	—	1 study	There is no significant change in total platelet count seen with 30 days supplementation of the basic root extract in otherwise healthy persons

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Serum T3

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Iodine	↓	☆☆☆ Minor	5 studies	500µg iodine or higher (in addition to the diet) appears to have a slight suppressive effect on thyroid function in otherwise healthy persons
B	Vitamin E	—	—	4 studies	The majority of evidence has failed to find any significant interaction with vitamin E supplementation and circulating levels of T3.
C	7-Keto DHEA	↑	☆☆☆ Minor	1 study	There appears to be an increase in circulating T3 hormone levels (active thyroid hormone) when 7-keto is paired with a caloric restriction and exercise (relative to placebo with the same regimen)
C	Zinc	↑	☆☆☆ Minor	2 studies	The decline in T3 hormone levels during prolonged exercise is abolished with supplementation of zinc.
D	Dehydroepiandrosterone	—	—	1 study	No significant influence on serum T3 has been noted

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Serum T4

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Iodine	↓	★☆☆ Minor	7 studies	Supplemental iodine above 500µg appears to be capable of suppressing T4 to a small degree whereas lower doses are not associated with such an effect.
B	Vitamin E	—	—	5 studies	Although one study noted a decrease with 600 IU, future studies in similar persons with multiple doses have failed to replicate these observations.
C	7-Keto DHEA	—	—	1 study	Insufficient evidence to support alterations in T4, with no changes detected when it is measured
C	Zinc	↑	★☆☆ Minor	2 studies	The decline in T4 hormone levels during prolonged exercise is abolished with supplementation of zin
D	Tetradecyl Thioacetic Acid			1 study	

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Severity of Sickness

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Andrographis paniculata	↓	★★★☆☆ Notable	1 study	Seems to have more efficacy against nasal, ear, and throat symptoms of sickness. Lack of evidence and comparisons to reference drugs limits strong evidence
C	Garlic	↓	★☆☆☆☆ Minor	1 study	Despite the potent efficacy in reducing the occurrence of sickness, the actual severity of symptoms is only modestly reduced with garlic.
C	Pelargonium sidoides	↓	★☆☆☆☆ Minor	1 study	In children with upper respiratory tract infections (URTIs), supplementation is effective in reducing symptom severity.
C	Colostrum	—	—	2 studies	While in children with IgA deficiency colostrum appeared to reduce the severity of sickness when supplemented at the onset of sickness, this same effect was not observed in adults with suspected upper respiratory viral infections.

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Sex Hormone Binding Globulin

Sex Hormone Binding Globulin (SHBG) is a globulin that is able to bind to and sequester steroid hormones such as estrogen, testosterone, and DHT. Its elevations are associated with less activity of the steroid hormones.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Dehydroepiandrosterone	↓	★☆☆ Minor	4 studies	There appears to be a decrease in SHBG concentrations in older individuals who also experience an increase in androgen/estrogen concentrations, but this is similarly unreliable
B	Red Clover Extract	—	—	6 studies	There are no significant alterations in the circulating levels of SHBG seen with red clover supplementation.
C	Fish Oil	—	—	1 study	No significant influence on SHBG levels
C	Eurycoma Longifolia Jack	—	—	1 study	No significant influence on circulating SHBG over the course of 12 weeks in otherwise healthy men.
C	Chromium	—	—	1 study	In women with PCOS, chromium supplementation does not alter SHBG concentrations in serum.
D	Licorice	—	—	1 study	No significant alterations in SHBG levels following supplementation

Sexual Function

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Maca	↑	★☆☆ Minor	1 study	An improvement in SSRI induced sexual dysfunction has been noted with Maca supplementation
C	Saffron	↑	★☆☆ Minor	2 studies	SSRI related sexual dysfunction in both men and women appears to be reduced with coingestion of saffron, although saffron does not alter the efficacy of SSRI therapy on depression.
C	Vitamin E	—	—	1 study	Vitamin E does not appear to influence sexual function or satisfaction in otherwise healthy persons with no known sexuality disorders.

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Skeletal Muscle Atrophy

Skeletal muscle atrophy (catabolism) is the loss of lean muscle tissue over time or during inactivity. Compounds that increase atrophy can accelerate this loss while compounds that reduce atrophy are known as 'anti-catabolic'.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Creatine	—	—	2 studies	One study noted a prevention of lean mass loss (did not distinguish between water and muscle), while the study measuring muscle mass specifically failed to find a protective effect during limb immobilization.
C	Ephedrine	↓	★☆☆ Minor	1 study	May decrease the rate of skeletal muscle breakdown over time
C	Clenbuterol	↓	★☆☆ Minor	1 study	The rate of muscle protein breakdown is decreased with clenbuterol usage
D	Coconut Oil	↓	★☆☆ Minor	1 study	Was able to attenuate the rate of skeletal muscle loss during a hypocaloric diet in obese persons; unknown if this applies to lean persons and may be related to ketone production.

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Skin Elasticity

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Pycnogenol	↑	★☆☆ Minor	1 study	An improvement in skin elasticity has been noted with Pycnogenol supplementation
C	Astaxanthin			1 study	
D	Raspberry Ketone	↑	★☆☆ Minor	1 study	Appears to benefit the skin when topically applied as part of a cream
D	Boswellia serrata	↑	★☆☆ Minor	1 study	Not enough evidence to evaluate potency, but an increase in skin elasticity has been noted with topical boswellia

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Skin moisture

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Coconut Oil	↑	★★★☆☆ Notable	2 studies	Appears to be comparable to mineral oil, the active control
C	Astaxanthin			1 study	
D	Salvia hispanica	↑	★★☆☆☆ Minor	1 study	An increase in skin moisture has been noted with topical chia seed application (4% of the solution being chia oil)
D	Ginkgo biloba	↑	★★★☆☆ Notable	1 study	The lone study assessing the effects of topical application of 0.3% ginkgo flavonoids in a cream noted a 28% increase in skin moisture content over 28 days, a highly relevant increase.
D	Saffron	—	—	1 study	Acute topical application of a cream containing saffron has failed to cause significant changes in skin moisture content over the course of seven hours.

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Skin Quality

Skin quality tends to refer to an overall evaluation on (facial) skin parameters such as tightness, moisture content, and clearness from acne. Supplements that improve skin quality can be taken orally or topically as a cream.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Green Tea Catechins	↑	★☆☆ Minor	1 study	Oral ingestion of high dose catechins (1400mg) has been shown to improve skin quality
C	Bladderwrack	↑	★☆☆ Minor	1 study	Limited evidence supports its efficacy, difficult to assess potency due to no reference drug.
C	Pycnogenol	↑	★☆☆ Minor	1 study	Oral supplementation of standard doses of procyanidins can improve skin quality in elderly women, other demographics not tested
C	Red Clover Extract	↑	★☆☆ Minor	1 study	There appears to be an overall increase in skin texture and moisture content associated with oral supplementation of the isoflavones, and a depigmenting activity should also apply (not yet shown in humans)
C	Astaxanthin			1 study	
D	Alpha-Lipoic Acid	↑	★☆☆ Minor	1 study	May improve skin quality when topically applied
D	Hemp Protein	—	—	1 study	No significant influence of topical hemp oil on skin quality
D	Boswellia serrata	↑	★☆☆ Minor	1 study	Somewhat effective, not enough evidence to fully evaluate potency.

D	Ginkgo biloba	↑	★☆☆ Minor	1 study	Skin smoothness/roughness is beneficially influenced with topical application of ginkgo flavonoids at 0.3%
D	Orthosiphon stamineus	↑	★★★☆☆ Notable	1 study	The lone study in women with oily skin noted that improvements in skin quality with a 2% <i>orthosiphon</i> cream were greater than the reference drug of 1% zinc gluconate on all parameters.

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Sleep Quality

Sleep quality refers to the restfulness of a nights sleep and how well it rejuvenates the body, and does not necessarily reflect sleep length.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Melatonin	↑	★☆☆ Minor	4 studies	An increase in sleep quality can occur following treatment of conditions known to impair sleep quality (insomnia and tinnitus)
B	Ginkgo biloba	↑	★☆☆ Minor	5 studies	There may be an increase in sleep efficiency (reduced waking during the night) without any apparent enhancement of REM sleep, this seems to be related to the flavonoid portion
B	Valeriana officinalis	—	—	4 studies	At least according to an overall meta-analysis on the topic, valerian does not appear to be much greater than placebo for aiding sleep in otherwise healthy persons. This may differ in persons with insomnia but that is not yet tested adequately
C	Kava	↑	★☆☆ Minor	2 studies	Sleep quality is enhanced via reducing the symptoms of anxiety which impair sleep
C	Magnesium	↑	★☆☆ Minor	2 studies	An improvement in sleep quality has been noted in persons with poor sleep quality, no studies assess persons with normal sleep function
C	Lavender	↑	★☆☆ Minor	7 studies	Improvements in sleep quality have been noted in insomniacs and persons with

					generalized anxiety disorder mostly, with some limited evidence suggesting this may benefit generally healthy persons. Both oral supplements and aromatherapy are implicated in these benefits, but overall the quality of the studies is somewhat less than desirable. The parameters that see benefit are less waking up during the night and reduction in insomniac symptoms
C	Echinacea	—	—	1 study	Likely related to the inefficacy in treating symptoms, but no significant ability to aid in sleep quality during or without sickness
C	Panax ginseng	↑	★☆☆ Minor	1 study	Has been noted to improve the first-night effect (impaired sleep when sleeping in a new location) after a week of supplementation; possibly of interest to frequent travellers
C	Quercetin	—	—	1 study	No significant influence on sleep quality
C	Ornithine	↑	★☆☆ Minor	1 study	The increase in sleep quality was secondary to reducing the adverse effects of excessive drinking, and was measured by self-report
C	Theanine	↑	★☆☆ Minor	1 study	Sleep quality has been noted to improve in persons with hyperactivity during sleep (such as ADHD). Sleep duration and latency do not appear to be affected
C	Dehydroepiandrosterone	—	—	1 study	No significant influence on sleep quality in menopausal women
C	Yamabushitake	—	—	1 study	No significant effects on sleep quality

C	Glycine	↑	★☆☆ Minor	3 studies	In persons undergoing mild sleep deprivation, 3g of glycine an hour prior to sleep is able to increase sleep quality and improve self-reports of fatigue and well being the next day due to better sleep.
C	Red Clover Extract	↑	★☆☆ Minor	1 study	In post menopausal women, there appears to be an increase in self reported sleep quality that was quite notable, reaching 70-73 points of improvement on a 0-100 rating scale (placebo at 10-16) although this needs to be replicated (independently) to assure quality of data.
D	Pyrroloquinoline quinone	↑	★☆☆ Minor	1 study	An improvement in sleep quality has been noted in persons with impaired sleep; it is not certain how PQQ affects persons with normal sleep cycles

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Sperm Count

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Zinc	↑	★☆☆ Minor	4 studies	An increase in sperm count has been noted in infertile men who also had low testosterone; it was ineffective in infertile men with normal testosterone
C	Tribulus terrestris	—	—	1 study	The increase in sperm count seen with tribulus failed to outperform placebo.
C	Astaxanthin			1 study	
C	Saffron	—	—	2 studies	Saffron supplementation does not appear to be effective in increasing sperm count in infertile men.
D	Ginger	↑	★☆☆ Minor	1 study	A somewhat minor increase in sperm count (16.2%) is seen with supplementation of ginger (amount undisclosed) to infertile men over three months.
D	D-Aspartic Acid	↑	★☆☆ Minor	1 study	Improvements of sperm count in infertile men have been noted to vary between 50-100% increases over baseline.
D	Ashwagandha	↑	★☆☆ Minor	1 study	There appears to be an increase in sperm count in normozoospermic men with infertility consuming 5g ashwagandha daily, with more potency seen in men who self-identify as stressed.

Sperm Quality

Sperm quality refers to the structural capacity of sperm cells and their ability to fertilize (and does not necessarily reflect sperm count nor motility). Supplements that improve sperm quality are thought to be pro-fertility agents.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	L-Carnitine	↑	★★★☆☆ Notable	5 studies	Carnitine at 3g daily appears to increase sperm quality mostly related to sperm morphology; there are mixed effects on sperm motility
B	Mucuna pruriens	↑	★★☆☆☆ Minor	3 studies	There appears to be an increase in seminal quality and oxidative parameters following 3-month ingestion of Mucuna pruriens, which is thought to be secondary to correcting the hypothalamic-pituitary-testes axis
C	Coenzyme Q10	↑	★★☆☆☆ Minor	4 studies	There may be some beneficial influences on the sperm quality, but they have not been reliably reported
C	Ashwagandha	↑	★★☆☆☆ Minor	2 studies	Appears to enhance seminal quality (in a fairly general sense) but needs more studies against reference drugs to properly assess potency.
C	Shilajit	↑	★★☆☆☆ Minor	1 study	Sperm quality (and thought to apply to fertility) has been improved with Shilajit supplementation
C	Vitamin C			1 study	
C	Eurycoma Longifolia Jack	↑	★★☆☆☆ Minor	1 study	May increase parameters of sperm quality and volume.

C	Tribulus terrestris	—	—	1 study	The increase in sperm quality seen with 6g tribulus root has failed to outperform placebo in infertile men.
C	Astaxanthin			1 study	
C	Saffron	—	—	2 studies	While preliminary evidence suggested benefit to seminal morphology, the best evidence to date does not support a role for saffron in enhancing seminal quality.
D	D-Aspartic Acid	↑	★☆☆ Minor	1 study	Appears effective, needs to be compared against a comparator.
D	Ginger	↑	★☆☆ Minor	1 study	Seminal viability (40.7%) and normal morphology () is increased in infertile men given ginger.

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Stomach Ulcers

Stomach ulceration (either by NSAID, alcohol, or bacterial infection) can be treated with oral supplementation or antioxidants. The cause of ulceration may be relevant in the treatment thereof, with a curative substance for alcohol not necessarily benefitting *heliobacter pylori* infections.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Melatonin	↓	★★★☆☆ Notable	3 studies	A notable protective effect against both aspirin and <i>heliobacter pylori</i> induced stomach ulceration is seen with melatonin either alone or with other agents (such as omeprazole) nearing absolute protection in some instances. Although less researched, these may apply to duodenal ulcers as well
C	Curcumin	—	—	1 study	No significant influence on stomach ulceration detected

Stress

Stress (particularly distress) is excessive stimulation of the body's resources that eventually manifests negative symptoms such as fatigue or depression. Several supplements, such as adaptogens, are thought to reduce the development of stress.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Dehydroepiandrosterone	—	—	1 study	No significant influence on parameters of stress
C	Melissa officinalis	↓	★☆☆ Minor	1 study	A decrease in self-reported stress has been reported with lemon balm
C	Rhodiola Rosea	↓	★☆☆ Minor	2 studies	Might be effective, but the reduction in stress (rating scale) appears to be less than that seen with fatigue
C	L-Tyrosine	↓	★☆☆ Minor	2 studies	Perceptions of stress during acute stressors, as well as related symptoms of acute stress, appear to be reduced following tyrosine ingestion
C	Lavender	—	—	1 study	No significant influences on stress
C	Soy lecithin	↓	★☆☆ Minor	1 study	May reduce perceived stress during stressful situations
C	Rose Essential Oil	↓	★☆☆ Minor	1 study	Self-reported ratings of stress are reduced with rose oil inhalation
C	Phosphatidylserine	↓	★☆☆ Minor	2 studies	Possible stress reducing effects that appear independent of cortisol and heart rate, although these effects are unreliable

C	Krill Oil	↓	★☆☆ Minor	1 study	Stress as a side-effect of PMS has been reduced with supplemental krill oil
C	Fish Oil	↓	★☆☆ Minor	1 study	Self-reported stress in distressed women given fish oil supplementation appears to be reduced
C	Theanine			1 study	
C	Ashwagandha	↓	★★★☆☆ Notable	1 study	Ashwagandha appears to significantly reduce the symptoms of stress and its comorbidities (fatigue, temporary cognitive impairment, etc.) as well as biomarkers such as cortisol.
C	Eurycoma Longifolia Jack	↓	★☆☆ Minor	1 study	Supplementation of eurycoma in stressed persons appears to reduce subjective perceptions of stress.
C	Ginkgo biloba	↓	★☆☆ Minor	1 study	There may be some anti-stress properties of ginkgo biloba supplementation when a single dose is taken prior to a stress test
C	Centella asiatica	↓	★☆☆ Minor	1 study	There appears to be stress reducing properties associated with supplementation of this herb at 1g daily, although they may be secondary to anxiety reduction.
D	Kava	↓	★☆☆ Minor	2 studies	Possible antistress effects of kava that requires larger studies
D	Pyrroloquinoline quinone	↓	★☆☆ Minor	1 study	A reduction in self-reported stress has been noted after 8 weeks in persons with self-reported sleep problems; this study also noted improvements in sleep

Stroke Recovery Rate

After a stroke, the next few weeks and months are associated with a gradual improvement and recovery of cognitive capacities to near pre-stroke levels. Some supplements have been noted to accelerate this recovery or help survivors of stroke.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Ginkgo biloba	—	—	1 study	Although there is some scattered evidence to support the role of ginkgo in stroke recovery rates, the best evidence currently available does not find a significant therapeutic benefit.
C	Piracetam	—	—	1 study	Ineffective in the one study where stroke recovery rate was assessed
C	Astragalus membranaceus	↑	★☆☆ Minor	1 study	Not remarkably effective, but does confer some protective and cognitive promoting effects following acute stroke.
C	Nefiracetam	—	—	1 study	No significant influence on the recovery rates from stroke has been noted.
C	Phenylpiracetam	↑	★☆☆ Minor	1 study	Symptoms (cognitive and physical) seen after a stroke appear to be more rapidly recovered with daily usage of phenylpiracetam than with placebo
C	Zinc	↑	★☆☆ Minor	1 study	In zinc deficient persons who recently suffered a stroke, supplementation of zinc appears to accelerate the rate of recovery.
D	Vitamin B12	↑	★☆☆ Minor	1 study	A slight improvement in verbal

					learning associated with 1,000mcg of B12 supplementation in persons with lacunar stroke, according to at least one pilot study

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Subjective Well-Being

Self-reported ratings of well being and happiness; either in general (euphoria-inducing compound) or reducing a disease state to enough of a degree to make the persons relatively happy.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Creatine	↑	★☆☆ Minor	11 studies	The influence of creatine on well being and general happiness is usually dependent on it treating a disease state; there does not appear to be a <i>per se</i> benefit to well being.
B	Dehydroepiandrosterone	—	—	4 studies	No significant influence on well being is noted with DHEA <i>per se</i> , although it may come secondary to other changes occurring during DHEA supplementation (such as improved functionality in elderly persons)
B	Kava	↑	★★★☆☆ Notable	4 studies	The increase in well being appears to be quite large, but secondary to reducing anxiety. At least one study has noted that, in healthy persons subject to a minor stressor (testing) that kava enhanced cheerfulness
B	Panax ginseng	↑	★☆☆ Minor	5 studies	There appears to be an increase in well being and happiness in persons who either have a disease state treated (ie, better glycemic control in diabetes or less erectile dysfunction) and this may also apply to acute usage of 400mg panax ginseng during acute mental stress. In an unstressed and healthy person, panax ginseng is unlikely to have benefit

B	Rhodiola Rosea	↑	★★★☆☆ Notable	4 studies	Increases in subjective well being and contentment in fatigued or stressed individuals appears to be greater than other supplements.
B	Ganoderma lucidum	↑	★☆☆☆☆ Minor	3 studies	Subjective well being increases in disease states where other symptoms (seen as adverse) are decreased; an inherent increase of well being is uncertain.
B	Ginkgo biloba	↑	★☆☆☆☆ Minor	3 studies	An improvement in mood has been noted in persons with cerebral injury, but not in otherwise healthy middle aged persons.
B	Pelargonium sidoides	↑	★☆☆☆☆ Minor	4 studies	Alongside improvements in sickness comes improved well being and vitality associated with supplementation over placebo.
B	Vitamin E	—	—	4 studies	Studies assessing well being in otherwise healthy persons or those with disease states not associated with depression have failed to find any interaction with vitamin E supplementation.
C	Green Tea Catechins	↑	★☆☆☆☆ Minor	1 study	An increase in well being has been noted in unhealthy persons given green tea catechins
C	Chlorogenic Acid	↑	★☆☆☆☆ Minor	1 study	Chlorogenic acid may have a mood enhancing effect independent of caffeine
C	L-Carnitine	—	—	3 studies	No significant changes in subjective well being associated with carnitine intake
C	Ephedrine	↑	★☆☆☆☆	1 study	

C	L-Phenylalanine	↑	★☆☆ Minor	1 study	Appears to increase well being acutely following the first doses of ephedrine, secondary to the psychostimulatory effects
C	Vitamin C	↑	★☆☆ Minor	1 study	An improvement in mood has been noted in hospitalized persons
C	Conjugated Linoleic Acid	—	—	2 studies	Insufficient evidence to support an inherent contentment boosting effect, as the lone study was confounded with weight loss.
C	Caffeine	↑	★☆☆ Minor	2 studies	May increase subjective well being and mood state, possibly secondary to reducing fatigue or from catecholamines
C	L-Tyrosine	↑	★☆☆ Minor	2 studies	There appears to be an increase in subjective well being during stress when tyrosine is preloaded (perhaps secondary to the antistress effects of tyrosine), although this is not overly reliable
C	Maca	↑	★☆☆ Minor	1 study	An increase in well being has been noted
C	Mucuna pruriens	↑	★☆☆ Minor	1 study	An increase in well being has been noted to be secondary to a reduction in cortisol
C	Pyruvate	↑	★☆☆ Minor	1 study	An increase in well being may occur secondary to weight loss, although due to the complications in weight loss with pyruvate this may not be feasible
C	Pycnogenol	↑	★☆☆ Minor	1 study	An increase in well being and mood has been noted in students undergoing academic testing, which correlated with improved test scores

C	Theanine	—	—	1 study	No significant influence on subjective well being and mood state per se
C	Phosphatidylserine	—	—	1 study	No significant influence on subjective well being noted
C	Fish Oil	↑	★☆☆ Minor	3 studies	An improvement in well being has been noted in nondepressed and nonelderly obese persons given fish oil supplementation to a small magnitude.
C	Arginine	—	—	1 study	In persons with peripheral artery disease (intermittent claudication), despite improving symptoms as assessed by a treadmill walking test there does not appear to be an improvement in self-reported well being
C	Ashwagandha	↑	★☆☆ Minor	2 studies	An improvement in well being has been noted secondary to reducing anxiety symptoms.
C	Eurycoma Longifolia Jack	↑	★☆☆ Minor	1 study	In otherwise normal men supplementing eurycoma, an increase in overall quality of life and happiness is seen (alongside increases in libido)
C	Modafinil	↑	★★★☆☆ Notable	2 studies	Subjective well being and enjoyment during cognitive tasks appears to be significantly improved modafinil supplementation, and this is notable as it has been noted to occur in otherwise healthy persons taking modafinil for nootropic purposes
C	Zinc	↑	★☆☆ Minor	2 studies	Although the evidence is mixed currently, zinc has been previously associated with an improvement in mood state

					and has mechanisms by which it can work. It likely has a small but positive influence.
C	Blueberry	↑	★☆☆ Minor	1 study	A slight improvement in subjective well being and happiness has been noted in elderly persons given blueberries over a few weeks as a daily supplement.
C	Nigella sativa	↑	★★★ Notable	1 study	Although only based on one study, in men with central obesity and a wide variety of general health complaints supplementation has outright abolished all measured complaints such as loss of libido, high appetite, pain, and forgetfulness.
C	Peppermint	↑	★☆☆ Minor	3 studies	Although mood state during cognitive testing is unaffected, quality of life is increased when headaches or abdominal pain is being treated with peppermint oil.
C	Centella asiatica	—	—	1 study	Acute ingestion of this herb in otherwise healthy individuals does not appear to alter subjective mood parameters.
C	Cocoa Extract			1 study	
C	N-Acetylcysteine			1 study	
C	Red Clover Extract	—	—	2 studies	Two differing studies have noted either no improvement of well being in menopausal women, or a significant (near 80%) improvement; more research is needed to refine the actual effect, but the study noting no effect is considered higher quality.
C	Ruscus aculeatus	—	—	1 study	Despite improving symptoms of chronic venous insufficiency in the afflicted persons, supplementation failed to lead to an increase in quality of life

					relative to placebo.
D	Black Cohosh	↑	★☆☆ Minor	1 study	May increase well being in those with menopause if a reduction of symptoms occurs.
D	Boswellia serrata	↑	★☆☆ Minor	1 study	Increase in well-being was likely secondary to reducing joint pain from osteoarthritis
D	Bromelain	↑	★☆☆ Minor	1 study	Minor improvements in well being secondary to reducing joint pain
D	Lavender	↑	★☆☆ Minor	1 study	An increase in well being has been noted with lavender aromatherapy, possible secondary to the relaxing effects
D	Vinpocetine	↑	★☆☆ Minor	2 studies	An increase in well being has been noted to be secondary to the reduced rate of cognitive decline

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Swimming Performance

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Creatine	—	—	27 studies	On the whole, there is no reliable improvement in swimming performance with creatine supplementation. In the instances where it could be beneficial, a loading period (no maintenance) is used prior to short sprint tests (50-100m for 1-3 sprints) in order to reduce time by around 2%, or prolonged swimming (400m) may have benefits in the last stretch only.

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Symptoms of Acute Bronchitis

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Pelargonium sidoides	↓	★★★ Strong	11 studies	The standard dose of EPs7630 appears to greatly reduce all symptoms of acute bronchitis, being able to outright eliminate symptoms in as little as 60% of patients (cough and hoarseness related) and up to 95% of persons (sputum and rhonchi related) with efficacy within three days increase over two weeks.

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Symptoms of Acute Mountain Sickness

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Ginkgo biloba	↓	★★★☆☆ Notable	9 studies	There appears to be a quite potent yet quite unreliable reduction in symptoms of AMS when ginkgo is taken at 240mg daily for 1-5 days prior to a trip up a mountain. The reason for this variability is not known.

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Symptoms of Alzheimers

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Ginkgo biloba	↓	★☆☆ Minor	5 studies	Cognitive impairment that is associated with Alzheimer's appears to be significantly reduced with ginkgo supplementation.
C	Fish Oil	—	—	1 study	Despite the benefit seen with high dose DHA in cognitive decline, there does not appear to be a proven significant protective effect in persons already with Alzheimer's
C	Alpha-GPC	↓	★★★☆☆ Notable	1 study	At least among nutraceuticals, Alpha-GPC appears to significantly improve cognition in persons with Alzheimer's disease at the dose of 1,200mg when taken as a daily supplement over a prolonged period of time.
C	Oxiracetam	—	—	1 study	The lone study in persons with Alzheimer's rather than organic cognitive decline has failed to find any benefit associated with supplementation
C	Inositol	—	—	2 studies	The preliminary evidence at this point in time using <i>scyllo</i> -inositol has failed to find a significant therapeutic benefit and <i>myo</i> -inositol shows a nonsignificant trend for improvement based on preliminary evidence.
C	Saffron	↓	★☆☆ Minor	2 studies	Mixed evidence on the efficacy of saffron, but it is possible that supplementation could delay an increase in symptoms without a therapeutic effect.

C	Vitamin E	↓	★★★☆☆ Notable	2 studies	Very high dose Vitamin E supplementation in the form of α-tocopherol (2,000 IU) appears to reduce the rate of cognitive decline in persons with moderate to severe Alzheimer's Disease with a potency comparable to selegiline. Currently no research on lower (more standard) doses, and there appears to be no influence on minor AD or cognitive decline not characterized by AD.

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Symptoms of Autism

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	N-Acetylcysteine			5 studies	
C	L-Carnitine	↓	★★★☆☆ Notable	1 study	High dose carnitine (50mg per kilogram) appears to reduce some symptoms of autism as assessed by rating scales; notable due to the rarity of a supplement towards this goal
C	Ginkgo biloba	—	—	2 studies	The better conducted trial and parts of the preliminary evidence suggest no therapeutic benefit of ginkgo biloba in the treatment of autism
D	Inositol	—	—	1 study	The preliminary evidence on autism does not support a role for inositol therapy

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Symptoms of Bipolar Disorder

Bipolar disorder (a condition characterized by manic and depressive phases) may be influenced by various nutritional supplements, although one of the two phases may be unaffected while the other benefits.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	↓	★☆☆ Minor	5 studies	There appears to be reduced depressive symptoms in bipolar disorder when the depression is of a large magnitude (similar to the anti-depressant effects of fish oil in general). There may not be a reduction in depressive symptoms with lower severity depression (a trend to increase has been noted) and manic symptoms do not appear to be significantly influenced.
C	CDP-choline	—	—	1 study	The lone study in persons with bipolar disorder was one investigating addiction, and when measuring symptoms of bipolar disorder they failed to find any influence of supplementation on symptoms.
C	Inositol	—	—	2 studies	Although a beneficial effect cannot fully be ruled out, the best evidence currently available does not support a significant role for inositol in the treatment of bipolar disorder.
C	Chromium	↓	★☆☆ Minor	4 studies	In persons with bipolar disorder given supplementation of chromium, benefits were only noted against depressive symptoms and while significant (statistically) were mild; manic symptoms were not affected.

D	Uridine	↓	★☆☆ Minor	1 study	Depressive symptoms of bipolar disorder are fairly strongly reduced with uridine supplementation, but currently only open label studies are in existence

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Symptoms of Crohn's Disease

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
D	Curcumin	↓	★☆☆ Minor	1 study	Possible reductions of symptoms associated with Crohns Disease
D	Glutamine	↓	★☆☆ Minor	3 studies	A possible reduction of symptoms associated with Crohn's disease may occur, but this appears to be unreliable

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Symptoms of Diabetic Neuropathy

Diabetic neuropathy is nerve pain associated with diabetes, and is commonly targeted to improve quality of life in diabetics.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Alpha-Lipoic Acid	↓	★★★☆☆ Notable	2 studies	Not yet compared to reference drugs, but it has been subject to a meta-analysis and appears to be more effective than other options for reducing nerve pain associated with diabetes. The lack of a reference comparison and some evidence suggesting no effect prevent a strong rating.
C	Magnesium	↓	★☆☆☆☆ Minor	1 study	A reduction in symptoms associated with diabetic neuropathy has been noted with magnesium supplementation
D	Sulbutiamine	—	—	1 study	Insufficient evidence to support a role in diabetic neuropathy associated with sulbutiamine supplementation

Symptoms of Fibromyalgia

Fibromyalgia is a nonspecific pain disorder with currently unknown causes, although supplements are still being investigated for the purpose of reducing this pain.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	L-Carnitine	↓	★☆☆ Minor	1 study	Fibromyalgic symptoms are reduced with carnitine ingestion
C	Coenzyme Q10	↓	★★★ Strong	5 studies	CoQ10 appears to be quite strongly effective for reducing symptoms of fibromyalgia (strong rating may be retracted at a later time when other reference drugs arise)
C	S-Adenosyl Methionine	↓	★☆☆ Minor	1 study	A decrease in soreness symptoms of fibromyalgia (with no apparent effect on force production) has been noted with SAMe supplementation.
D	Chlorella	↓	★☆☆ Minor	1 study	May have efficacy in reducing pain associated with fibromyalgia, but requires more evidence

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Symptoms of Intermittent Claudication

Intermittent claudication is a disorder of blood flow that limits mobility, and some supplements that aid in blood flow are known to prolong walking time and quality of life in persons with this condition.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Ginkgo biloba	↓	★☆☆ Minor	6 studies	There appears to be reduced symptoms of intermittent claudication with ginkgo supplementation, although it seems to vary significantly from one individual to another and despite some persons experiencing large benefit the overall 'net' benefit is relatively minor.
B	L-Carnitine	↓	★★★☆☆ Notable	3 studies	Symptoms of intermittent claudication are notably reduced with L-Carnitine supplementation (the rate of improvement over time, as assessed by walking distance, seems to be doubled; ie. from 40% to 60% or 60% to 90%) and associated with the Propinyl-L-Carnitine form (found in the supplement GPLC). The role of propinoic acid cannot be ruled out at this time, and studies have not used basic L-carnitine or ALCAR
C	Alpha-Lipoic Acid	↓	★★★☆☆ Notable	1 study	The reduction of claudication symptoms appears to be fairly potent with ALA supplementation, although there is not a large body of evidence overall.
C	Arginine	↓ ↑	★☆☆ Minor	2 studies	Both an improvement and an impairment have been noted on walking distance in persons with intermittent claudication, and it is not exactly known why

					this occurs (may be related to time, with prolonged usage being impairing)

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Symptoms of Irritable Bowel Syndrome

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Peppermint	↓	★★★☆☆ Notable	8 studies	In persons with IBS, supplementation of peppermint oil appears to reliably and effectively reduce abdominal pain for as long as it is taken. Benefits are no longer seen two weeks after supplement cessation and abdominal pain is the only symptom notably reduced.

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Symptoms of Menopause

Symptoms of menopause (climacteric symptoms) are issues that affect women after menopause, such as hot flashes or disturbed sleep. Supplements that reduce these symptoms on self-report surveys are thought to help women cope with menopause.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Black Cohosh	↓	★☆☆ Minor	13 studies	Although there appears to be some benefit over placebo, more recent studies note that the magnitude of benefit is much less than previously though (in the past, a false positive occurred when unblinded studies noted remarkable benefits with black cohosh; the placebo effect appears to be quite potent in regards to menopause)
A	Red Clover Extract	—	—	14 studies	While isolated studies have noted some benefits, the best evidence at this moment in time (Independently conducted and larger, better conducted, studies) tend to note no significant influence on the main climacteric symptoms such as hot flashes with supplementation.
B	Panax ginseng	↓	★☆☆ Minor	3 studies	May decrease some symptoms associated with menopause, mostly related to libido, but this is unreliable.
C	Pueraria mirifica	↓	★★★☆☆ Notable	4 studies	The effects of Pueraria Mirifica on menopausal symptoms appear to be potent, with one study suggesting comparable efficacy to estrogen replacement therapy itself. Requires more robust evidence, however.

C	Maca	↓	★☆☆ Minor	1 study	One study noted reduced symptoms associated with menopause; libido was possibly independently increased, but anxiety and depression appear to also be reduced.
C	Pycnogenol	↓	★☆☆ Minor	1 study	A decrease in some symptoms of menopause has been noted with Pycnogenol supplementation
C	Yamabushitake	↓	★☆☆ Minor	1 study	Menopausal symptoms have been reduced, but this was mostly due to the reported antidepressant and anxiolytic properties of the mushroom.
C	Valeriana officinalis	↓	★☆☆ Minor	2 studies	Limited evidence suggests efficacy in the treatment of menopausal symptoms with valerian extract, with one study measuring benefits to hot flash frequency and the other insomniac symptoms.
D	Dehydroepiandrosterone	↓	★☆☆ Minor	2 studies	Decreases in menopausal symptoms have been noted with DHEA supplementation
D	Pueraria lobata	—	—	1 study	No significant influence detected on symptoms of menopause (as assessed by rating scales)
D	Royal Jelly	↓	★☆☆ Minor	1 study	A decrease in symptoms related to menopause have been noted with Royal Jelly ingestion

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Symptoms of Multiple Sclerosis

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	L-Carnitine	↓	★☆☆ Minor	1 study	Some symptoms associated with multiple sclerosis are noted to be reduced with carnitine ingestion.
C	Modafinil	↓	★☆☆ Minor	2 studies	Memory impairment in multiple sclerosis may be attenuated with supplementation of modafinil (250mg armodafinil), although other cognitive impairments associated with MS do not appear significantly affected.
C	Ginkgo biloba	—	—	1 study	Supplementation of ginkgo has failed to significantly benefit the cognition of persons with multiple sclerosis
D	Vitamin D	↓	★☆☆ Minor	1 study	There appears to be a lower relapse rate in multiple sclerosis patients when Vitamin D is present at higher concentrations

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Symptoms of OCD

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Zinc	↓	★☆☆ Minor	1 study	High dose zinc (220mg twice daily) may have a minor additive role to standard OCD therapy (fluoxetine), although the small magnitude of benefit and the high dose used suggest that it is not the best supplemental option.
C	Inositol	↓	★☆☆ Minor	1 study	Although a small decrease, there appear to be benefits to OCD symptoms associated with high dose inositol supplementation
C	N-Acetylcysteine			1 study	
C	Valeriana officinalis	↓	★☆☆ Minor	1 study	The lone study assessing the effects of valerian and OCD found a benefit with treatment relative to placebo.

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Symptoms of Osteoarthritis

Symptoms of osteoarthritis (OA) tend to reflect mobility, joint pain and stiffness, as well as quality of life in persons with OA. Supplements that benefit these symptoms according to self-reported rating scales are prophylactic.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Glucosamine	↓	★☆☆ Minor	19 studies	There appears to be a small decrease in osteoarthritis symptoms associated with glucosamine (as sulfate, not hydrochloride) which is somewhat unreliable but consistently outperforms placebo on meta-analyses. The magnitude of reduction, however, is somewhat minor but still comparable to acetaminophen
B	Ginger	↓	★☆☆ Minor	5 studies	There may be a small reducing effect, but it does not appear to be greater than the active control of Ibuprofen
B	Boswellia serrata	↓	★★★☆☆ Notable	4 studies	The reduction observed with Boswellia serrata for pain and other symptoms of osteoarthritis are more profound than other supplements including that of glucosamine (reference), but study robustness is limited by industry influence.
B	S-Adenosyl Methionine	↓	★★★☆☆ Notable	4 studies	Decreases in symptoms of osteoarthritis appear to be reduced to similar levels with SAMe as with pharmaceuticals like Naproxen, although SAMe requires a longer period of time for efficacy to occur
B	Rose Hip	↓	★☆☆ Minor	3 studies	There appears to be benefit to osteoarthritis symptoms with

					supplementation of rose hip relative to placebo, with benefits more apparent over longer periods of supplementation.
C	Curcumin	↓	★★★☆☆ Notable	3 studies	There appears to be significant reductions in symptoms of osteoarthritis, with the largest decrease noted occurring after eight months of supplementation and reaching 41% of baseline (more than a halving of symptoms).
C	Stinging Nettle	—	—	4 studies	Highly difficult to assess the efficacy of stinging nettle on osteoarthritic symptoms due to a wide degree of variance in study methodology
C	Feverfew	—	—	1 study	No significant interaction between supplemental Feverfew and osteoarthritic symptoms
C	Bromelain	—	—	1 study	No significant influence on symptoms of osteoarthritis when tested
C	Microlactin	↓	★☆☆☆☆ Minor	2 studies	Appears to reduce pain symptoms and improve functionality associated with osteoarthritis, with one study suggesting comparable efficacy to Glucosamine sulfate
C	Methylsulfonylmethane	↓	★☆☆☆☆ Minor	1 study	A decrease in symptoms of osteoarthritis has been noted and seems to be somewhat comparable in potency to Glucosamine sulfate
C	Pycnogenol	↓	★★★☆☆ Notable	2 studies	The preliminary evidence at this point in time (promising and independent, but limited) support the usage of pycnogenol in reducing all symptoms of osteoarthritis, reaching up to a halving of

					symptoms but requiring 90 days for effects to occur
C	Vitamin D			1 study	
C	Creatine	↓	★☆☆ Minor	1 study	Appeared to increase functionality, although not to a remarkable degree.
D	Vitamin C	—	—	1 study	No significant influence on the symptoms of osteoarthritis
D	Guggul	↓	★☆☆ Minor	1 study	Possible reductions in the symptoms associated with osteoarthritis
D	Harpagophytum procumbens	↓	★☆☆ Minor	3 studies	Symptoms of osteoarthritis appear to be reduced following ingestion of devil's claw, but insufficient robust evidence exists

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Symptoms of Parkinsons Disease

Parkinson's Disease is a form of dementia characterized by cell loss (usually dopamine producing cells) in a brain region called the substantia nigra, resulting in movement abnormalities. Some supplements may reduce movement and cognitive impairment of this state.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Mucuna pruriens	↓	★★★☆☆ Notable	3 studies	Possible symptoms reduction in Parkinson's Disease related to the L-DOPA content and theorized (but not proven) peripheral dopamine decarboxylase inhibitor; this is notable as a L-DOPA and carbidopa combination supplement is the reference for reducing parkinson's symptoms
C	D-Serine	↓	★☆☆☆☆ Minor	1 study	Preliminary evidence suggests that the standard dosage of D-Serine can alleviate some symptoms of Parkinson's disease

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Symptoms of PMS

Premenopausal symptom (PMS) appears to be affected by a few supplements, with continual usage of these supplements able to reduce the symptoms of PMS including bloat and emotional instability.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Vitex agnus castus	↓	★★★ Strong	6 studies	Vitex is the reference drug used for reductions in PMS symptoms, with about half of users experiencing a halving of menopausal symptoms with prolonged use (3+ cycles)
C	Krill Oil	↓	★☆☆ Minor	1 study	PMS and its symptoms (breast tenderness, stress, and irritability mostly) have been reduced with krill oil supplementation
C	Ginkgo biloba	↓	★☆☆ Minor	2 studies	There appear to be reductions in the symptoms of PMS associated with ginkgo supplementation, the degree of reduction being reported at up to 23.68%
C	Inositol	↓	★☆☆ Minor	2 studies	Myo-inositol supplementation appears to be effective in reducing dysphoric and depressive symptoms during PMS
C	Valeriana officinalis	↓	★☆☆ Minor	1 study	Abdominal pain associated with menstruation appears to be reduced relative to placebo in women who complained of above average levels of pain during their menstrual cycles.
C	Saffron	↓	★★★ Notable	1 study	One study assessing saffron on PMS symptoms noted that supplementation caused 76% of the participants to have more than a halving of overall

					symptoms (placebo reaching 8%), suggesting relatively potent effects.
D	Magnesium	↓	★☆☆ Minor	1 study	A slight reduction in symptoms of PMS has been noted with magnesium supplementation

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Symptoms of Rheumatoid Arthritis

Rheumatoid arthritis is an autoimmune form of arthritis that is associated with increases in inflammation and edema at joints, usually the more flexible and softer joints such as the hands. Some supplements target rheumatoid arthritis.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Velvet Antler	—	—	2 studies	No significant influence of velvet antler on symptoms of rheumatoid arthritis
C	Andrographis paniculata	↓	★☆☆ Minor	1 study	Reductions in joint pain and swelling were somewhat minimal in magnitude
C	Alpha-Lipoic Acid	—	—	1 study	No significant interaction between ALA supplementation and symptoms of rheumatoid arthritis
C	Feverfew	—	—	1 study	Preliminary evidence has failed to find an effect of Feverfew on reducing symptoms of Rheumatoid arthritis
C	Krill Oil	↓	★★★☆☆ Notable	1 study	500mg Krill oil reduced symptoms of osteoarthritis up to 30%, which is a pretty significant effect size that requires future research to investigate.
C	Nigella sativa	↓	★☆☆ Minor	1 study	A modest reduction in symptoms of rheumatoid arthritis (9%) has been noted with ingestion of the seeds
C	Hesperidin	↓	★☆☆ Minor	1 study	Preliminary evidence suggests a mild decrease in symptoms of rheumatoid arthritis seen with high (3,000mg) supplemental doses of G-

					hesperidin.
C	Rose Hip	↓	★☆☆ Minor	2 studies	There appears to be mild benefits to joint symptoms in rheumatoid arthritis when rose hip is supplemented over the course of months, and these benefits may be seen at low (5g) dosages. Short term supplementation has not shown much benefit.

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Symptoms of Schizophrenia

Schizophrenia is a disorder with positive (hallucinations and delusions) and negative (anhedonia and depression) symptoms alongside slight cognitive impairment, and some supplements are currently being investigated to aid in these symptoms.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	D-Serine	↓	★☆☆ Minor	6 studies	D-Serine supplementation is able to reduce symptoms of schizophrenia (more efficacy on negative and cognitive symptoms rather than positive) in a dose-dependent manner between 30-120mg/kg, but possibly due to the unreliable increases in blood D-serine its benefits are also unreliable
B	Sarcosine	↓	★★★☆☆ Notable	4 studies	While the magnitude of benefit seen with Sarcosine is comparable to both D-serine and glycine, it appears to require a much lower (more practical) dose than does glycine and is more reliable than D-serine
B	Ginkgo biloba	↓	★☆☆ Minor	6 studies	Symptoms of schizophrenia appear to be reduced with supplementation of ginkgo biloba (EGb-761 at 240-360mg daily), although all studies currently use ginkgo alongside standard antipsychotic therapy. It appears effective as an add-on
B	Inositol	—	—	3 studies	At the dose that showed anti-depressant effects, inositol failed to improve any symptoms associated with schizophrenia.
C	Theanine	↓	★☆☆ Minor	1 study	Activation and anxiety symptoms of schizophrenia

					appear to be reduced with high dose (400mg) Theanine
C	Glycine	↓	★☆☆ Minor	1 study	Is able to decrease symptoms of schizophrenia similar to both D-serine and sarcosine, but this occurs at an impractically high dose (minimum effective dose being around 800mg/kg bodyweight)
C	Chromium	—	—	1 study	The addition of low dose chromium to antipsychotic therapy in schizophrenic persons failed to augment the efficacy of treatment.

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Symptoms of Systemic Lupus Erythematosus

Systemic Lupus Erythematosus (SLE or just Lupus) is an autoimmune disorder associated with outbreaks on skin tissue (and other immunological side-effects). Some supplements are thought to improve quality of life in persons with lupus.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	↓	★★★☆☆ Notable	9 studies	The decrease in symptoms of lupus as assessed by SLAM-R and BILAG at times reaches up to 50% symptom reduction and tends to exceed 30%, and the first pilot studies noted remission in all subjects (although they have not been replicated since). Oddly, benefit may come from lower doses (160mg EPA and 140mg DHA) with higher doses conferring less benefit
C	Vitamin D	↓	★★☆☆☆ Minor	1 study	Inflammatory symptoms associated with Lupus appear to be reduced with Vitamin D ingestion

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Symptoms of the Common Cold

Symptoms of the common cold refer to the actual symptoms experienced during sickness, rather than the risk of developing URTIs or the length of sickness. Reducing symptoms of sickness tends to make the process to health more tolerable despite not actually affecting the healing rate.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Echinacea	—	—	4 studies	Insufficient evidence to support modification of symptoms of sickness
C	Garlic	↓	★☆☆ Minor	2 studies	Similar to symptoms of sickness in general and the length of sickness, the therapeutic efficacy of garlic appears to be modest at best.
C	Pelargonium sidoides	↓	★★★☆☆ Notable	1 study	All symptoms appear to be reduced with treatment of the standard dose of EPs7630. With symptom reduction after five days and the amount of persons with full resolution of symptoms being more than doubled relative to placebo.

Symptoms of Tinnitus

Tinnitus (pathological ringing of the ears) is known to be affected by various supplements, which may reduce the degree tinnitus disturbs sleep or impairs quality of life.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Melatonin	↓	★☆☆ Minor	4 studies	Melatonin may reduce symptoms associated with tinnitus in persons who suffer from the state, as assessed by questionnaire
B	Ginkgo biloba	—	—	4 studies	There does not appear to be a significant and reliable therapeutic effect of ginkgo on tinnitus symptoms, although limited evidence suggests that if tinnitus is a side-effect of cognitive decline that it may be attenuated.
C	Zinc	↓	★☆☆ Minor	1 study	Zinc supplementation at higher levels (50mg) appears to be able to reduce subjective symptoms of tinnitus in most persons supplemented with zinc.
D	Magnesium	↓	★☆☆ Minor	1 study	Decreased symptoms associated with tinnitus have been noted following magnesium supplementation

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Symptoms of Ulcerative Colitis

Ulcerative colitis (UC) is a subset of inflammatory bowel disease (the other being Crohn's Disease), and supplements that are thought to be preventative or therapeutic to UC are those that increase remission chance or prolong the time until symptoms arise.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Curcumin	↓	☆☆☆ Minor	2 studies	Symptoms of ulcerative colitis reduced with supplementation of curcumin
C	Andrographis paniculata	↓	☆☆☆ Notable	2 studies	Appears to be quite effective based on preliminary evidence, with one study being comparable to sustained release mesalazine in potency.
C	Colostrum	↓	☆☆☆ Notable	1 study	One study using a solution of colostrum (as enema) in persons with distal colitis noted a large suppression of symptoms and inflammation relative to placebo. No studies available on oral supplementation of colostrum for inflammatory bowel diseases.
D	Psyllium	↓	☆☆☆ Notable	1 study	The potency of psyllium husk in controlling remission of ulcerative colitis is comparable to the reference drug mesalamine.
D	Vitamin E	↓	☆☆☆ Notable	1 study	Rectal administration of high doses of vitamin E appears to be effective in reducing symptoms of ulcerative colitis, with preliminary research noting remission in the majority of patients.

Symptoms of Vitiligo

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Picrorhiza kurroa	↓	★★★☆☆ Notable	1 study	The one study using <i>picrorhiza kurroa</i> for the purpose of treating vitiligo noted that after daily usage that 27% of the subjects experienced complete resolution of symptoms (curative effect)
C	Polypodium leucotomos	—	—	1 study	Currently no evidence to support a role of <i>polypodium leucotomos</i> in the treatment of vitiligo
C	Ginkgo biloba	↓	★★★☆☆ Minor	2 studies	EGb-761 appears to be associated with skin repigmentation in persons suffering from vitiligo, although the degree of this effect is fairly modest

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T Cell Count

T-lymphocytes are a subset of white blood cells that mediate active immunity, and their reduction with immunosuppressants precedes an increased risk of getting sick. Conversely, elevating T-cells is thought to support the immune system (but may aggravate autoimmune disorders).

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	—	—	4 studies	Although there is some evidence to suggest an immunosuppressive effect on T cells, most evidence suggest no significant effect. When the immunosuppression does occur, it is due to the EPA content
C	Polypodium leucotomos	—	—	1 study	The increase in T cell count does not appear to be statistically significant, although a possibly relevant increase cannot be ruled out.
C	Tinospora cordifolia	—	—	1 study	Overall concentrations of T-cells (including CD4+ Lymphocytes) do not appear to be significantly influenced
C	Hesperidin	—	—	1 study	There do not appear to be any significant influence on the overall count of T Lymphocytes (collectively referring to Th1 and Th2 cells) with hesperidin supplementation.
C	Colostrum	—	—	1 study	In otherwise healthy individuals, colostrum does not alter overall levels of T cells relative to baseline or control proteins.

Testosterone

The manly man hormone, testosterone is the most well known androgen that mediates androgenic processes such as muscle building, fat loss, some aspects of cognition and hair loss in some persons; important in puberty, it is sought after for its muscle building potential in men.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Dehydroepiandrosterone	↑	★★★☆☆ Notable	20 studies	There appears to be an increase in testosterone following DHEA supplementation, but the vast majority of literature is in menopausal women (where testosterone contributes to libido). There is variability in the results, and DHEA is unreliable in increasing testosterone, but this unreliability extends to all demographics and subjects (with limited evidence of DHEA increasing testosterone in all studies including youthful athletes, which are less studied).
B	Creatine	↑	★★☆☆☆ Minor	6 studies	Degree of testosterone spike is not overly notable, although it appears to be present
B	Tribulus terrestris	—	—	4 studies	In otherwise healthy males, testosterone is not influenced with supplementation of <i>tribulus terrestris</i> . There may be an increase in infertile men, but this is weak.
B	Fenugreek	—	—	3 studies	Although there is limited evidence to support an increase in testosterone, more evidence than not denies such an increase
B	Alcohol	↓↑	★★☆☆☆ Minor	9 studies	There appears to be a time-dependent influence on

					testosterone, with acute doses of alcohol increasing testosterone secondary to creating energy influx in the liver (small enough of an increase to be 'somewhat' effective but may contribute to libido) whereas abuse is known to reduce testosterone levels more notably. The acute increase in testosterone is thought to be related to spikes in libido
B	Caffeine	↑	★☆☆ Minor	4 studies	A very small (usually 12%) increase is noted in trained athletes consuming caffeine above 250mg prior to exercise, this may be dependent on exercise as studies without exercise fail to find alterations in testosterone. This increase is unlikely to lead to significant testosterone-like effects
B	Maca	—	—	4 studies	No significant influences on testosterone in any tested demographic
B	Velvet Antler	—	—	3 studies	Repeated trials have failed to find an increase in testosterone associated with velvet antler supplementation
B	HMB	—	—	3 studies	No significant influence of acute usage on testosterone levels
B	Zinc	↑	★☆☆ Minor	7 studies	Both chronic/excessive exercise as well as a zinc deficiency are associated with abnormally low testosterone concentrations, and in these states supplementation of zinc increases testosterone. There is no inherent increase in testosterone with zinc if either of those two conditions are not met
B	Red Clover Extract	—	—	3 studies	The majority of evidence has

					suggested no significant influence of red clover supplementation on the testosterone concentrations in postmenopausal women
B	Colostrum	—	—	5 studies	While one study noted a preservation of testosterone circadian rhythm during a five day cycling race (where testosterone tends to flatline), other studies have failed to find any influence on basal testosterone concentrations.
C	Vitamin D	↑	★☆☆ Minor	1 study	An increase in testosterone has been noted in men with 3,332 IU of Vitamin D over the course of a year
C	Chrysin	—	—	1 study	Has failed to increase testosterone levels in one study.
C	Panax ginseng	↑	★☆☆ Minor	2 studies	May increase testosterone in infertile men, has also failed in fertile men to influence testosterone; likely a mere antioxidative effect in damaged testicles
C	Nicotine	—	—	1 study	No significant influence on testosterone levels
C	Beta-Alanine	—	—	1 study	
C	D-Aspartic Acid	↑	★☆☆ Minor	3 studies	There appears to be an increase in testosterone in most subjects acutely (6-12 days), and while this may persist to the tune of 30-60% in infertile men it is reduced to baseline within a month in otherwise healthy men with normal testosterone at baseline.
C	Magnesium	—	—	2 studies	No significant influences on testosterone levels noted with magnesium intake

C	Licorice	↓	★☆☆ Minor	6 studies	There appears to be a testosterone reduction associated with intake of licorice above 500mg, but the magnitude of this reduction is quite variable and there is no robust information on the topic
C	Garcinia cambogia	—	—	1 study	Testosterone appears to be unaltered following ingestion of garcinia cambogia
C	7-Keto DHEA	—	—	1 study	Insufficient evidence to support changes in testosterone following 7-keto supplementation.
C	Ashwagandha	↑	★☆☆ Minor	3 studies	Testosterone may be increased in infertile men (who have a reduction in testosterone), but there is currently no evidence to suggest an inherent testosterone boosting effect in otherwise normal men.
C	Coleus forskohlii	↑	★☆☆ Minor	1 study	Increase of testosterone observed in men not overly potent and is highly variable.
C	Eurycoma Longifolia Jack	—	—	3 studies	Although the protective effects of tongkat ali on the testicles and the profertility effects may result in a slight increase in testosterone in infertile men and the adaptogenic effects may cause a preservation of testosterone in stressed men, there is no evidence in otherwise healthy and unanxious men.
C	Shilajit	↑	★☆☆ Minor	1 study	A 23.5% increase has been noted in infertile men, it is not certain if this applies to fertile men.
C	Stinging Nettle	—	—	1 study	No detectable influence on testosterone levels

C	Coenzyme Q10	↑	★☆☆ Minor	1 study	Not the largest increase, and was in infertile men; may not apply to fertile men.
C	Ecdysteroids	—	—	1 study	No alterations noted in serum testosterone associated with ecdysterone consumption
C	Gamma Oryzanol	—	—	1 study	No detectable influence on testosterone levels in otherwise healthy men
C	Ganoderma lucidum	—	—	1 study	No significant influence on testosterone levels following ingestion of Reishi
C	Green Tea Catechins	—	—	1 study	No significant influence on serum testosterone
C	L-Carnitine	—	—	1 study	No significant alterations noted
C	Mucuna pruriens	↑	★☆☆ Minor	2 studies	An increase in testosterone is seen in infertile men. It is unsure if this increase in testosterone occurs in fertile and otherwise healthy men
C	Royal Jelly	↑	★☆☆ Minor	1 study	A small increase in testosterone has been noted with 3g Royal Jelly for 6 months in older men and women, no studies in youth currently and practical significance of such a small increase unknown
C	Glutamine	—	—	1 study	No significant alterations in testosterone noted
C	Fish Oil	—	—	1 study	No detectable influence on testosterone levels in serum
C	Phosphatidylserine	—	—	1 study	No significant influence on testosterone noted with PS supplementation

C	Arachidonic acid			1 study	
C	Arginine	—	—	1 study	No significant influence on circulating testosterone concentrations
C	Astaxanthin			1 study	
C	Chromium	—	—	1 study	Testosterone is not affected by chromium in women with PCOS. Currently no evidence in otherwise healthy men.
C	Saffron	—	—	2 studies	Neither aromatherapy nor oral supplementation appear to significantly influence testosterone concentrations in serum.
D	Boron	↑	★☆☆ Minor	2 studies	There appears to be an interaction with Boron and testosterone in both genders, but it is seemingly unreliable
D	Yohimbine	—	—	1 study	No significant influence on testosterone seen with yohimbine supplementation
D	Punicalagins	—	—	1 study	No significant influence on testosterone levels in men at risk for prostate cancer
D	Ginger	↑	★☆☆ Minor	1 study	An increase in testosterone has been noted to reach 17.7% in infertile men given an undisclosed amount of ginger over three months.
D	Calcium			1 study	
D	Rubus coreanus	—	—	1 study	Despite the highly promising evidence in rats, there is no significant influence of the berries on testosterone levels of otherwise healthy men.

Thermic Effect of Food

The thermic effect of food (TEF) is known as the amount of calories required to metabolize food products (in order to get their calories to the body), and ranges from 1-3% for carbohydrates and fats while it can reach 20% for protein. Some supplements modify TEF values.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Green Tea Catechins	—	—	1 study	No significant influence on the thermic effect of food
D	Ginger	↑	★☆☆ Minor	1 study	Ginger has been found to increase the thermic effect of coingested food products
D	Psyllium	—	—	1 study	Failed to modify the thermic effect of food.
D	Coconut Oil	—	—	1 study	Insufficient evidence to support alterations in the thermic effect of food compared to other oils

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Thyroid-Stimulating Hormone

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Iodine	↑	☆☆☆ Minor	3 studies	An increase in Thyroid Stimulating Hormone (TSH) occurs both at the doses that suppress T3 and T4 and sometimes at lower doses where thyroid function is not impaired
C	Trimethylglycine	—	—	1 study	No significant influence of betaine on circulating TSH concentrations in serum.
D	Tetradecyl Thioacetic Acid			1 study	

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TNF-Alpha

Tumor necrosis factor alpha (TNF-α) is a proinflammatory cytokine that is used as a marker of inflammation. Its reduction is thought to reflect a lesser state of inflammation in the body.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Conjugated Linoleic Acid	—	—	4 studies	Insufficient evidence to support changes in TNFα, a biomarker of inflammation.
B	Fish Oil	↓	★☆☆ Minor	6 studies	May decrease TNF-a
C	L-Carnitine	—	—	1 study	No significant influence on TNF-a
C	Punicic Acid	—	—	1 study	No significant influence on serum TNF-a levels
C	Stinging Nettle	—	—	1 study	No apparent effect on circulating TNF-a at baseline (may reduce TNF-a secretion from proinflammatory signals, see inflammation)
C	Resveratrol	↓	★☆☆ Minor	1 study	A significant decrease in circulating TNFα levels have been detected with resveratrol supplementation; linked to antiinflammatory effects of resveratrol
C	Ganoderma lucidum	↓	★☆☆ Minor	2 studies	A reduction in TNF-alpha levels have been noted in persons with elevated baseline TNF-alpha levels
C	Japanese Knotweed	↓	★☆☆ Minor	1 study	A decrease in TNF-a has been noted following oral consumption of japanese knotweed

C	Vitamin D	↓	★☆☆ Minor	1 study	A decrease has been noted over time relative to placebo, of relatively minor magnitude
C	Tetradecyl Thioacetic Acid	↓	★☆☆ Minor	2 studies	A decrease in serum levels of TNF-a has been noted with supplemental TTA
C	Blueberry	—	—	1 study	No significant changes in TNF-alpha concentrations
C	Garlic	↓ ↑	★☆☆ Minor	2 studies	Decreases have been noted in inflammatory states (indicative of antiinflammatory effects) and increases seen in healthy persons; suggesting an immunomodulatory effect
C	Creatine			1 study	
C	Trimethylglycine	—	—	1 study	No significant influence on TNF-α concentrations following supplementation of betaine to persons with fatty liver.
C	Rose Hip	—	—	1 study	At this point in time, there is no evidence to suggest modifications in the circulating levels of TNF-α relative to control.
C	Vitamin E	—	—	1 study	TNF-α does not appear to be influenced with supplementation of vitamin E relative to placebo.
C	Colostrum	—	—	2 studies	TNF-a is not affected by supplementation of colostrum.
D	Zinc	↑	★☆☆ Minor	1 study	A zinc deficiency is associated with reduced circulating TNF-a concentrations, which are normalized upon zinc sufficiency.
D	Perilla Oil			1 study	

Total Cholesterol

Total Cholesterol is a phrase used to refer to all circulating cholesterol molecules, and is totalled by adding LDL-C, HDL-C and vLDL-C together. It is distinct from Triglycerides.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Policosanol	↓	☆☆☆ Minor	12 studies	There may be some limited efficacy of policosanol on cholesterol (when excluding the studies from cuba, which are highly suspicious, there is still some scattered but unreliable evidence) whereas it does not appear to be potent in any way.
A	Fish Oil	—	—	18 studies	Although some decreases have been noted, overall there does not appear to be a significant clinical reduction in total cholesterol like there is with triglycerides
A	Garlic	↓	☆☆☆ Notable	17 studies	Garlic supplementation or the raw garlic bulb appears to reduce cholesterol (total cholesterol, mostly due to LDL reductions) reliably and in the range of 10-15%
A	Red Clover Extract	—	—	16 studies	The majority of evidence does not support a role for reducing total cholesterol with supplementation of red clover extract, except perhaps a minor (less than 10%) reduction in overweight postmenopausal women.
A	Chromium	—	—	17 studies	Similar to its actions on LDL and HDL individually, chromium does not appear to have a significant role in improving total cholesterol levels in type II diabetic

					subjects.
B	Creatine	—	—	4 studies	In otherwise healthy males given creatine supplementation, overall levels of cholesterol are unaffected.
B	L-Carnitine	—	—	4 studies	For the most part, there does not appear to be a significant influence of carnitine on total cholesterol levels
B	Curcumin	—	—	5 studies	More robust evidence suggests no significant influence of curcumin on total cholesterol, although there may be a potential role
B	Spirulina	↓	★☆☆ Minor	6 studies	Reductions in cholesterol seen are positive, but not overly remarkable
B	Berberine	↓	★★★☆☆ Notable	2 studies	Total cholesterol appears to be decreased by around -0.58mmol/L (95% CI -1.02 to -0.14), which is not overly potent. The reduction is notable as if this mechanism is via PCSK9 inhibition then it would work very well with statin drugs.
B	Psyllium	↓	★☆☆ Minor	4 studies	Not unique to psyllium, but has the standard slight reduction of cholesterol that affects persons with high cholesterol. Not strong enough for monotherapy, can be a nice addition to more potent supplements or drugs
B	Olive leaf extract	↓	★☆☆ Minor	4 studies	There appears to be somewhat of a decrease in total cholesterol (mostly due to LDL) with olive leaf consumption; it is not overly reliable
B	Grape Seed Extract	↓	★☆☆ Minor	3 studies	May decrease total cholesterol

					to an unremarkable degree when taken either at high (600mg) doses or in high risk populations; reductions in cholesterol are definitely not reliable
B	Royal Jelly	↓	★☆☆ Minor	2 studies	A decrease in total cholesterol is noted in the range of 10% associated with 50-100mg of Royal Jelly daily; the evidence this conclusion was drawn from (via a meta-analysis) is a bit lacklustre
B	Nigella sativa	↓	★☆☆ Minor	8 studies	Decreases have been sporadically noted in persons with high cholesterol initially, the cholesterol reductions are mild at best and do not affect persons with normal cholesterol.
B	Hesperidin	—	—	5 studies	While there may be a slight decrease which only applies to those with very elevated cholesterol at baseline, in normal persons or those with mild to moderately high cholesterol there is no significant influence.
B	Trimethylglycine	↑	★☆☆ Minor	3 studies	One study noted a stasis in total cholesterol when placebo decreased (a relative increase). Reasons for this unknown and the data needs to be replicated.
B	Astaxanthin			4 studies	
B	Vitamin E	—	—	10 studies	There does not appear to be a significant influence of vitamin E supplementation on cholesterol levels whether used by a healthy person or one with elevated cholesterol.
C	ECA	—	—	1 study	No significant influence on total cholesterol levels

C	Ginger	↓	★☆☆ Minor	1 study	Possible cholesterol reducing effects associated with ginger consumption
C	Coenzyme Q10	—	—	2 studies	No significant or consistent effects on total cholesterol levels noted with CoQ10
C	Vitamin C	—	—	2 studies	No significant influence on total cholesterol seems apparent with vitamin C supplementation
C	Punicic Acid	—	—	1 study	No significant influence on total cholesterol levels
C	Whey Protein	—	—	2 studies	No significant influence on circulating cholesterol has been demonstrated with whey protein
C	Grapefruit	↓	★☆☆ Minor	1 study	A decrease in total cholesterol has been noted, this is confounded with weight loss (also occurred)
C	Vanadium	—	—	2 studies	No significant alterations in the levels of total cholesterol <i>per se</i> , but a decrease has been noted to be secondary to attenuating diabetic symptoms
C	Artichoke Extract	↓	★☆☆ Minor	4 studies	Despite its traditional usage, the decreases in cholesterol are not remarkable and are quite small in magnitude.
C	Licorice	—	—	1 study	No significant influence on total cholesterol is observed following licorice ingestion
C	Green Coffee Extract	—	—	1 study	No significant alterations in total cholesterol seen with green coffee extract
C	Nattokinase	—	—	1 study	No significant influence on

					total cholesterol seen with supplementation
C	Eleutherococcus senticosus	—	—	1 study	No significant influences yet known for total cholesterol
C	Benfotiamine	—	—	1 study	No significant changes in total cholesterol
C	Cissus quadrangularis	↓	★☆☆ Minor	1 study	Reductions in total cholesterol not overly remarkable relative to placebo and confounded with weight loss which occurred with cissus
C	Ashwagandha	↓	★★★☆☆ Notable	3 studies	There is a decrease in total cholesterol of around 10% when ashwagandha (water extract of the roots) is ingested. It is notable, however, since this appears to occur in all persons regardless of whether they have high cholesterol or not
C	Stevia	—	—	1 study	No significant effect on total cholesterol levels have been detected with stevia consumption
C	Theaflavins	—	—	1 study	No significant influence on total cholesterol levels with theaflavins supplementation
C	Ecklonia cava	↓	★☆☆ Minor	2 studies	A possible reduction in total cholesterol concentrations
C	Ecdysteroids	—	—	1 study	In resistance trained males, no significant influence of ecdysterone supplementation on cholesterol
C	Salvia hispanica	—	—	2 studies	No significant influence on total cholesterol levels after inclusion of chia seeds into the diet

C	Gamma Oryzanol	—	—	2 studies	No significant alterations seen in total cholesterol levels with supplementation
C	Garcinia cambogia	—	—	1 study	No significant alterations seen in total cholesterol levels
C	Ganoderma lucidum	—	—	1 study	No significant alterations in total cholesterol observed with reishi ingestion
C	Green Tea Catechins	↓	★☆☆ Minor	1 study	A decrease in cholesterol is noted with green tea catechins, but to a small degree
C	Hibiscus sabdariffa	—	—	3 studies	No significant changes in total cholesterol noted
C	HMB	↑	★☆☆ Minor	2 studies	One underpowered study noted an increase in total cholesterol while another suggested no significant effect. The exact effect of HMB on total cholesterol is not currently known and required replication
C	Japanese Knotweed	—	—	1 study	No significant alterations in cholesterol seen with Japanese Knotweed ingestion
C	Irvingia gabonensis	↓	★☆☆ Minor	2 studies	A decrease in total cholesterol has been noted, but is confounded with weight loss
C	Magnesium	—	—	2 studies	No significant influence on total cholesterol levels seen with magnesium supplementation
C	Melatonin	—	—	1 study	No significant influence on total cholesterol levels
C	Microlactin	↓	★☆☆ Minor	2 studies	May be able to reduce total cholesterol by a moderate to low degree (8-10%), but requires more robust evidence

C	Soy lecithin	↓	★★☆ Notable	1 study	A decrease in total cholesterol, mostly due to LDL-C, has been noted to the magnitude of 40.66-42.00% which is astounding; requires replication.
C	Resveratrol	—	—	1 study	No significant effect on total cholesterol levels
C	Pyruvate	↓	★☆☆ Minor	1 study	A reduction in total cholesterol has been noted once in response to a high fat hypercaloric diet; practical relevance unknown
C	Guggul	↓	★☆☆ Minor	2 studies	Possible decrease in total cholesterol, but this is unreliable (and paired with a possible increase in LDL-C, this is likely to be not desirable)
C	Tetradecyl Thioacetic Acid	↓	★☆☆ Minor	3 studies	Possible reductions in total cholesterol with supplementation of TTA
C	Panax ginseng	↓	★☆☆ Minor	2 studies	Possible cholesterol reducing effect, but appears unreliable
C	Phosphatidylserine	—	—	1 study	No significant influence with PS supplementation on total cholesterol
C	Krill Oil	↓	★☆☆ Minor	2 studies	A decrease in total cholesterol has been noted with krill oil, to a fairly normal degree (reduction is lessened from the remarkable increase in HDL)
C	Lactobacillus casei			1 study	
C	Citrulline	—	—	1 study	No significant influence on total cholesterol concentrations

C	Vitamin K	—	—	1 study	No significant interactions with total cholesterol concentrations in persons given vitamin K supplementation
C	Sea Buckthorn	—	—	1 study	Total cholesterol does not appear to be affected with supplementation of sea buckthorn in otherwise healthy persons.
C	Blueberry	—	—	2 studies	No significant influence on total cholesterol concentrations in the blood.
C	Dehydroepiandrosterone	↓	★☆☆ Minor	3 studies	There may be a decrease in cholesterol seen with DHEA in hypercholesterolemics, but it is not overly reliable
C	Zinc	↓	★☆☆ Minor	2 studies	A decrease in cholesterol, due to LDL-C being reduced, seems to occur following oral supplementation of zinc in persons who are obese and likely zinc deficient
C	Inositol	↓	★☆☆ Minor	4 studies	A small decrease in total cholesterol has been noted with supplementation of inositol in women with PCOS
C	Tribulus terrestris	↓	★☆☆ Minor	1 study	A decrease in cholesterol levels has been noted with tribulus supplementation
C	Rooibos	↓	★☆☆ Minor	2 studies	May decrease total cholesterol to a small degree in unhealthy persons
C	Anethum graveolens			2 studies	
C	Citrullus colocynthis	↓	★☆☆ Minor	2 studies	There may be a reduction in total cholesterol in those with high cholesterol, but it has a large degree of variability.

C	Phosphatidylcholine			1 study	
C	Yacon	—	—	1 study	No significant influence on total cholesterol has been noted despite changes in LDL and accompanying weight loss.
C	Rose Hip	↓	★☆☆ Minor	3 studies	A decrease in total cholesterol has been noted to a mild degree in obese persons, although a study in rheumatic patients without any abnormalities in cholesterol metabolism failed to find such an effect.
D	Coffee	↑	★☆☆ Minor	1 study	An increase in cholesterol has been noted in one study which attributed most of the increase to HDL
D	Quercetin	↑	★☆☆ Minor	1 study	An increase in total cholesterol has been noted, but mostly attributed to HDL
D	Tauroursodeoxycholic Acid	↓	★☆☆ Minor	1 study	A decrease in total cholesterol in serum has been noted secondary to treating cholestasis
D	Pueraria lobata	—	—	1 study	No significant influence have been detected on total cholesterol
D	Coconut Oil	↓	★☆☆ Minor	1 study	A decrease in total cholesterol (both the LDL and HDL portions) has been noted with coconut oil to a minor degree relative to longer chain fatty acids
D	Aronia melanocarpa	↓	★☆☆ Minor	2 studies	Requires more studies before conclusions can be made, appears to simply be exerting anti-oxidant effects.
D	Yerba mate	↓	★☆☆ Minor	1 study	A decrease of total cholesterol has been noted with Mate

					consumption
D	Eclipta alba	↓	★☆☆ Minor	1 study	A decrease in total cholesterol has been noted with supplementation of eclipta alba
D	Pycnogenol	↓	★☆☆ Minor	2 studies	Possible cholesterol lowering effects of small magnitude, but these are not wholly reliable
D	Emblica officinalis	↓	★☆☆ Minor	1 study	A decrease in cholesterol has been noted and appears to affect both healthy controls as well as diabetics
D	Rubus coreanus	—	—	1 study	Currently the only study is in otherwise healthy men with no cholesterol problems, and there was no influence of berry consumption.
D	Perilla Oil			1 study	
D	Ruscus aculeatus	↓	★☆☆ Minor	1 study	A decrease in total cholesterol (9.4%) has been noted in diabetic persons alongside an increase in HDL-C. Requires replication.
D	Colostrum	↓	★☆☆ Minor	1 study	A mild decrease in total cholesterol has been noted with supplementation of colostrum in type II diabetics.

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Training Volume

Training volume refers to the amount of physical work that can be conducted in one session, either by enhancing recovery between sets or increasing the amount of work performed in one set. Supplements that enhance training volume may improve gains from exercise.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Caffeine	↑	★☆☆ Minor	3 studies	There appears to be an increase in training volume (overall work performed during a workout) associated with caffeine ingestion relative to placebo, extending to both weightlifting and anaerobic cardiovascular exercise
B	HMB	—	—	3 studies	No significant influence on training volume when used acutely
B	Sodium Bicarbonate	↑	★☆☆ Minor	10 studies	There might be an increase in work output conducted in tests that are anaerobic (high intensity) and associated with metabolic acidosis ('the burn') but may not extend to other contexts
C	Methylsulfonylmethane	—	—	1 study	No significant influence on the total training volume able to be conducted
C	Pyruvate	—	—	1 study	No significant influence on training volume in otherwise healthy persons given an exercise protocol
C	Choline	—	—	2 studies	No significant improvements in training volume independent of choline depletion
C	Ornithine	—	—	1 study	No significant influence on the

					amount of work that can be conducted on a cycle ergometer during short-term testing
C	Citrulline	↑	★★☆ Notable	1 study	The increase in work capacity seen with citrulline supplementation appears to be time dependent. While there are no inherent and immediate effect, the reduction of fatigue later in a weight lifting workout causes a relative increase that has at least one doubled reps conducted (on set 8 of exhaustive exercise)
C	Quercetin	—	—	1 study	Training volume does not appear to be significantly influenced with quercetin supplementation.
C	Creatine	—	—	2 studies	Swimming training volume is unaffected by creatine supplementation.
C	Trimethylglycine	↑	★☆☆ Minor	1 study	One study noted an increase in overall training volume (6.5%) when the whole workout was assessed, and this was without any apparent changes in the volume conducted in any individual set or any changes in the rate of perceived exertion.
C	Astaxanthin			1 study	

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Treatment of Amyotrophic lateral sclerosis (ALS)

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Creatine	—	—	6 studies	Short term usage may increase power output like usual, but prolonged supplementation of creatine has failed to alter the deterioration of muscle and lung function. While no reduction in mortality has been noted statistically, two studies have noted a trend towards reductions in mortality suggesting an unknown protective effect.

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Treatment of COPD

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	N-Acetylcysteine	↑	★☆☆ Minor	4 studies	N-Acetylcysteine may reduce some symptoms of COPD by acting as a mucolytic agent and reducing sputum formation, but it does not appear to be effective at aiding the lungs themselves or reducing disease progression.
B	Creatine	—	—	3 studies	The main parameters of concern when treating COPD (lung and heart function, cardiovascular exercise performance) are not affected with creatine supplementation.

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Treatment of Headaches

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Pelargonium sidoides	↑	☆☆☆ Minor	10 studies	Headaches as a side effect of acute bronchitis are pretty much abolished with the treatment of acute bronchitis from this herb; it is doubtful that headaches from other causes aside from sickness are treated in a similar manner.
C	Peppermint	↑	☆☆☆ Notable	2 studies	Preliminary evidence suggests that topical application of peppermint oil is effective in reducing tension headache severity when applied at the start of the headache (can work within 15 minutes), and is comparable to 1,000mg acetaminophen in potency
D	Creatine	↑	☆☆☆ Notable	1 study	In children and adolescents subject to traumatic brain injury who then received 400mg/kg creatine supplementation, headache frequency as a side effect is reduced from around 90% down to 10%.

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Treatment of Hepatic Encephalopathy

Hepatic Encephalopathy is a liver condition associated with excessive ammonia which impairs cognitive function, and supplements that either aid liver function or independently reduce ammonia are seen as therapeutic.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	L-Carnitine	↑	★☆☆ Minor	4 studies	Cognitive side effects of hepatic encephalopathy are alleviated with carnitine supplementation, notably fatigue and cognitive performance.

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Treatment of PCOS

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Inositol	↑	★★★☆☆ Notable	14 studies	Supplementation of inositol in the range of 200-4,000mg daily appears to be effective in improving fertility in women with PCOS, while doses in the 2,000-4,000mg range appear effective in improving testosterone levels and insulin sensitivity.

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Triglycerides

Triglycerides is a term used to refer to the circulating levels of fatty acids (similar in structure to dietary fatty acids, and fat mass) that can be measured via a blood test. Although crucial for energy usage, excessively high circulating Triglycerides is a risk factor for circulatory problems.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Fish Oil	↓	★★★ Strong	46 studies	Fish oil, both EPA and DHA, are reference drugs for the purpose of reducing triglycerides with highly reliable reductions in the range of 15-30% (higher reductions seen in persons with higher baseline triglycerides)
A	Garlic	↓	★☆☆ Minor	15 studies	There appears to be quite an unreliable decrease in triglycerides following garlic supplementation. When looking at meta-analyses, there is either a significant but small decrease or a reduction that fails to reach statistical significance.
A	Red Clover Extract	—	—	11 studies	Isolated reports have noted minor (less than 10%) reductions in triglycerides in overweight or hyperlipidemics mostly, but overall there is not a significant reduction in triglycerides noted with Red clover extract.
A	Chromium	—	—	16 studies	Chromium does not appear to have a role in reducing triglyceride concentrations in the serum of subjects, including diabetic subjects given chromium supplementation.
B	Curcumin	↓	★☆☆ Minor	5 studies	Some reducing effects have been noted, but they seem to

					be unreliable and not overly potent
B	Dehydroepiandrosterone	—	—	3 studies	Mixed evidence, but it seems that DHEA doesn't have a significant influence on triglycerides
B	Conjugated Linoleic Acid	↑	★☆☆ Minor	7 studies	May possible increase triglycerides, but is unreliable in doing so and not overly potent.
B	Policosanol	—	—	5 studies	When excluding older cuban studies (which are highly suspicious) there is no evidence to support a reduction of triglycerides.
B	Spirulina	↓	★★★☆☆ Notable	8 studies	In populations with metabolic syndrome or related morbidities (diabetes, hyperlipidemia, hypetension, etc.) spirulina in a variety of doses between 1-8g daily is able to reduce triglycerides up to 10-15%.
B	Magnesium	—	—	6 studies	For the most part, no significant influence of magnesium supplementation on triglycerides
B	Berberine	↓	★☆☆ Minor	2 studies	Degree of reduction according to meta-analysis was −0.48mmol/L (95% CI −0.57 to −0.39) which was not overly remarkable.
B	Psyllium	—	—	4 studies	Currently, it does not seem like there is a significant influence of psyllium on circulating triglycerides
B	Olive leaf extract	—	—	5 studies	The majority of the evidence suggests that there is no impressive effect on triglycerides with olive phenolic consumption

B	Grape Seed Extract	—	—	3 studies	No significant influence of grape seed extract on triglycerides even in a high risk population at a high oral intake of GSE (600mg)
B	L-Carnitine	—	—	2 studies	No significant influence on triglycerides
B	Inositol	↓	★☆☆ Minor	4 studies	There may be a small decrease in triglycerides associated with supplementation of inositol to women with PCOS
B	Nigella sativa	↓	★☆☆ Minor	8 studies	The decreases in triglycerides only affect those with high triglycerides, and the decrease scales with severity of hyperlipidemia (mild elevation of TGs is met with a 1-5% decrease, significantly elevated TGs are met with a 15-20% reduction).
B	Hesperidin	—	—	8 studies	There is no significant influence on triglycerides noted with supplementation of hesperidin; if an effect occurs, it is of very minor magnitude and only lasts for as long as supplementation persists.
B	Astaxanthin			4 studies	
B	Vitamin E	—	—	8 studies	No evidence to support changes in triglycerides associated with vitamin E supplementation in any tested person.
C	Fenugreek	↓	★☆☆ Minor	1 study	May reduce triglyceride levels
C	Ephedrine	↓	★☆☆ Minor	2 studies	There appears to be a decrease in triglycerides over time with ephedrine ingestion, which may be due to either the fat burning effects of ephedrine

					or the weight loss that tends to ensue
C	Ginger	↓	★☆☆ Minor	1 study	May decrease triglycerides
C	Black Cohosh	—	—	2 studies	No significant effect on triglyceride concentrations in serum
C	Punicic Acid	↓	★☆☆ Minor	2 studies	A possible slight reduction in triglycerides has been noted with pomegranate oil, but this appears to be unreliable
C	Whey Protein	↓	★☆☆ Minor	2 studies	Possible reductions in triglycerides, but it is not sure if this is exclusive to whey protein or due to protein in general.
C	Melatonin	↓	★☆☆ Minor	2 studies	A possible reduction in triglycerides to a minor degree is noted with melatonin supplementation, but this is not reliable
C	Vanadium	↑	★☆☆ Minor	2 studies	A slight increase in triglycerides has been noted with vanadium supplementation
C	Artichoke Extract	—	—	4 studies	The two better controlled trials noted no change, whereas a decrease and increase has been noted otherwise. Unclear overall effects on triglycerides
C	Licorice	—	—	1 study	No significant influence on triglycerides
C	Gynostemma pentaphyllum	—	—	1 study	No significant alterations in triglycerides noted with supplementation
C	Hibiscus sabdariffa	↓	★★★☆☆ Notable	4 studies	Mixed effects on triglycerides, but the lone study that noted a decrease noted comparable

					potency to pravastatin; requires more literature
C	Green Coffee Extract	—	—	1 study	No significant influence on triglycerides following oral intake
C	Hemp Protein	—	—	2 studies	No significant influence of oral hemp seeds on triglycerides
C	Nattokinase	—	—	1 study	No significant influence on triglycerides
C	Eleutherococcus senticosus	—	—	1 study	No significant influences yet known for triglycerides
C	Benfotiamine	—	—	1 study	No significant influence on triglycerides.
C	Cissus quadrangularis	↓	★☆☆ Minor	1 study	Reduction in triglycerides is not overly potent and occurred alongside weight loss, which was likely a confounding factor.
C	Ashwagandha	↓	★☆☆ Minor	4 studies	The best evidence at this point in time suggests a slight decrease in triglycerides seen with Ashwagandha supplementation, although it does not appear to extend to persons with normal triglyceride levels but occurs in those with metabolic impairments.
C	Caffeine	—	—	1 study	No significant influence on triglyceride levels
C	Stevia	—	—	1 study	No significant influence on circulating triglycerides has been noted with stevia consumption
C	Resveratrol	↓	★☆☆ Minor	1 study	A decrease in triglycerides has been noted with resveratrol supplementation

C	Shilajit	↓	★☆☆ Minor	1 study	Minor decrease in triglycerides has been noted with shilajit
C	Theaflavins	—	—	1 study	No significant influence of theaflavins on triglycerides (hypercholesterolemic persons)
C	Ecklonia cava	—	—	1 study	No significant influence on triglycerides noted with ecklonia cava
C	Ecdysteroids	—	—	1 study	No significant influence on triglycerides
C	Salvia hispanica	—	—	2 studies	No significant influence on triglycerides
C	Fucoxanthin	↓	★☆☆ Minor	1 study	A decrease in circulating triglycerides is noted with fucoxanthine
C	Gamma Oryzanol	—	—	1 study	No significant alterations in plasma triglycerides seen with supplementation
C	Garcinia cambogia	—	—	1 study	No detectable influence on triglyceride levels
C	Ganoderma lucidum	↓	★☆☆ Minor	2 studies	There may be a small decrease in triglycerides (8% or so) in unhealthy persons, but this has not been observed in otherwise healthy individuals
C	Green Tea Catechins	—	—	1 study	No apparent influence on triglycerides
C	Japanese Knotweed	—	—	1 study	No significant influence of Japanese Knotweed on triglycerides
C	Irvingia gabonensis	↓	★☆☆ Minor	1 study	A decrease in triglycerides has

					been noted, confounded with weight loss
C	Microlactin	—	—	1 study	No significant influence on fasting triglycerides noted
C	Vitamin C	—	—	2 studies	No significant influence on fasting or postprandial triglycerides seems apparent with Vitamin C
C	Vitamin D	↓	★☆☆ Minor	1 study	The decrease in triglycerides is present after long term ingestion of Vitamin D, although it isn't to a highly significant degree
C	Soy lecithin	—	—	1 study	No significant influence on triglycerides
C	Royal Jelly	—	—	3 studies	Although there may be a reduction in triglycerides associated with Royal Jelly, currently the best evidence suggests no such change
C	Guggul	—	—	2 studies	No significant influence of Guggul on triglycerides is detectable
C	Tetradecyl Thioacetic Acid	↓	★★★☆☆ Notable	3 studies	The one trial using TTA to reduce triglycerides noted a reduction of around 15%, which is notable and requires replication
C	Panax ginseng	—	—	2 studies	No significant alterations in triglycerides and fatty acids in the fasted state or during exercise
C	Phosphatidylserine	—	—	1 study	No significant influence on triglycerides seen at rest or during exercise with PS supplementation
C	Krill Oil	↓	★☆☆☆☆	2 studies	A decrease in triglycerides has

			Minor		Reduction in triglycerides has been noted with krill oil
C	Lactobacillus casei			1 study	
C	Vitamin K	—	—	1 study	No significant influence on circulating triglycerides seen with MK-4 supplementation
C	Sea Buckthorn	—	—	1 study	Although it may attenuate postprandial lipidemia (spikes in triglycerides following a meal), supplementation does not appear to significantly affect fasting triglyceride concentrations.
C	Cocoa Extract			1 study	
C	Blueberry	—	—	2 studies	No known interactions with serum triglycerides following supplementation of blueberries.
C	Zinc	—	—	2 studies	No significant reduction in circulating triglycerides has been detected with zinc supplementation.
C	Rooibos	↓	★☆☆ Minor	2 studies	A minor reduction of triglycerides occurs with daily ingestion of Rooibos tea only in unhealthy persons
C	Anethum graveolens			2 studies	
C	Citrullus colocynthis	↓	★☆☆ Minor	2 studies	The decrease seen in triglycerides in one study was statistically significance, but the average reduction in hyperlipidemics (16%) has a very large range
C	Creatine			3 studies	
C	Trimethylglycine	—	—	2 studies	No significant alterations in serum triglycerides are noted with prolonged supplementation of betaine supplementation.

C	Phosphatidylcholine			1 study	
C	Yacon	—	—	1 study	Despite a triglyceride reducing effect of fructooligosaccharides in rats, the limited evidence in humans (with mildly elevated triglycerides) failed to find any appreciable effect despite weight loss.
C	Rose Hip	—	—	1 study	No significant influence of rose hip on triglyceride concentrations has been noted.
D	Coconut Oil	—	—	1 study	Insufficient evidence to support changes in serum triglycerides.
D	Aronia melanocarpa	↓	★☆☆ Minor	1 study	Requires more studies before conclusions can be made, appears to simply be exerting anti-oxidant effects.
D	Eclipta alba	↓	★☆☆ Minor	1 study	Decreases in triglycerides have been noted, but not to a remarkable degree
D	HMB	—	—	1 study	No significant influence on triglycerides
D	Pycnogenol	—	—	1 study	No significant alterations on triglycerides
D	Safflower Oil	—	—	1 study	No significant alterations in triglyceride concentrations
D	Emblica officinalis	↓	★☆☆ Minor	1 study	Appears to have triglyceride reducing properties
D	Rubus coreanus	—	—	1 study	No significant influence of this berry on the triglycerides of otherwise healthy men.
D	Perilla Oil			1 study	
D	Pyrroloquinoline	—	—	1 study	

D	quinone				Short term supplementation of PQQ has failed to significantly influence triglycerides in otherwise healthy adults
D	Ruscus aculeatus	—	—	1 study	No significant influence on circulating triglycerides in diabetic persons given <i>ruscus aculeatus</i> supplementation.
D	Colostrum	↓	★☆☆ Minor	1 study	In type II diabetics, triglycerides in fasting conditions were noted to be reduced relative to baseline with colostrum ingestion.

Upper Respiratory Tract Infection Risk

Upper respiratory tract infections (URTIs) are sicknesses that mostly affect the lung and breathing capacities, and is the cause of many cold symptoms. Supplements that reduce the risk of developing URTIs are said to promote immunity.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Echinacea	↓	★★★☆☆ Notable	11 studies	The reduction in rate of sickness seen with echinacea as a daily supplement is highly effective in some instances, but subject to a high degree of variability. It is notable due to it being a comparator.
C	Vitamin C	—	—	2 studies	No significant influence on the rate of acquiring sickness
C	Vitamin D	—	—	1 study	Lack of efficacy in reducing rate of sickness
C	Andrographis paniculata	↓	★★☆☆☆ Minor	1 study	Appears to be better than placebo, although it is difficult to assess potency.
C	Zinc	—	—	1 study	Despite having lower sickness rates overall, the reduction seen in URTIs specifically does not appear to reach significance.
C	Garlic	↓	★★☆☆☆ Minor	1 study	There appears to be a reduction in the lung infection risks with garlic supplementation.
C	Vitamin E	↓	★★☆☆☆ Minor	1 study	Supplementation of 200 IU vitamin E in elderly persons has been noted to reduce overall occurrence of upper, but not lower, respiratory tract infections.

C	Colostrum	↓	★☆☆ Minor	3 studies	There may be a minor reduction in the incidence of upper respiratory tract infections (URTIs) seen with colostrum, although more evidence is needed to confirm this activity as current trials are usually underpowered.
D	Polypodium leucotomos	↓	★☆☆ Minor	1 study	Appears to reduce infection risk, although it did not appear to be overly remarkable in doing so.

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Urea

Urea is a metabolic byproduct of amino acid metabolism that is excreted by the kidneys.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Glutamine	↑	★☆☆ Minor	1 study	An increase in urea has been noted with glutamine supplementation
C	Citrulline	↑	★☆☆ Minor	1 study	An increase in urea is seen with citrulline supplementation (possibly due to increased serum Ornithine sequestering ammonia)
C	Ornithine	↑	★☆☆ Minor	2 studies	Mixed effects, but it appears that when ammonia is decreased that urea is also increased but if ammonia is unchanged whatever reason for this also means that urea is unchanged.
C	Arginine	—	—	1 study	Although it is theoretically plausible that arginine can increase urea concentrations (secondary to the actions of ornithine), it does not appear to reliably occur
C	Citrullus colocynthis	—	—	1 study	No significant alterations in serum urea, suggesting no renal toxicity with the low doses (300mg) of this supplement
C	Creatine			4 studies	
C	Astaxanthin			1 study	
C	Chromium	—	—	1 study	The lone study assessing urea failed to find a significant interaction between it and supplementation of chromium.

D	Hibiscus sabdariffa	—	—	1 study	No significant influence on urea
D	HMB	↑	★☆☆ Minor	1 study	A slight increase in urea has been noted, requires replication

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Uric Acid

Uric acid is a molecule (a byproduct of purine metabolism) that, in excessive levels, can contribute to gout and kidney stones. Despite this, uric acid is a potent antioxidant compound.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Creatine	↓	★☆☆ Minor	2 studies	Minor reductions in uric acid.
C	Ganoderma lucidum	—	—	1 study	No changes in serum uric acid seem apparent
C	Gynostemma pentaphyllum	—	—	1 study	No significant influences on uric acid
C	L-Carnitine	↓	★☆☆ Minor	1 study	A decrease in uric acid has been noted
C	Glutamine	↑	★☆☆ Minor	1 study	An increase in serum urate has been noted in the range of 10-20% acutely, but attenuates with time and is likely not a concern within a week. Practical significance of this increase unknown.
C	Quercetin	—	—	1 study	No significant influence on uric acid concentrations
C	Nigella sativa	—	—	2 studies	No statistically significant alterations in uric acid concentrations in serum
C	Rooibos	—	—	1 study	No significant influence on uric acid is seen with Rooibos tea ingestion.
C	Psyllium	↓	★☆☆ Minor	1 study	An 11% decrease in uric acid has been noted in diabetics supplementing with psyllium husk.

D	Hibiscus sabdariffa	—	—	1 study	Does not appear to influence uric acid concentrations in serum
D	Tetradecyl Thioacetic Acid	—	—	2 studies	No significant alterations in serum uric acid seen with supplemental TTA
D	Garlic	—	—	1 study	No significant interactions with uric acid concentrations in serum.

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Vaccine Augmentation

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Panax ginseng	↑	★☆☆ Minor	1 study	Has been noted to increase the antibody response to vaccinations when taken prior
C	Chlorella	—	—	1 study	Has once failed to act effectively as a vaccine adjuvant
C	Vitamin E	↑	★☆☆ Minor	2 studies	There appears to be an increased antibody response to vaccinations in otherwise healthy persons who supplement with a low dose of vitamin E relative to those receiving placebo with their vaccination; this applies to both youth and the elderly.
C	Colostrum	↑	★☆☆ Minor	2 studies	Tenuous evidence for an increase in vaccine efficacy, as while the one study assessing antibody titres failed to find any influence (suggesting no benefit) there does appear to be a reliable increase in the secretion of IgA and IgG in response to the vaccine.

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Verbal Fluency

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Oxiracetam	↑	☆☆☆ Minor	2 studies	Appears to favor improvements in verbal fluency in persons with cognitive dementia, despite benefiting most parameters measured
C	Ginkgo biloba	—	—	2 studies	No significant influence of supplemental ginkgo on verbal fluency even in persons with cognitive injuries.
C	Vitamin E	—	—	1 study	Verbal fluency does not appear to be significantly altered with vitamin E supplementation relative to placebo.

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Viral Load

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Colostrum	—	—	1 study	Administration of colostrum to persons with HIV already on antiretroviral therapy does not further modify viral titres.
D	Nigella sativa	↓	★★★☆☆ Notable	1 study	A pilot study in hepatitis C noted that the viral load was reduced to 38.6% of baseline with a modest dosage of the seed oil, a fairly drastic reduction.
D	Chromium	—	—	1 study	In persons with HIV, supplementation of chromium did not alter the levels of the virus in their body despite showing actions on glucose disposal rates.
D	Tetradecyl Thioacetic Acid			1 study	

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Visual Acuity

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
C	Caffeine	—	—	1 study	No significant influence on visual acuity has been noted with caffeine on hand-eye or target-based visual tasks
C	Ginkgo biloba	↑	★☆☆ Minor	1 study	Improvements have been noted in the visual field in persons with normal tension glaucoma, which is characterized by damage to this parameter. It is uncertain whether ginkgo increases visual acuity in otherwise healthy persons.
C	Saffron	↑	★☆☆ Minor	2 studies	Supplementation of saffron appears to increase visual acuity in persons with age-related macular degeneration.
D	CDP-choline	↑	★☆☆ Minor	1 study	In persons with glaucoma, CDP-Choline ingestion appears to be somewhat protective of vision and has been noted to cause improvements in visual acuity
D	Ruscus aculeatus	—	—	1 study	The improvement in visual acuity seen with supplementation of this herb failed to reach statistical significance in diabetic persons with retinopathy.

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vLDL-C

Very low density cholesterol (vLDL-C) is the lipoprotein synthesized in the liver, and is able to convert to LDL-C when in circulation.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Fish Oil	↓	★☆☆ Minor	6 studies	May decrease vLDL cholesterol
B	Chromium	—	—	3 studies	No significant influence on vLDL cholesterol seen in diabetics supplementing chromium.
C	Shilajit	↓	★☆☆ Minor	1 study	Minor decreases in vLDL concentrations have been noted
C	Guggul	—	—	1 study	No significant influence on vLDL cholesterol levels
C	Quercetin	—	—	1 study	No significant changes in vLDL-C are detected with quercetin supplementation.
C	Creatine			1 study	
D	Eclipta alba	↓	★☆☆ Minor	1 study	Decreases in fasting vLDL have been noted

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VO2 Max

VO₂ Max refers to the maximal oxygen consumption during exercise, and is thought to reflect the abilities of the cardiorespiratory system (heart and lungs) to handle high intensity cardiovascular exercise (anaerobic exercise).

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Creatine	↑	★☆☆ Minor	6 studies	Improvements in VO ₂ max are not wholly reliable, and appear to be low in magnitude.
B	Beta-Alanine	—	—	5 studies	Highly unreliable effects on VO ₂ max and currently is thought to have no significant effect.
B	Fish Oil	—	—	3 studies	There is no evidence to support an improvement of VO ₂ max when fish oil is consumed alongside an exercise routine
B	Sodium Bicarbonate	—	—	7 studies	For the most part, peak VO ₂ consumption is not significantly influenced by supplemental sodium bicarbonate (although VO ₂ kinetics that are not referring to VO ₂ max may be influenced somewhat)
B	Colostrum	—	—	6 studies	All studies assessing the effects of colostrum in athletes subject to cardiovascular training have failed to find any difference between colostrum and whey protein (control) for influencing VO ₂ max.
C	Coenzyme Q10	↑	★☆☆ Minor	2 studies	An increase in VO ₂ max of untrained persons has been noted following CoQ10 supplementation.

C	Vitamin C	—	—	1 study	Does not appear to have a role in altering VO2 max
C	Echinacea	↑	★☆☆ Minor	1 study	Not an astounding increase in VO2 max, requires replication.
C	Cordyceps	—	—	2 studies	No significant influence on VO2 max in otherwise healthy persons.
C	Rhodiola Rosea	—	—	1 study	May slightly improve oxygen consumption during submaximal exercise in untrained persons, but overall the improvement in VO2 max does not appear to be highly potent or reliable.
C	Caffeine	—	—	1 study	No significant influence on VO2 max ratings
C	Green Tea Catechins	↑	★☆☆ Minor	1 study	An increase in VO2 max has been noted in untrained persons
C	L-Carnitine	—	—	1 study	No detectable influence on VO2 max associated with carnitine supplementation
C	Ashwagandha	↑	★☆☆ Minor	2 studies	A slight increase in VO2 max has been detected over the course of 8 weeks supplementation in otherwise untrained persons.
C	Curcumin	—	—	1 study	In postmenopausal women, curcumin supplementation does not improve VO2 max.
C	Capsaicin			1 study	
C	Trimethylglycine	—	—	1 study	Although a minor increase in oxygen uptake was noted in certain situations (final sprint of testing), overall VO2 max is not significantly affected.

D	Eleutherococcus senticosus	↑	★☆☆ Minor	1 study	Possible increases in VO2 max, but requires more evidence to ascertain potency and reliability
D	HMB	—	—	1 study	No significant influence on VO2 max in trained athletes

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Weight

Weight is the result of your body's fight against Earth's gravity. It is sometimes used as a measurable parameter in some studies as it is cheap to measure the weight of many people, but more expensive to measure fat mass and lean mass separately.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
A	Creatine	↑	★★★ Strong	28 studies	Appears to have a large effect on increasing overall weight due to water retention in persons who respond to creatine supplementation. Degree of increase is variable.
A	Fish Oil	—	—	14 studies	For the most part, no significant influence on body weight over time
A	Conjugated Linoleic Acid	—	—	21 studies	CLA is considered ineffective for weight loss to the high degree of unreliability in the results, with most evidence suggesting no effects and some sparse evidence to suggest both increases and decreases.
A	Chromium	—	—	33 studies	There is no significant influence of chromium on weight in either healthy persons or those with diabetes, and although a possible interaction may occur in some instances of better glucose control or reduced appetite they are not frequent enough to establish a solid relationship to chromium.
A	Colostrum	—	—	13 studies	The majority of studies fail to find any significant influence of colostrum on body weight that is atypical of protein sources, although as it confers protein and calories it remains

					possible to gain weight from colostrum.
B	Pyruvate	—	—	5 studies	Most evidence suggests that standard oral doses of Pyruvate supplementation do not have a reducing effect on weight, but the effects of high dose pyruvate during severe caloric restriction cannot be ruled out
B	Ephedrine	↓	★★★☆☆ Notable	10 studies	Ephedrine tends to result in reliable weight loss over time relative to control (assuming calories are held equal), which is mostly due to a loss of body fat
B	Whey Protein	—	—	8 studies	The influence of whey protein on weight <i>per se</i> is highly unreliable, and is subject to the overall context of the diet. Protein in general can aid weight loss attempts and is required to build lean mass, with whey not having any demonstrated benefit over other protein sources.
B	Nicotine	↓	★★☆☆☆ Minor	4 studies	Possible minor weight reducing effects occur in interventions using nicotine, but they are highly unreliable and likely mediated by lesser food intake rather than inherent fat burning effects
B	Green Coffee Extract	↓	★★☆☆☆ Minor	3 studies	There may be a weight reducing effect, but currently the literature is too influenced by industrial producers of GCE and the magnitude of effect seems too large. Independent replication is needed.
B	Psyllium	—	—	4 studies	No convincing evidence for a weight reducing effect of psyllium.
B	5-HTP	↓	★★★☆☆	3 studies	

B			Minor		The reduction in weight appears to be mostly secondary to a reduction in food intake, and is not too remarkable in magnitude
B	Garcinia cambogia	—	—	3 studies	Although there is some counter evidence, it tends to be less robust and for the most part there is no significant weight reducing effect of garcinia cambogia supplementation
B	Magnesium	—	—	4 studies	No evidence to support a role for magnesium in inducing alterations in body weight
B	Vitamin K	—	—	3 studies	In studies that measure weight changes over time (usually as a secondary piece of data), there do not appear to be any significant alterations associated with vitamin K supplementation.
B	Inositol	↓	★☆☆ Minor	7 studies	Decreases in body weight have been noted in women with PCOS, as inositol is effective in treating PCOS. They seem to influence leaner and overweight women more than obese women.
B	Nigella sativa	↓	★☆☆ Minor	4 studies	One study has noted weight loss, but due to the reduction in appetite and no records of food intake the possibility of subjects losing weight due to eating less cannot be ruled out. Other studies have failed to find an influence of treatment.
B	Red Clover Extract	—	—	7 studies	No studies, even those using up to 120mg total isoflavones for up to a year, have noted significant weight loss associated with Red Clover supplementation in postmenopausal women.

B	Trimethylglycine	—	—	4 studies	No significant alterations in weight are seen with supplementation of betaine, which is different than what is seen with another popular sports osmolyte (creatine).
B	Astaxanthin			3 studies	
B	Vitamin E	—	—	7 studies	There does not appear to be any influence of vitamin E supplementation at any tested dose in any subject on weight loss nor gain.
C	Coleus forskohlii	↓	★☆☆ Minor	4 studies	Mixed effects on overall weight, may be more effective in men rather than women. Overall, it requires more evidence to see if it has a role in weight loss regimens.
C	Green Tea Catechins	—	—	2 studies	
C	ECA	↓	★★★☆☆ Notable	1 study	Due to both the increase in metabolic rate and reduction in appetite reported, there are notable weight reductions with the ECA stack
C	Tauroursodeoxycholic Acid	—	—	1 study	No significant influence on weight in obese persons
C	Vitamin C	—	—	2 studies	Vitamin C does not appear to have a weight reducing effect
C	Punicic Acid	—	—	1 study	No significant influence on weight has been noted
C	Alpha-Lipoic Acid	↓	★☆☆ Minor	4 studies	It is possible that high doses (1,800mg) may have a body weight reducing effect in obese persons, but this requires more evidence.
C	Grapefruit	↓	★☆☆ Minor	3 studies	There appears to be a weight reducing effect of grapefruit consumption relative to

					isocaloric controls (such as apple juice)
C	Chlorella	—	—	1 study	No significant effects on body weight
C	Licorice	—	—	1 study	No significant interactions with body weight associated with licorice ingestion
C	Hibiscus sabdariffa	—	—	2 studies	Weight appears to be unaffected following ingestion of Roselle tea
C	Spirulina	—	—	2 studies	Currently not enough evidence to support any significant interaction with weight
C	7-Keto DHEA	↓	★☆☆ Minor	1 study	A weight loss of 2.88kg (1.8% body fat) was seen with 7-keto over placebo (0.97 kg loss with 0.28% bodyfat) which is significant but not overly notable, since the study used obese persons and exercise
C	Caralluma fimbriata	—	—	1 study	Study was too short for the appetite suppressing effects to manifest as weight loss, and thus no evidence exists for weight reducing effects.
C	Chlorogenic Acid	↓	★☆☆ Minor	2 studies	Although the reductions seen with chlorogenic acid seem remarkable, the studies conducted at this moment in time are somewhat industry influenced
C	Cissus quadrangularis	↓	★☆☆ Minor	1 study	There may be a small weight loss associated with 300mg cissus (2.5% ketosteroids) which was seen alongside a reduction in appetite in obese persons; no known direct fat burning properties.
C	Rhodiola Rosea	—	—	1 study	Unable to modify weight over

					time
C	Olive leaf extract	—	—	2 studies	Overall, there does not appear to be a significant effect of olive phenolic consumption on weight
C	Stinging Nettle	—	—	1 study	No significant influence on body weight with consumption of stinging nettle
C	Shilajit	—	—	1 study	No significant influence detected on weight
C	Dehydroepiandrosterone	—	—	1 study	No significant influence on weight noted with DHEA supplementation
C	Fucoxanthin	↓	★★★☆☆ Notable	1 study	The lone study in obese menopausal women noted a large degree of weight loss over time relative to control, which was thought to be due to increasing the metabolic rate (secondary to alleviating fatty liver). Needs to be replicated in other demographics
C	Ganoderma lucidum	—	—	1 study	No significant alterations in body weight seen with ganoderma ingestion
C	Gynostemma pentaphyllum	↓	★★☆☆☆ Minor	1 study	Long term, but not short term, ingestion of gynostemma tea appears to reduce fat mass in diabetics; no studies in healthy persons yet
C	Irvingia gabonensis	↓	★★☆☆☆ Minor	2 studies	Decreased body weight has been noted when african mango is consumed before meals, which may be secondary to reduced food intake; studies are somewhat confounded by industry influence.
C	Vitamin D	—	—	2 studies	No significant alterations noted

					in weight, even when fat mass is lost, in obese persons
C	Royal Jelly	—	—	1 study	No significant alterations in weight over the long term with Royal Jelly supplementation
C	Panax ginseng	—	—	2 studies	Does not appear to have any weight reducing properties, although it has been reported in one study secondary to improving the glycemic profiles of diabetics
C	Krill Oil	—	—	1 study	No significant influence on weight over time
C	Lactobacillus casei			1 study	
C	Leucic Acid	↑	★☆☆ Minor	1 study	The lone study using leucic acid in athletes has noted a minor but statistically significant increase in weight, attributable to lean mass (muscle plus water; bone mass unchanged)
C	Ashwagandha	↓	★☆☆ Minor	2 studies	A decrease has been noted in one study where overweight persons with anxiety were being treated, and while the 1-2kg loss over 8 weeks was significant it is not sure if this applies to otherwise normal weight non-anxious persons.
C	Curcumin	—	—	1 study	Currently no demonstrable anti-obese effect of isolated curcumin supplementation.
C	Eurycoma Longifolia Jack	↓	★☆☆ Minor	1 study	A decrease in weight has been noted in overweight and obese men, but did not extend to men of normal weight. Mechanisms unknown.
C	Modafinil	—	—	1 study	There is currently no evidence to suggest a significant reduction of weight associated

					with modafinil, although as a trend to reduce weight has been noted alongside appetite reduction it is thought that modafinil could have a role in weight control.
C	Zinc	↓	★☆☆ Minor	2 studies	In children who are likely deficiency, zinc supplementation can reduce body weight.
C	Quercetin	—	—	1 study	No significant alterations detected in body weight with quercetin supplementation.
C	Garlic	—	—	2 studies	Although there are theoretical benefits of garlic to weight loss, prolonged supplementation of garlic in other studies (where weight is measured as a secondary parameter of interest) is not altered. The weight loss effects are either small or nonexistent in otherwise normal conditions
C	D-Aspartic Acid	—	—	1 study	No significant alterations in body weight when D-aspartic acid is taken alongside resistance training.
C	Anethum graveolens			1 study	
C	Hoodia gordonii	—	—	1 study	No significant influence on overall body weight (due to no fluctuations in appetite and thus no significant fat loss)
C	Hesperidin	—	—	2 studies	In studies measuring weight as well as other parameters, weight is not influenced by supplementation of hesperidin relative to placebo
C	Citrullus colocynthis	—	—	1 study	In assessing the influence of the fruit extract on blood glucose, there was no significant influence on weight

C	Yacon	↓	★☆☆ Minor	1 study	A decrease in weight has been noted in obese women given Yacon, although this study could potentially be explained by a reduction in food intake (due to an increase in self-reported satiety and no tracking of calories noted).
C	Saffron	↓	★☆☆ Minor	1 study	A reduction in weight has been noted to a very mild degree which may be wholly related to a reduction in snacking that has been observed with saffron supplementation in overweight women.
C	Rose Hip	—	—	1 study	Despite some evidence to suggest antiobese effects in the mouse, limited human evidence has failed to find evidence in otherwise healthy but obese humans.
D	Coconut Oil	↓	★☆☆ Minor	1 study	Appears somewhat effective in reducing weight of obese persons to a greater degree than an isocaloric amount of longer chain fatty acids
D	Black Cohosh	—	—	1 study	No significant influences on body weight
D	Tetradecyl Thioacetic Acid	—	—	2 studies	Although increased mitochondrial fat oxidation was created for underlying the reductions in lipids and blood pressure, no significant influence on body weight was noted in obese men
D	Taurine	—	—	1 study	No significant influence on weight noted with supplementation
D	Safflower Oil	—	—	1 study	No significant changes in total body weight appear to be visible following ingestion of safflower oil in the diet

D	Sodium Bicarbonate	—	—	1 study	Despite the potential increase in metabolic rate and increase in ketone body production, there is currently no evidence to support more fat loss with sodium bicarbonate over placebo
D	CDP-choline	—	—	1 study	No significant effects of CDP-Choline on weight, despite the small appetite reducing effect
D	Blueberry	—	—	1 study	No significant influence on weight when taken as a daily supplement in obese individuals.

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White Blood Cell Count

Total white blood cell count is measured commonly in toxicology testing, and some supplements that are known to support the immune system may also act via increasing levels of immune cells.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	Garlic	—	—	3 studies	While there are significant modifications in the subpopulations of white blood cells (ie. <i>which</i> immune cells you have) the overall quantity does not appear significantly affected.
B	Vitamin E	—	—	6 studies	Supplementation of vitamin E does not appear to alter overall content of white blood cells relative to placebo.
C	Green Coffee Extract	—	—	1 study	No significant alterations in WBC count
C	Spirulina	↑	★☆☆ Minor	1 study	Minor increase, needs more evidence in a non-aged cohort to assess potency
C	Glutamine	—	—	1 study	In safety testing, no significant alterations in white blood cell count is noted.
C	Anethum graveolens			1 study	
C	Hesperidin	—	—	1 study	No significant influence on total white blood cell count is seen with supplemental hesperidin.
C	Astaxanthin			2 studies	
C	Saffron	↓	★☆☆ Minor	2 studies	A decrease in white blood cell count has been noted with supplementation of saffron at 60mg for over eight weeks.

C	Colostrum	—	—	2 studies	White blood cell count does not appear to be chronically modified with colostrum supplementation, although a transient (one day) elevation was noted in one study.
D	Uncaria tomentosa	↑	★☆☆ Minor	1 study	An increase in white blood cell count has been noted with Cat's Claw by 9% over 9 weeks with a water extract, which is thought to be related to the immunoenhancing properties. The white blood cells that were increased were not assessed
D	Nigella sativa	↑	★☆☆ Minor	1 study	A normalization of WBC count has been noted in persons with hepatitis C being treated with the seed oil.
D	Stephania tetrandra	—	—	1 study	No significant alterations in white blood cell count are noted with oral supplementation of this plant.
D	Moringa oleifera	—	—	1 study	No significant alterations in white blood cell count following ingestion of the seeds of <i>Moringa oleifera</i>
D	Ashwagandha	—	—	1 study	During toxicology testing in otherwise healthy persons, there is no significant alterations in white blood cell count seen with supplementation.
D	Tetradecyl Thioacetic Acid			1 study	

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Working Memory

Working memory is the ability to transiently keep information in the brain until it can be processed into longterm memory, and person's with high working memory capacities are said to have a 'steel trap' mind. Some supplements may improve working memory in particular.

LEVEL OF EVIDENCE	SUPPLEMENT	CHANGE	MAGNITUDE OF EFFECT CHANGE	SCIENTIFIC STUDIES	COMMENTS
B	L-Tyrosine	↑	★☆☆ Minor	4 studies	Appears to preserve working memory during acute stressors without inherently having a memory boosting effect
B	Modafinil	↑	★☆☆ Minor	5 studies	An improvement in working memory is noted in most persons tested, even otherwise healthy and nonfatigued controls.
B	Ginkgo biloba	—	—	3 studies	Despite the improvement in short term memory and recall, there does not appear to be a significant improvement in working memory.
C	Coconut Oil	—	—	1 study	Insufficient evidence to support an increase in working memory
C	Melissa officinalis	—	—	2 studies	No significant influence appears to exist on working memory associated with lemon balm
C	Choline	—	—	1 study	No significant improvement in working memory
C	Phosphatidylserine	↑	★☆☆ Minor	1 study	Improvement in working memory may be due to improved attention
C	Nigella sativa	—	—	1 study	

					Despite improvements in logical memory and 30 minute recall, digit span tests are not affected by supplementation of <i>nigella sativa</i> .
C	Cocoa Extract			1 study	
C	PRL-8-53	↑	★☆☆ Minor	1 study	Memory acquisition appears to be mildly increased in the range of 18-31% in persons with poorer performance on a word recollection memory test, but is not improved in high performers.
D	Peppermint	—	—	1 study	Working memory does not appear to be influenced with the aroma of peppermint