Examine® Liver Health Supplement Guide

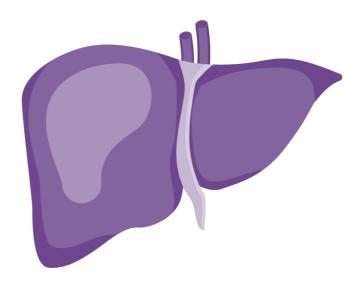


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Introduction

The liver participates in so many vital processes that its nickname should be the Swiss Army organ. It doesn't receive as much attention as other organs, because <u>cardiovascular disease</u>, cancer, and various other diseases are more likely <u>causes</u> of <u>death</u> than <u>liver disease</u>, but if the liver isn't functioning well, the effects can be felt throughout the body.

Perhaps a more specific analogy for the liver would be a factory: it is responsible for the production, breakdown, transport, and storage of a wide variety of chemicals, acting as the central hub for many of the components of metabolism.

Liver function basics

So what specifically does the liver do?

First, it continuously takes a large amount of <u>blood glucose</u> (i.e., blood sugar) from the bloodstream, stores it as glycogen, and then converts it back to glucose, releasing it as needed. If the body needs more glucose and the liver is low on glycogen, it turns individual amino acids into glucose in a process called gluconeogenesis. Additionally, because glucose is the body's main monosaccharide, other ones — namely, <u>fructose</u> and galactose — are converted to glucose, and this happens primarily in the liver. —

Depiction of glycogen

MONOSACCHARIDE

DISACCHARIDE

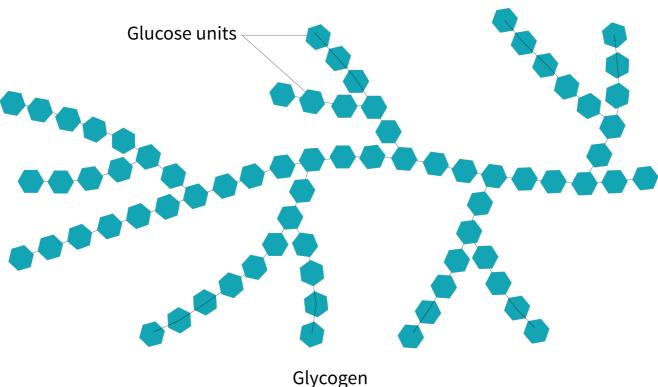




Glucose

Sucrose, a.k.a. table sugar (Glucose + Fructose)

POLYSACCHARIDE



When food intake provides an excess of energy, the liver converts more carbohydrates into fatty acids, takes fatty acids from the bloodstream, and either uses them, stores them, or packages them to be circulated once again. Under conditions of starvation or very low intake of carbohydrates, it's the liver that creates ketone bodies from fatty acids.

Besides its role in the metabolism of the body's main energy sources, the number of important molecules that the liver synthesizes is too long to list, but it includes albumin, cholesterol, uric acid, bile acids, growth factors, and proteins involved in the inflammatory response, among many others.[2]

The liver is also pivotal for the detoxification of xenobiotics (substances foreign to the body) and transforming them into more benign and excretable forms.[3] These include pharmaceutical drugs, environmental toxins, alcohol, bacterial by-products, and more — things you definitely don't want building up in your system.

There is widespread misunderstanding about detoxification in the body. Products, protocols, and diets claim to remove toxins from the body with no real evidence or understanding of how detoxification works. On the other hand, some of the backlash to detoxing makes it sound like all you need are a functioning liver and kidneys to deal with toxins optimally. However, nutrients are needed to support optimal functioning of

the liver and its detoxification enzymes. This makes some "detox" supplements plausible, but they usually lack rigorous research.[4]

Anyone who looks into the nutritional information of liver will immediately notice something: it stores huge amounts of <u>vitamin A</u>, <u>copper</u>, and <u>vitamin B12</u>. These, along with many other nutrients and compounds, are stored in the liver and released as needed. So with the liver storing, transporting, detoxifying, and synthesizing so many things, it's clear that it's intimately linked to the rest of the body, and a healthy liver is essential to overall health.

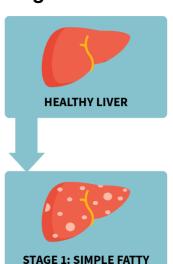
When liver function goes wrong

There are numerous diseases that can affect the liver, but many of them are beyond the scope of this guide; here, we're focused mainly on those that are influenced by diet and lifestyle and are particularly common: *nonalcoholic fatty liver disease* (NAFLD) and more advanced manifestations, such as *nonalcoholic steatohepatitis* (NASH) and cirrhosis. NAFLD is estimated to affect roughly 25% of adults in the US and Europe, making it especially worth our attention.^[8]

Fatty liver disease

Fatty liver disease is generally defined by steatosis, an accumulation of excess fat in the liver; lesions, such as fibrosis, where connective tissue replaces normal tissue; ballooning; excessive accumulation of various compounds; and inflammation, causing permanent scarring and cirrhosis when damage has progressed enough that the liver loses function.[9]

Progression of non-alcoholic fatty liver disease (NAFLD)



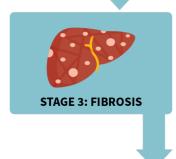
• Normal, functioning liver

- Excess fat builds up in the liver cells but is considered harmless.
- There are usually no symptoms, and you may not even realize you have it until you get an abnormal blood test result.



LIVER (STEATOSIS)

- NASH is a more aggressive form of the condition in which the liver has become inflamed.
- Inflammation is the body's healing response to damage or injury and, in this case, a sign that liver cells have been damaged.



- Some people with NASH develop fibrosis, which is characterized by persistent inflammation in the liver, resulting in the generation of fibrous scar tissue around the liver cells and blood vessels.
- This fibrous tissue replaces some of the healthy liver tissue, but there is still enough healthy tissue for the liver to function normally.



- At this most severe stage, bands of scar tissue and clumps of liver cells develop.
- The liver shrinks and becomes lumpy. This is known as cirrhosis.

When a major cause of this is excessive alcohol consumption, it's called *alcoholic fatty liver disease* (AFLD), and when alcohol abuse isn't present, it's *nonalcoholic fatty liver disease* (NAFLD). While they share some similarities, they are not the same condition. AFLD tends to be more severe and have more diverse pathological features.

NAFLD often goes hand in hand with <u>metabolic syndrome</u> and type 2 diabetes. Likely causes include overeating and subsequent obesity; lack of physical activity; smoking; and the metabolic impairments and inflammation that follow. What's worse, because the liver is so important to the metabolic health of the body, its impairment is likely to start a vicious cycle where worse liver function leads to worse metabolic function and vice versa.

[11]

Fatty liver and diabetes

Many molecular mechanisms are involved in the vicious circle linking fatty liver to diabetes and diabetes to progressive liver injury.

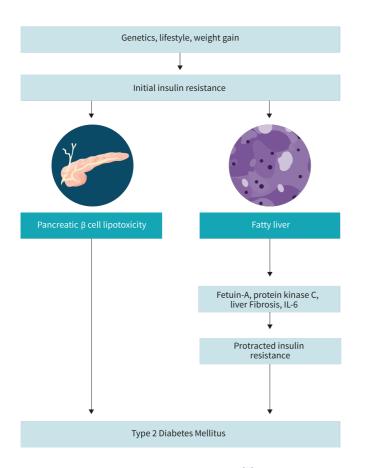
On the left portion of the below image is the first part of the journey, leading from initial insulin resistance to fatty liver and eventually to the development of type 2 diabetes (T2D) in those predisposed individuals in whom pancreatic lipotoxicity occurs.

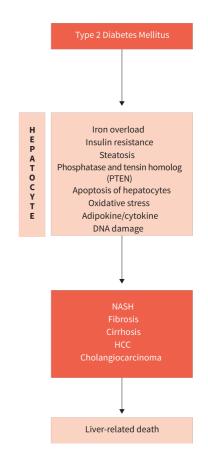
On the right is the mechanism which – triggered by long-lasting/decompensated T2D – may be conducive to progressive liver disease including primary liver cancer in predisposed individuals.

The vicious circle of fatty liver and diabetes

FROM FATTY LIVER TO DIABETES

FROM DIABETES TO PROGRESSIVE LIVER INJURY VIA DISREPAIR





Adapted from Loria et al. Hepatol Res. 2013.[11]

HCC, hepatocellular carcinoma; IL, interleukin; NASH, non-alcoholic steatohepatitis; PTEN, phosphatase and tensin homolog; T2D, type 2 diabetes.

Assessing liver health

The most common way to assess liver injury is through liver enzyme tests, mainly alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), γ -glutamyl transferase (GGT), and a handful of others. These enzymes participate in the metabolism of amino acids, among other functions, and tend to be elevated in the bloodstream when liver cells are injured. However, they can be present in the muscles and other organs, be elevated in other diseases, and sometimes rise due to factors other than liver

damage.

ALT is more prevalent in the liver than AST, and adding in GGT and other markers can help paint a clearer picture. There are newer biomarkers based on mitochondrial damage, cell death, DNA damage, inflammation, and more, but the vast majority of liver damage in short-term trials continues to be evaluated mainly by the aminotransferase tests. When it comes to fatty liver disease and its progression, ultrasound and biopsies that measure the amount of steatosis, fibrosis, and other markers are commonly used, and researchers have come up with grading schemes based on them. [13][14]

Other ways to measure liver health include approximating its function by using markers that would be altered if the liver weren't performing its functions properly. Common tests that do this are bilirubin, albumin, ceruloplasmin, and the ability to produce blood-clotting factors. Various other tests are being added all the time.

Liver health: where supplements fit in

In this guide, we have assembled a list of several promising supplements for the general defense of the liver. Their mechanisms differ, but a common theme is increasing the levels of endogenous antioxidants the body produces and regulating inflammation to protect the liver when it's under stress from toxins, pollutants, infection, and metabolic dysfunction.

Beyond what we have included in this guide, the lifestyle modifications generally associated with metabolic and cardiovascular health apply to the liver as well: weight loss, a highly nutritious diet, and exercise can be considered the basis of liver health, with supplements potentially adding an extra boost. [17]

Wyatt Brown, Researcher

Combos

Core Combo

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

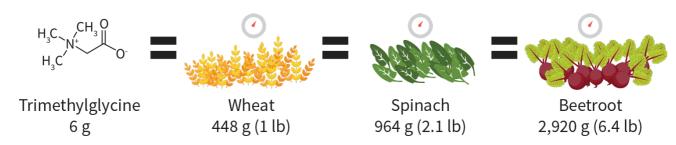
If you have an MTHFR gene mutation, replace the SAMe by 7.5–15 mg of <u>L-methylfolate</u> once a day and 1,500–2,000 mg of <u>TMG</u> twice or thrice a day (i.e., 3–6 g/day). TMG can be consumed as a powder or simply through foods, notably wheat bran (1,339 mg of TMG per 100 g), spinach (600–645 mg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

Getting enough trimethylglycine through foods

LOW DAILY DOSE



HIGH DAILY DOSE



Tip: Try one combo alone for a few weeks

Taking too many supplements at once may prevent you from determining which ones are truly working. Start with just one of the combos suggested here for a couple of weeks before you consider making any modification, such as adding another supplement, altering a supplements dosage, or incorporating the supplements from an additional combo.

When adding another supplement to your regimen, be methodical. For example, you may wish to take all the supplements from two combos. Select the combo that you wish to try first and take this for a couple of weeks. Then, add one supplement from the second combo and wait another week to see how it affects you. Continue this process until you've added all the supplements you wish to.

If a supplement appears in two combos you wish to combine, don't stack the doses; instead, combine the ranges. For instance, if the range is 2–4 mg in one combo and 3–6 mg in the other, your new range becomes 2–6 mg. Always start with the lower end of the range — especially in this case, since the reason why one of the ranges has a lower ceiling in one combo may be due to a synergy with another supplement in the same combo. Reading through the full supplement entry may help you decide which dose to aim for, but if you're not sure, lower is usually safer.

Specialized Combos

For people with a fatty liver

Take 4.5–8 g of <u>spirulina</u> per day, with or without food. Additionally, drink 1–4 cups (1 cup = 177–237 mL / 6–8 oz) per day of regular, half-caffeinated, or decaffeinated coffee.

For people with hepatitis C

Take 1.5–8 g of <u>spirulina</u> per day, with or without food. Additionally, drink 1–4 cups (1 cup = 177–237 mL / 6–8 oz) per day of regular, half-caffeinated, or decaffeinated coffee. Before bed, take <u>TUDCA</u> (500–1,750 mg) without food.

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

Take 500–1,750 mg of 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, 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, take 4 mg of <u>picroliv</u> per kilogram of body weight (i.e., 12 mg/kg/day) and 400 mg of <u>NAC</u> (i.e., 1,200 mg/day).

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

Primary Supplements

S-Adenosyl-Methionine (SAMe)

What makes SAMe a core supplement

S-adenosylmethionine (SAMe) works with enzymes in a process called <u>methylation</u>: 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 <u>liver disease</u>, 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 <u>cholestasis</u>, alcoholic liver disease, and possibly even *nonalcoholic fatty liver disease* (NAFLD).

Preliminary evidence suggests that ingesting <u>choline</u> or its derivative <u>trimethylglycine</u> (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 SAMe

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 <u>foods rich in choline</u> before you consider taking 250–500 mg of *choline bitartrate* once a day with food.

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

Adequate Intake (AI) for choline (mg)

AGE	MALE	FEMALE	PREGNANT	LACTATING
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AGE	MALE	FEMALE	PREGNANT	LACTATING
0–6 months	125	125	_	_
7–12 months	150	150	_	_
1–3 years	200	200	_	_
4-8 years	250	250	_	_
9–13 years	375	375	_	_
14-18 years	550	400	450	550
>18 years	550	425	450	550

Reference: Institute of Medicine. Choline (chapter 12 in Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6 , Folate, Vitamin B_{12} , Pantothenic Acid, Biotin, and Choline. The National Academies Press. 1998.) [18]

Tip: Why don't you recommend brands or specific products?

For two reasons:

- We don't test physical products. What our researchers do all day, every day is analyze
 peer-reviewed studies on supplements and nutrition.
- We go to great lengths to protect our integrity. As you've probably noticed, we don't sell
 supplements, or even show ads from supplement companies, even though either option
 would generate a lot more money than our Supplement Guides ever will and for a lot less
 work, too.

If we recommended any brands or specific products, our integrity would be called into question, so ... we can't do it. That being said, in the interest of keeping you safe, we drew <u>a short list of steps</u> <u>you should take</u> if a product has caught your interest.

Secondary Supplements

Milk Thistle

What makes milk thistle 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., <u>alcohol</u> or <u>some medications</u>) are not likely to benefit from milk thistle.

High doses of silymarin (420–600 mg) have shown efficacy against death cap mushroom poisoning (*Amanita phalloides*); 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 means take some silymarin ... *after* you've called emergency services, or on your way to the hospital!

Silymarin may lower the effectiveness of oral contraceptives.

Milk thistle vs. the death cap



The Amanita phalloides, also known as death cap, is a lethal mushroom.

The lethal dose is 0.1 mg of death cap per kilogram of body weight (0.045 mg/lb).





Symptoms include vomiting, diarrhea, and liver dysfunction.

The death cap's main toxin, α-amanitin, prevents DNA from creating new proteins.





The silymarin in milk thistle can help your body get rid of α-amanitin.

How to take milk thistle

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.

N-Acetylcysteine (NAC)

What makes NAC 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 *nonalcoholic fatty liver disease* (NAFLD).

High NAC doses are used acutely in cases of toxin-induced liver damage, particularly when caused by an overdose of <u>acetaminophen</u> (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 <u>nausea</u> and vomiting, but much lower doses can be taken daily to support glutathione levels and thus, indirectly, the liver.

How to take NAC

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

Tauroursodeoxycholic Acid (TUDCA)

What makes TUDCA 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 <u>apoptosis</u> (i.e., programmed cell death).

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

TUDCA supplementation can help prevent endoplasmic reticulum stress in your cells 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 <u>gallstone</u> formation and even dissolve cholesterol-rich non-calcified gallstones. It cannot, however, dissolve gallstones rich in <u>bilirubin</u> or in <u>calcium</u> and other minerals.

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

How to take TUDCA

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

Promising Supplements

Coffee

What makes coffee a secondary option

Coffee is a <u>wildly popular drink worldwide</u> that may also have some health benefits for the liver. This caffeinated beverage contains a mix of anti-inflammatory and bioactive antioxidant compounds that are thought to be responsible for these benefits. [19][20][21]

Numerous prospective observational studies, a handful of case–control studies, and one RCT have seen people who consume coffee regularly to have decreased odds for *nonalcoholic fatty liver disease* (NAFLD), liver fibrosis, liver cirrhosis, complications from chronic hepatitis C, and liver cancer compared to those who drink coffee infrequently or not at all. [22][23][24][25][26][27][28][29][30][31][32][33] Additional associations have been seen between coffee consumption and improvement in liver enzyme profiles (ALT, AST, and GGT). [34]

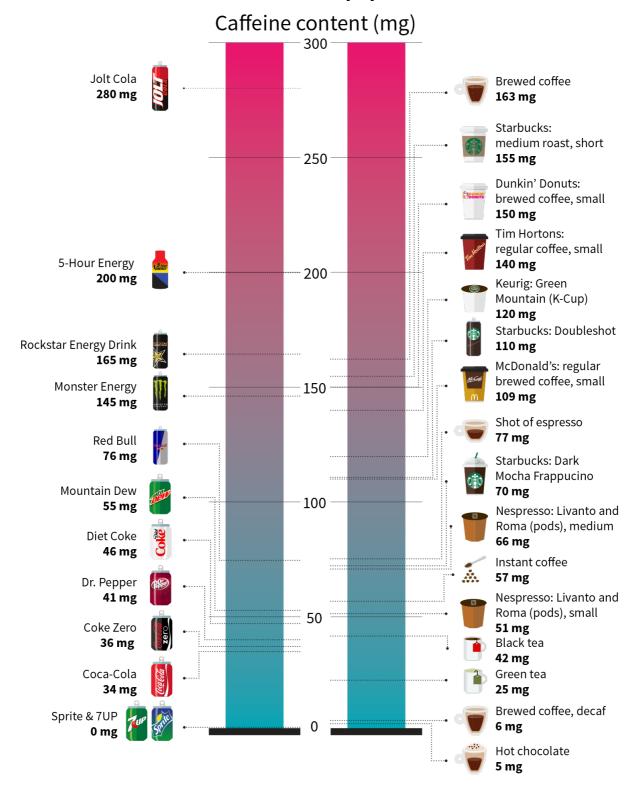
You can experience caffeine *dependence* when you become *tolerant* to some of its effects. When tolerance occurs, and you stop consuming caffeine, you can experience symptoms of <u>withdrawal</u>, such as <u>fatigue</u>, <u>irritability</u>, <u>headaches</u>, and — ironically — sleeplessness.

Caffeine also interacts dangerously with <u>several pharmaceuticals</u>, notably <u>tizanidine</u> and a type of antidepressant called *monoamine oxidase inhibitors* (<u>MAOIs</u>). It can also interfere with glucose metabolism, raise <u>blood pressure</u>, raise <u>heart rate</u>, and increase urination (though the effect is usually mild), but those four effects fade away as your tolerance to caffeine develops.

Caffeine can also decrease blood lithium levels. Suddenly eliminating all caffeine from your diet may cause your lithium levels to rise. If you are on <u>lithium medication</u>, keep your day-to-day caffeine intake roughly the same. [35] If you wish to stop taking caffeine, talk with your physician about slowly weaning yourself from it.

You might already be consuming more caffeine than you think. When you calculate your daily intake, consider all your <u>beverages</u>, foods, and supplements (pre-workouts and energy boosters, particularly). Bear in mind that caffeine can be "hidden" in a product — for instance, if you read "<u>guarana seeds</u>" on a label, remember that those are richer in caffeine than coffee seeds.

Caffeine content of popular drinks



References: McCusker et al. J Anal Toxicol. 2006. [36] ● Desbrow et al. Nutr Health. 2019. [37] ● Ludwig et al. Food Funct. 2014. [38]

● Fox et al. *J Agric Food Chem.* 2013.[39] ● McCusker et al. *J Anal Toxicol.* 2003.[40] ● Angeloni et al. *Food Res Int.* 2019.[41]

How to take coffee

Drink 1–4 cups a day of regular, half-caffeinated (half-caf), or decaffeinated coffee (decaf). The definition of what a "cup" of coffee constitutes varies from study to study. Generally speaking, one cup is 177–237 mL (6–8 oz) so your total daily intake should be between 177–946 mL (6–32 oz).

The liver benefits of coffee appear to be additive, with 1-2 cups providing better outcomes than <1, and 3-

4 cups outperforming 1–2. More than 4 cups a day may also provide additional benefits but, should you choose to consume >4 cups/day, be mindful of your overall caffeine intake. After your 4th cup of caffeinated coffee, switching to decaf is advisable to keep your daily caffeine intake at safe levels.

Removing caffeine from coffee changes its composition little. [42] Yet, <u>caffeine</u> itself may play a role in coffee's beneficial liver effects. [43][20][44] It is plausible that decaffeinated coffee might have less potent effects on liver health, but this hypothesis does not have much research looking into it. [31]

If you consume caffeinated coffee, monitor your overall caffeine intake to ensure you're not <u>consuming</u> <u>unsafe levels</u>.

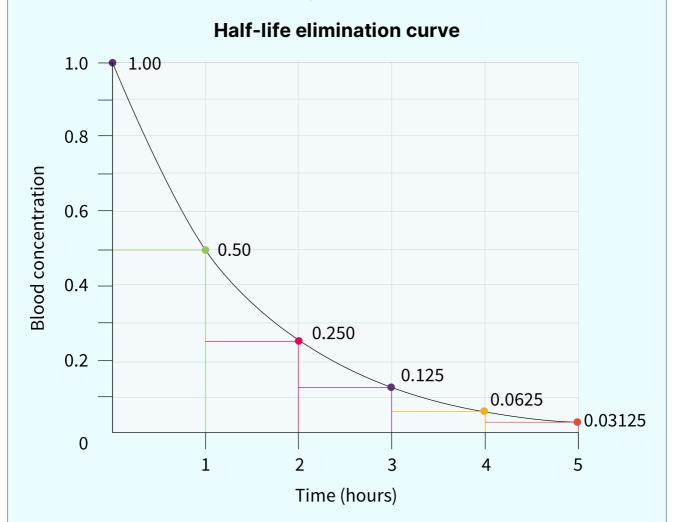
- For *healthy adults*, caffeine intakes up to 400 mg/day don't raise any general health concerns. [45][46][47] While you *can* consume more, 400 mg is how much caffeine most healthy people can regularly consume in a day without suffering lasting harm.
- If you are *pregnant or breastfeeding*, the scientific evidence differs on what constitutes a safe upper intake: either 200 or 300 mg of caffeine per day. [45][47][48][49][50] The clinical evidence being scarce, it is advisable to keep consumption on the lower side of these recommendations.
- If you have *cardiovascular health concerns*, the long-term implications of regular caffeine intake are less clear low to moderate intakes could be safe, but consult your physician first. [48][51]

Caffeine can disrupt sleep when consumed in the evening, or even in the afternoon; even if it does not prevent you from falling asleep, caffeine will impair the *quality* of your sleep. In healthy adults, the average <u>half-life</u> of caffeine falls between 5 and 6 hours, but this number can vary greatly between individuals, from 1.5 to 9.5 hours, because of genetics and other factors — heavy smoking can double the rate of caffeine metabolism, pregnancy can halve it, [52] etc. [53]

Q Digging Deeper: What is "half-life"

In its simplest definition, <u>half-life</u> is the time it takes for a compound to reach half of its initial concentration in the blood. For example, say you consume one cup of coffee that contains 200 milligrams of caffeine. In 5–6 hours, the caffeine concentration in your blood should drop to 100 milligrams, on average.

Below is an example of a half-life elimination curve. For the hypothetical compound being measured, it has a half-life elimination rate of 1 hour. This means that for every hour that goes by its concentration in the bloodstream is reduced by 50%.



Adapted from. Hallare et al. StatPearls. 2020. [54]

Picrorhiza Kurroa

What makes *Picrorhiza kurroa* 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 (<u>Amanita phalloides</u>). Milk thistle, however, is backed by more 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 Picrorhiza kurroa

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.

Daily	Picrorhiza	kurroa	intake	bv	bod	vweiaht

POUNDS	KILOGRAMS	PER DOSE (mg)	TOTAL INTAKE (mg)
100	45	180	540
125	57	230	685
150	68	270	815
175	79	315	950
200	91	365	1,090
225	102	400	1,225
250	113	450	1,355
275	125	500	1,500

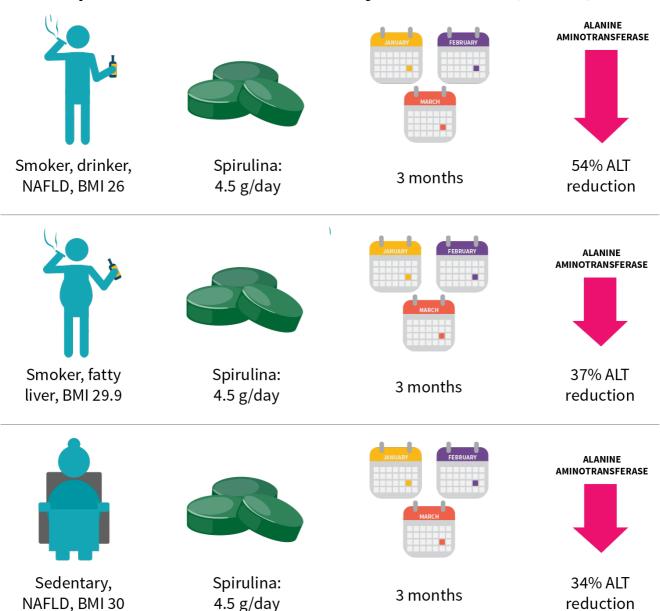
Spirulina

What makes spirulina 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 <u>Gilbert's Syndrome</u>, 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 <u>hepatitis C</u> and *nonalcoholic fatty liver disease* (<u>NAFLD</u>).

Spirulina vs. _non-alcoholic fatty liver disease_ (NAFLD)



Reference: Ferreira-Hermosillo et al. J Med Case Rep. 2010. [55]

How to take spirulina

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.

Unproven Supplements

Of the supplements we have reviewed, none currently fit the above description.

Inadvisable Supplements

Alcohol

The amount of alcohol to consume for optimal liver health is likely close to none (or in more translatable terms, drinking very infrequently). Yet, many people enjoy having a drink, so it's important to understand how to do so in a way that minimizes potentially harmful effects.

There are two important factors to consider when it comes to alcohol intake: amount and time.

- 1. A moderate drinking amount is considered up to 1 drink per day for females and up to 2 drinks per day for males. For reference, 1 drink is typically 355 mL (12 oz) of 5% alcohol beer, 150 mL (5 oz) of 12.5% wine, or 45 mL (1.5 oz) of drinks with a higher (≥30%) alcohol content.
- Spreading your alcohol intake over a longer period of time will be less taxing to your liver.
 Consuming 2 drinks in under 30 minutes will be more harmful compared to consuming the same amount over an hour or two.

As a general rule of thumb, if you wake up with a hangover you've almost certainly drank too much alcohol.

FAQ

Q. What about the supplements not covered in this guide?

Our guides are regularly updated, often with new supplements. We prioritize assessing (and reassessing) the most popular of them and those most likely to work. However, if there is a specific supplement you'd like to see covered in a future update, please let us know by <u>filling out this survey</u>.

Q. Can I add a supplement not covered in this guide to my combo?

Supplement with your current combo for a few weeks before attempting any change. Talk to your physician and <u>research each potential addition</u>. Check for known negative interactions with other supplements and pharmaceuticals in your current combo, but also for synergies. If two supplements are synergistic or additive in their effects, you might want to use lower doses of each.

Q. Can I modify the recommended doses?

If a supplement has a recommended dose 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. Taking less could render the supplement ineffective, yet starting with half the regular dose could be prudent — especially if you know you tend to react strongly to supplements or pharmaceuticals.

Q. At what time should I take my supplements?

The answer is provided in the "How to take" section of a supplement entry whenever the evidence permits. Too often, however, the evidence is either mixed or absent. Starting with half the regular dose can help minimize the harm a supplement may cause when taken during the day (e.g., <u>fatigue</u>) or in the evening (e.g., <u>insomnia</u>).

Q. Should I take my supplements with or without food?

The answer is provided in the "How to take" section of a 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 (\underline{A} , \underline{D} , \underline{E} , \underline{K}), for instance, are better absorbed with a small meal containing fat than with a large meal containing little to no fat.

Q. What are DRI, RDA, AI, and UL?

The <u>Dietary Reference Intakes</u> (DRIs) is a system of nutrition recommendations designed by the Institute of Medicine (a US institution now known as the <u>Health and Medicine Division</u>). RDA, AI, and UL are part of this system.

- Contrary to what the name suggests, a Recommended Dietary Allowance (RDA) doesn't represent
 an ideal amount; it represents the minimum you need in order to avoid deficiency-related health
 issues. More precisely, it represents an amount just large enough to meet the minimum requirements
 of 97.5% of healthy males and females over all ages which implies that the RDA is too low for
 2.5% of healthy people.
- The Adequate Intake (AI) is like the RDA, except that the number is more uncertain.
- The Tolerable Upper Intake Level (UL) is the maximum safe amount. More precisely, it is the
 maximum daily amount deemed to be safe for 97.5% of healthy males and females over all ages —
 which implies that the UL is too high for 2.5% of healthy people.

As a general rule, a healthy diet should include at least the RDA of each nutrient — but less than this nutrient's UL. This rule has many exceptions, though. For instance, people who sweat more need more salt (i.e., sodium), whereas people who take <u>metformin</u> (a diabetes medicine) need more <u>vitamin B12</u>.

Moreover, the DRIs are based on the median weight of <u>adults</u> and <u>children</u> in the United States. Everything else being equal (notably age, sex, and percentage of body fat), you likely need a lesser amount of nutrients if you weigh less, and vice versa if you weigh more. The numbers, however, are not proportional — if only because the brains of two people of very different weights have very similar needs. So you can't just double your RDIs for each nutrient if you weigh twice as much as the median adult of your age and sex (even if we overlook that people weighing the same can differ in many respects, notably body fat).

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

Oral <u>glutathione</u> gets digested into its constituent amino acids: cysteine, <u>glycine</u>, and glutamic acid. Of those three, cysteine is the rate-limiting factor in endogenous glutathione production. Oral N-Acetylcysteine (<u>NAC</u>) 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.

Q. I don't have any liver problems, 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 <u>core supplement</u> (<u>SAMe</u>).

Q. A lot of spirulina is farm-grown and

harvested. How do I know it is safe?

Spirulina is considered a food grade product and is generally <u>rigorously tested</u>. For example, it undergoes microbiological and chemical composition tests as well as tests for contaminants like heavy metals, pesticides, and extraneous materials.

That being said, here's a list of steps you can take to find a high quality spirulina supplement.

Q. What are some of the dietary recommendations for people with NAFLD?

Since there are no approved medicines to treat *nonalcoholic fatty liver disease* (NAFLD), lifestyle and dietary recommendations are the staple. Recommendations include: [57]

- Reducing bodyweight by 7–10%
- Reducing saturated fat to less than 7% of total calories
- Minimizing trans fat intake
- Minimizing sugar intake
- Maintaining cholesterol intake below 200 milligrams per day
- Keeping fat intake to 25-35% of caloric intake

A simpler guideline is to follow a Mediterranean-type diet with emphasis on legumes, fruits, vegetables, fish, nuts, whole grains, with or without caloric restriction. [58]

Q. What about detox diets and cleanses?

Despite their popularity, "<u>detox diets</u>" are not backed by the evidence, nor are they even based on scientifically sound principles.

While your body can accumulate toxicants, detox diets aren't supported by toxicological mechanisms or trial evidence, and they can occasionally be dangerous. Your liver, lungs, kidneys, and other organs work nonstop to "detoxify" you; a diet rich in protein, vegetables, and fruits will provide them with the nutrients they need to properly function.

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