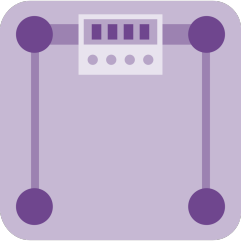


**Fat Loss Supplement Guide **

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**Introduction**

As a graduate student, I pooh-poohed the posers who flaunted “sub-10% body fat” unconfirmed by DXA or at least hydrostatic weighing. How ignorant they were, whereas I — being quantified and verified — was so much better than them. (No matter how balanced I seemed on the outside, inwardly I was a bit of a jerk.)

| **Digging deeper: DXA**  DXA scans (dual-energy X-ray absorptiometry scans, aka DEXA scans) are one of the more accurate ways to estimate changes in lean mass, fat mass, and bone density. When you get a DXA scan, you lie down on a bed while a robotic arm moves up and down the length of your body, emitting very low-level X-rays and measuring how much radiation gets absorbed.  A DXA scan is fairly quick (usually 3–10 minutes), and it delivers measurements that are, on average, within 3 percentage points of those you’d obtain from the 4-component method — a more accurate but impractical, time-consuming, and expensive method restricted to scientific and medical studies.[1][2] This means that if your body-fat percentage is 20% as measured by the 4-component method, a DXA scan should report a number between 17% and 23% (on average; individual variations can reach 8 percentage points, which would give results between 12% and 28%).  Originally, DXA scans were used to measure bone density for detecting (or tracking the development of) bone thinning or weakening (i.e., osteoporosis). Modern DXA machines can use equations to estimate body fat and lean mass. This means that modern DXA is a “3-component method”: it gives readings for fat, lean soft tissue, and bone mineral. Note that what many studies report as “lean mass” from a DXA scan is more often “lean soft tissue” mass, i.e., the lean mass minus the bone mass. |
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As part of my quest for the lowest BF%, I took all the fat loss supplements — nearly literally all of them. Having read a few studies selected by the supplements’ manufacturers, I believed myself to be the repository of fat-loss secrets unknown to the crowd.

Then I took years of biostatistics and epidemiology, and I realized that most of the studies I’d trusted were of extremely poor quality. Years later, when I first worked with patients in an obesity clinic, I started to record on their intake forms the very same supplements I’d been taking. It makes sense…who wouldn’t want a quick fix if at all possible?

Everyone wants quick fixes, whether it’s a client at an obesity clinic who is trying to shed a hundred pounds or a gym rat trying to hit a BF% goal. Some gym rats who don’t carry too much fat are easily convinced that they do and thus suffer from poor body image and tarnished self-esteem. But they’ll never admit it, even if they’re secretly jealous of their friend’s intricate arm veins.

These same insecurities plague those of us who don’t aim for a freaky-low BF% but just want to be “toned”. When we see bodybuilders or even health models on the covers of magazines, we can’t help imagining them looking shredded year round, even when we know they can’t be. And by the way, my fellow humans, even if you do manage to bring your BF% down to the same level as a bodybuilder’s on contest day, you still won’t look as cut unless you dehydrate yourself until your skin is paper-thin (which, need I mention it,

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isn’t healthy).

| **Caution: Female BF% vs. male BF%**  The average woman carries a lot more body fat than the average man, and women’s essential body fat is also a lot higher (10% vs. 3%) than men’s. A man with 5% body fat can be ripped. A woman with 5% body fat is dead.  In short, women shouldn’t compare their BF% to that of their male friends. That said, it can be fun to compare the BF% of men with that of women for the same body-composition category, and you can do that by comparing this graph to that one. |
| --- |

So what does it all mean? Well, it means that you need to ask yourself the right questions, to begin with. In this case, the first question isn’t “How do I lose fat?” — that isn’t even the second question. The first question is “How much fat do I carry?”, the second is “What’s my fat goal?”, and finally, the third is “How do I get there?” (which usually translates to “How do I lose fat?”).

**How much fat do I carry?**

Scales (the normal kind) can’t answer that question. They can tell you how much you weigh, but not how much of that weight is fat, how much is muscle, and how much is water.

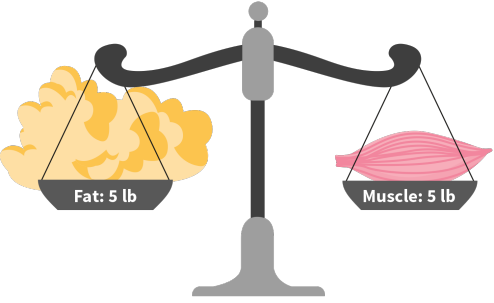
| **Digging Deeper: Mass vs. weight**  Mass: A measure of how much matter is in an object. Unlike its weight, the mass of an object is constant. If an object’s mass is 1 gram on Earth, its mass is 1 gram on the Moon.  Weight: An object’s relative mass. Unlike mass proper, weight is affected by gravity — it will be different on Earth and on the Moon, and it can even vary on Earth (a given object is slightly heavier at sea level than at the top of a mountain and at the poles than at the equator).  For our purpose, mass and weight are pretty much interchangeable. It just happens that “weight” is commonly appended to some nouns (e.g., body, water) and “mass” to others (e.g., fat, muscle). So we use “body weight” and “water weight” but “fat mass” and “muscle mass”. |
| --- |

Scales can mislead you in several ways. People who start an exercise program to shed fat often despair when their scales show that they’re gaining weight, but don’t forget that weight gain doesn’t equal fat gain — when you exercise, you build muscle. Similarly, don’t forget that weight loss doesn’t equal fat loss. In fact, most of the weight lost during a short detox diet is water, not fat, and that weight is quickly regained.

Note that if you lose as much fat mass as you gain muscle mass, you become leaner because fat is more voluminous than muscle for the same mass.

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**Fat vs. muscle**

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Because scales are so widespread, they are commonly used to estimate one’s “fitness level” — you [calculate your BMI by dividing your body weight in kilograms by your height in meters squared (kg/m2). Overweightness starts at a BMI of 25 and obesity at 30.

However, as the name implies (BMI stands for body mass index), this “measure of body fat based on height and weight” uses total body mass, not body fat mass. And because BMI was designed for use in sedentary people, it routinely classifies athletes — who, as a rule, carry more muscle than people who don’t exercise — as “overweight”.

BMI Classification

| **CATEGORY** | **BMI\*** | **BMI FOR ASIAN AND SOUTH ASIAN POPULATIONS** |
| --- | --- | --- |
| Severely underweight | <16.5 |  |
| Underweight | 16.5–18.4 | <18.5 |
| Normal weight | 18.5–24.9 | 18.5–22.9 |
| Overweight | 25–29.9 | 23–27.5 |
| Obesity | ≥30 | >27.5 |
| – Obesity class I | 30–34.9 |  |
| – Obesity class II | 30–34.9 |  |
| – Obesity class III | ≥40 |  |

\* kg/m2

Adapted from Weir and Jan. StatPearls. 2019.[3] ● WHO Expert Consultation. Lancet. 2004.[4]

Don’t throw away your measuring tape just yet, though. If you use it more, you can get a better idea of your body fat. For instance, whereas the BMI formula is based on just weight and height, the U.S. Navy formula

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also includes neck and abdomen/waist, plus hips for women.

And if you want to be really precise, you can take a dunk. Hydrostatic weighing, the old gold standard for determining body fat, has you weigh yourself on land and then again under water. This method is based on a simple fact: fat floats. Yet the method itself doesn’t qualify as simple — it requires some heavy, expensive equipment and thus is mostly used for research.

Dual energy X-ray absorptiometry (DXA) is commonly used to measure bone density, as we saw, but it’s also edging out hydrostatic weighing as the gold standard for determining body fat. DXA scans take just a few minutes, and although they used to be expensive and available only in medical facilities, now some health centers offer them for less than a hundred U.S. dollars.

| **Digging Deeper: Why do some people look more “ripped” than others?**  As the popularity of DXA scans increases, one question keeps coming back: why do some people look more ripped than others (of the same sex), even when their BF% isn’t lower?  There’s more than one possible reason.  When we look at other people, we tend to focus on the upper body — we look at a man’s forearms when he’s wearing rolled-up sleeves, at his upper arms when he’s wearing a T-shirt, at his abs when he’s stalking the beach. The quads and glutes are much bigger muscles, yet we’re much less likely to linger on them, especially when they’re clothed. And because people can differ substantially as to where they carry their fat (on their lower or upper body,[5] under their skin, or around their abdominal organs[6]~~)~~, they can also differ substantially in how ripped they look.  Another reason is water. The reason why bodybuilders have paper-thin skin when on stage isn’t just their very low BF%, they’re also dangerously dehydrated. Bodybuilders take diuretics and reduce their water intake in the days leading to a competition, as do many fitness models shortly before a photoshoot.  Finally, you can trick the eye. Darker skin makes you look more cut, which is why light-skinned bodybuilders slather themselves with sunless tanning lotion.[7]  They’ll also shed and shave their body hair, which would otherwise obscure their muscle lines. And on the other side of the lens, a photographer can play with angles, lights, and shadows to accentuate a bulge or deepen an interstice.  And of course, there’s Photoshop software. |
| --- |

All right, but chances are that your neighborhood still doesn’t have such a health center, and even if it does, a hundred bucks isn’t pocket change to most of us — getting regular scans to assess your progress can become expensive. So what method can be used at home?

One option is a BIA device, which uses bioelectrical impedance analysis to estimate body water, and from there, lean mass (aka fat-free mass), and from there, body fat. To obtain numbers in pounds or kilograms rather than in percentages requires the use of a scale, so most BIA devices also function as scales.

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In fact, most BIA devices look exactly like scales, with the current traveling through your bare feet, whereas in more expensive models, the current travels through your feet and hands. But even the professional models you’ll find in gyms aren’t overly trustworthy.

Too many factors can affect the result, starting with your hydration level — the less water you carry, the more fat your BIA device will think you have.[8]If you own such a device, use it only in the morning, after going to the toilet but before eating or exercising, because the result will also be skewed if you are still digesting[9] or have exercised within the past couple of hours.[10][11][12]

Another at-home option is body fat calipers. Calipers look like a pair of compasses and require that you (lightly) pinch your skin in several places; you can then use one of several formulae (the two most common are the Jackson and Pollock 3-site and 7-site formulae[13][14]~~)~~ to calculate your percentage of body fat and from there, your body fat in pounds (as long as you know your weight).

Don’t put too much stock in your first result, though; it can be off, especially if you currently carry too much fat.[15] The strength of calipers lies not so much in their providing an accurate number than in their accurately tracking changes in body composition.

In other words, as long as you pinch your skin at the same places in the same way, a caliper will tell you reliably if your percentage of body fat increases or decreases. (There are tricks that you can use to pinch your skin at the same places each time; you can, for instance, refer to personal landmarks such as belly button, moles, scars, etc.)

As it stands, a near-ideal “combo” would be to start with a DXA scan, measure your body fat with a caliper or BIA on that same day, compare the numbers, and then use the caliper or BIA at regular intervals (such as once per week) to track your trends.

**Tip: How to accurately measure body composition changes**

There are many factors that can affect your body composition measures. Take the following into account to help ensure you are getting the most accurate readings possible.

Various diets can influence body composition measures. For example, in the first week or so of a ketogenic diet, you will drop water weight and use up much of your glycogen. Because these changes can throw off the tools used to measure fat mass and lean mass (DXA, BIA, BOD POD®), it's best not to use pre-keto measurements as your baseline.

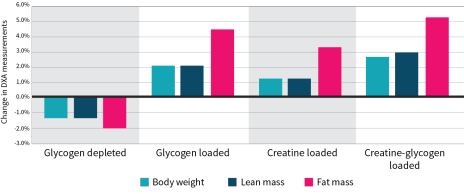
On the flip side, a high-carb diet could cause your glycogen stores to fill up and increase water weight. To help avoid erroneous measures caused by these shifts, wait 1–2 weeks for your body to adapt to your new diet. Then have measurements taken and use these as your baseline against which to compare future measurements.

This advice still applies if, instead of the tools listed above, you use calipers or calculations from limb measurements. It also applies if you decide to switch from a low-carb diet to a higher carb diet (or vice versa): eat your higher-carb diet for 2 weeks, then take new baseline measurements.

Another confounding factor you need to be aware of is creatine.[16] Like glycogen, creatine causes water retention and thus can mess up with your measurements. So if you want to be able to compare two measurements, use creatine consistently or not at all.

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**Different methods of body-water manipulation lead to different DXA readings**

****Reference: Bone et al. Med Sci Sports Exerc. 2017.[16]

Creatine is just one example of a general rule: to reduce potential sources of error, try to standardize the conditions under which measurements are taken.

Test at the same time of day (e.g., at 9 a.m.).

Test under the same feeding conditions (e.g., before breakfast).

Test under similar hydration statuses. Don’t be overhydrated or underhydrated. Empty your bladder. Don’t make any major dietary changes for 3 days before the test.

Don’t exercise for 24 hours before the test.

Don’t apply moisturizing lotions for 24 hours before the test.

Wear the same or similar clothing (or none, if practicable).

Use the same equipment, software/algorithm, technician, and body position.

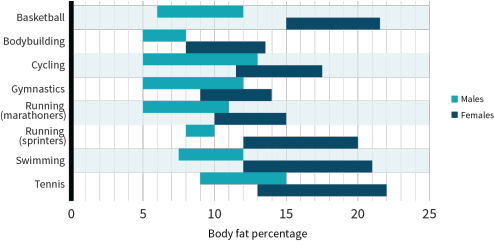
**What’s my fat goal?**

The answer never starts with a number. Do you want to look great at the beach? Or just to avoid the health problems linked to an excess of body fat? Or are you an athlete? And if you are an athlete, does your sport have weight classes?

You may have noticed that fighters carry more fat than contest-day bodybuilders. Even when weight class is a concern, there are still some performance advantages to keeping some fat on you because very low body fat in athletes has been associated with physical and mental fatigue, chronic pain, and impaired immunity.

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**Body-fat percentage ranges per sport**

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Adapted from Kenney, Wilmore, and Costill. Body Composition and Nutrition for Sport (chapter 15 in Physiology of Sport and Exercise, 5th ed. Human Kinetics. 2011. ISBN:https://lccn.loc.gov/2011035158) ● Jeukendrup and Gleeson. Body Composition (chapter 13 in Sport Nutrition, 2nd ed. Human Kinetics. 2009. ISBN:https://lccn.loc.gov/2009034956)

As this graph shows, female athletes tend to carry more fat than their male counterparts. This is perfectly normal. Remember: you need some fat. You can’t “burn” it all and keep on living. Your minimal percentage of body fat — the percentage below which your health is compromised — is called essential fat, and as we saw, it is not the same for men (3%) and women (10%).

For that reason, at the end of this intro, you’ll find 2 graphs: one for women and one for men. Each will give you an idea of your “fat fitness” and of the range you should aim for to reach a certain goal.

Those graphs should remind you that your percentage of body fat matters more than your total body fat and a lot more than your weight. When people say they want to lose weight, most often they should really say they want to lose fat.

Let’s say you start at 150 lb with 20% body fat. At that point, you carry 30 lb of fat. Then, after training for half a year, you reach 153 lb (the horror!) with 17% body fat. At that point, you carry 26 lb of fat.

So you’ve gained 3 lb of weight, but you’ve lost 4 lb of fat, which means you’ve gained 7 lb of lean mass. And if you’ve taken care of weighing yourself at the same time of the day (before breakfast but after going to the toilet, usually), that lean mass is muscle.

As we saw, fat takes up a lot more space than muscle, so you can weigh more yet be leaner. And women, don’t worry that gaining muscle will make you look “masculine”; it doesn’t work that way. Even if you lift weights (and really, most of you should), you won’t develop the same musculature that a man can — not without the same testosterone levels that a man has.

In other words, gaining some muscle will make you look toned, not muscular.

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| **Tip: Diet is key**  Exercising can help you build muscle and lose fat, but if we only consider fat loss, eating better usually trumps exercising more.  Compared to exercise changes (alone), diet changes (alone) have been shown to produce around three times the weight loss.[17]  The calories burned by a 5’10” man weighing 154 pounds and running a 5K (3.1 miles) are offset by just 7 small chocolate-chip cookies (367 vs. 379 kcal). |
| --- |

**How do I lose fat?**

Finally we’re getting there. The answer is as simple as calories in vs. calories out — except, not really. There are many reasons why weight loss, or weight gain, can’t be boiled down to a simple equation (i.e., there are 9 kcal in 1 gram of fat and there are 454 grams in 1 pound, so if I ingest 4,086 kcal more than I need, I gain 1 pound of fat).

Calories are units of energy. To measure the caloric content of any item, edible or not, you can burn it in a bomb calorimeter. However, unlike a bomb calorimeter, your body can’t extract energy from everything — it can’t even extract energy from all carbs (dietary fibers are carbs, but you can’t digest them, though some of your gut bacteria can).

Not only that, but even when you can digest something and convert it into calories, the process requires that you “burn” calories. This so-called thermic effect of food is greater for protein than for fat or carbs, and it can be affected by your age, the timing of your meal, and various other factors.

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| **Digging Deeper: Know your fat**  There are 3 predominant types of fat in your body.  White adipose tissue (WAT). This is the type of fat that your physician warns you about. It can be damaging to health, particularly when it overaccumulates around your midsection. Fat’s role as an endocrine organ is increasingly a topic of research, and hormones like leptin and adiponectin play critical roles in metabolic health.[18]  Brown adipose tissue (BAT). Considered a “healthy” fat in the body, this type of fat is a very metabolically active and highly thermogenic tissue. Although it is found in significant quantities in infants, adults tend to have very small deposits. It is thought that stimulating brown fat growth in adults could help fight weight gain. Some evidence suggests an association between having more brown fat and being less likely to develop metabolic dysfunction.[19]  Beige adipose tissue. This type of fat can be thought of as the child of white and brown fat. It is found within white fat but displays many of the beneficial qualities of brown fat. White fat contains stromal vascular cells that help to shift the structure and function of the white fat cell to those of a brown fat cell. The total amount of brown and beige fat tissue in the body has been inversely associated with body mass index.[20] |
| --- |

Some supplements discussed in this guide can also affect the “calories in-out” equation through thermogenesis, lipolysis, and better nutrient partitioning (more nutrients sent to the muscles, less stored as fat).

Still, “calories in vs. calories out” is the simple answer to a complicated question, and for all the caveats it implicitly carries, it has practical applications. Start by assessing the amount of calories you need just to maintain your weight based on your level of activity, and then compare this number to the amount of calories you consume daily. That should give you a very rough idea of where you stand.

As the weeks and months go by, record how much you consume (of each macronutrient) and how much weight, body fat, and lean mass you gain or lose. In this way, you’ll draw a much clearer picture of your actual caloric needs.

To lose fat, you’ll need to end up in a caloric deficit on most days. You’ll also need to keep yourself in check on “cheat days” because unrestrained binging can easily torpedo a diet through sheer caloric load and the reinforcement of bad habits. Supplements can help, but you’ll have to help yourself too, either by eating less or by exercising more. Or both.

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| **Caution: Don’t let binging become a habit**  You can partially compensate for the occasional binge by eating less the next day or exercising more,[21] but you should be wary of letting binges turn into habits. Binges are often triggered by specific events — a stressful situation, maybe, or hunger-inducing TV ads or the tantalizing scent of tasty food. If you let yourself react by binging, then the next time you encounter the trigger, you’ll be more likely to binge again.  **Yearly weight change in Germany, Japan, and the U.S.** Adapted from Helander et al. N Engl J Med. 2016.[22]  Binge habits aren’t easy to break, especially when you’ve had them for a long period of time, so you might want to start by weakening them. Rather than reacting to a binge trigger by eating a plain salad or a big plate of nothing, you could try indulging less than the previous time (and start with a satiating helping of protein[23]~~)~~. Or you could reward yourself in another way — a way not related to food. Regular small improvements can add up over time. |
| --- |

Don’t overdo it, though. Drastic diets aren’t only hard to maintain, they can also deprive you of some of the nutrients you need to stay healthy,[24] and they make it hard to exercise. Correspondingly, don’t go crazy with exercise — even if you don’t overcompensate with excess food. Regular exercise helps maintain your basal metabolism, but going overboard can easily lead to injury, especially while on a diet.

In this guide, you’ll learn about supplements that can help you lose weight, with or without exercise. Just as important, you’ll learn to optimize your protein intake to lose more fat and less muscle.



Kamal Patel, Co-founder and Director

MPH, MBA, PhD(c) in Nutrition

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**Female body-composition categories based on age and percentage of body fat**

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Adapted from American College of Sports Medicine. Body Composition (chapter 5 in ACSM’s Health-Related Physical Fitness Assessment Manual, 4th ed. Lippincott Williams & Wilkins. 2013. ISBN:978-1451115680)

13

**Male body-composition categories based on age and percentage of body fat**

****

Adapted from American College of Sports Medicine. Body Composition (chapter 5 in ACSM’s Health-Related Physical Fitness Assessment Manual, 4th ed. Lippincott Williams & Wilkins. 2013. ISBN:978-1451115680)

14

**Combos**

**Disclaimer about supplement quality**

We expect that readers will do their due diligence when choosing products. Depending on the manufacturer, supplements may have inaccurate labels (i.e., they contain too much or too little of the ingredients they claim or, in some cases, significant amounts of other ingredients not listed). They may also contain significant amounts of contaminants such as heavy metals or pesticides. It is also possible for supplements to contain ingredients that people are commonly allergic to, and it’s important to be aware of the nonmedicinal ingredients as well. As a brief introduction to vetting manufacturers, we drew up a short list of steps you should take if a product has caught your interest.

| **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. |
| --- |

**Core Combo**

Consume protein throughout the day, in place of a significant percentage of fats and carbohydrates, particularly before large meals if using protein supplements. In general, the higher you go with protein, the more effect you will see, but there is no reason to go past 30% of calories from protein. Depending on a number of variables, the necessary protein intake may differ, so consider using our calculator. Casein or pea protein may be somewhat more effective than whey and soy, but all should work.

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| **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 supplement 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 that 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, because 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**

**If you have a lot of body fat to lose and tolerate caffeine**

In addition to the core supplement of protein, it's probably advisable to take highly viscous fiber, as detailed in the fiber entry of this guide.

After a few weeks of protein, fiber, and anything else you may be trying, consider adding the following if you are not seeing sufficient results:

The combination of caffeine (no more than 400 mg per day) and green tea (500 mg of EGCG) may synergistically accelerate your fat loss.

15 to 25 grams/day of medium-chain triglycerides can be taken as a substitute for fat or carbohydrates.

**If you have a lot of body fat to lose and do not tolerate caffeine**

Refer to the aforementioned combo, but don’t include caffeine. Also be sure that your source of green tea has been decaffeinated.

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**If you overeat due to stress, depression, or insomnia**

You may not actually need to take caffeine or other fat burners. Instead, it may be best to focus on whichever psychological issues that are causing you to overeat and address them. Do you eat in response to stress? Reducing stress may cause weight loss. Do you overeat due to depression? Treating depression may cause weight loss. These challenges are mostly beyond the scope of this guide, however.

Within this guide, 5-HTP at 200–300 mg, taken 3 times per day (before each major meal) may help to reduce the tendency to overeat.

Saffron has research support, and it may be worth reading the saffron entry; however, it is unproven as far as the evidence standards for this guide are concerned, but, saffron is likely effective for reducing depression and anxiety in its own right.

For people with stress and sleep issues, any stimulants or fat burners in this guide may be especially unwise because they may exacerbate these issues.

**What has changed since the last time?**

It should be noted that we changed the names of our ranking categories. “Core” (the highest) is now “primary”, “primary” is now “secondary”, and “secondary” is now “promising”. This nomenclature has already been implemented for some guides, but this is the first update to the Fat Loss Guide that uses this new terminology. For example, if it was a core supplement in the previous issue and is now a secondary supplement in this issue, we’ll say that it was a primary supplement in the previous issue and is now a secondary supplement.

Added:

L-Carnitine

Garcinia cambogia

Irvingia gabonensis

Yerba mate

Paullinia cupana

Saffron

Changed ranking:

5-HTP

Downgraded from secondary to promising. This is simply a matter of our new standards for evidence. Although some evidence supports it, more research is needed.

Yohimbine

Downgraded from secondary to promising. This is simply a matter of our new standards for evidence. Although some evidence supports it, more research is needed.

Synepherine

Downgraded from promising to unproven. After a new evaluation of the evidence, we were not convinced 17

of a clear benefit due to the scarcity of trials that use it on its own, rather than as one of many ingredients in an overall fat-burning stack.

White willow bark

Downgraded from promising to unproven. There was insufficient evidence based on our new standards. Berberine

Upgraded from unproven to promising. New research suggests a benefit, though much more evidence is still necessary before we can be very confident in it.

Green coffee extract

Upgraded from unproven to promising. A new analysis of the evidence suggested a small benefit, though it is still unlikely to be particularly effective.

Raspberry ketone

Downgraded from unproven to inadvisable. Not only does it probably not work, but we were concerned about the possibility of insulin resistance and liver damage if taken in the long-term. Although there isn’t a great deal of evidence for this, the risk-to-benefit ratio is unfavorable.

Clarifications:

Paullinia cupana (Gurana) and Yerba mate were previously listed under “Atypical caffeine sources” as promising supplements, but we decided to review them separately. They are both unproven in the sense that there are insufficient studies to demonstrate efficacy, although logically, their caffeine content should make them effective. The reason why it possibly doesn’t make sense to treat them as a substitute for caffeine supplements, coffee, or tea is because their safety is much less clear.

Theanine was previously its own entry in the guide under “promising supplements”, but the only reason it was there was as an adjunct to caffeine to prevent jitteriness. Now it’s simply mentioned in the caffeine entry.

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**Primary Supplements**

**Protein**

**What makes protein a primary supplement**

A high-protein diet is one of the most popular methods for weight loss, and the reasoning makes sense. First, protein digestion and utilization (the thermic effect of food) expends more calories than fat and carbohydrate digestion.[25][26][27] Although this is unlikely to lead to significant fat loss by itself, it is one small factor out of many that may lead to greater long-term success.

Another reason why protein may help to reduce body fat is its effects on appetite. Depending on the individual, protein improves overall satiety when taken right before a meal.[26] This is likely related to enhanced ghrelin reduction and GLP-1 secretion, in comparison with other macronutrients.[28] However, this meta-analysis is unable to tell us if there are minimal or optimal effective doses or which types of protein are most effective.

From a thermogenesis standpoint, it probably doesn’t matter because the effects of different amino acids are unlikely to differ substantially.

From a satiety standpoint, there may be some differences between protein types, although it may not matter very much. Dairy protein is made up of whey (20%) and casein (80%) and they are absorbed at different rates, with whey absorbed much faster than casein. There is some evidence to suggest that whey is more satiating in the short term (a couple hours), whereas casein is more satiating in long-term (longer than that), though the evidence is inconsistent on short-term satiety.[29][30][30] So casein may be preferable for extending the time between meals, but for the purpose of preloading to reduce energy intake at meals, it is less clear.

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**Kinetics of whey (fast) vs casein (slow) digestion**

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One trial found that pea protein and casein were more satiating than egg protein and whey protein when taken 30 minutes before a meal, though more research is needed to corroborate this finding.[30]In general, it doesn’t appear that there is a difference between soy and whey protein.[31]

It is also worth noting that this result is largely based on acute effects. In nonacute trials of a longer duration, although a modest benefit on appetite is possible, the current research is inconclusive for the effects of protein on satiety.[32] The takeaway is not that continuously taking protein for fat loss doesn’t work, just that protein may be best used as an acute preload to reduce subsequent energy intake, or simply to replace other macronutrients that are easier to overeat.

Based on studies on satiety, 20% of energy intake or less is considered to be “normal protein” and anything higher is “high protein”. Safety concerns with protein intake don’t start to appear until 30% or more of energy, so a protein intake of 30% of total kilocalories is a good spot for fat loss.

One more reason why a high protein intake may be beneficial for fat loss is that it can help to preserve muscle mass, which contributes to energy expenditure.[33] Regardless of the potential effects on energy expenditure, retaining muscle mass during low-calorie diets is desirable.

**Warnings about protein**

Unless you have a pre-existing condition that affects your liver or kidneys, the intakes suggested below will not harm these organs.[34]

**How to take protein**

**For dieting**

In general, high-protein diets start at 20% of calories, and 30% of kilocalories is a reasonable stopping point, so depending on your tolerance, somewhere between 20%–30% of protein should be ideal, with the 20

higher end being more effective. We also have a guide and a calculator that are worth checking out.

Taking protein before meals is likely the ideal way to use protein to reduce energy intake, and using protein to replace other macronutrients that are easier to overeat is another approach. Even though protein has a slightly higher thermic effect of food, it should still be counted fully as calories to compensate for natural inaccuracies in calorie counting.

There may be some benefit of pea protein or casein over whey protein, but more research is needed. Any protein should work.

Beyond that, what works for an individual will require experimentation and close observation. Is it possible to replace a normal meal with a lower-calorie protein shake? Great! As long as both hunger and stress are kept at bay, that is. If a high protein intake allows a person to eat less, but stress levels rise due to a low calorie intake, then although there may be short-term success, stress makes long-term rebounding and subsequent yo-yoing more likely.

**For maintenance**

In the United States, the RDA of 0.8 grams per kilogram of body weight (0.36 grams/lb) is considered the minimum amount of protein that a healthy adult must consume daily to prevent muscle wasting when total caloric intake is sufficient.[35]

However, the current evidence suggests that this amount has been underestimated. Recent studies point to 1.0–1.2 grams/kg as the minimum daily intake for sedentary adults who wish to maintain muscle mass without losing or gaining weight,[36][37][38] whereas adults with fat loss goals can benefit from 1.5–2.7 grams/kg (0.68–1.23 grams/lb). Even a reanalysis of the data used to establish the above RDA suggests that the minimum daily intake should be at least 1.0 grams/kg.[39]

So, how much protein does an individual need daily? Here’s a quick rundown of how much protein may be needed in different situations. For more information, check out our in-depth article on protein needs.

A person who is at a healthy weight, is active, and wishes to lose fat should aim for 1.8–2.7 grams/kg (0.82–1.23 grams/lb), skewing toward the higher end of this range as they become leaner or if they increase their caloric deficit (by eating less or exercising more).

A person with overweight or obesity should aim for 1.2–1.5 grams/kg (0.54–0.68 grams/lb). This range, like all the others in this list, is based on a person’s total body weight (most studies in people with overweight or obesity report their findings based on total body weight, but some calculators determine optimal protein intake based on lean mass or ideal\* body weight).

A person who follows a vegan diet or obtains most of their protein from plants may have higher protein requirements because plant-based proteins are usually inferior to animal-based proteins with regard to both bioavailability and amino acid profile.

Daily protein intake

| **BODY WEIGHT** | **BODY WEIGHT** | **0.45** | **0.54** | **0.68** | **0.82** | **0.91** | **1.00** | **1.23** | **grams/lb** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **LBS** | **KGS** | **1.0** | **1.2** | **1.5** | **1.8** | **2.0** | **2.2** | **2.7** | **grams/kg** |
| 100 | 45 | 45 | 54 | 68 | 81 | 91 | 100 | 122 | grams |
| 125 | 57 | 57 | 68 | 85 | 103 | 113 | 125 | 154 | grams |
| 150 | 68 | 68 | 82 | 102 | 122 | 136 | 150 | 184 | grams |
| 175 | 79 | 79 | 95 | 119 | 142 | 159 | 175 | 213 | grams |
| 200 | 91 | 91 | 109 | 136 | 164 | 181 | 200 | 246 | grams |
| 225 | 102 | 102 | 122 | 153 | 184 | 204 | 225 | 275 | grams |

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| **BODY WEIGHT** | **BODY WEIGHT** | **0.45** | **0.54** | **0.68** | **0.82** | **0.91** | **1.00** | **1.23** | **grams/lb** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **LBS** | **KGS** | **1.0** | **1.2** | **1.5** | **1.8** | **2.0** | **2.2** | **2.7** | **grams/kg** |
| 250 | 113 | 113 | 136 | 170 | 203 | 227 | 250 | 305 | grams |
| 275 | 125 | 125 | 150 | 187 | 225 | 249 | 275 | 338 | grams |

References: Schoenfeld and Aragon. J Int Soc Sports Nutr. 2018.[40] ● Jäger et al. J Int Soc Sports Nutr. 2017.[41] ● Thomas et al. Med Sci Sports Exerc. 2016.[42] ● Institute of Medicine. Protein and Amino Acids (chapter 10 in Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. The National Academies Press. 2005. DOI:10.17226/10490

Consume 20–40 grams of protein within the 2 hours preceding or following a workout to help stimulate muscle growth. Spread the rest of the protein intake over a few meals, starting with breakfast, to provide the body with a consistent flow of amino acids.

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**Secondary Supplements**

**Caffeine**

**What makes caffeine a secondary option**

By causing epinephrine (aka adrenaline) and dopamine to be released, caffeine has beneficial effects on energy, mood, and fat loss. However, after prolonged consumption, only the ability of caffeine to ward off sleep remains strong. Euphoria and excitability both fade away, and the fat loss effect is at least significantly diminished.

Two distinct effects contribute to caffeine’s fat-burning properties: a thermogenic effect (in the short term, caffeine increases heat production) and a weaker lipolytic effect (in the long term, caffeine causes triglycerides to release fatty acids, which the body can then use for fuel).

**Three ways caffeine can assist in fat loss**

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More precisely, by inhibiting a category of enzymes called phosphodiesterases (PDEs), caffeine can increase the body’s levels of cyclic adenosine monophosphate (cAMP). Elevated cAMP levels are associated with lower triglyceride levels in fat cells (due to cAMP increasing lipolysis) and improved protein synthesis in muscle cells. Moreover, when PDEs are inhibited, compounds that increase cAMP levels (such as synephrine and forskolin) might become even more effective at increasing heat production.

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**Warnings about caffeine**

Even though coffee is a popular beverage worldwide, caffeine is not innocuous. Regular consumption leads to tolerance and often to dependence and withdrawal. Caffeine interacts dangerously with several pharmaceuticals, notably tizanidine and a type of antidepressant called monoamine oxidase inhibitors (MAOIs)[43].

Caffeine may also decrease blood lithium levels. Suddenly eliminating all caffeine from the diet can cause lithium levels to rise. Individuals who are on lithium medication should keep their day-to-day caffeine intake roughly the same. A person who wishes to stop taking caffeine should talk with a physician about slowly weaning from it.

Caffeine can also interfere with glucose metabolism, raise blood pressure, raise heart rate, and increase urination (and thus the risk of dehydration during exercise, though the effect is usually mild), but those 4 effects fade away as tolerance to caffeine develops.

An individual might already be consuming more caffeine than they think. When calculating the daily intake of caffeine, consider all beverages, foods, and supplements. Bear in mind that caffeine can be “hidden” in a product — for instance, if “guarana seeds” appears on a label, remember that this product is richer in caffeine than coffee seeds.

**How to take caffeine**

For healthy adults, a caffeine intake of up to 400 mg/day doesn't raise any general health concerns. Although it’s possible to consume more, 400 mg is how much caffeine most healthy people can regularly consume in a day without suffering lasting harm.

24

**Caffeine upper limit (400 mg) in number of drinks**

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References: McCusker et al. J Anal Toxicol. 2006.[44] ● Desbrow et al. Nutr Health. 2019.[45] ● Ludwig et al. Food Funct. 2014.[46] ● Fox et al. J Agric Food Chem. 2013.[47] ● McCusker et al. J Anal Toxicol. 2003.[48] ● Angeloni et al. Food Res Int. 2019.[49]

To supplement with caffeine for a prolonged period of time, take 100–200 mg twice per day (i.e., 200–400 mg/day). Caffeine in this range can be consumed via coffee or tea. People who get enough caffeine through dietary sources should not supplement with caffeine. People who are unused to caffeine should start at the low end of this range. People who are sensitive or new to stimulants should supplement with caffeine by itself before introducing other stimulants (such as synephrine).

Supplementing with caffeine on an empty stomach can increase the rate of absorption, but it can also cause gastrointestinal upset. Caffeine can disrupt sleep when consumed in the evening, or even in the

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afternoon; even if it does not prevent a person from falling asleep, caffeine will impair the quality of the sleep. In healthy adults, the average half-life of caffeine falls between 5 and 6 hours, but this number can vary greatly between individuals because of genetics and other factors — heavy smoking can double the rate of caffeine metabolism, pregnancy can halve it, etc.

| Although theanine (the amino acid L-theanine) does not directly influence fat loss, it can be of use to people who are supplementing with stimulants, notably caffeine. Its calming effect on the nervous system can reduce the overexcitability caused by stimulants without decreasing the stimulant derived benefits to focus and attention span. In fact, the improvements in concentration induced by caffeine and theanine have been shown to be synergistic.  Theanine can be added to any stimulant that provides too much nervous energy at the standard dose.  People who take caffeine should take an equal dose of theanine. At the lower end of the range, if a person takes 100 mg of caffeine twice a day, they should also take 100 mg of theanine twice per day (i.e., 200 mg/day). At the higher end of the range, if a person takes 200 mg of caffeine twice per day, they should take 200 mg of theanine twice per day (i.e., 400 mg/day). |
| --- |

**Green Tea**

**What makes green tea a secondary option**

Tea is the most popular beverage in the world after water.[50] Although there are many kinds of herbal infusions, actual teas are made from the leaf of Camellia sinensis. From least to most fermented, the best known types of tea are green, yellow, oolong, black, and pu-erh. In most of the world, white tea undergoes little to no fermentation (a little more or a little less than green tea), but in China, it is a fermented tea.

Catechins are phytochemicals with antioxidant properties, and the less fermented the tea, the richer it is in catechins. Of the catechins found in tea, epigallocatechin gallate (EGCG) is the most bioactive and abundant (48%–55% of total catechin content).[51]

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**Processing tea impacts the type of polyphenols it contains **Reference: Higdon and Frei. Crit Rev Food Sci Nutr. 2003.[52]

As a fat burner, EGCG may work by inhibiting catechol-O-methyltransferase (COMT), an enzyme that helps degrade catecholamines (the hormones and neurotransmitters dopamine, epinephrine, and norepinephrine).[53] Catecholamines help break down stored body fat, which can then be used or excreted by the body. When EGCG inhibits COMT, it allows catecholamines to liberate stored fat over a longer period of time. Additionally, green tea has been observed to activate AMPK, which may increase fatty acid metabolism and has appetite-regulating effects, potentially leading to a double effect of increased fat burning and lower appetite.[54][55]

When it comes to hard evidence in humans, a meta-analysis of randomized placebo-controlled trials evaluated the overall effects of green tea products (green tea, green tea extracts, including isolated green tea catechins such as EGCG) on body weight (22 studies with 2,357 participants), BMI (22 studies with 1,124 participants) and waist circumference (13 studies with 65) and found a statistically significant reduction in all.[56]It was unclear whether doses higher than 800 mg were more effective than lower doses, and an additional analysis found potentially greater effects when the dose was less than 500 mg, though with few studies at that level, it is difficult to say that this was a genuine effect, The vast majority of studies used higher doses with a significant cluster around 500 mg. Therefore, 500 mg can be viewed as a reasonable maximum dose.

It was also unclear whether studies lasting longer than 12 weeks yielded different effects than shorter studies.

In general, the study quality was good according to the assessment, and so although there are questions remaining regarding green tea’s long-term effects, it is more probable that it has a meaningful effect than not.

It is unclear from this research whether most of the effect comes from fat burning or effects on appetite. Although some fat-burning effect is likely, it should not be assumed that green tea will be effective in the absence of a reduction in calorie intake.

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**Warnings about green tea**

Green tea may cause adverse effects on the liver if taken in high supplemental doses. Specifically, increases in liver enzymes have largely been found when taking doses that correspond to 800 mg or more of EGCG.[57] However, it is possible that long-term use of lower doses could also be detrimental to the liver.

Green tea can also cause adverse gastrointestinal effects such as nausea, abdominal pain, diarrhea, and dyspepsia/indigestion, and less commonly, vomiting, constipation, and flatulence/belching.[57].

The aforementioned hepatotoxicity may be partially caused by its combination with acetaminophen, according to one study in mice,[58] though more research is needed to confirm this. In any case, taking green tea with medications known to be hepatotoxic may simply compound the risks.

Green tea contains a moderate amount of caffeine and so theoretically has the same adverse events as caffeine if taken in sufficiently high doses.

Green tea contains vitamin K, which may cause it to interfere with warfarin and other vitamin K antagonist blood thinners.[59] However, this is likely less of a problem with extracts or brewed green tea due to much lower levels than for whole leaves.

One study found that green tea reduced the increase in concentration of nadolol, a beta-blocker.[60] **How to take green tea**

When it comes to green tea extracts, there is probably no point in going over 500 mg per day, and it’s possible that less is needed, but how much less is unclear.

A typical 250 mL cup of green tea will tend to contain 30–50 mg of caffeine and 50–100 mg of EGCG, and so 8 cups is generally recognized to be the upper limit for safety (not surpassing 400 mg of caffeine) and likely provides sufficient green tea catechins. More than 4 cups may not be necessary for the effect of the caffeine itself.

Taking EGCG on an empty stomach leads to an increase in blood concentrations but can cause nausea. 28

**Promising Supplements**

**Yohimbine**

**What makes yohimbine a promising option**

Yohimbine is an alkaloid found in the bark of the African yohimbe tree (Pausinystalia johimbe). Outside of the sports and fitness community, yohimbine is probably best known for its use as a virility booster in traditional medicine and a clinically proven treatment for erectile dysfunction.[61]In contrast, athletes and dieters hope to benefit from the bark extract's purported ability to elevate plasma testosterone levels, promote skeletal muscle hypertrophy, and most prominently, shed “stubborn” body fat.

Yohimbine's purported fat burning effects are commonly credited to its somewhat unique ability to block the antilipolytic alpha-2 receptors on our fat cells. These receptors control and limit the stress-hormone induced breakdown and release (lipolysis) of stored triglycerides and free fatty acids from the cells.[62][63].

There are two things that make yohimbine particularly interesting for dieters. First, yohimbine theoretically stacks well with other stimulants such as ephedrine and caffeine because it augments their lipolytic effects by widening a well-established physiologically relevant bottleneck of lipolysis. Second, and probably more

important, yohimbine specifically targets the hard-to-shed subcutaneous fat depots covering the abdominals, obliques, glutes and other regions of the body, which harbor what people often refer to as “stubborn” body fat, and are characterized by a significantly increased expression of antilipolytic alpha-2 receptors on the surface of the fat cells.[64][65] Because these receptors are coactivated by adrenergic hormones, these (mostly subcutaneous) “stubborn” body fat stores with their high alpha-2-to-beta-1 receptor ratios will react much less favorably to the lipolytic stimulus of epinephrine and other hormones… unless the stress hormones’ self-inhibitory effects are blunted by an alpha-2 antagonists like yohimbine.

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| **Digging deeper: Why exactly is yohimbine supposed to be consumed on an empty stomach, before workouts, and alongside classic stimulants such as caffeine?**  As counterintuitive as this may sound, epinephrine — one of the primary stress hormones in our body — inhibits its own lipolytic effects on fat cells as it activates both the prolipolytic beta-1 as well as the antilipolytic alpha-2 receptors on the cell surfaces.[66] Hence, the total lipolytic effect of beta adrenergic stimulants, such as caffeine, and the effects of exercise, will increase if the alpha-2 receptors (which would otherwise act like the parking brake on a car) are blocked by receptor specific antagonists such as yohimbine.[67][68]  The stimulation of the alpha-2 receptors is not the only bottleneck that limits triglyceride breakdown and free-fatty-acid release from our fat cells. Insulin, for example, has also been shown to significantly reduce the lipolytic effects of catecholamines. Additionally, its effect appears to be specifically pronounced in the same subcutaneous fat depots, where the so-called “stubborn” fat (which yohimbine supposedly targets) resides.[69]In conjunction with yohimbine's very own ability to potentiate postprandial (postmeal) insulin secretion, this information clearly warrants the recommendation that yohimbine should not be taken with foods and/or during the postprandial period.[67] |
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That all sounds nice in theory, but If we look at the actual evidence from trials, the effect turns out to be unexpectedly limited, with only 2 out of a meager total of 4 studies showing beneficial effects of yohimbine supplementation on body weight and/or body composition.

Some critics even argue that yohimbine's whole reputation as a potent weight loss adjuvant hinges on the results of a single study.[68] The corresponding paper published in “Research in Sports Medicine” in 2006 reported a statistically significant 2.2% reduction in body fat in already lean top-level soccer players who had been randomized to receive either 2x10 mg of yohimbine HCL or an identically appearing placebo supplement twice per day for 21 days (9.3% ± 1.1% to 7.1% ± 2.2%). Despite the large standard deviations, this is quite an impressive result — specifically, in view of the fact that the body fat levels of the young men in the placebo group, who had also been told to stick to their regular diet and exercise regimen, remained essentially unchanged (8.9% ± 1.4% preintervention, 9.2% ± 1.9% postintervention).

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| **Important note “There is a fundamental difference between lipolysis and fat loss”**  An increase in lipolysis, which is the process of breakdown of triglyceride bonds of stored body fat and the subsequent release of free fatty acids into the bloodstream, does not equate to “fat loss”. Unlike the former, the latter critically depends on a hypoenergetic environment — in other words, unless a person is in a caloric deficit that forces the body to actually burn the fatty acids, instead of just restoring or redistributing them towards their original or alternative body fat stores, they will not lose a single gram of body fat. In fact, in a worst-case scenario, body fat could be redistributed from the “stubborn” but metabolically rather benign subcutaneous body fat towards other storage sites in the body —- including the dreaded inter-organ (visceral) fat. And although this effect has yet not been documented in the pertinent literature on yohimbine's use as a fat burner, it has repeatedly been observed in response to the surgical removal of “stubborn” subcutaneous in longer-term follow-ups of several clinical studies.[70][71][72] |
| --- |

Other “supplementation-only studies” (studies in which the participants did not make mandatory changes to their lifestyle, diet, and physical activity) seem to refute an independent effect of yohimbine supplementation on the body composition of normal-weight participants. For example, a 6-month dose escalation trial found no difference in body weight, BMI, body fat, and fat distribution between 47 male participants who received progressively increasing amounts of yohimbine (peak intake: 43 mg/day) and those who had been randomly assigned to a placebo group.[73]

Similarly, contradictory results can be found in the 2 other papers in Table 1.[74][75] Both were randomized controlled trials but were methodologically very different from the previously discussed experiments. Both studies were conducted in participants with obesity who were following energy-reduced diets (1000 kcal/day). Both studies used almost identical amounts of yohimbine, i.e., 18 mg/day and 20 mg/day (total daily doses). Unfortunately, both studies failed to assess the changes in body fat and body composition of their participants and stuck to weight loss as their primary metric of yohimbine's usefulness as a weight loss adjuvant. Despite these methodological similarities, the results of the 2 studies diverge significantly. Although Kucio et al. reported a significant weight loss advantage of 1.34 kg in their short 3-week study, Berlin et al. did not find statistically significant differences in the weight trajectory between the participants in the yohimbine group and the placebo group over the course of their significantly longer 8-week treatment period.

When it comes to a final assessment of the usefulness of yohimbine as a putatively site-specific “fat burner”, we must (and do) acknowledge the plethora of anecdotal evidence suggesting that the alpha-2 inhibitor should join the ranks of primary or at least secondary options. From a science perspective, however, the paucity of evidence and the conflicting outcomes of the 4 pertinent studies warrant that yohimbine be classified as a “promising” option only. There are a couple of things that set this indole alkaloid apart from other agents in the same category, namely, yohimbine's well-established mechanism of action, its unique site-specific fat loss effects, and its synergy with classic, readily available, well researched and perfectly safe stimulants such as caffeine. Hence, yohimbine should — despite being classified as “promising” only — occupy a top spot in the “supplements to test” list for dieters who are trying to get rid of the hard-to-shed last body fat reservoirs on their thighs, buttocks, abs, obliques and other fat storage sites where adipocytes have a high alpha-2-to-beta-1 receptor-ratio.

**Warnings about yohimbine**

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As for most compounds, the toxicity of yohimbine is dose dependent and differs from individual to individual. The most common side effects include agitation, anxiety, palpitations, chest pain, sweating, blurred vision, and hypertension. Overdoses can also cause hypotension, tachycardia, seizures, paralysis, and coma.[76][77] Deaths from overdose have even been reported in the literature. Therefore, it is important to note that the concentration of yohimbine in the decedents' blood suggested that they accidentally consumed 5–10 grams instead of 5–10 milligrams of yohimbine.[78]

Unlike other fat burning agents, yohimbine has not been linked to serum enzyme elevations or clinical liver disease in either clinical studies or case reports.[77] Only anecdotal evidence exists for dermatological side effects and kidney damage.[79][80] Prolonged use of yohimbine has not been adequately studied, and its potential for long-term toxic effects cannot be extrapolated from the existing short-term safety data that we have. It is important to be aware of potential adverse effects that may worsen pre-existing conditions when considering the use of yohimbine. Yohimbine may raise blood pressure, which could exacerbate hypertension (high blood pressure) in affected individuals[81][76][82]. Additionally, yohimbine may trigger anxiety and agitation, potentially aggravating symptoms in people who already suffer from anxiety[81][76]. It is important to consider these risks before deciding to use yohimbine.

There are no known reports of cross-contamination of yohimbine supplements.

**How to take yohimbine**

Take 10–20 mg per day (or 0.25 mg per kg of body weight; 0.25 mg/kg) of yohimbine HCL\* preferably while fasted and/or 30 minutes before physical activity. Titrate the dosage upward starting at 2 mg. Do not escalate the dosage. There is neither enough safety data nor reliable evidence of beneficial effects of doses beyond the 20 mg/kg margin.

\* Avoid taking supplements containing rauwolscine (aka “alpha-yohimbine” or yohimbe bark extracts) instead of yohimbine HCL. There’s no scientific evidence to prove the efficacy and safety of rauwolscine, and the actual yohimbine content of bark extracts varies substantially, often deviating significantly from the label claims. For example, a 2016 analysis of 49 “yohimbe” or “yohimbine” products on the U.S. market found deviations ranging from 23% to 147%.[82]In addition, the extract often contains various other compounds from the bark that may provoke unpredictable side effects.

The dose can be split, but each dose should be taken at least 1.5 hours after the most recent meal to avoid any interference between postprandially elevated insulin levels.

Each individual will have to experiment with optimal dosing schemes because the individual rate at which yohimbine is metabolized has been shown to vary by a factor of up to 1000. Individuals with European heritage seem to be particularly likely to be slow or “nonmetabolizers” of yohimbine and are thus significantly more susceptible to side effects due to a significantly greater activation of their sympathetic nervous system.[83]

When taken at dosages of greater than 0.3 mg per kg of body weight (ideally ≥0.6 mg/kg), caffeine triggers a significant increase of epinephrine[84] and consequent increases in lipolysis. When caffeine is coadministered with yohimbine, its effects are no longer (self-)limited by the catecholamine's interaction with the alpha-2 receptors on fat cells. Thus, a person can expect a significant increase in the lipolytic effects of caffeine, not only, but particularly, in areas where a high density of alpha-2 receptors makes body fat particularly resistant to dieting efforts.

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**L-Carnitine**

**What makes L-carnitine a promising option**

L-Carnitine is an amino acid that is synthesized in the body from lysine and methionine and that can be obtained from the diet, primarily from animal products, including meat, fish, and dairy.[85]. Because L carnitine plays important roles in lipid metabolism (by transporting long-chain fatty acids into the mitochondria) and glucose metabolism, it has been studied for its potential antiobesity effects.

According to 2 meta-analyses,[86][87] supplementation with L-carnitine resulted in small reductions in BMI (−0.40 and −0.36), body weight (−1.2 and −1.1 kilograms), and fat mass (−2.1 and −1.2 kilograms) over the course of an average of 16 and 19 weeks, respectively. That said, in subgroup analyses, the weight reducing effects of L-carnitine were statistically significant in individuals with overweight or obesity, but not in individuals with normal body weights. Also, in one of the meta-analyses in which the researchers performed subgroup analyses based on trial quality, L-carnitine’s effect on BMI became statistically insignificant in high-quality trials, and the effect on body weight was reduced to a loss of 0.6 kilograms.[86] Considering that the average duration of high-quality trials was around 23 weeks, an extra loss of 0.6 kilograms in that time frame can be considered negligible, especially for people with overweight or obesity for whom this would represent a smaller relative drop in body weight.

Because of the very small effect size of L-carnitine on body weight and composition, it can only rank as a promising option.

**Warnings about carnitine**

Adverse effects are generally rare, but some cases of upset stomachs have been reported. Higher doses of L-carnitine (2 grams/day or more) can be converted into the compound trimethylamine, which, in some people, can give a fishy odor to urine, sweat, or breath.[88]

Carnitine and its derivatives might interact negatively with some pharmaceuticals, including anticoagulants (such as warfarin/Coumadin/Jantoven and acenocoumarol/Sintrom/Nicoumalone). People on thyroid medication or with hypothyroidism may also wish to forgo carnitine because it might depress thyroid hormone levels.[89]

**How to take L-carnitine**

The greatest weight reduction has been observed with a dosage of 2,000 milligrams per day of L carnitine.[86]In most trials, this dosage was split into 2–4 daily doses of 500–1,000 milligrams.

**5-HTP**

**What makes 5-HTP a promising option** 33

5-Hydroxytryptophan (5-HTP) is the immediate precursor for the “feel good” neurotransmitter, serotonin. Research shows that 5-HTP crosses the blood-brain barrier and readily converts to serotonin. Orally ingested 5-HTP supplements are therefore expected to boost serotonin levels in the brain and thus to elevate mood, mitigate stress, and reduce appetite.[90] This reduction in stress and appetite may lead to a reduction in food intake and, eventually, a reduction in body weight. Unfortunately, the number of studies is very limited. Between 1989 and 2022, only 5 randomized clinical trials investigated the usefulness of 5-HTP as a weight loss adjuvant. In 3 studies, the participants were allowed to maintain their regular diet and eat to satiety (ad libitum diet).[91][92][93]In one study, the participants followed a hypocaloric diet designed to induce an energy deficit of 800 kcal per day.[94]In 2 studies, the participants were fed an ad libitum diet for 5 or 6 weeks and were then switched to a diet that provided 1,200 kcal per day for another 5 or 6 weeks.[92][95]

**A more in-depth discussion of the studies for readers who are so inclined**

Except for a very recent study by Evans et al., which enlisted 48 normal-weight, well-trained men and women (30 women, 18 men with 15 +/-10 years of training, on average),[93] all studies were conducted in participants with overweight or obesity. Only 2 of the remaining studies recruited both male and female participants — in both studies, the women outnumbered the men significantly.[91][93] Moreover, in 2 studies, the participants had been diagnosed with “hyperphagia”, which means that their ad libitum diet contained significantly more energy than their caloric requirements (calculated according to sex, age and physical activity) would dictate.[92][95] A comparison of the dosage schemes in the earlier studies from the 1990s and the two more recent ones reveals that the former used significantly higher doses of 5-HTP than the Rondanelli et al. study from 2011[94] and the 2022 study by Evans et al.[93] The former was the only study that used an oral spray that was administered 5 times per day (fasting in the morning, at mid-morning, before lunch, fasting in the afternoon, and before dinner) instead of capsules, and these more recent studies averaged total daily doses of 150 mg and 100 mg of 5-HTP. That's only about 15% of the dosage in the 3 earlier trials in which the participants consumed 250–400 mg of 5-HTP at approximately 30 minutes before each of the main meals.

Overall, the results of the previously described studies support statistically significant but (in all but one instance[95]~~)~~ hardly meaningful weight loss benefits of 5-HTP over the respective control treatments. It may be noteworthy that unlike the higher-dose early trials, more studies did not observe significant reductions in body weight on an energy-reduced (−800 kcal/day; 1 study) and habitual dietary regimen (the other study). What both studies do report is evidence in favor of reductions in body fat, with Rondanelli et al. reporting a larger reduction of skinfold, arm, and hip circumference measures in 4 weeks,[94] and Evans et al. reporting a significant difference between the 0.7 kg reduction in body fat in the fit participants of the treatment arm of the study compared to the 0.2 kg increase in body weight in the participants in the placebo arm.[93] Because the already small loss of body fat failed to achieve statistical significance in within-group analysis and changes in body fat percentage were not detected, the authors themselves advised to interpret what they deem a “modest loss of fat mass” with caution.

The results look slightly better for the studies that were conducted before the year 2000. Although they did not reliably assess the effects on their participants’ body composition, all of these studies reported statistically significant reductions in body weight compared to the control groups. The greatest weight loss benefit of approximately −5 kg was observed in the initially mentioned two

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phase study by Cangiano et al.,[95] a study that was conducted in the exact group of dieters that appear to be most likely to benefit from supplementation from 5-HTP — hyperphagic individuals.

The participant specificity of the outcome doesn't come as a surprise. After all, it should be obvious that people whose weight problems can be clearly ascribed to episodic or chronic overeating will benefit most from the appetite-suppressing effects of 5-HTP, which became most apparent in Cangiano et al.'s study in which the provision of 5-HTP significantly reduced the ad libitum food intake of participants on an ad libitum diet and improved their ability to stick to the prescribed kcal deficit in the second phase of the study. With 90% vs. only 30% of the participants in the treatment group experiencing “early satiety” during this 6-week dieting period, the study provides the most convincing evidence of the usefulness of 5-HTP as an appetite suppressant and weight loss aid.

| **Digging deeper: Will 5-HTP reduce my craving for sweets?**  Although evidence that favors a certain nutrient specificity of the appetite-suppressing effects of 5- HTP exists, the number of pertinent studies is very limited. One study that could provide some practically relevant insights is the previously discussed two-phase trial by Cangiano et al.,[95]in which hyperphagic female participants with overweight stuck to their original regular dietary habits for 6 weeks before they were switched to an energy-reduced 1,200 kcal/day diet. After all, the 20 women whose data was finally analyzed didn't just reduce their energy intake in the ad libitum period of the study from more than 2700 kcal/day to approximately 1800 kcal/day (p < 0.001), but they did so to a large extent at the expense of carbohydrates, the intake of which was reduced by almost 50% (p < 0.002) by the end of the initial 6-week period. What is often ignored when this impressive result is cited is that the participants also reduced their fat consumption by almost 40% (p < 0.002). Overall, the results still support the claim that 5-HTP supplements may curb cravings for “sweets”. After all, most people think of chocolate, cookies, and other snacks with the particularly savory combination of sugar and fat when they complain about craving sweets.  Unfortunately, evidence of similar benefits in individuals without overweight or obesity is insufficient, and the number of male participants in pertinent studies is so low that a phenotype-specific and sex specific effect of 5-HTP on “carb cravings” cannot be excluded and would thus be an interesting target for future investigation. |
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There is indication that 5-HTP works to some extent. However, the evidence is too limited for it to be ranked higher. Most importantly, there is a lack of studies involving male and/or nonhyperphagic participants with normal weights, for whom the existing research seems to suggest smaller to nonexistent benefits from supplementing with this appetite-suppressing serotonin precursor. People with very high energy intakes are most likely to benefit from 5-HTP, whereas it may not be very useful for people who are simply trying to reach their ideal weight and are able to maintain a caloric deficit already.

**Warnings about 5-HTP**

5-HTP supplementation may cause dose-dependent gastrointestinal upset.[96] There are also reports of dose-related nausea and vomiting.[97] At higher doses, 5-HTP may cause serotonin syndrome, a serious

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condition caused by high levels of serotonin in the body, though this is unlikely to result from normal human doses, and there are few reports of it happening.[98]

5-HTP should not be taken alongside antidepressants, antipsychotics, or other medications that affect serotonin, such as dextromethorphan and tramadol.

Use of 5-HTP supplements may lower blood pressure,[99] so caution should be exercised by people with low blood pressure and those with high blood pressure who are currently taking blood pressure medications. 5- HTP may interfere with surgical procedures due to its effects on serotonin levels in the brain, which may affect the vascular and nervous systems.[100][101] Therefore, it is advisable to stop taking 5-HTP supplements prior to surgery.

Supplemental 5-HTP has been under careful watch for its safety and toxicity because supplemental L tryptophan, a precursor to 5-HTP, was once suspended due to the occurrence of eosinophilia-myalgia syndrome (EMS), a rare and potentially fatal condition. The occurrence was traced back to contaminated tryptophan from one manufacturer.[102] 5-HTP supplements have a potential risk for contamination by chemicals that can induce EMS, and analyses of samples of 5-HTP supplements have provided evidence of the presence of these chemicals.[103][104][105]

**How to take 5-HTP**

Take 200–300 mg of 5-HTP three times per day (3 x 200–300 mg) on an empty stomach, approximately 30 minutes before the three main meals for at least 4–6 weeks. Regular 5-HTP capsules containing standardized Griffonia simplicifolia extracts are preferred over alternative products such as oral sprays, the efficacy of which is not yet supported by a sufficient number of studies.

**Fiber**

**What makes fiber a promising option**

Dietary fiber refers to a long list of carbohydrates (as well as lignin) found primarily in plant food. Although the gut microbiota can feed on fiber, the body cannot absorb it directly.

However, this doesn’t mean that fiber can’t provide calories to the body because when the gut microbiome ferments it, this process leads to the production of short-chain fatty acids that can be absorbed. Some fibers can yield as much as 2.4 calories per gram of fiber, though most contribute far less than that.[106][107] Conversely, some fiber types even prevent the absorption of fat and may be negative calorically. However, fiber generally won’t be very significant in the big picture when it comes to the calories it can produce.

Fiber can also reduce overall energy intake through its effect on appetite and food intake. The short-chain fatty acids from fiber fermentation can interact with the brain to regulate energy intake and have a variety of potential metabolic benefits.[108][109] Fiber can also produce a satiating effect by adding bulk to meals, slowing digestion, and prolonging satiety signals to the brain.

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There are distinctions between types of fiber, which have implications for their function. The most common types are described as follows.

Soluble fiber dissolves in the stomach into a gel that slows down the passage of food from the stomach to the small intestine. This gel also helps lower blood sugar by delaying and reducing carbohydrate absorption in the body.[110]

Insoluble fiber does not dissolve in the stomach but gently “scrubs” the digestive tract. It speeds up the rate at which food moves through the intestinal tract, and it may also increase insulin sensitivity and bind to potentially harmful chemicals, such as carcinogens, allowing them to be excreted.[110][111][112]

Because soluble fiber slows digestion and is generally more fermentable, it has attracted more attention for fat loss.

A meta-analysis of randomized controlled trials specifically on highly prebiotic (able to feed our gut bacteria) fiber for people with BMI of 25 or greater didn’t find evidence for a meaningful or statistically significant reduction in body fat.[113] However, it is important not to generalize this finding to all highly fermentable fibers because there are other differences in characteristics that could be relevant.

Highly fermentable fiber, although great for health, may not be ideal for weight loss. Highly viscous fiber, in contrast, may be a better choice.

A set of recent meta-analyses specifically evaluated highly viscous fiber. The first meta-analysis was performed in the context of calorie-restricted diets and included studies on agar, alginate, β-glucan, guar gum, konjac, psyllium, or xanthan.[114]It found a reduction in body weight of 0.74 kg in the subgroup of participants with overweight/obesity over a period of 10.1 weeks on average and 0.89 kg in the subgroup with increased CVD risk over the course of 14 weeks; BMI (overlapping but a different subset of studies) didn’t change in the former group, whereas the latter saw a reduction of 0.45 over the course of 13.1 weeks. Body fat percentage was reduced by 1.39% over the course of 11.3 weeks for the subgroup with overweight/obesity, and there was insufficient evidence for the subgroup with cardiovascular risk. There was insufficient evidence to evaluate waist circumference. In some studies, the viscous fiber was compared 37

to no fiber, and in others, it was compared to a different kind of fiber, namely, wheat and other grains, with viscous fiber appearing to be more effective.

The other meta-analysis evaluated the effects of viscous fiber in the context of ad libitum diets, and far more studies were available in this context.[115] This meta-analysis found a reduction in waist circumference of 0.63 cm over a median study length of 12 weeks, with a particularly large effect for participants with metabolic syndrome and elevated cardiovascular risk. The researchers also found a reduction in body fat percentage of 0.85% over a median study length of 8 weeks for participants with overweight or obesity.

It is difficult to determine which types of viscous fiber are best, but the most researched types with benefits are psyllium, guar, and β-glucan, as well as combinations of viscous fibers.

**Warnings about fiber**

To date, no Tolerable Upper Intake Level (UL) has been set for fiber.[116][117]Ill effects from a higher fiber intake vary greatly from person to person and may include flatulence, bloating, cramping, diarrhea, or general intestinal discomfort. These effects may be more common under the following circumstances:

When consuming isolated fiber supplements

When fiber intake is abruptly increased

When consuming very high levels of fiber (>50 grams/day)

When consuming highly fermentable fibers (e.g., guar gum, inulin/chicory root, pectin, beta-glucan, konjac glucomannan)

If not consumed with sufficient fluids, a high-fiber diet may cause a blockage in the intestines (aka an intestinal obstruction). This is a particular concern in people who may have impaired intestinal motility, which occurs when the nerves or muscles in the intestinal tract don’t function properly, and may cause intestinal muscle contractions to occur at an abnormally slow rate, which may cause food to get stuck.

A common ingredient in protein bars — isomalto oligosaccharide (IMO) — was once thought to be fiber because it isn’t broken down early in the digestion process. But it was later found that IMO gets mostly absorbed in the small intestine, providing 2.7–3.3 calories per gram (compared with 4 kcal/gram for fully digestible carbohydrates).[118][119][120]

Although not inherently low in fiber, very-low-calorie, low-carbohydrate, and ketogenic diets can sometimes be lower in fiber than other diets due to a reduction in plant matter intake.[121][122][123]

Supplemental fiber may interfere with the absorption of digoxin (Digox, Lanoxin Pediatric, Digitek),[124] carbamazepine (Tegretol XR, Equetro, Epitol),[125]levothyroxine (Synthroid, Tirosint, Unithroid),[124] and lithium.[124] Do not take fiber within at least 30 minutes of taking these medications. It's possible that supplemental fiber may interfere with other medications not listed above. Out of caution, it may be prudent to separate pharmaceutical intake from fiber intake by at least 30 minutes as well. (This advice can also apply to other supplements).

Fiber supplements are not known to cause low blood sugar (i.e., hypoglycemic events), but it is theoretically possible — though not probable — when taken with other supplements or pharmaceuticals that can lower blood sugar, such as most antidiabetic drugs.

**How to take fiber**

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There are two ways to think about how to take fiber: general daily fiber intake from food and supplemental fiber. In general, most dietary fiber will come from food, and there are guidelines for different demographics.

Dietary requirements for fiber have been established as Adequate Intake (AI) levels.[35] The AI for fiber can be thought of as the minimum level needed to ensure nutritional adequacy. Although the recommended intake for adults ranges from 21 to 38 grams per day, the US average intake is just 16 grams, which falls 23.8%–57.9% below the AI.[126]

Adequate Intake (AI) for total fiber (grams)

| **AGE** | **MALE** | **FEMALE** | **PREGNANT** | **LACTATING** |
| --- | --- | --- | --- | --- |
| 0–6 months | — | — | — | — |
| 7–12 months | — | — | — | — |
| 1–3 years | 19 | 19 | — | — |
| 4–8 years | 25 | 25 | — | — |
| 9–13 years | 31 | 26 | — | — |
| 14–18 years | 38 | 26 | 28 | 29 |
| 19-30 years | 38 | 25 | 28 | 29 |
| 31–50 years | 38 | 25 | 28 | 29 |
| 51–70 years | 30 | 21 | — | — |
| >70 years | 30 | 21 | — | — |

Reference: Institute of Medicine. Dietary, Functional, and Total Fiber (chapter 7 in Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. The National Academies Press. 2005. DOI:10.17226/10490

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**What 25 grams of fiber a day looks like**

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Fiber supplements should consist of highly viscous fiber and generally the aforementioned psyllium, guar, β glucan types, or a combination of viscous fibers.

Fiber should be taken before a meal to slow digestion. In general, 6–15 grams per day, divided between major meals, is the most effective range, though there will be interindividual variability, and it may be possible to judge what suits an individual best through observation. For example, if a certain dose of fiber before a meal makes a person the least likely to overeat, that matters more than what happened on average in studies.

Future editions will attempt to uncover and compare a wider variety of dietary fiber types.

Regardless of where fiber comes from (foods, supplements, or both), take these 3 steps to minimize unwanted adverse effects.

1. Gradually increase fiber intake over a period of 1–2 weeks. This will allow time for the microbiome to adjust and help identify your tolerance threshold. If taking a fiber supplement, begin with 3–4 grams per day for the first few days before increasing the dose.

2. Take in enough fluids as fiber intake is increased. A fiber intake of 40–70 grams per day can be generally well tolerated, with sufficient fluid intake, in healthy adults without intestinal issues (e.g., IBD, IBS, celiac, Crohn’s, ulcerative colitis, low intestinal motility).[35] Consume at least 240 mL (8 oz) of fluids when taking fiber. This amount is suitable for up to a 10-gram fiber dose, although individual results will vary. People who are particularly sensitive should drink 296 mL (10 oz) of fluid for every 5-gram fiber dose.

3. Split the fiber intake evenly across meals to ease digestion.

**Medium-chain Triglycerides (MCTs)** 40

**What makes MCTs a promising option**

Compared to their long-chain cousins, medium-chain triglycerides (MCTs) consist of shorter, "medium chain" fatty acids such as caproic acid (6 carbons), caprylic acid (8 carbons), capric acid (10 carbons), and lauric acid (12 carbons). MCTs occur naturally in varying amounts in milk (4%–12%), palm kernel or coconut oil (both up to 50%).[127]

Due to the comparatively short length of their fatty acid chains, dietary MCTs are rapidly broken down, absorbed, and converted to ketones such as acetoacetate, acetone, and beta- hydroxybutyrate in the liver, whereas for long(er)-chain triglycerides, which provide their consumers with almost exactly 9 kcal of energy per gram of LCT they ingest, a single gram of MCTs delivers only 8.2 kcal of readily accessible energy.[128]

MCTs have been observed to reduce energy intake in the short term relative to other fatty acids. The mechanisms are still poorly understood though, and the effect apparently isn’t influenced by the most commonly measured appetite-related hormones such as gastric inhibitory polypeptide (GIP), peptide YY (PYY), or glucagon-like peptide-1 (GLP-1).[129]

Meta-analyses of randomized trials have found small but statistically significant reductions in body weight, body fat, and waist circumference.[130][131] Over the course of roughly 10 weeks, on average, the reduction in body fat in the treatment groups was roughly 0.39 kg and 0.89 kg greater than in the control groups, which constitutes a small but potentially meaningful effect if sustained over the long term. However, there is some evidence that the effects of MCTs lessen over time. In the long term, the averages may be even smaller.[132]

The reason that medium-chain triglycerides didn't make the ranks of primary or secondary fat loss options is because of the small if not practically negligible benefit that MCTs offer to the average dieter and the necessity of using medium-chain triglycerides as a substitute and not a supplement that is consumed on top of the long-chain triglycerides in their diet. All things considered, MCT oils are potentially effective but, regarding their efficacy, they are a rather mediocre fat loss agent in the extensive list of “promising options” listed in this guide.

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| **Digging deeper: How might MCTs work to reduce body fat? We're not entirely sure, but we have some leads**  One of the most frequently proposed mechanisms by which medium-chain triglycerides facilitate weight loss relates to their supposed satiety effects. Proponents of this hypothesis claim that the increase in satiety triggers unconscious reductions of the overall energy intake on ad libitum diets and promotes adherence to prescribed energy deficits.  Studies investigating the effects of acute MCT intake on participant food intake during subsequent meals do indeed support a small effect of MCTs on ad libitum energy intake. This effect tends to be greater when LCTs are replaced with purified MCT formulas, instead of natural MCT sources such as coconut or palm kernel oil.[129] The nature of the effect is generally transient, and studies that report weight-loss-relevant 400–600 kcal/day reductions in 24-hour energy intake[133][134] found that the benefits are predominantly limited to the first meal after ingestion of the MCTs.  The underlying mechanisms behind the voluntary reductions in energy intake are yet not fully understood because most LCT substitution studies fail to measure and analyze potential mechanisms, such as increasing levels of satiety hormones or vagal afferent activity.[135]In their 2021 review, scientists from King’s College in London and the University of Reading found only 4 studies that measured the satiety hormone response to high MCT vs. high LCT test meals. Among those studies, only 1 study reported the expected increase in satiety hormones.[129] The other studies even found comparatively larger effects on CCK, PYY, or GLP-1 for LCTs, compared to their allegedly more satiating medium-chain cousins, suggesting that long-chain (and not medium-chain) triglycerides should be the more satiating types of fat.[136][137]  The authors of the previously cited 2015 meta-analysis discuss several potential reasons for the rather disappointing 0.39 kg and 0.89 kg decreases in unwanted body fat. Of these, the most convincing hypothesis relates to the thermic effects of MCTs.[138][139][140] These effects are probably transient and apparently start to diminish after 2 weeks of increased MCT consumption.[132] At least in theory, the corresponding increase in fat oxidation and energy expenditure could nevertheless contribute to the observed weight loss effects of medium-chain triglycerides. Practically speaking though, it seems very unlikely that a body-weight-dependent increase in energy expenditure in the range of 0.1 kcal per minute, which lasts only for a limited time after the ingestion of a meal, will make a relevant difference for the average dieter.[140] The same goes for the repulsive taste of medium-chain fatty acids (MCFAs). These MCT metabolites can form when larger quantities of medium-chain-triglycerides are exposed to triglyceride-breaking lipase enzymes in the mouth. And we must not forget the well-known gastrointestinal side effects that have limited and still limit the use of MCTs in medical interventions.[141][142] These gastrointestinal effects may make a negligible contribution to the observable weight loss via reductions in food intake and a purported decrease in nutrient availability. |
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| **Digging deeper: Will MCTs spare muscle mass when dieting?**  It has been hypothesized that MCTs can help preserve muscle mass during periods of caloric restriction, but the study results thus far have been equivocal. Benefits have been reported predominantly from studies in which the comparator diets were artificially enriched with high or very high amounts of long-chain triglycerides.[143][144] The practical relevance of this (often unnaturally high) LCT content of the control diets becomes particularly obvious in a 2001 study in women with obesity. In that study, the already small muscle-preserving effect —2.7 vs. 3.2 kg of lean mass loss in 4 weeks on a very-low-calorie (578.5 kcal/day) diet — vanished when the comparator that the scientists used was not an LCT-enriched version but the common low-fat version of a commercial meal replacement shake.[145]  With individual studies measuring increased — and not decreased — nitrogen losses during high MCT vs. high LCT diets,[146] and the totality of contemporarily available evidence reporting only small to nonexistent effects of MCT oils on lean mass losses due to reductions in energy intake, we must assume that the efficacy of MCTs as protein-sparing agents is very limited. However, it is conceivable that in individuals who are on (very-)low-carbohydrate or ketogenic diets with naturally high levels of LCTs, the muscle preserving effects of MCT–LCT substitution could reach practical relevance. |
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**Warnings about MCTs**

Medium-chain triglyceride supplements, specifically oil formulations, are reported to cause gastrointestinal upset as well as instances of diarrhea.[147] A maximum dose of medium-chain triglycerides should be limited to 30 grams at one time because higher doses are associated with increased gastrointestinal distress.[148][147] It’s unclear how long to wait between doses in order to minimize this risk. For example, if someone takes 20

grams before a workout session and then takes an additional 20 grams 4 hours later, will that lead to gastrointestinal issues? We don’t know.

Medium-chain triglycerides currently do not have any known drug interactions. More research and data are required to determine whether interactions exist between medium-chain triglycerides and other drugs and supplements.

People with diabetes should be aware that medium-chain triglycerides supplements may increase ketone levels in the body, which may worsen diabetes complications.[149][150][151] Medium-chain triglycerides are primarily metabolized by the liver, so people with liver disease such as hepatic cirrhosis should exercise caution when taking medium-chain triglycerides.[150]

Currently, there are no notable issues or concerns for contamination of medium-chain triglycerides. However, the processing of oils (which is similar to how to medium-chain triglyceride supplements are processed) can lead to the formation of impurities that may be hazardous to health,[152] but there has been no concern for this occurring with medium-chain triglyceride supplementation.

**How to take MCTs**

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Do not use medium-chain triglycerides (MCTs) as a “supplement” but as a “substitute”. Replace 15–25 grams per day of long-chain triglycerides in the diet with MCTs for a period of at least 8 weeks. Do not escalate the dosage because studies don't support that increasing MCT intake beyond 30 grams per day will accelerate the loss of weight and/or body fat.

Practically speaking, this substitution can be achieved by replacing sources of high amounts of LCTs in the diet — such as soybean, canola, or corn oil, tallow fat, butter/ghee and even olive oil — with either purified MCT oils or natural sources of medium-chain triglycerides such as coconut or palm kernel oils. In addition, it may be worth spending some extra money on high-MCT alternatives of favorite processed foods. Some of the high-MCT pancakes, smoothies, muffins, ice creams, milk shakes, tomato sauces, etc., that the food industry have to offer have even been used in scientific studies. Be careful though, because many of the manufacturers of these “functional foods” do not properly “substitute” but simply “supplement” their products with MCTs. The obvious consequence is an often significant increase in energy content that must be considered to avoid sabotage of dieting efforts.

**Garcinia cambogia**

**What makes Garcinia cambogia a promising supplement**

Garcinia cambogia (GC) is an edible fruit that grows in parts of South Asia and Africa. With its sharp and sour taste, GC has traditionally been used to cure and preserve foods. It has also been used as an herbal tonic to cure intestinal discomfort, eradicate parasites, and ameliorate rheumatism.[153] Today, GC is sold as a “natural antiobesity agent” and is often standardized for its purportedly primary active ingredient hydroxycitric acid (HCA). Studies on Garcinia or purified HCA support some but not all the label claims of GC supplements.

Garcinia seems to promote weight loss by 2 distinct mechanisms: reductions in food intake and amelioration of body fat gain. These effects are thought to be brought about by HCA's modulatory effect on satiety-related serotonin levels, as well as increased fat oxidation and decreased de novo lipogenesis (aka fat storage).[153] Moreover, ex vivo studies on human adipocytes from women with obesity who supplemented with HCA reported increases in fat-cell leptin expression and a significant downregulation of 348 and induction of 366 fat-related and obesity-related genes.[154]

A 2020 meta-analysis of 8 randomized controlled trials in 530 participants with overweight or obesity reported an average weight loss of 1.34 kg and a literally meager reduction of body fat percentage of approximately 1%.[155]Interestingly, the reviewers observed a rather large 4.16 cm reduction in waist circumference (WC). Unfortunately, this result was based on only those 3 out of 8 trials that measured the changes in this important marker of a potentially health-relevant reduction of proinflammatory belly fat.

The 8 input studies lasted 8 to 12 weeks, and the dosages of Garcinia cambogia ranged from 166 to 4,667 mg per day. No study seems to have investigated the effects of GC in apparently healthy individuals or athletes with normal weights. Only a single 10-day randomized controlled trial that probed the effects of a combination of GC with L-carnitine and an algae extract supported the appetite suppressive effects of GC[156] and thus the idea that GC or HCA supplements may aid the weight-loss and weight-maintenance efforts of normal-weight individuals, too.

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**Warnings about Garcinia cambogia**

Numerous case reports warn against liver damage from GC supplements.[157][158][159][160] Many of the complications resolved with early discontinuation of the supplement.[160] Nevertheless, data from 22 cases recorded by the Drug-Induced Liver Injury Network (DILIN) from 2004 to 2018 indicated that liver injury occurred 13–223 days (median of 51 days) after supplementation was initiated.[161]It is noteworthy that many of the published case reports document signs and symptoms of liver damage in response to Hydroxycut®, a multi-ingredient “fat burner”[162][163][164][165][166]in which HCA was one of the primary ingredients (but not the only ingredient) that could have been responsible for the adverse effects. Moreover, a recent study reported that the HCA content of 33% of the Garcinia cambogia supplements in a sample of 18 deviated significantly from the label claims and contained often undeclared additives.[167]

In view of the established risk of idiopathic hepatic damage and individual case reports of ocular side effects,[168] myocarditis,[169] and mania,[170] even the authors of a generally positive recent review of GC’s ability to promote weight loss in participants with overweight and obesity acknowledge that the potential side effects, supplement/supplement interactions, and supplement/drug interactions of Garcinia still warrant further investigations.[171]

**How to take Garcinia cambogia**

In view of its potential albeit idiosyncratic (i.e., highly individual) side effects, it would be wise to start at the lower range of the dosing spectrum with 1,000 mg of GC extract or 300–500 mg of HCA per day in 2–3 separate servings, preferably taken with food.

Current research does not support increased weight or fat loss in response to higher dosages or treatment durations.ly, it is not recommended to exceed intakes of 2,000 mg of GC extract or 500–750 mg of HCA per day or to consume GC supplements for longer than 30 days. For additional considerations regarding the often debated safety of GC supplements, please refer to the “warnings” section of this article.

**Irvingia gabonensis**

**What makes Irvingia gabonensis a promising option**

Irvingia gabonensis, also known as the African mango, wild mango, or bush mango, is a species of African trees that bears edible mango-like fruits. Extracts from its seeds are marketed as weight loss adjuvants that work by increasing the breakdown and inhibiting the synthesis of fatty acids, as well as modulating appetite and food intake via their effects on leptin and adiponectin.[172][173][174] The putative weight loss benefits of African mango are often ascribed to ellagic acid, Irvingia's best-known bioactive constituent. Whether ellagic acid is the most important or even the only active ingredient in the seed extracts is not clear. Although it does exist, clinical evidence to support the weight loss effects of Irvingia is rather scarce. An older systematic review from 2013 found only 3 clinical randomized clinical trials and concluded that, based on the contemporarily available evidence, Irvingia could “not be recommended as a weight loss aid.”[175] A more recent meta-analysis from December 2019 found a total of 5 randomized controlled trials[176] and came to a slightly different conclusion. Based on data from participants aged 19–55 with overweight 45

and obesity, the 2019 meta-analysis calculated a statistically significant 8.71% (95% CI: −11.10, −6.32) net reduction of body weight that was accompanied by potentially clinically meaningful reductions in body fat percentage (−4.23%) and waist circumference (−7.6%).

The interventions lasted 28–90 days (8.8 weeks on average). The supplement dosages ranged from 2x150 mg per day to 3x350 mg per day taken before meals (when the corresponding details were reported). Two industry-funded studies used the standardized Irvingia seed extract IGBO131. One study used the extract in

combination with 250 mg of Cissus quadrangularis[177]In the 2 remaining, non-industry-funded studies, regular seed extracts were used.

Even though the results of the previously discussed meta-analysis sound quite convincing, there are good reasons why we've classified Irvingia as only a “promising” but not as a “secondary" — let alone “primary” — option for fat loss. Most importantly, the authors of the meta-analysis found a high risk of bias in 4 of the 5 studies. Furthermore, it is worth considering that 2 studies were directly funded by the supplement industry and that the practical relevance of one of these studies, which also happens to report the largest reductions in body fat percentage and waist circumference, was limited by confounding effects due to cosupplementation with Cissus quadrangularis.[178][177]It's also noteworthy that the only study rated at a low risk of bias did not detect significant reductions in body weight or body fat in response to 90 days of daily Irvingia supplementation at a dosage of 2x150 mg per day in its 24 participants with obesity (BMI > 30) and diagnosed metabolic syndrome.[179] What this low risk of bias study did find, though, was a statistically significant 3 cm reduction in waist circumference that was accompanied by significant improvements in glucose and lipid metabolism, suggesting that Irvingia may be best suited for dieters who are interested specifically in reductions of proinflammatory visceral body fat, rather than lower numbers on the display of their bathroom scales.

**Warnings about Irvingia gabonensis**

Research has found no significant difference in side effects between people who take Irvingia gabonensis and placebo, although the evidence is sparse and further research is needed[175]. Some of the potential side effects that have been reported include headaches, difficulty sleeping, and flatulence (gas).[175]

There is no clear research on possible drug interactions of Irvingia gabonensis. However, based on its proposed mechanisms of action, there could be a very speculative drug interaction with diabetes medication that may cause hypoglycemia[180] or may possibly affect how well certain antidiabetes drugs like rosiglitazone or pioglitazone work.[181] People who are taking anti-diabetic medications or who have problems with blood sugar regulation should be cautious and talk to their doctor before taking Irvingia gabonensis.

It is important to note that Irvingia gabonensis may pose a risk to individuals with certain medical conditions. Research on rats found that Irvingia gabonensis extract taken in high doses (over 2,500 mg/kg/day) did not cause any harmful effects.[182] However, it is unclear whether this applies to humans with kidney problems because it has not been researched. However, one case study reported that a person with high blood pressure and some kidney damage experienced kidney failure after taking Irvingia gabonensis.[183] For individuals with kidney problems, it is important to exercise caution when supplementing with Irvingia gabonensis.

There are no known reports of cross-contamination of Irvingia gabonensis supplements.

**How to take Irvingia gabonensis**

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Take 150–250 mg of Irvingia seed extracts 2–3 times per day at 30 minutes before meals.

With only 5 studies and no direct dose-effect comparisons, it is impossible to tell whether escalating the doses will yield better results. In fact, the study that used the highest amounts of Irvingia (3x350 mg/day) reported the smallest reductions in body weight and body fat percentage.[172] Hence, it appears rather unlikely that taking more than the previously recommended 300–750 mg of Irvingia per day will yield better results.

Due to the same lack of head-to-head comparisons, it is also not clear whether extracts like IGOB131, which is standardized for its albumin (≥7%) and ellagic acid (≥1%) content, should be preferred over other forms of Irvingia gabonensis seed extracts. This is particularly true in view of the fact that the purported effects of the albumin content of the seed extract, which the patent holder almost advertised in a 2015 paper,[184] are based on hypotheses and outright speculation.

**Green Coffee Extract**

**What makes Green coffee extract a promising option**

Green coffee extract (GCE) is an extract of unroasted, green coffee beans that is rich in chlorogenic acid (CGA). Among the various polyphenols in coffee beans, CGA is believed to be the primary driver of GCE's beneficial effects on fat loss efforts. To deliver sufficient amounts of CGA, scientists and supplement vendors alike rely on extracts that are standardized for a certain amount of the antioxidant and anti inflammatory free radical scavengers[185] and contain reduced levels of caffeine.

Two larger meta-analyses have reviewed the effects of GCE on body weight and body fat in selected clinical trials.[186][187] The dosages of GCE ranged from 46 to 6000 mg per day and were administered for 1 to 12 weeks (median of 8 weeks) to adults aged 18–51 years with several pre-existing health conditions, including overweight/obesity, hypertension, nonalcoholic fatty liver disease, high blood lipids, and metabolic syndrome. Two studies in participants without apparent health conditions were also included.

Because there is a large overlap between the studies that were included in the 2 meta-analyses, it is not surprising that the overall results of the 2019 and 2020 papers are very similar. Based on slightly different sets of 15 studies and data from 723[186] and 897 participants,[187] both meta-analyses report significant reductions of body weight (−0.94 kg and −1.23 kg, respectively) in response to green coffee extract or beverages. Regarding the more fat-loss-relevant outcomes of waist circumference and body-fat percentage, the results differ only in their statistical significance The earlier analysis,[186] which investigated only the effects on the participants’ waist circumference, reported a technically nonsignificant (p = 0.07) reduction of 0.85 cm.[186] Having included data from 2 additional studies, the more recent meta-analysis from 2020[187] reported similar, albeit statistically significant (p = 0.006) mean reductions of 1.00 cm.

Only the more recent of the 2 meta-analyses[187] assessed the effects on body fat directly. With only 4 studies and 175 participants in this subgroup analysis, the researchers were unable to detect a significant effect on percentage of body fat (−0.40%, p = 0.58).

Although the absolute effects on body weight and, more importantly, waist circumference and body fat 47

percentage don't seem to be of great practical relevance, a closer look at the subgroup analyses of the 2 meta-analyses shows why GCE can still be considered a “promising” fat loss supplement, at least for some people: Participants with overweight and obesity (BMI >25) lost more than twice as much weight (−2.054 kg, p < 0.001 versus 0.008 kg, p = 0.929 in normal-weight subjects).[186] Women seem to be more likely to see weight loss benefits than men. Furthermore, there’s evidence of significant appetite reduction and improved insulin sensitivity[188]in participants with metabolic disease; both could facilitate greater fat loss in this part of the population.

**Warnings about Green coffee extract**

Similar to regular coffee intake, green coffee extract naturally contains caffeine. With high caffeine intake, adverse effects such as headache, irregular heartbeat, and frequent urination can occur. An animal study found that green coffee extract may result in calcium depletion in bones, but more research, —specifically human studies — are required to determine the validity of this effect.[189]In general, studies involving green coffee extract have reported few adverse effects.[190][187]

Green coffee extract should not be taken with other stimulant drugs and supplements such as ephedrine because concurrent use could result in overstimulating effects that may lead to heart problems.

The caffeine present in green coffee extract may worsen symptoms of anxiety and increase blood pressure, so people with anxiety and hypertension should not consume large amounts of green coffee extract and should use caution in moderate use of the supplement.

Coffee beans and other products of coffee, including green coffee extract, can be subject to contamination, which may affect the quality and safety of the product. Samples of green coffee extract have been studied, and these studies found the presence of contamination from toxigenic fungi.[191] Mycotoxins may be resistant to the roasting process and thus present a possible risk of exposure.[192] Although there is potential for contamination, there does not seem to be a high occurrence of illness from consumption of green coffee extract due to toxigenic fungi.

**How to take Green coffee extract**

The current evidence suggests that the effective dose of green coffee bean extract (GCE) is 400–800 mg per day, standardized for 45%–55% chlorogenic acid (CGA), taken with or without food for at least 4 weeks. Women and people with overweight/obesity are most likely to benefit.

Significant dose-response effects were not detected in meta-analyses,[186][187] and individual studies comparing the efficacy of different amounts of GCE do not exist but could help specify the recommendations.

**Berberine**

**What makes berberine a promising option**

Berberine is an alkaloid that can be found in various plants, including Berberis aquifolium, Berberis aristata, 48

and Argemone mexicana.[193] Traditionally the roots, rhizomes, and stems of these plants have been used as a herbal treatment for diarrhea, intestinal parasites, and related ailments.[194] More recently, berberine has caught the attention of medical researchers. Recent studies have suggested that berberine supplements may even rival metformin, the world's most prescribed diabetes drug,[195] for its gluco-regulatory and lipid regulatory effects.[193] Studies also suggest that, despite significant structural differences, berberine and metformin seem to exert their beneficial health effects via similar if not almost identical mechanisms.[193] Therefore, It is unsurprising that individual clinical trials suggest that berberine shares metformin's antiobesity effects in participants with a variety of metabolic and inflammatory diseases.[196][197][198]

Unfortunately, reliable clinical evidence of berberine's effects on body fat, specifically, is almost nonexistent. The pertinent studies so far have focused on changes in body weight and BMI, improvements in blood glucose management, or reductions of elevated blood lipids as primary outcomes and have been conducted almost exclusively in participants with overweight/obesity and/or metabolic dysregulation. Based on this admittedly limited evidence, 2 recent meta-analyses investigated the effects of berberine on body weight/BMI and waist circumference.[196][197]

Both meta-analyses were published in 2020 and included only randomized clinical trials with a comparator or placebo group. Accordingly, there is a huge overlap between the set of 9 and 12 studies that were included in the analyses. The clinical trials that were analyzed lasted 4–24 weeks, with a median study duration of 12 weeks. They were conducted almost exclusively in participants with overweight or obesity who were treated with an average dose of 1,500 mg of berberine HCL per day (dosages ranged from 750 to 5,000 mg of berberine HCL per day).[196][197]

Despite the large overlap in input studies, the meta-analysis reported slightly different effects on body weight and BMI. One of the 2 meta-analyses reported a statistically significant (p < 0.001) 2.07 kg reduction in body weight but did not detect a significant effect on BMI.[197] The other meta-analysis, which used a marginally different set of studies, found only insignificant effects on body weight but a significant reduction in BMI (−0.29, p = 0.006).[198] What is important is that both meta-analyses reported statistically significant improvements in the participants’ waist circumferences of −1.79 cm (p = 0.001) and −0.59 cm (p = 0.03).[197][198] Against the background equivocal reductions in body weight and BMI, this reduction in waist circumference may be taken as a surrogate marker of body fat reductions.[199]

Overall, there's little doubt that the results of individual studies on berberine's weight loss effects in specific populations are impressive. In one study, for example,184 participants with nonalcoholic fatty liver disease lost twice as much weight over the course of a 16-week lifestyle intervention when they supported their weight loss efforts with a dosage of 3 x 500 mg of berberine HCL per day.[200] However, the entirety of the contemporarily available evidence is not sufficient to classify berberine as an empirically proven fat loss supplement. After all, the average reductions in body weight and waist circumference observed in clinical trials are small. Changes in body fat have not been directly measured with body impedance or dual-energy X-ray absorptiometry (DXA) in clinical trials. Additionally, data from studies in participants with normal weights and without apparent health conditions are not available. This absence of studies in healthier, fitter, and more active study populations is particularly problematic. After all, it is all but certain that berberine — which scientists believe that it works mostly by activating the malfunctioning AMPK pathway in people with obesity and metabolic dysregulation[201] — would have similar effects in a population whose cellular energy gauge (because that’s basically what AMPK is) is still intact.[202]

**Warnings about berberine**

Although low blood sugar (i.e., hypoglycemic events) has not been readily observed in clinical trials, no 49

long-term trials have tracked this outcome. It is possible that berberine may cause low blood sugar, so some caution is warranted, particularly if it is taken with supplements or pharmaceuticals that can lower blood sugar.[203] People who are taking any medication that can lower blood sugar should not begin taking berberine without talking with a physician.

The research assessing berberine’s safety tends to be short term, making it difficult to predict adverse effects with prolonged use. The larger, more effective doses (1.5 grams/day or more) of berberine may lead to a higher occurrence of adverse effects.[204] Although major adverse events haven’t been associated with berberine supplementation, gastrointestinal symptoms such as nausea, diarrhea, constipation, and abdominal swelling from gas or fluid may result from taking high doses.

Berberine should only be taken by people with elevated fasting blood sugar (≥5.55 mmol/L; ≥100 mg/dL) or HbA1c (≥5.7%). Most of the research has been conducted in the context of type 2 diabetics, and much of the remaining research focuses on people at risk for becoming diabetic. Although it’s possible that berberine could help people with normal blood sugar levels and insulin sensitivity maintain lower fasting blood sugar, it’s not clear whether the benefits outweigh the risks when used consistently for years. Additionally, it’s unclear whether berberine can provide any benefit for people with gestational diabetes or polycystic ovary syndrome (PCOS),[205] a condition that is often accompanied by insulin resistance.[205]

Berberine interacts with several enzymes and thus has the potential to interact with many pharmaceuticals. Not all are known, but the documented drug interactions include losartan (Cozaar), dextromethorphan (Vicks, Robitussin, Tussin Cough, Delsym), midazolam (Versed), and various oral contraceptives.[206] Individuals who are on cyclosporine (Neoral, Sandimmune, Gengraf) should not take berberine because it may interfere with drug metabolism.

Do not supplement with berberine if pregnant or breastfeeding because it has barely been studied under these conditions. The studies that do exist point to some potential harm (unusual uterine contractions, miscarriage, and kernicterus in jaundiced newborns), but these events are not confirmed to be caused by berberine.[207][208] Even so, caution is warranted until more research has been conducted.

Lastly, berberine can increase bilirubin levels (a substance found in bile, which aids digestion), which may interfere with lab tests of bilirubin. Individuals who are planning on being tested for bilirubin should stop taking berberine at least 7 days prior to testing.

**How to take berberine**

The current evidence suggests that effective dosages of berberine range from 500 to 1,500 mg of berberine HCL per day. To avoid gastrointestinal distress, the participants in clinical trials are usually advised to consume the capsules with food, with higher doses (>500 mg) broken down into two (2x500 mg) or three (3x500 mg) smaller servings.

Based on the currently available evidence, there is no reason to believe that supplementing with more than the previously recommended maximum of 1,500 mg of berberine HCL per day would augment its fat loss effects. However, the treatment duration seems to matter, with studies lasting 12–16 weeks reporting the largest reductions in BMI.[197]

Putative alternatives to berberine HCL — like barberry juice[209] and a plethora of plant or fruit extracts — exist but lack scientific studies to prove their efficacy and make sensible dosage recommendations.

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**Unproven Supplements**

**Yerba Mate**

**What makes yerba mate an unproven supplement**

Yerba mate, orIlex paraguariensis, is a small shrub native to South America that grows primarily in Argentina, Paraguay, Uruguay, and Brazil. Yerba mate contains a variety of bioactive molecules, including flavonoids (such as quercetin, kaempferol, and rutin), cinnamic acids, xanthines (such as caffeine and theobromine), saponins, amino acids, vitamins, and minerals.[210]

Although a small number of animal studies have suggested that yerba mate may have antiobesity effects,[211][212] the only randomized controlled trial looking at the effects of yerba mate on anthropometric parameters in humans has produced less than convincing results.[213] More specifically, the aforementioned study examined the effects of supplementation with 3 grams per day of yerba mate extract for 12 weeks in 30 men and women with obesity. Compared to placebo, yerba mate supplementation prevented small increases in fat mass and body fat percentage and caused a small reduction in waist–hip ratio, but had no effect on BMI, body weight, abdominal visceral or subcutaneous fat, or the circumference of the waist, hip, thigh, or arm. It’s worth noting that the trial was exploratory in nature and was funded by the manufacturer of the yerba mate supplement.

In short, the lack of high quality human trials looking at the effect of yerba mate on body composition makes yerba mate an unproven supplement for fat loss.

**Guarana**

**What makes guarana an unproven supplement**

Guarana, also known as Paullinia cupana, is a fruit-bearing tree. Its seeds are ground into powder, and the powder is best known for its stimulant properties. Guarana is primarily produced in the Brazilian states of the Amazonas region (16%) and Bahia (77.4%), and approximately 70% of the world production of guarana is used by the beverage industry. Guarana is added to various soft drink and energy drinks as a highly marketable “natural source of caffeine”.[214]In the Amazonian medical tradition, guarana has been used as a diuretic and tonic against headache, fever, and cramps. Weight loss, on the other hand, was added to the list of allegedly “traditional” uses only when guarana gained popularity in the urban centers of Brazil.[214]

Guarana contains xanthines, primarily caffeine, as well as a range of phenols, including catechins, tannins, and procyanidins. Although all of these compounds have been touted as “fat burners” for marketing purposes in the past, there is insufficient evidence of putative synergistic effects from the 2.5%–6%

caffeine in the seeds and higher amounts of the world's best-known stimulant in commercially produced 51

standardized guarana extracts.[215]

Rodent studies comparing the effects of regular to decaffeinated guarana extracts do not support the notion that the putative beneficial effects that guarana exerts on weight loss and fat loss are attributable to anything other than its highly bioavailable caffeine content.[216] This lack of evidence of additive or synergistic effects of caffeine with the phenol content of the Paulinia cupana seeds clearly relativizes the significance of the results of 2 often-cited animal studies that investigated the effects of pure guarana extracts on metabolic parameters relevant to weight loss.[217][218][219] Perhaps even more importantly, it would explain the lack of clinical trials that support a non-caffeine-dependent effect of guarana on weight loss and/or weight maintenance in humans.

Overall, the currently available research indicates that supplement consumers can use guarana as an alternative to straight caffeine HCL and/or other caffeine sources. However, users must not expect fat or weight loss advantages that go beyond those provided by equivalent doses of caffeine from different sources.

**White Willow Bark**

**What makes white willow bark an unproven supplement**

White willow bark — which usually comes in the form of an extract from the bark of the eponymous willow tree — is a natural source of salicin, which is metabolized into salicylic acid, a cousin of acetylsalicylic acid, better known as aspirin. Although both share similar anti-inflammatory effects, the common effective dose

for white willow bark (240 mg) is significantly lower than the one that's recommended for aspirin (500 mg).[220] This is due to the higher potency of the plant extract that has been ascribed to various polyphenolics and flavonoids that may act synergistically with the aspirin precursor and related molecules.[221][222]

Rumors about the weight loss benefits of white willow bark date back to the late 1990s and early 2000s, when it was added to the highly popular ephedrine-containing ECA “fat burners”. Supplement manufacturers and vendors claimed that the bark extract would act synergistically with the supplements' two other eponymous ingredients, i.e., “E” as in ephedra/-ine and “C” as in caffeine.

The formerly commonly accepted rationale that the salicin content of the bark would prolong the cAMP related fat loss effects of ephedrine has never been experimentally validated. The same goes for the possible standalone weight loss effects of aspirin, salicin, or any of the mostly uncharted polyphenolics and flavonoids in the bark extracts.[222] [221] As far as fat loss is concerned, white willow bark must thus be filed in the “unproven supplements” category.

**Coleus forskohlii**

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**What makes Coleus forskohlii an unproven supplement**

Coleus forskohlii is an aromatic herb from the family of mints and lavenders and is indigenous to India. It has a long history of use in Ayurvedic medicine.

More recently, one of its phytochemical constituents, forskolin, has been shown to increase the body's levels of cyclic adenosine monophosphate (cAMP) and, subsequently, the rate of lipolysis (i.e. the release of stored body fat). Because this effect occurs independent of hormonal stimulation, forskolin could make a good complement to stimulant “fat burners” such as caffeine, which act primarily via catecholamines.[223][224][225]

Unfortunately, there is still insufficient evidence from clinical trials to confirm individual and/or complementary effects of forskolin on the loss of body fat in humans who are following either energy sufficient or calorically reduced diets. Of the 4 available industry-funded (or at least supported) 8-week to 12-week studies, 3 were conducted in participants with overweight or obesity.[224][226][225] Only one of these randomized double-blinded clinical trials reported significant reductions in total body fat and body fat percentage compared to the placebo treatment (−4.52 ± 5.74 kg vs. −0.51 ± 1.91 kg; p < 0.05).[224] The other 2 trials, which involved a total of 60 male and female participants with overweight or obesity, did not find beneficial effects of forskolin on either body weight or body composition over the course of a 12-week supplementation period. Lastly, the fourth and only open-label study in young normal-weight participants, which reported reductions in body fat, was limited by the lack of a control group and the low number of only 15 participants. Accordingly, the study can hardly be seen as convincing evidence of the putative fat loss effects of Coleus forskohlii. It should also be mentioned that it is impossible to say whether and to which extent the efficacy of the supplement may have been hampered by suboptimal dosing schemes. All 5 studies used a standardized (10% forskolin) ethanol extract from C. forskohlii. The supplement was consumed at a dosage of 250 mg twice per day (500 mg/day in total), approximately 30 minutes before meals. Putative synergistic effects with stimulant weight loss adjuvants such as caffeine have not been evaluated in clinical trials.

Due to the lack of experimental data as well as heavy industry support and funding, Coleus forskohlii must currently be considered an unproven supplement option for fat loss, and it is unlikely to become proven in the future.

**Fucoxanthin**

**What makes fucoxanthin an unproven supplement**

One human study showed a benefit from a dosage of 2.4–8 mg per day, but it used a proprietary seaweed extract; the study has never been replicated, and its results seem too good to be true — an average fat loss of 3.6 kg (7.9 lb) in 16 weeks. More research is needed before fucoxanthin can be recommended for fat loss.

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**Saffron**

**What makes saffron an unproven supplement**

Saffron has antidepressant and potentially antistress/antianxiety effects,[227] and depression and stress can potentially lead to excessive, hedonic eating.[228][229] There is some evidence from trials that saffron can improve satiety and alter eating behavior.[230][231] Additionally, saffron may reduce fat digestion by inhibiting pancreatic lipase and may have beneficial metabolic effects on skeletal muscle and adipocytes.[232]

When it comes to the clinical trials investigating saffron’s effects on measurable body composition, positive studies are few and far between. One 8-week study in participants with coronary artery disease found a reduction in waist circumference and body fat percentage from 30 mg of an aqueous saffron extract,[230] and a 12-week study in participants with diabetes found a reduction in waist circumference from 200 mg of saffron powder.[233] Other studies have not found meaningful effects.[231][234][235][236][237]It’s important to note that none of these studies set out to specifically test the effects of saffron on weight loss and, notably, they didn’t use saffron in the context of a weight loss diet. It’s possible that saffron, when combined with a weight loss diet, could lead to greater adherence in the long term. More research in that context is needed.

In conclusion, saffron is unproven for this purpose, but future studies that use it in conjunction with a weight loss diet could be informative.

**Synephrine**

**What makes synephrine an unproven supplement**

Synephrine (p-synephrine) is a protoalkaloid found in high doses in Citrus aurantium (bitter orange) and some other citrus fruits. It is a stimulant and has thermogenic properties, leading to its use in preworkout and fat loss products.[238] However, the mere observation that it can elevate metabolic rate is insufficient on its own to demonstrate meaningful fat loss over the long-term.

One study evaluated the effects of 20 mg of synephrine taken 15–30 minutes prior to exercise and at breakfast on nonexercise days.[239] Synephrine was also combined with a very long list of preworkout supplements in the intervention group, which was compared to the same supplements without synephrine and also to a placebo group. Over the course of 8 weeks, there didn’t appear to be any effect of synephrine on body fat.

Other studies have used synephrine in combination with other supplements and compared the combination to a placebo.[240][241][242][243] As such, these studies can’t provide information on the effects of synephrine in particular, and we don’t know how much, if any, of their results were due to synephrine.

In conclusion, synephrine has not been properly tested for its effects on body composition, and it is unproven.

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**Inadvisable Supplements**

**Hoodia gordonii**

**What makes Hoodia gordonii an inadvisable supplement**

Hoodia gordonii, parviflora, and all the other roughly 330 species from 31 genera of Hoodia plants are often mislabeled as “cactuses” or “desert cactuses”. Rather than a true cactus, which belongs to the Cactaceae family, all Hoodia genera belong to the Apocynaceae, the milkweed family.[244]

In contrast to many other commercial weight loss adjuvants, Hoodia does not have a well-documented history of use in traditional medicine as an intestinal tonic or appetite suppressant. According to a 2008 paper in the Journal of Ethnopharmacology, there was only a single scientific paper referring to the use of Hoodia species as an anorexiant agent prior to the publication of the first patent application in 1998.[244] Currently, roughly two decades and astonishingly few human studies later, scientists are still not sure which of a variety of metabolites in the various species of Hoodia that have been studied would cause its putative anorexigenic effects.[245]

Not knowing the mechanism by which a “fat burner” works is one thing. However, what's even more important for our assessment that Hoodia lacks sufficient scientific backing is the mere absence of convincing evidence of its rumored effects on appetite and downstream effects on body weight or body fat levels in humans. One of the few studies, in which researchers observed a statistically significant but practically irrelevant weight loss of 0.58 kg (p = 0.046) in the 204 participants in a 40-day single-blind, randomized, placebo-controlled consumer trial, was unable to establish a measurable effect on appetite, hunger, and craving control.[246] More recent studies seem to confirm that Hoodia cannot live up to its reputation as a powerful appetite suppressant that facilitates practically meaningful reductions in energy intake.[247][248]

Moreover, the often advertised safety of Hoodia as a nonstimulant and thus safe(r) alternative to stimulant based “fat burners” has received some scrutiny ever since a double-blinded, placebo controlled study in 49 women with overweight reported not just the previously known intestinal side effects, including nausea and emesis, but also potential neurological disturbances of skin sensation and unexpected significant increases

in blood pressure, pulse, heart rate, bilirubin, and alkaline phosphatase (p < 0.05), which are indicative of unwanted cardiovascular and hepatic side effects. Over the 15-day study period, the participants had received 2 servings per day of 1,110 mg of a commercially available purified Hoodia gordonii extract in the form of a yogurt drink, without significant effects on the ad libitum energy intake, body weight or the 36.6% (range 25%-45%) body fat of the human participants.[247]In the absence of evidence of both efficacy and safety,[245] Hoodia supplements can currently not be recommended as fat loss adjuvants.

**Senna alexandrina**

**What makes Senna alexandrina an inadvisable** 55

**supplement**

Senna alexandrina, or just senna, is an herb frequently marketed as a dietary cleanser and detoxifier. However, although senna can cause temporary weight loss due to its potent laxative effect, it is unclear whether it has an inherent effect on fat loss. One study in rats found that senna reduced weight gain in response to a high fat diet, though this is far from the high standard of evidence we require.[249]

Daily or chronic use of any potent laxative (except for fiber and caffeine) may result in colon damage, and so there is a potential risk from using senna consistently.

**Raspberry Ketone**

**What makes raspberry ketone an inadvisable supplement**

Raspberry ketones (RK) are naturally occurring aromatic phenolic compounds. Originally extracted from red raspberries, kiwifruit, peaches, and apples, they are now mass produced synthetically for use in perfumes and cosmetics.[250] Supplement manufacturers started to use RKs in their products in the mid-2000s and still advertise and sell them based on claims related to the purported antiobesogenic, antidiabetic, cardiovascular, and hepatoprotective effects of RKs.[251]

In 2005, scientists first observed that raspberry ketones, which are structurally similar to capsaicin and synephrine, can actively promote lipolysis and fat oxidation while suppressing fat storage when they are applied directly to fat cells in a cell culture dish.[252][253] Encouraged by subsequent rodent studies in which researchers observed statistically significant decreases in body weight (and more importantly, liver and adipose tissues weights of mice fed with a high-fat diet,[254][255][256]~~)~~ obesity researchers hypothesized that RKs may prove to be a new, valuable tool in the antiobesity toolbox. Until today, however, convincing evidence to support this hypothesis does not exist.

Only 2 clinical trials so far have investigated the efficacy of RKs as a weight loss adjuvant in humans. A 12- week randomized single-blind clinical trial in women with obesity[257] found no significant difference between the reduction in body weight of 20 participants who received dietary counseling plus 500 mg/day of pure raspberry ketones and that of the 18 women in the control group who received only the counseling. Essentially similar results were reported 2 years later in an industry-funded study from the U.S. The study investigated the effect of a multi-ingredient supplement containing an undisclosed amount of raspberry ketones, capsaicin, caffeine, garlic, Citrus aurantium, B vitamins, and chromium (Prograde Metabolism™) on the weight loss success of 36 men and women with overweight.[258] Over the course of 8 weeks, all participants followed an energy-reduced diet (500 kcal/day deficit) and supervised progressive exercise training 3 times per week. Both groups lost significant amounts of weight and body fat, but there was no statistically significant weight loss advantage for the treatment group. The evidence from clinical trials is thus not just insufficient. Rather, the 2 studies prove that raspberry ketones, at the commonly recommended dosage of up to 500 mg per day, do not have a statistically significant weight or fat loss effect in human beings — and even worse, higher doses of RKs (equivalent to 2,000 mg/day for a 50- kilogram human), as used in the previously referenced rodent studies, have only recently been linked to elevated glucose levels and higher mortality rates in initially healthy mice, as well as elevated markers of 56

liver damage in obese rodents.[259]In short, raspberry ketones are an unproven if not disproven fat loss supplement in humans and will probably disappear completely from the overcrowded fat loss supplement market due to their inefficacy and their recently questioned safety.

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**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 filling out this survey.

**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 research each potential addition. 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., fatigue) or in the evening (e.g., insomnia).

**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 (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.

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

The Dietary Reference Intakes (DRIs) is a system of nutrition recommendations designed by the Institute of Medicine (a US institution now known as the Health and Medicine Division). 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 metformin (a diabetes medicine) need more vitamin B12.

Moreover, the DRIs are based on the median weight of adults and children 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. Isn’t soy protein bad for males?**

Phytoestrogens are plant compounds structurally similar to estradiol, the main estrogen in males and premenopausal females. Because soy contains isoflavones, a type of phytoestrogen, concern has been raised about soy affecting male health.

To this day, two case reports have documented adverse effects (gynecomastia, hypogonadism, reduced libido, and erectile dysfunction) from an estimated 360 mg of soy isoflavones per day for 6–12 months. However, a meta-analysis of 15 randomized controlled trials (RCTs, a much higher level of evidence than case reports) found that males’ levels of total and free testosterone were not notably affected by either 60–240 mg of isoflavones or 10–70 grams of soy protein per day.

Accordingly, a couple of scoops of soy protein powder are unlikely to have estrogenic effects in males. If you’d like to take more, however, look for a soy protein concentrate or isolate produced through the alcohol-wash method, which dramatically lowers the isoflavone content.[260]

Keep in mind that the isoflavone content of different soy products can vary depending on several factors, such as the variety of soybeans used, differences in growing and storage conditions, and differential food processing techniques employed.[261] You can see how it varies below

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**Isoflavone content of common soy foods**

****Reference: USDA FoodData Central Databases. Accessed Jan 18, 2019. https://fdc.nal.usda.gov/

**Q. Don’t dietary proteins reduce bone density?**

More protein in the diet has been linked to more calcium in the urine. Two reasons have been suggested to explain this phenomenon. Your body draws from its calcium stores (in bones) to buffer the acid load caused by dietary protein. This has led researchers to suggest that higher protein intake could increase bone loss.[262]

Most studies that looked at protein intake and calcium excretion list dairy products as a protein source,[263] 60

so higher urinary calcium could simply be the result of higher calcium intake (i.e., more calcium in, more calcium out).

Therefore, looking only at calcium excretion wasn’t enough. Subsequent studies showed that dietary protein promotes dietary-calcium absorption[264] and that high protein intake “promotes bone growth and retards bone loss whereas low-protein diet is associated with higher risk of hip fractures.”[265] High-protein diets have also been shown to modestly suppress the decrease in bone mineral density caused by weight loss.[266]

What happens is that when you ingest more protein, you absorb more of the calcium in your food, so less calcium ends up in your feces. Later, your body gets rid of the calcium it doesn’t need, so more calcium ends up in your urine, but not as much as would have otherwise ended in your feces.[267] Therefore, an increase in protein intake leads to an overall decrease in calcium excretion, which points to an increase in calcium retention. High-protein diets also raise your insulin-like growth factor-1 (IGF-1),[268] which promotes notably bone growth.[269]

All in all, current evidence suggests that protein’s effect on bones is either neutral or beneficial.[267][270]

**Q. Should I continue using white willow bark if it aggravates my heartburn?**

No, you shouldn’t. Although a study reported that, “in contrast to synthetic aspirin, willow bark [did] not damage the gastrointestinal mucosa” (probably thanks to some phenolic compounds in the plant),[271] there is still a risk of it exacerbating stomach ulcers. Keep in mind that your body metabolizes salicin into salicylic acid, a close cousin of acetylsalicylic acid (aspirin), which several studies have shown can damage the lining of the digestive tract.

**Q. Why isn’t ephedrine included in this guide?**

Ephedrine, an alkaloid from the plant Ephedra sinica, cannot be marketed as a fat burner. Its sale is prohibited or restricted in various countries, so it cannot be recommended in this guide.

Synephrine is similar to ephedrine. It is a safer compound, though it is also less effective. **Q. Why isn’t DNP included in this guide?**

DNP (2,4-dinitrophenol) is most often sold as an herbicide or a pesticide; it cannot legally be sold as a food supplement. Ingested, it creates a leak in the energy pathway of mitochondria, the ATP generators in our cells, so that everything you do, from exercising down to breathing, burns more calories (as heat). For that reason, DNP has been studied as a potential obesity drug, and it has proven very effective. Alas, the adverse effects include dysgeusia (a distortion of the sense of taste), cataracts, and death. Because the efficacious dose and the lethal dose are very close and vary between individuals, even what was once considered a safe dosage has killed.

Since our bodies all react differently, and since the line between the efficacy and lethality of DNP is thin, what was safe for your friend may not be safe for you. At any dose, taking DNP is very much like playing Russian roulette.

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**Q. Is there a “best diet” for fat loss?**

Usually, in diet studies, weight loss differs little between diet groups but a lot within each group. In other words, individual results will vary. Let’s use as an example the Diet Intervention Examining The Factors Interacting with Treatment Success (DIETFITS) RCT, for which 600 participants were randomly assigned to either a low-fat or low-carb (non-keto) diet for 1 year, with intensive support from dietitians and research staff.[121] (You can read our detailed review of this 2018 study here.)

Here were the reported weight-loss averages:

5.3 kg (11.7 lb) in the low-fat group

6.0 kg (13.2 lb) in the low-carb group

As you can see in the figure below, in which each bar represents the weight change of a single participant, individual changes were all over the place in both groups: they ranged from −32 to +11 kg (−70 to +24 lb).

**12-month weight change for each DIETFITS participant **Adapted from Gardner et al. JAMA. 2018.[121]

One reason is simply that some people stick to their diets while others don’t (a support network is very helpful for diet adherence), but another may be that some diets do work better for some people than for others, for reasons that aren’t completely understood.

If there’s one takeaway to keep in mind after looking at all the evidence, it is that no one diet is inherently superior. Different diets work differently for different people, but your best fat-loss diet will have at least two qualities: it’ll be hypocaloric (it’ll make you eat less than your burn) and sustainable (it’ll fit your food preferences and lifestyle well enough that you can stick to it).

**Q. What about intermittent fasting for fat loss?** 62

Intermittent fasting is an eating pattern that involves alternating periods of little or no energy intake with intervening periods of normal food intake, on a recurring basis. The scientific literature on the effects of intermittent fasting on health and body composition is steadily growing, but differences between studies relating to populations used, intermittent fasting protocols employed, study durations, and so on, mean that it’s difficult to compare studies and draw firm conclusions.

Common types of fasting regimens

| **TYPE** | **FAST** | **FEED** | **DURATION** |
| --- | --- | --- | --- |
| Alternate Day Fasting | 36-hour fast | 12-hour feed | Every other day |
| Eat Stop Eat | Full-day fast | 1–2 days per week | 1–2 days per week |
| Warrior Diet | 20-hour fast | 4-hour feed | Every day |
| Lean Gains | 16-hour fast | 8-hour feed | Every day |
| 5:2 Diet | 500-600 kcal per fast day | 5 consecutive days per week | 2 successive days per week |

Studies in animals and humans suggest that intermittent fasting can reduce weight and fat mass, and may improve several markers of health. Yet, current evidence suggests that intermittent fasting and continuous energy restriction result in similar reductions in body weight and fat mass.[272][273][274] The results recent systematic review and meta-analysis also seem to confirm the above conclusions.[275][276][277]

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