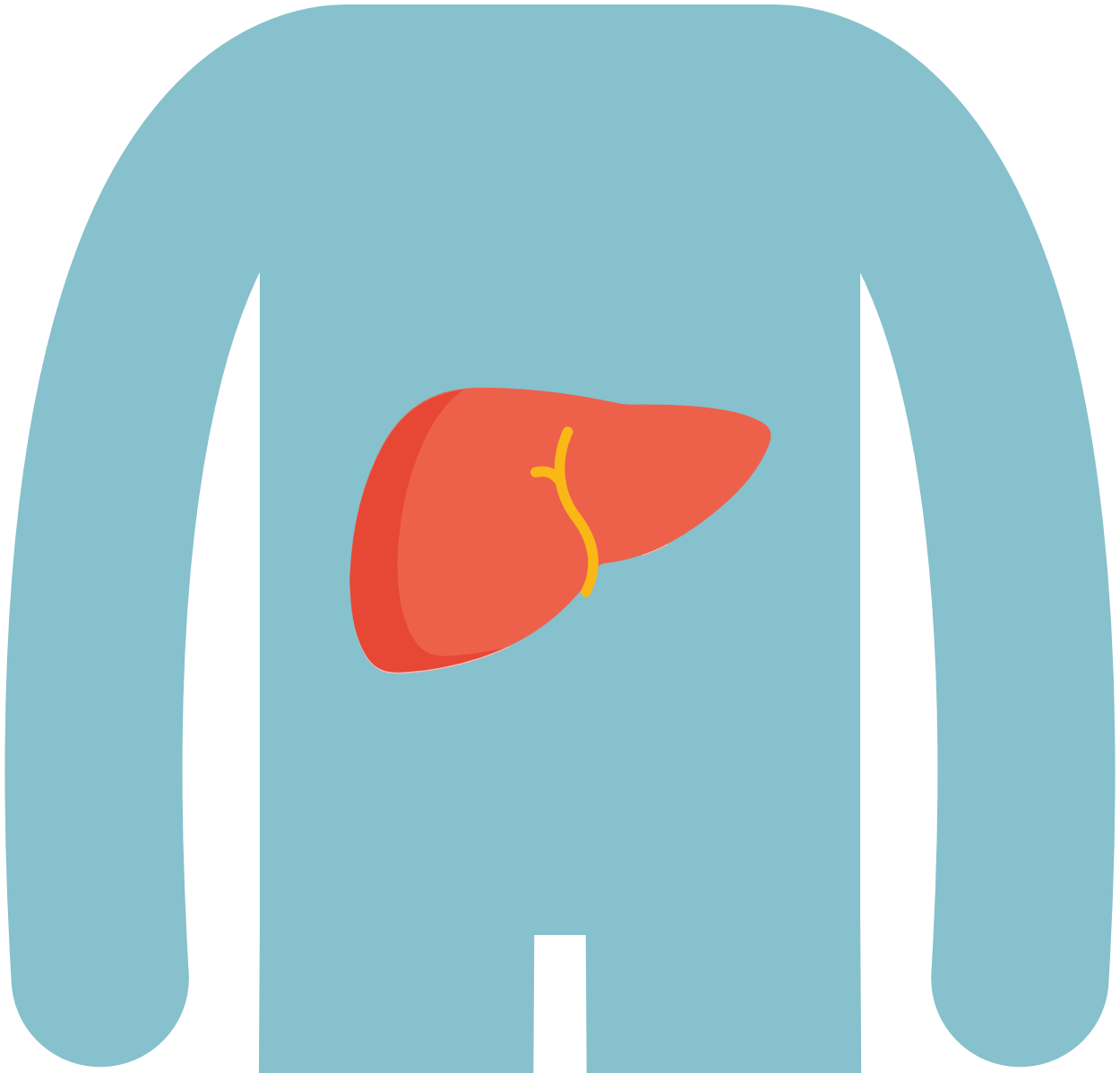
Examine.com

Liver Health Supplement Guide



Written by the editors of Examine.com

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Medical Disclaimer

This guide is a general-health document for adults over 18. Its aim is strictly educational. It does not constitute medical advice. Please consult a medical or health professional before you begin any exercise-, nutrition-, or supplementation-related program, or if you have questions about your health.

This guide is built on scientific studies, but study outcomes are never homogeneous: individual results do vary. If you engage in any activity or take any product mentioned herein, you do so of your own free will, and you knowingly and voluntarily accept the risks. While we mention major known interactions, it is possible for any supplement to interact with other supplements, as well as with foods and pharmaceuticals.

A product may not contain the exact compounds and amounts listed on its label. Before you decide whether to take it, investigate it and its manufacturer. More than isolated compounds, herbs are prone to batch-to-batch variability, which can alter their efficacy and safety.

For evidence supporting the claims mentioned in this guide, please visit Examine.com.

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How to Use This Guide

The Examine.com team has been publishing research on nutrition and supplementation since March 2011. Drawing from all we've learned, we've designed this Stack Guide to help you figure out which supplements can help you reach your health goal, and which can hinder you or just waste your money.

Core supplements have the best safety-efficacy profile. When used responsibly, they are the supplements most likely to help and not cause side effects.

Primary options may provide substantial benefit, but only in the right context. A primary option is not for everyone, but if you read the entry and find that you meet the criteria, consider adding the supplement to your stack.

Secondary options have less evidence for their effects. They could work or be a waste of money. Keep them in mind, but think twice before adding them to your stack.

Promising supplements are backed by tradition or by mechanistic, animal, epidemiological, or anecdotal evidence, but not yet by convincing human trials.

Inadvisable supplements are either potentially dangerous or simply ineffective, marketing claims notwithstanding. Do not add them to your stack. At best, they'll be a waste of money; at worst, they can cause you harm.

Now that you've been presented with various supplements worthy of your interest, the time has come to combine them based on your objective. We'll guide you in **assembling your stack**.

Then comes the **FAQ**, in which we cover common questions that may arise when assembling your stack.

Lastly, we include information on **precautions and troubleshooting**.

With all this combined, you should be able to identify and assemble the supplement stack best suited to your objective.

Core Supplements

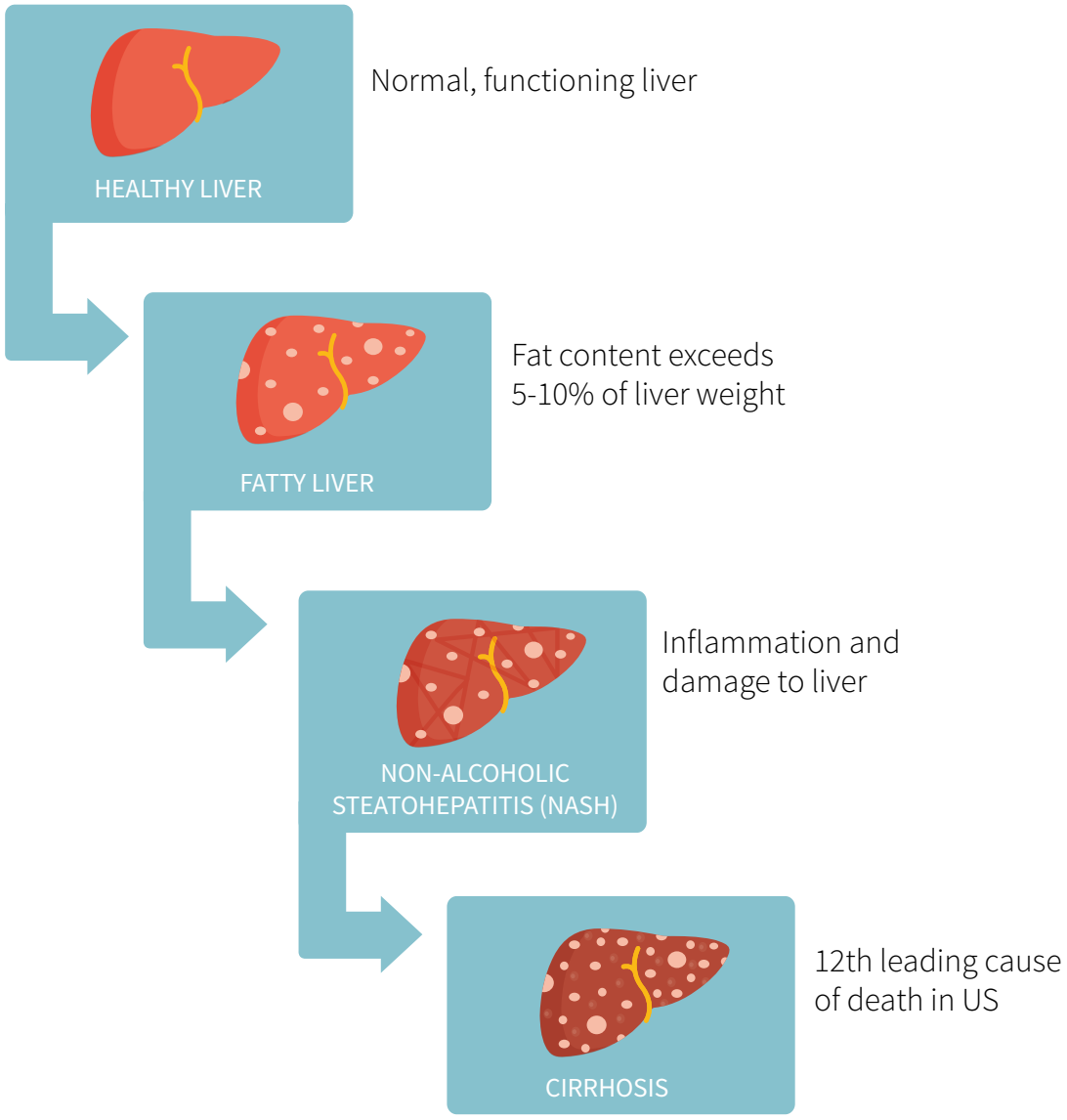
SAMe

Why it's a core supplement

S-adenosylmethionine (SAMe) works with enzymes in a process called methylation: when a molecule in your body needs a methyl group in order to undergo a chemical reaction, SAMe provides that group.

Since SAMe synthesis decreases with chronic liver disease, oral SAMe can benefit the person afflicted, but it doesn't follow that SAMe affects the disease itself. Current evidence suggests, however, that oral SAMe can support normal liver functions and may help fight cholestasis, alcoholic liver disease, and possibly even *non-alcoholic fatty liver disease* (NAFLD).

Figure 1: Progression of *non-alcoholic fatty liver disease* (NAFLD)



Methylenetetrahydrofolate reductase (MTHFR) is an enzyme that helps process amino acids. If you have an MTHFR gene mutation, SAMe can still benefit your liver, but it may also cause a "backlog" of a potentially harmful metabolite known as homocysteine. In this scenario, it would be safer to replace SAMe by L-methylfolate (aka levomefolic acid, 5-methyltetrahydrofolate, and 5-MTHF).

Preliminary evidence suggests that ingesting choline or its derivative trimethylglycine (TMG, aka betaine) can raise SAMe levels, though to a lesser extent than ingesting SAMe. Unlike choline, TMG also has preliminary evidence for benefiting the liver. Both choline and TMG lower homocysteine levels in normal people, which makes them less likely than SAMe to raise homocysteine levels in people with an MTHFR gene mutation.

How to take them

First choice is SAMe; second, TMG; third, choline. If you have an MTHFR gene mutation, however, do not take SAMe; instead, take L-methylfolate, with or without TMG or choline.

Take 400 mg of **SAMe** thrice a day (i.e., 1,200 mg/day), with or without food.

Take 1.5–2 g of **trimethylglycine** (TMG) twice or thrice a day (i.e., 3–6 g/day). TMG can be consumed as a powder or simply through foods, notably wheat bran (1,339 mg of TMG per 100 g), spinach (600–645 mg of TMG per 100 g), and beetroot (114–297 mg of TMG per 100 g).

Most people get enough choline through their diet. Track what you eat for a week; if, on average, you are getting less than 80% of your Adequate Intake (AI), try eating more foods rich in choline before you consider taking 250–500 mg of **choline bitartrate** once a day with a meal.

Take 7.5–15 mg of **L-methylfolate** once a day.

Primary Options

Milk Thistle

Why it's a primary option

Milk thistle (*Silybum marianum*) has been used to protect the liver as far back as ancient Greece. Nowadays, limited evidence suggests that **silymarin**, its bioactive compound, can increase the synthesis rates of protein and DNA in the liver. In the presence of liver toxins, it can also act as an anti-inflammatory agent. People who are not using compounds that may harm the liver (e.g., alcohol or some medications) are not likely to benefit from milk thistle.

High doses of silymarin (420–600 mg) have shown efficacy against death cap poisoning; for obvious reasons, however, there have been no controlled trials to confirm the conclusions from the case studies. If you ever get death cap poisoning, by all mean take some silymarin … ***after*** you've called emergency services, or on your way to the hospital!

Silymarin may lower the effectiveness of oral contraceptives.

How to take it

Take 140 mg of **silymarin** twice a day (i.e., 280 mg/day), with or without food. This translates to 187.5 mg twice a day (i.e., 375 mg/day) of a milk thistle extract standardized to 80% silymarin.

Figure 2: Milk thistle vs. the death cap

Death Cap (Amanita phalloides) is a highly lethal mushroom

The lethal dose is 0.1 mg/kg, which my be as little as a single mushroom

Symptoms include vomiting, diarrhea, and liver dysfunction

The mushroom toxin, Amanitin, prevents DNA from creating new proteins

The Milk Thistle extract, silymarin, can aid in clearing the toxin from the system

NAC

Why it's a primary option

N-acetylcysteine (NAC) can increase the body's production of the antioxidant glutathione. Low levels of glutathione are associated with various inflammatory and oxidative diseases, such as *non-alcoholic fatty liver disease* (NAFLD).

High NAC doses are used acutely in cases of toxin-induced liver damage, particularly when caused by an overdose of acetaminophen (aka paracetamol). The most common oral protocol in US hospitals is based on the weight of the patient in kilograms: one 140 mg/kg dose followed by sixteen 70 mg/kg doses 4 hours apart. Such high doses have been known to cause nausea and vomiting, but much lower doses can be taken daily to support glutathione levels and thus, indirectly, the liver.

How to take it

Take 400 mg of NAC once to thrice a day (i.e., 400–1,200 mg/day). If you are prone to nausea, take your NAC with food.

TUDCA

Why it's a primary option

Tauroursodeoxycholic acid (TUDCA) is a water-soluble, taurine-conjugated bile acid. It exists in trace amounts in the human body, where it helps regulate apoptosis (programmed cell death).

In hospitals, TUDCA is used to treat cholestasis, an impairment of the flow of bile (a digestive fluid secreted by the liver). It has also been shown to benefit people suffering from hepatitis C or from primary biliary cirrhosis, two diseases that damage bile ducts, but studies on other liver diseases, such as alcoholic or nonalcoholic fatty liver diseases, are still lacking.

TUDCA supplementation can help prevent endoplasmic reticulum stress and the resulting inflammation and oxidative stress, but more evidence is needed to determine if this property translates to a protective effect on the liver.

On the other hand, there is already significant evidence that TUDCA supplementation can induce cholesterol efflux and thus regulate cholesterol levels in cells. Combined with a low-cholesterol diet, TUDCA can reduce the risk of gallstone formation and even dissolve cholesterol-rich non-calcified gallstones. It cannot, however, dissolve gallstones rich in bilirubin or in calcium and other minerals.

One study in obese people reported that TUDCA supplementation increased insulin sensitivity in muscle and liver cells, but these results have not been replicated.

How to take it

Take 500–1,750 mg of TUDCA before bed, without food.

Secondary Options

Picrorhiza Kurroa

Why it's a secondary option

In Ayurvedic medicine, *Picrorhiza kurroa* is a liver tonic. **Picroliv**, its bioactive compound, is composed of picroside I and picroside II.

Picrorhiza kurroa has antioxidant properties, can improve the flow of bile (a digestive fluid secreted by the liver), and might reduce fat accumulation in the liver. In animal studies, it was more effective than milk thistle at protecting the liver against all kinds of toxins, including death cap mushroom. Milk thistle, however, is backed by human studies.

Picrorhiza kurroa is an endangered plant. Should you decide to take it, seek out a company that focuses on plant sustainability.

How to take it

Choose a *Picrorhiza kurroa* extract standardized for its picroliv content. Take 12 mg of **picroliv** per kilogram of bodyweight per day (5.4 mg/lb/day) in three divided doses, with or without food.

- If you weight 100 lb (45 kg), take 180 mg of picroliv thrice a day.
- If you weight 150 lb (68 kg), take 270 mg of picroliv thrice a day.
- If you weight 200 lb (91 kg), take 360 mg of picroliv thrice a day.
- If you weight 250 lb (113 kg), take 450 mg of picroliv thrice a day.

Spirulina

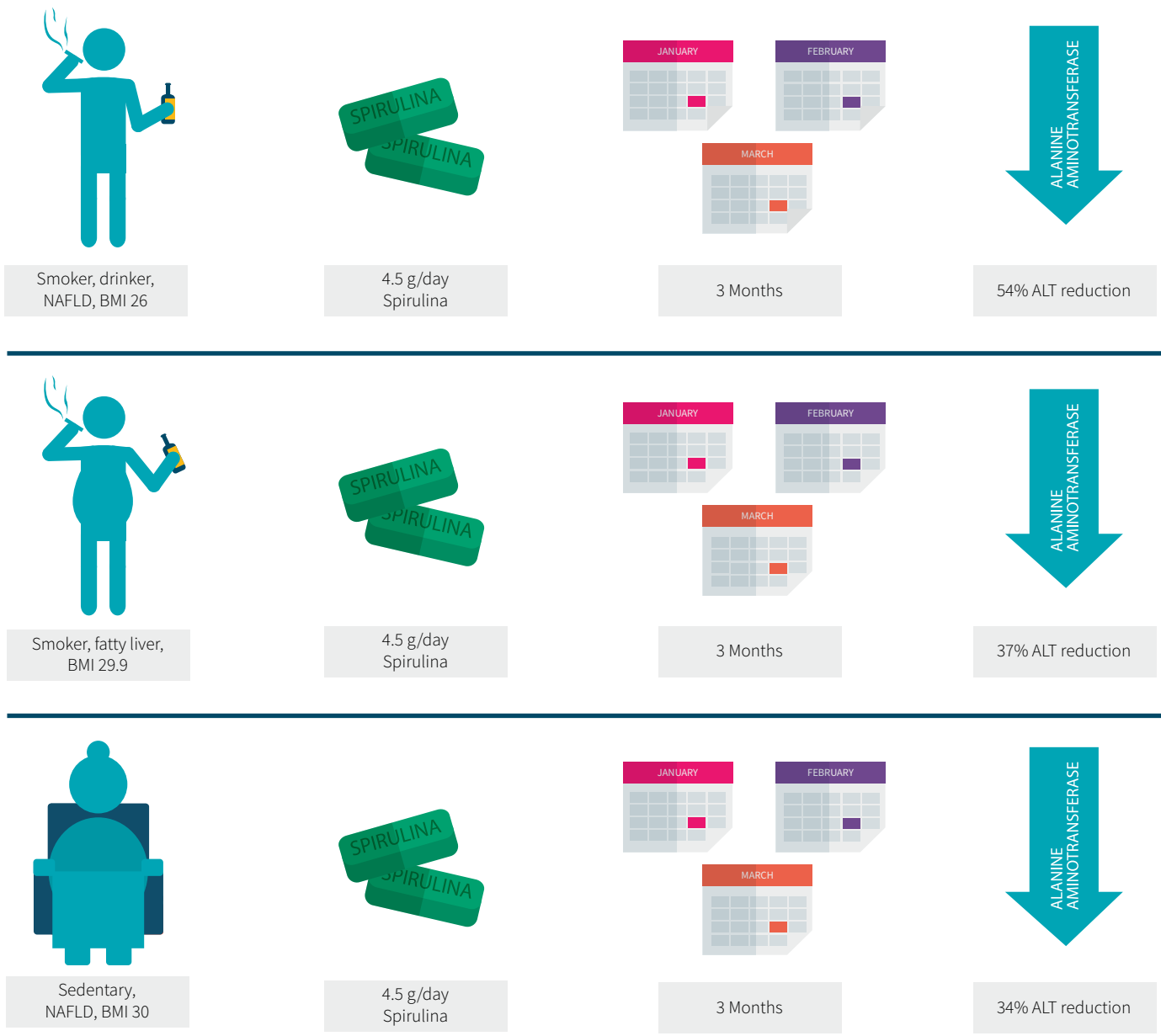
Why it's a secondary option

Spirulina, a protein-rich blue-green algae, has been shown to reduce inflammation and oxidative stress. Moreover, one of its bioactive compounds, c-phycocyanin, is a bile acid mimetic, which is why spirulina supplementation is thought to mimic Gilbert's Syndrome, a medical condition characterized by high levels of bile acids in the body. Elevated bile acid levels

are associated with a reduced risk of obesity, diabetes, and cardiovascular complications. People with Gilbert's Syndrome tend to have longer lifespans.

Preliminary evidence suggests that spirulina might help treat hepatitis C and *non-alcoholic fatty liver disease* (NAFLD).

Figure 3: Spirulina vs. *non-alcoholic fatty liver disease* (NAFLD)



Source: Ferreira-Hermosillo et al., *J Med Case Rep*. 2010 Apr.

How to take it

Take 1.5–8 g of spirulina per day, with or without food. Spirulina is available as bulk powder, as powder in capsules, and in tablet form.

Inadvisable Supplements

Despite their current popularity, "detox diets" are not backed by the evidence, nor are they even based on scientifically sound principles. A healthy, balanced diet is more likely to help your liver detoxify itself, simply by allowing it to function optimally.

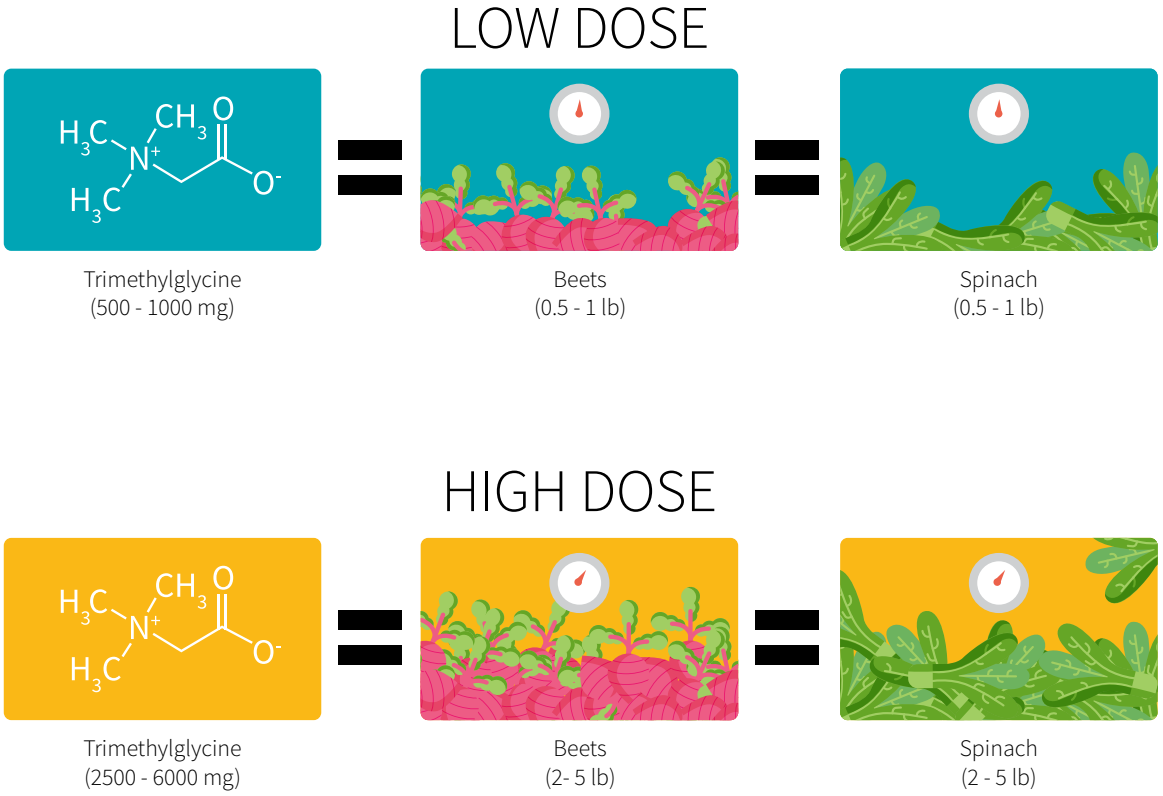
Assembling Your Stack

Incorporating Core Supplements

Take 400 mg of SAMe thrice a day (i.e., 1,200 mg/day), with or without food.

If you have an MTHFR gene mutation, replace the SAMe by 7.5–15 mg of L-methylfolate once a day and 1,500–2,000 mg of TMG twice or thrice a day (i.e., 3–6 g/day). TMG can be consumed as a powder or simply through foods, notably wheat bran (1,339 mg of TMG per 100 g), spinach (600–645 mg of TMG per 100 g), and beetroot (114–297 mg of TMG per 100 g).

Figure 4: Getting enough trimethylglycine through foods



Incorporating Options

For people with a fatty liver

In addition to the core supplements, take 4.5–8 g of spirulina per day, with or without food.

For people with hepatitis C

In addition to the core supplements, take 1.5–8 g spirulina per day, with or without food. Before bed, take TUDCA (500–1,750 mg) without food.

For people with cholesterol-rich non-calcified gallstones in their liver

In addition to the core supplements, take 500–1,750 mg TUDCA before bed, without food.

For people who regularly drink or take acetaminophen

The following protocols can help your liver process reasonable amounts of alcohol or acetaminophen, but ***they won't save you in case of abuse of either substance.***

Twice a day, in addition to the core supplements, take 140 mg of silymarin (i.e., 280 mg/day) and 400 mg of NAC (i.e., 800 mg/day).

Silymarin may reduce the efficacy of oral contraceptives. If you take or might take an oral contraceptive, replace the above protocol by this one:

Thrice a day, in addition to the core supplements, take 4 mg of picroliv per kilogram of body weight (i.e., 12 mg/kg/day) and 400 mg of NAC (i.e., 1,200 mg/day).

If you are prone to nausea, take your NAC with food.

FAQ

Can I add to my stack a supplement not covered in this guide?

Supplement your current stack for a few weeks before attempting any change. Talk to your doctor and research each potential new addition in advance. Check for known negative interactions with other supplements in your current stack, but also for synergies. If two supplements are synergistic or additive in their effects, you might want to use lower doses for each.

Can I modify the recommended doses?

If a supplement has a recommended dosage range, stay within that range. If a supplement has a precise recommended dose, stay within 10% of that dose. Taking more than recommended could be counterproductive or even dangerous.

Should I take my supplements with or without food? And at what time?

Answers are provided in each supplement entry whenever the evidence permits. Too often, however, the evidence is either mixed or absent. Besides, a supplement's digestion, absorption, and metabolism can be affected differently by different foods. Fat-soluble vitamins (A, D, E, K), for instance, are better absorbed with a small meal containing fat than with a large meal containing little to no fat.

Starting with half the regular dose can help minimize the harm a supplement may cause when taken during the day (e.g., tiredness) or in the evening (e.g., insomnia).

Why take NAC to make glutathione? Why not take glutathione directly?

Oral glutathione gets digested into its constituent amino acids: cysteine, glycine, and glutamic acid. Of those three, cysteine is the rate-limiting factor in endogenous glutathione production. Oral N-Acetylcysteine (NAC) is simply a more efficient (and cheaper) way of providing your body with cysteine. Multiple studies have reported greater increases in circulating glutathione from oral NAC than from (an equal dose of) oral glutathione.

I don't have any liver problem, can I still supplement for general liver health?

A supplement will not make a liver that is neither damaged nor diseased "even healthier". If you are into preventive supplementation, just take this guide's core supplement (SAMe).

Precautions and Troubleshooting

Stack components are seldom studied together. The safest way to add supplements to your daily routine is one at a time, at least a couple of weeks apart, to better assess the effects (and side effects) of each new addition. Start at half the regular dose for a week, then slowly increase to the regular dose if you are not experiencing the desired effects.

Since minerals and vitamins (especially the fat-soluble vitamins: A, D, E, and K) can accumulate in the body, it is best to consider supplementation only after a dietary evaluation. Track what you eat for a week; if, on average, you are getting less than 80% of your Recommended Dietary Allowance or Adequate Intake, supplementation becomes an option, though first you should try eating more foods rich in the desired vitamin or mineral.