Examine

Muscle Gain & Exercise Performance Supplement Guide

Written By: Mike Murray, Antonis Damianou, & Adel Moussa
Edited By: Molly Gregas
Reviewed By: Wyatt Brown, & Molly Gregas

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Introduction

There's a holy trinity of exercise:

- Better performance
- More muscle
- Less fat

These are the primary goals of most exercise programs. So why are we covering muscle gain and exercise performance together and separately from fat loss?

There's a simple answer — because the latter (fat loss) is merely *associated* with exercise. More precisely, the issue with fat loss is one of fuel: how do you convince your body to burn its precious energy stores? Exercise does help, but not as much, in itself, as a hypocaloric diet (i.e., eating less than you burn).[1]

To lose fat, exercise is a *plus*. To build muscle, exercise is a *necessity*. Any supplement that helps you exercise harder and longer can also help you build stronger muscles. And because stronger muscles allow you to exercise harder and longer, any supplement that promotes muscle growth can also benefit exercise performance.

Note that we said it can benefit exercise performance, but it not always *does*. The upper-body muscles of a wrestler would be a literal burden to a marathoner. The type of exercise that you undertake will influence the kind of muscle you grow, and the kind of muscle that you grow will make you fitter for some sports than for others.

Even similar sports can lead to very different musculatures. Running marathons is an aerobic activity and builds more "slow twitch" muscle fibers (more endurance than strength). Running sprints is an anaerobic activity and builds more "fast twitch" muscle fibers (more strength than endurance).

🔍 **Digging Deeper: Types of muscle fiber**

Your heart and stomach are muscular organs, but when you think of muscle building, you think of building your *skeletal* muscle — the type of muscle that moves your skeleton. This type of muscle is made of two types of fibers: *type I* (slow twitch) and *type II* (fast twitch). Type II fibers are further classified into *type IIa* and *type IIx*, but that's not relevant here.

Slow-twitch muscle fibers have more mitochondria, myoglobin, and capillaries in order to process more oxygen. In other words, they're optimized for aerobic metabolism and thus slow but consistent energy production. They don't fatigue easily but are relatively weak, and they can't support high-intensity efforts (i.e., efforts above the anaerobic threshold). These are the fibers we use for prolonged submaximal exercise activities and postural control.

Fast-twitch muscle fibers have less myoglobin and fewer capillaries and mitochondria — they'd rather use the space to store more glucose (as glycogen). They are also larger and more contractile (their larger size makes them more contractile, which in turn gives them more growth potential, creating a positive feedback loop). Their contractile properties are part of what makes them ideal for short, powerful bursts of effort. However, their reliance on anaerobic metabolism makes them fatigue quickly. These are the fibers we use for weightlifting or sprints.

Still, the basics of muscle building stay the same, whichever type of exercise you choose to focus on.

1. *Take it slow.* Exercise hard enough to stimulate muscle growth, but not so hard as to injure yourself or impair recovery. Muscle growth takes time and patience; it can only happen so fast.

How fast (or how slow) depends on many factors, starting with genetics. In a 12-week trial, untrained women gained an average of 1.2 kg (2.6 lb) of muscle;[2] in a 10-week trial, men with some lifting experience also gained an average 1.2 kg (4.4 lb) of muscle.[3] However, in both trials, interpersonal variability was very high, so those numbers may not apply to you — don't let them either constrain or daunt you.

2. *Don't give up.* At some point, you'll probably experience a plateau, either in strength or muscle mass. Few people — few lifters, in particular — deal with plateaus appropriately.

Because they are scared of fat gains, many people refuse to increase their caloric intake as their muscle mass increases.

Because they are scared of muscle loss, many lifters refuse to ever reduce their lifting volume or intensity (a deload period). Yet muscle and strength are largely maintained even when total lifting volume is reduced by two-thirds,[4] and deloads increase the body's sensitivity to anabolic signals.[5] So, take advantage of those temporary breaks when you seem to hit a wall.

⚠️ Caution: Sometimes, less is more

Muscle doesn't grow at a linear rate, such as "0.5 kg or 1 lb per month." Everyone has a physiological limit with regard to muscle size, and the closer you get to this limit, the harder it becomes to make any gain. Even worse, sometimes your progress suddenly stalls for no apparent reason. It can be tempting then to try some of the new "breakthrough" supplements that companies produce on a regular basis, but that's seldom the solution. More likely, you need more calories or protein, you need to alter your workout routine (to stimulate your muscles differently), or maybe you need to exercise *less* for a while to let your body recover.

As surprising as it may sound, exercising *more* is less likely to help. Lifting twice as much or twice as often won't double your gains. In fact, according to the vast majority of studies, you won't experience significantly greater gains if you exercise a muscle group more than twice a week.[6]

However, taking a break by exercising less intensely and less often differs greatly from taking a break by spending days glued to your couch, barely moving at all. One study found muscle and strength losses after only 5 days of disuse (*complete* disuse, mind you, because the entire leg was in a cast).[7]

3. *Don't go crazy with cardio. Some* cardio can increase blood flow to the muscles, thus speeding nutrient delivery and thus speeding recovery. *Some* cardio can reduce fat gains in people on a hypercaloric diet by keeping fat-burning pathways active. *Too much* cardio can hinder progress by burning up calories, which cuts into recovery and interferes with anabolic signaling pathways.[8]

4. *Eat enough, but not too much.* Most people only need a couple of hundred kilocalories per day above maintenance to maximize muscle growth.[9] If you eat too much above maintenance, you risk accumulating too much fat, which you'll later struggle to shed. But if you eat *below* maintenance — if your primary goal is to lose fat — keep in mind that you won't be able to exercise as hard or build as much muscle.

💡 **Tip: Choose a body recomposition strategy**

Bodybuilders aren't typically thought of as brainy, but some among their ranks are experts on the science and practice of fat loss and muscle gain (the two faces of body recomposition). Genetics and even steroids can only take you so far; an effective dietary strategy is what separates the ridiculously ripped and veiny from the average bodybuilder.

You can choose between two "recomp" strategies: *steady* and *cycling*. The former involves eating around your maintenance level of calories to slowly accrue muscle and shed fat. The latter cycles between prolonged bulking (during which large caloric surpluses enable a highly anabolic state) and intense cutting (during which substantial caloric deficits lead to fat being rapidly stripped from the body).

The *steady* strategy is ideal for most people; it is easier to finely tune, and you'll look good year-round, not just for shows or competitions.

The *cycling* strategy is reserved for competitors and other individuals with significant training and dieting experience. Your ideal caloric surplus — how much you should eat above maintenance to maximize muscle gain without accumulating too much fat — depends on many factors, such as training intensity and frequency, surrounding temperature, genetics, and so forth. If you overbulk, which is all too easy to do, cutting will be hard and take longer, and you'll end losing too much of your hard-won muscle.[10]

5. *Eat meals, don't graze.* Meal frequency is a topic of much debate. For decades, "6 meals per day" has been a bodybuilding mantra, but now the intermittent-fasting crowd claims we can be awake for hours, even a whole day, without eating a bite — and be healthier for it!

The truth probably lies somewhere in the middle.

Skeletal muscle protein synthesis changes with amino acid concentrations in the blood; our bodies become desensitized to the anabolic stimulus of protein after about 3 hours.[11] Therefore, eating too frequently can impede muscle protein synthesis.

In contrast, you don't want to deprive your muscles of the amino acids they need to grow. Because a moderate-sized meal might take up to 5 hours to digest, it seems prudent to eat something every 4–6 hours, which translates to 3–4 meals per day.

6. *Eat enough protein.* Protein is aggressively pushed both on athletes and on the general population, and with good reason — it's essential for many biological functions, including muscle gain or preservation. In this guide, we'll tell you how much you need and when.

💡 **Tip: Don't assume that protein powders are necessary**

Protein powders are used by more than 40% of men who regularly go to the gym and by more and more people who don't go to the gym.[12] Remember our advice: *eat* enough protein. Not that powders are bad — except when used to make up for (or even *replace*) a good diet.

Protein-rich foods taste better than protein shakes, and, by affecting gut hormones and through other mechanisms, they're also more filling.[13] So when you think *protein*, think *food* first — not *powder*.

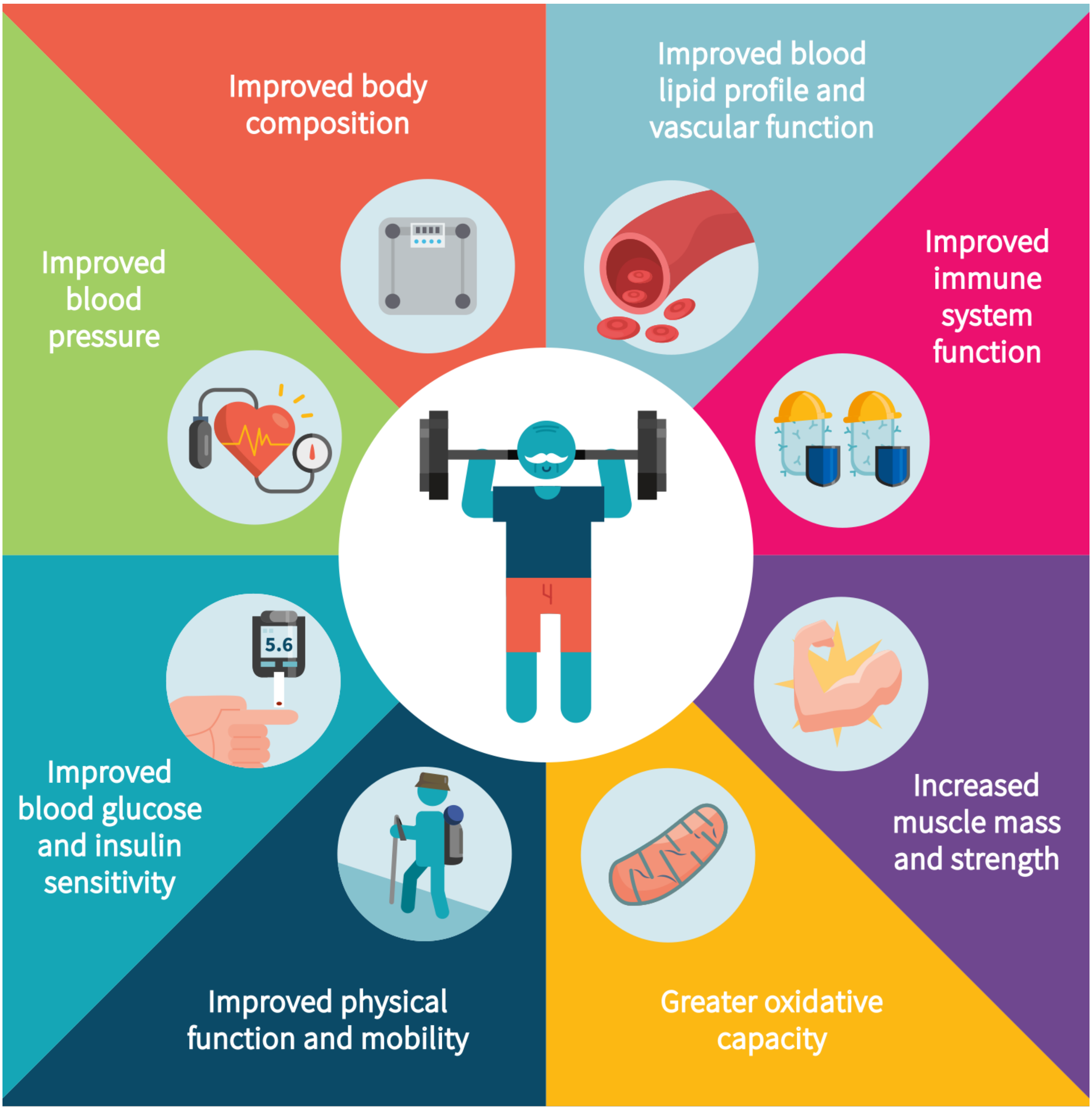
7. *Eat enough fat*. Eating a diet that is too low in fat (less than 15% of your daily caloric intake) can reduce testosterone levels to the point of impairing muscle gains.[14]

8. *Time your carbs.* You can gain strength and build muscle without much carbs, as shown in ketogenic diet studies involving gymnasts[15] or college-aged weightlifters.[16] But if you do eat carbs, we'll tell you how much you need and when — there are ways to time your carbohydrate intake to maximize exercise performance and recovery.

As you can infer from those 8 points, the "food factor" is as crucial to muscle gain as the "exercise factor". Before you turn to supplements to give you an edge, make sure that you're eating a healthy, balanced diet that is rich in micronutrients. Vitamins and minerals support many of the functions that promote muscle gain, such as immune function, hormonal regulation, fuel use, and so on.

As you read this guide and learn about different supplements, remember that the most effective (e.g., protein, creatine, etc.) were originally food components.

The influence of resistance training on chronic disease risk



Adapted from Mcleod et al. *Front Physiol.* 2019.[17]

Kamal Patel, Co-founder and Director
MBA, MPH, PhD(c) in Nutrition

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

There’s no core combo because supplement needs vary by activity. Refer to any specialized combos that apply.

💡 **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 that 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

For weightlifters (muscle growth and power)

Consume protein throughout the day (1.6–2.4 grams per kilogram of body weight or g/kg), with the help of protein powder if necessary. Your intake should probably be more towards the lower end of the range if you are also doing endurance sports. If you are also trying to lose body fat, up to 3.3 g/kg may be helpful, though this is speculative. Consult the protein entry to set the intake level best suited to your needs.

Consult the carbohydrates entry to set your carbohydrate intake.

The following supplements can be used for additional effects.

Creatine can be taken as 5 grams of creatine (or approximately 0.3 g/kg) 4 times per day (20 grams total) for 5–7 days, followed by a maintenance dose of 3–5 grams daily, or it can simply be taken at a dose of 3–5 grams per day right from the beginning, though it might take a little longer to see the effects.

Caffeine, can be taken at 3–6 mg/kg an hour before a workout. If you find that caffeine makes you jittery in an uncomfortable way, even with normal doses, taking 250 mg of theanine may help to reduce this.

Nitrates can be taken at a dose of at least 5.1 mmol and up to 25 mmol (378.2–1,550 mg) of nitrate 2–3.5 hours before exercise.

For athletes who exercise for 1 hour or more (alertness and endurance)

Roughly 1.8 g/kg of protein is probably the sweet spot, because there's always a trade-off between protein and carbohydrate intake, and too little carbohydrate is going to be detrimental. Peri-workout doses of 0.4 g/kg may yield additional benefits.

Consult the carbohydrates entry to set your carbohydrate intake.

Caffeine can be taken at 3–6 mg/kg of body mass an hour before a workout. If you find that caffeine makes you jittery in an uncomfortable way, even with normal doses, taking 250 mg of theanine may help to reduce this.

Nitrates can be taken at doses of at least 5.1 mmol and up to 25 mmol (378.2–1,550 mg) of nitrate 2–3.5 hours before exercise.

Beta-alanine can be taken at 3.2–6.4 g/day, split into doses of 0.8–1.6 grams every 3–4 hours to avoid paraesthesia — an uncomfortable sensation described as tingling, itching, or "pins and needles" on the surface of the skin — for 4–24 weeks.[18] Higher doses may be necessary to maximize muscle carnosine levels for some people, and taking sodium bicarbonate simultaneously may augment the effects.

Other options

If working in a fasted state, taking 20–40 grams of protein within the 2 hours following the workout will help preserve muscle mass.

People with *a lot* of muscle mass can increase the creatine dose from 5 to 10 grams.

If it is impractical to consume a lot of nitrate-rich vegetables, try 6 grams of citrulline (or 10 grams of citrulline malate) instead. Because glutathione may slow the rate of nitric oxide breakdown in the bloodstream, adding 200 mg of *N-acetylcysteine* (NAC) to nitrates or citrulline might prove synergistic.

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 Muscle Gain & Exercise Performance guide that uses this new terminology. For example, if it was a core supplement in the previous issue and now it's 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:

- Citrulline (previously discussed in "Nitric Oxide Boosters")
- Tart cherry
- Alpha-GPC
- Capsaicin
- Betaine
- Choline
- Maca
- *Rhodiola rosea*
- Arginine
- Fenugreek

- *Panax ginseng*
- Phosphatidic acid
- *Tribulus terrestris*

Changed ranking:

Beta-alanine

Upgraded from secondary to primary. On the one hand, it won't have a large effect, but on the other hand, we're sure enough of its effects that it could be worthwhile, especially in the case of competitive sports, where a small advantage matters a lot. If there were more great supplements for exercise performance, it may be back at secondary, but there aren't.

Caffeine

Upgraded from secondary to primary. Besides the potential for psychological issues such as jitteriness and sleep impairment, there doesn't seem to be much downside, even when taken consistently despite tolerance (it continues to work, just maybe a little less well).

BCAAs

Upgraded from promising to secondary. The evidence does support a benefit, though the question of whether or not there's a point to taking them specifically vs. protein powder is still valid. And there probably isn't a point other than digestive issues with protein powders,

Sodium bicarbonate

Upgraded from promising to secondary. The evidence has improved since last time.

HMB

Downgraded from promising to unproven. It probably doesn't work. Mechanistic plausibility only justifies studies, not the assumption of efficacy.

Removed:

The broad categories of Nitric Oxide Boosters, Cholinergics, Testosterone Boosters, and Adaptagens have been removed, and in their place, the individual supplements have been reviewed. Different supplements may have different effects and shouldn't necessarily be considered equivalent.

Primary Supplements

Beta-alanine

What makes *beta-alanine* a primary option

Beta-alanine is a nonessential amino acid that has attracted interest as an ergogenic aid due to its role in carnosine synthesis. Carnosine is a dipeptide composed of the amino acids L-histidine and beta-alanine. It is abundant within skeletal muscle and primarily acts as an intracellular pH buffer.

During intense exercise, a high release of protons (i.e., hydrogen) occurs, which leads to a decrease in pH, an increase in muscle fatigue, and a decline in performance. Carnosine acts as the immediate defense against proton accumulation in the contracting musculature. Therefore, it’s postulated that increasing muscle carnosine content will delay fatigue during exercise and enhance performance. Carnosine may also improve exercise tolerance by regulating calcium handling, scavenging free radicals, and detoxifying reactive aldehydes.[19]

The focus on carnosine prompts the question of “why not just supplement with carnosine directly?” Carnosinase, the enzyme that breaks down carnosine, is present in the blood, liver, and kidneys, but not in skeletal muscle.[20] As a consequence, most oral carnosine is rapidly broken down before reaching the skeletal muscle, making it an inefficient option to increase muscle carnosine levels.

In contrast, beta-alanine has been identified as the rate-limiting factor for endogenous synthesis of carnosine within skeletal muscle, and chronic supplementation has been shown to significantly elevate muscle carnosine content in a variety of populations.[21]

A robust body of evidence demonstrates that beta-alanine supplementation has a small effect on exercise capacity and performance in exercise durations of 30 seconds to 10 minutes, with a larger effect on exercise capacity (i.e., time to exhaustion) than performance (i.e., time trial).[22]

The efficacy of beta-alanine is similar for continuous vs. intermittent exercise and in untrained vs. trained individuals, although slightly smaller effects have been reported in trained populations.[22] With regard to the former, several studies report that supplementation with beta-alanine improves performance during level 2 variants of the Yo-Yo test (a popular way to evaluate high-intensity intermittent exercise performance)[23] and the 2000-meter rowing ergometer test.[24]

Based on these findings, it’s logical to assume that beta-alanine is useful for resistance training. A limiting factor during resistance training is the ability to overcome localized muscular fatigue caused by an accumulation of lactate and hydrogen ions, which causes a drop in pH. Beta-alanine could delay fatigue during resistance exercise sets, leading to the completion of more repetitions (reps) and augmented muscular adaptations.

Despite this sound rationale, few studies have examined the effect of beta-alanine on resistance exercise performance. Moreover, the results have been inconclusive. An early study in collegiate football players reported a nonsignificant increase in overall training volume for the back squat and bench press over 3 total training sessions in 3 weeks;[25] however, a study in collegiate rugby players observed no effect of beta-alanine on total reps performed across 5 sets of bench press and back squat at 70% of *1-repetition maximum* (1RM) to fatigue with 2 minutes of rest between sets.[26] Similarly, a study in strength-trained men reported no effect of beta-alanine on total reps performed across 8 sets of bench press and leg press at 70% 1RM to failure with 2 minutes of rest between sets.[27] In a 4-week trial in resistance-trained men, the participants trained each muscle group twice per week, and each training session was composed of multiple exercises performed for 3 sets of 10 repetitions to muscular failure, with 60 seconds of rest between sets and 120 seconds between exercises. Compared to placebo, beta-alanine increased overall training volume while reducing perceived effort.[28]

In untrained participants, one study in college-aged women reported an increase in the number of leg press reps at 65% 1RM following beta-alanine supplementation, but no effect was found for bench press.[29] Another study in Vietnamese sports science students found no difference between beta-alanine and placebo on performance during a high-rep set (20–40 reps) of biceps curls.[30] Lastly, beta-alanine failed to improve performance on 20-rep leg press and chest press tests in older adults (aged 66–70 on average).[31]

From a practical standpoint, beta-alanine supplementation is recommended for events such as 400–1500-meter running, 4 km cycling, 100–400-meter swimming, boxing,[32][33] etc. It is unlikely to benefit activities such as 100-meter running or 25-meter swimming. Additionally, the available evidence does not support the use of beta-alanine for moderate-intensity resistance exercise.

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

Warnings about *beta-alanine*

Supplementation with beta-alanine very frequently causes acute paraesthesia, a tingling or prickling sensation in the nerves. This sensation usually subsides soon after supplementation and doesn't appear to be harmful.[34] Another finding is a modest increase in ALT and ALP, two liver enzymes that often indicate liver damage when elevated in the bloodstream, though it's not clear in this case if this increase is due to liver damage or some other explanation. More specific liver damage tests are needed to determine this.

How to take *beta-alanine*

The current recommendation for beta-alanine supplementation is to ingest 3.2–6.4 grams per day split into doses of 0.8–1.6 grams taken every 3–4 hours to avoid paraesthesia — an uncomfortable sensation described as tingling, itching, or "pins and needles" on the surface of the skin — for 4–24 weeks.[18]

Increases in muscle carnosine content are the most pronounced during the early stages of beta-alanine supplementation, but it seems to take longer than 4 weeks to achieve peak muscle carnosine content.[35] In one study, the average time to maximal muscle carnosine content was 17 weeks. However, in several participants, carnosine content continued to increase up to the end of the study at 24 weeks. In the same study, 1 participant achieved maximal carnosine content at week 4, and several others did so at week 12. These results are particularly captivating because some evidence suggests that performance improvements following beta-alanine supplementation are strongly associated with changes in muscle carnosine content.[35][36]

According to a recent analysis, commonly used supplementation protocols, such as 6.4 grams per day for 4 weeks, may not come close to saturating muscle carnosine content.[37] Based on these findings, it's clear that there is large variability in the response to beta-alanine supplementation, and chronic supplementation (for 12 to 24 weeks or more) is likely necessary to maximize the ergogenic effect. For people who are interested in maximizing the ergogenic effect, it's also worth highlighting that cosupplementation of beta-alanine with sodium bicarbonate may provide further benefits than beta-alanine alone.[22]

Creatine

What makes *creatine* a primary supplement

Creatine is among the most well-researched and effective supplements for increasing high-intensity exercise performance and muscle mass.[38] It is a naturally occurring compound that is present in meat and fish and is also produced in the liver (and to a lesser extent in the kidneys and pancreas) from reactions involving the amino acids arginine, glycine, and methionine.[39]

Supplementing with creatine increases the body's creatine stores, which are located primarily in skeletal muscles in the form of phosphocreatine (PCr). As *adenosine triphosphate* (ATP) is degraded into *adenosine diphosphate* (ADP) to provide energy during exercise, PCr is broken down.[40] One of its byproducts, inorganic phosphate, is donated to ADP to resynthesize ATP. In short, more creatine enhances the capacity of ATP resynthesis, boosting exercise performance.

The performance of maximal effort exercises lasting less than 30 seconds is typically improved following creatine supplementation, and this beneficial effect is most evident when there are repeated bouts of exercise. More specifically, 5%–15% improvements in maximal power and strength, anaerobic capacity, and work performance during repetitive sprint performance commonly occur, whereas improvements in single-effort sprint performance range from 1% to 5%.[41] Most studies have reported a small improvement in jump performance as well.[41]

🔍 **Digging Deeper: Creatine and androgens**

Creatine has also been investigated for its effects on androgens, with most studies concluding that it had none.[42][43][44][45][46][47][48][49][50][51] A lone study noted a tiny increase in dihydrotestosterone (DHT) with no change in testosterone — a puzzling result that has yet to be replicated.[42]

A robust body of evidence indicates that creatine enhances lower body and upper body strength performance during exercise that is less than 3 minutes long, including maximal weight lifted in the squat, leg press, and bench press in addition to the number of bench press repetitions.[52][53] Notably, these effects were observed independent of age, sex, and training status. Other research supports that creatine supplementation augments increases in chest and leg press strength in older adults (>50 years of age) as well.[54]

Naturally, because creatine increases the amount of volume that can be lifted in a workout, it tends to lead to gains in muscle mass.[55] Creatine may also have direct effects on skeletal muscle.[56][57][58] In one particular study, creatine increased satellite cell number and myonuclei concentration to a greater extent than resistance training alone.[59]

With regard to endurance exercise, creatine generally has no direct effect on performance. This is unsurprising because exercise bouts longer than 2 to 3 minutes in duration rely predominantly on the oxidative system (not ATP-PCr) for the resynthesis of ATP. Therefore, it's possible that creatine may benefit endurance athletes indirectly. For example, supplementing with 20 grams per day of creatine 5 days before a half-ironman triathlon, full ironman triathlon, or 30-kilometer race attenuated increases in inflammatory cytokines (e.g., TNF-α, interleukin1-β) and muscle damage biomarkers (i.e., creatine kinase, lactate dehydrogenase) in trained athletes.[60][61][62]

Additionally, creatine loading (20 g/day) has been shown to enhance glycogen synthesis.[63][64][65] In one study that used a glycogen depletion protocol, followed by creatine and carbohydrate (8 grams per kilogram of body weight per day or g/kg/day) loading, glycogen resynthesis was 82% greater in the creatine group compared to placebo.[63] These findings are particularly compelling because glycogen replenishment is critical for promoting recovery and preventing overtraining during intense training and competition periods.

Another potential benefit of creatine is related to its osmotic properties (i.e., it helps with water retention). Endurance athletes must deal with hot and humid environments as part of their sport, which can compromise thermoregulation and, as a consequence, performance. Collectively, the evidence suggests that creatine supplementation is a highly effective hyperhydrating strategy[40] and may reduce the risk of muscle cramping and heat related-illness during exercise.[66]

Warnings about *creatine*

Decades of research have demonstrated that creatine is generally well tolerated. The only recorded adverse effects are nausea, diarrhea, and stomach cramps in people taking more than 10 grams at once, and even at such high doses, these effects are rare.[40] Still, a person who is particularly sensitive to creatine's digestive side effects should split the daily dose, take it with some food, and drink more fluids.

Another alternative is *micronized* creatine monohydrate, which dissolves more easily in liquids.

Concerns about creatine supplementation can be divided into 3 main categories: kidney function, muscle function, and thermoregulation.

Both blood and urinary creatinine may be increased by creatine supplementation, which has led to the hypothesis that if the kidneys are forced to excrete higher-than-normal levels of creatine or creatinine, some sort of damage and impairment in function will eventually take place.[67] In support of this hypothesis, evidence from some rodent studies showed that creatine may negatively affect kidney function.[68][69] However, animals respond differently from humans to creatine ingestion,[70] and in healthy people, supplementing with up to 10 grams of creatine per day for 10 months to 5 years has not been shown to adversely affect kidney function.[71][72] Moreover, one study in participants with type 2 diabetes and one study in participants with peripheral artery disease (two populations at an increased risk of chronic kidney disease) found that daily creatine supplementation for 8–12 weeks did not affect markers of kidney function.[73][74] These results may not be generalizable to other populations (i.e., other disease states), but they do provide further evidence against the postulated link between creatine supplementation and kidney function.

The rationale behind the claim that creatine supplementation causes dehydration and muscle cramping is based on creatine's ability to drive water into cells. It's postulated that creatine preferentially increases intracellular water uptake and retention[75] and that the bound intracellular water might not be released into the extracellular compartment for thermoregulation during exercise, leading to muscle cramping, dehydration, electrolyte imbalances, and other heat-related issues.[66] However, there is no scientific evidence to support these claims.[66] Several trials have investigated the effects of creatine supplementation on muscle cramps, muscle tightness, muscle strains, injuries, and missed practices, and the results have suggested that creatine use may reduce the likelihood of muscle injury and dysfunction compared to nonuse of creatine.[76][77] In the clinical setting, creatine supplementation has been shown to decrease the incidence of muscle cramps during hemodialysis treatment by 60%.[78]

Out of caution, people who are taking medications that can increase the risk of harm or damage to the kidneys (i.e., nephrotoxic drugs) may want to skip creatine supplementation.

🔍 Digging Deeper: ATP and muscular contractions

Adenosine triphosphate (ATP) can be viewed as the body's main energy source. Carbohydrates, fats, proteins, and ketones are technically not directly used as energy but are rather used to make a certain amount of ATP that the body can then use to perform an action, like contracting a muscle.

For a muscle contraction to occur, the brain sends an electrical signal to the muscle that tells a calcium reserve, called the sarcoplasmic reticulum, to release calcium into the muscle. The calcium is necessary for the ATP to do its job, allowing the muscle to contract. Conversely, ATP is necessary for the calcium to be pumped back into the sarcoplasmic reticulum in preparation for a future muscle contraction.

🔍 **Digging Deeper: Creatine and testosterone**

You may have heard that creatine can raise testosterone, the precursor to *dihydrotestosterone* (DHT), and can thereby accelerate or cause hair loss. To date, though, the overall body of evidence suggests that creatine doesn't affect testosterone or hair loss.[42][79][45][46][47][48][49][80][43][44][50][51]

Creatine can cause water retention, which may notably increase body weight. Avoiding high-dose creatine loading and cosupplementation with carbohydrates to augment PCr increases and glycogen storage can limit the transient dreaded "bloating" to a minimum.[81][82][83] This side effect is largely harmless and is reversed when creatine supplementation is stopped. Theoretically, this water retention could harm people whose kidney disorders are being treated with diuretics, which cause water loss.[40] This possible harm is based on known mechanisms rather than human trial data.

How to take *creatine*

There are many different forms of creatine on the market, but creatine monohydrate is the cheapest and most effective. The most efficient way to increase muscle creatine stores is to ingest 5 grams of creatine (or about 0.3 grams per kilogram of body weight) four times per day (20 grams total) for 5–7 days.[40] Following saturation of muscle creatine stores, a maintenance dose of 3–5 grams per day can be consumed, although some studies indicate that larger athletes may need to ingest as much as 5–10 grams per day to maintain creatine stores.[40]

With that being said, creatine loading is not necessary. It's been shown that supplementing with 3 grams per day for 28 days can lead to a similar increase in muscle creatine stores as loading for 6 days.[84] Furthermore, several variables can be manipulated to potentially expedite muscle creatine saturation while using a low daily dose. Creatine accrual in muscles is enhanced following exercise[85][86] and when coingested with carbohydrate[87] and/or protein.[88]

The response to creatine supplementation is highly variable, and in some individuals, there is a lackluster increase in muscle creatine stores following creatine loading.[89][90] This heterogeneity is related to differences in baseline creatine levels,[85] diet,[91] age,[92] and muscle fiber type composition.[90] For instance, in a study that had children, omnivorous adults, vegetarian adults, and older adults (ages 62 to 84) supplement with creatine for 7 days, PCr increases were greater in older adults than in children and omnivorous adults, and there was a significant increase in muscle PCr content in vegetarians, but not in omnivores.[93]

Protein

What makes *protein* a primary supplement

Any protein found in food or supplements is called dietary protein. During the digestive process, dietary protein is broken down into its amino acid constituents and ultimately serves as building blocks that are needed to build, maintain, and repair bodily tissue, produce enzymes and hormones, construct neurotransmitters, manufacture antibodies for immune defenses. and much more.[94][95]

Although muscle is made out of proteins, which are made out of amino acids, amino acids should not be thought of as merely bricks in a wall. At least some amino acids, most prominently leucine, also act as signaling molecules that can trigger or augment biological processes, with direct effects on exercise performance and body composition. This happens via their direct and direct effects in muscle repair, hypertrophy, and function or via neurotransmitters, hormones, nucleotides, and coenzymes, which are similarly made up primarily of amino acids.

Simply eating more protein won't build more muscle on its own, though it may reduce muscle breakdown. However, in the presence of a sufficient physical stimulus such as weight training, an increased protein intake can increase muscle strength and hypertrophy significantly.

The debate over optimal protein intake in sports is ongoing, and it's even trickier than a person might think. On the one hand, too little protein will reduce muscle protein synthesis, but on the other hand, increased protein intake will come at the cost of fats and carbohydrates that are necessary to fuel training and performance, and some athletes may even be hindering themselves by eating too much protein.[96]

For this reason, protein guidelines should ultimately be based on the specific sport or purpose, and no size fits all. Various guidelines for athlete nutrition recommend that athletes involved in strength/power related training should ingest as much as 1.5–2.2 grams of protein per kilogram of body weight per day, depending on the activity.[97][98]

In our guide, our distinction is largely between strength and endurance exercise.

Acute effects of protein on muscle performance and recovery

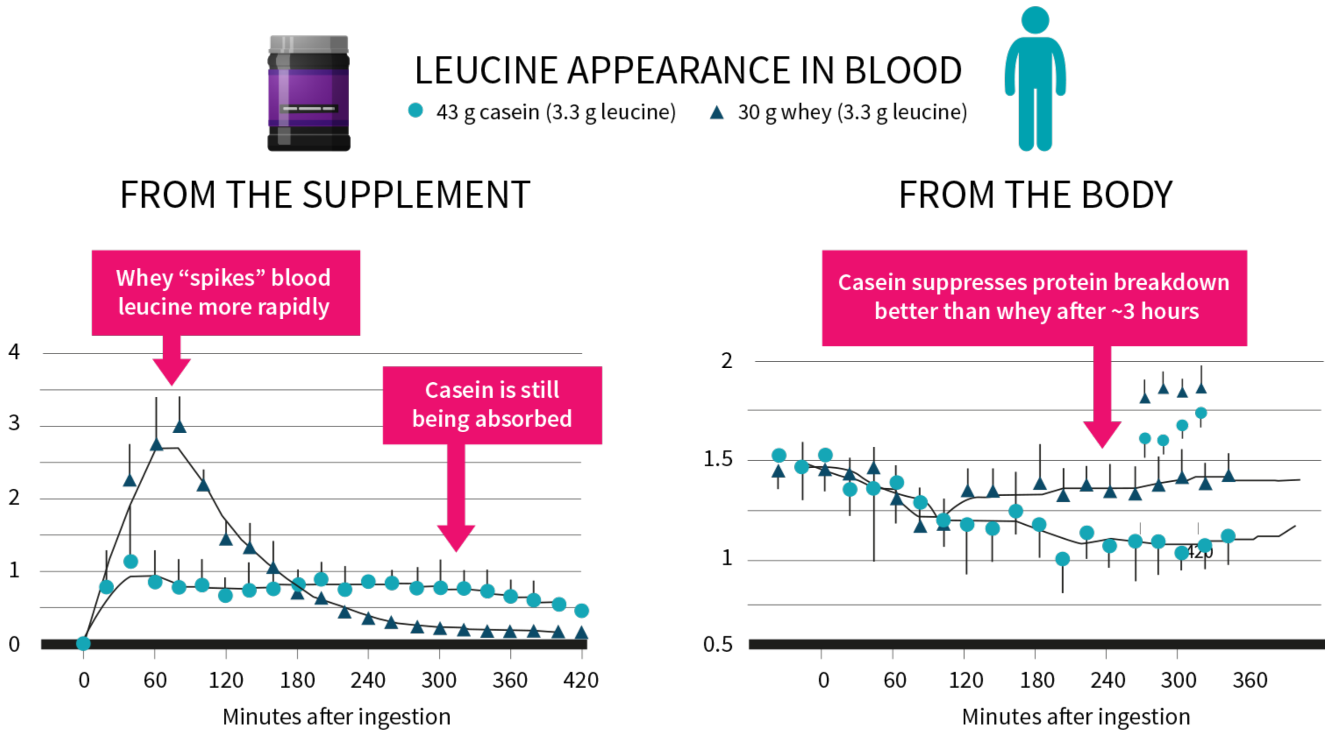
The limited data that we have do not suggest that resistance trainees will see immediate benefits from the short-term use of protein supplements when carbohydrate supplementation is delivered at optimal rates during or after exercise.[99] A slightly more promising image emerges for the effects of protein supplements on the intermediate recovery (24–96 hours postexercise) from a potentially muscle-damaging resistance training regimen. In a meta-analysis of 13 studies investigating the effects of at least 20 grams of whey protein consumed before or after workouts, the authors reported a small to medium-sized positive effect on the temporal restoration of contractile function and thus muscle recovery compared to the control treatment.[100]

Several explanations have been proposed to explain the medium-term recovery benefits of protein supplements, ranging from the putative increases in postworkout glycogen (re)synthesis that have been observed especially in trainees on low carbohydrate diets,[101][102][103][104] to the general antioxidant and anti-inflammatory effects of protein supplementation.[105]

It should also be noted that the majority of pertinent studies have used different forms of dairy protein. Hence, it is not clear to what extent the previously discussed prorecovery effects depend on the proven insulinogenic, antioxidant, and anti-inflammatory effects of dairy proteins, in general, and whey protein, in particular,[106][107][108] or whether other EAA-rich and leucine-rich protein sources would yield similar or maybe even superior improvements in intermediate muscle recovery and beyond.

Adequate amounts of leucine (≥2 grams/serving) can be found in many proteins. However, whey delivers leucine the fastest and has thus been considered one of the most protein-anabolic (dairy) proteins.

Leucine kinetics of whey (fast) vs casein (slow)



Adapted from Boirie et al. *Proc Natl Acad Sci USA*. 1997.[109]

Acute effects of protein on muscle protein synthesis

A large part of the contemporary research on the benefits of protein supplements has focused on their beneficial effects on trainees' postworkout protein synthesis rates. The pertinent studies consistently show significant increases in this putative predictor of long-term muscle gains in response to 20 grams or more of proteins with high essential amino acid contents, most prominently dairy (milk, whey, or casein), soy, or pea proteins. However, the “optimal” amount of protein is still the object of ongoing research.

What is clear is that a certain dose-response relationship exists at least for the immediate (0-4 hours) increase in post-resistance-exercise protein synthesis, but the additive effect of each extra gram of protein does decline. Although this decline is indicative of the existence of a ceiling effect for high protein intakes, the data that were taken from a 2021 review[110] clearly indicate that this ceiling, if it even exists, does not nullify further increases in protein synthesis in response to the ingestion of 40 grams compared to 20 grams of supplemental protein after a standardized resistance training workout.

In view of the 13% difference and an overall increase in postexercise protein synthesis by almost 50%, it is by no means clear whether and to what extent this acute increase in fractional protein synthesis — which was measured over a time frame of only 4 hours after the workout — will manifest in the form of actual muscle gains after weeks or months of training.[111][112]

Chronic effects of protein on muscle and strength gains

Resistance-training-induced increases in muscle size and strength take time, more time than the monitoring window of 4–8 hours that scientists use to assess the influx of amino acids into their participants’ muscles (e.g., quadriceps, biceps brachii, and gastrocnemius). This time window is inadequate to capture the complete picture of muscle adaptation and growth. Hence, the previously discussed studies — which focus on the immediate impacts of protein supplementation on strength and the frequently referenced effects of varying amounts of protein on the protein synthetic response within a short time window (4–8 hours postexercise) — provide only a limited perspective on the practical advantages of protein supplements for individuals engaged in resistance training.[111][112]

Even though the debates about the optimal types, time of ingestion, serving sizes, etc. are ongoing, there seems to be a relatively broad consensus that the meager recommended daily allowance for protein of 0.8 grams per kilogram of body weight issued by the NIH[113] will not support maximal strength or size gains in either recreational or professional resistance trainees.

In fact, a recent meta-analysis used data from 69 pertinent randomized controlled trials as part of its dose-effect analysis of increases in daily total daily protein intake and their effects on resistance-training-induced strength gains. This analysis quantifies the optimal protein intake at 1.6 grams per kilogram of body weight (g/kg) per day or higher — at least twice the FNB's previously cited RDA.[114]

This is also remarkable because the vast majority of studies was conducted in participants who did not habitually participate in resistance training before the intervention. Based on their dose-response analyses using spline curves, the Japanese authors of the study were also able to estimate the strength increase per additional 0.1 g/kg per day at 0.72%. Notably, this almost linear increase peaked at total intakes of 1.5 g/kg per day, and no further gains in response to extra protein were observed thereafter. The intuitive concept of “more protein helps more” thus seems to apply only within a relatively narrow range of total protein intakes.

Both the concept of a ceiling level for the benefits of increased protein intakes and where this ceiling could probably be found are corroborated by at least 3 additional meta-analyses.[115][116][117] The most recent of these studies,[117] which sought to quantify both the muscle strength and size response to resistance training, concluded an (almost) identical level of 1.6 g/kg of body weight per day, a figure that is identical to the one reported by the 2 other meta-analyses.[115][116] With even higher total protein intakes, additional increases in muscle size begin to diminish, and the already small effect of less than a pound of extra muscle that the previously cited meta-analyses calculated for each 0.1 g/kg of extra protein (based on studies lasting, 8 to 12 weeks on average) starts to fade.

Although the increases in protein intake in the studies included in the meta-analyses discussed above were generally achieved through the administration of protein supplements, the extent to which powders, drinks, and bars provide a significant advantage over food proteins remains unclear. After all, it seems that the chronic response to increased protein intakes is less dependent on the timing and type of protein that is consumed than on the initially discussed and often-cited acute effects on muscle protein synthesis. Although FSR, MyoPS, and others clearly benefit from the use of fast-digesting high EAA proteins in the form of protein concentrates, isolates, and hydrolysates taken near the time of of resistance training workouts, contemporary evidence suggests that the more practically relevant effects of chronically elevated protein intakes are primarily determined by the absolute amount of protein that a trainee consumes[118][119] — provided that the protein sources consumed have a sufficiently high content of essential amino acids (roughly 25%–50% of the total protein content) and leucine.[120][121] This also means that consuming a significant portion (let alone all of one's dietary protein) in the form of whey or other high-EAA, high-leucine, fast-digesting protein supplements would not promote a trainee's longer-term muscle gains beyond levels that could be achieved with eggs, fish, meats, dairy, legumes, etc.

Effects on endurance exercise

Protein is still mostly thought of as a supplement that's useful primarily for bodybuilders, strength athletes, martial artists, and all other trainees for whom muscle mass and strength rank highest among their professional or recreational training goals. Nevertheless, the interest in high(er) protein diets, protein supplements, and (more recently) functional foods with extra protein has increased significantly in endurance and team sports.

According to data from a network analysis of 20 randomized controlled trials published in and before 2019 that included mostly studies in endurance athletes (i.e. cyclists, runners, triathletes, basketballers, soccer players), increased protein intakes can have significant benefits on classic markers of endurance exercise performance such as the participants *rating of perceived exertion* (RPE).[122] It is important to note that performance boosts were found only in studies in which the protein (usually whey or other fast-digesting dairy proteins) was supplied on top of the mainstay carbohydrate supplements. In other words, benefits were not detected for either RPE or other direct measures of athletic performance in the meta-analysis — including VO_2max, maximum power, and average power — if the protein replaced the readily available sugar water.

Benefits cannot be guaranteed, however. Disappointing results have been reported in a meta-analysis of trials involving concurrent training regimens (strength and cardio simultaneously).[123] Although beneficial effects on muscle strength and body composition were observed in the majority of the 11 studies that were included in the meta-analysis, the three 4-week to 8-week interventions that measured the more endurance-specific VO_2max capacity of their participants found no evidence of beneficial effects for 20 grams per day,[124] 38.6 grams per day,[125] and 50 grams per day of extra protein, compared to placebo supplements.[126] This raises the question of how the divergent study outcomes can be explained.

The answer may sound surprising and seems to refute the previously introduced concept of dietary protein as the LEGO bricks of the muscles. Persistently lower aminotransferase levels (ALT and AST), which indicate reduced use of muscle protein as an energy source (some may say "protein-wasting"), clearly suggest that the benefits are due more to a reduced protein breakdown of muscle tissue as an energy substrate and due less to the incorporation of “protein bricks” into the muscle architecture.[127] Even if that's not the primary mechanism, it becomes increasingly clear that these “muscle-protective” effects of extra protein are of previously underappreciated value in endurance athletes, where they may play a significantly greater role than they would for resistance trainees, for example.

One thing that seems to refute the idea that protein may simply be used as fuel is the observation of a 2022 study in which the levels of ALT and AST, the two key enzymes which facilitate the conversion of the amino acids alanine and aspartate to glucose in the liver (gluconeogenesis), were significantly reduced when 0.4 g/kg of carbohydrates were given to 10 recreationally trained male runners 60 minutes before an standardized running protocol at intensities of 70% VO_2max and subsequent running to exhaustion at 80% VO_2max.[127] If it were just due to the energy, the observed advantage of 0.4 g/kg of protein over the same amount of carbohydrates (which served as a control) would not have occurred. A similar statement can be made for the benefits that scientists observed during recovery periods lasting longer than 8 hours, as were reported by 2 out of 3 studies in a 2020 meta-analysis[128] that investigated concomitant administration. A common classic belief is that carbohydrates fuel endurance athletes. Recent insights, however, suggest that proteins promote recovery and adaptation on a subsequent bout of endurance exercise 12–24 hours later.[129][130] Overall, the cited acute response data thus suggest the existence of both recovery and even putative prerecovery effects of (extra) protein, effects that seem to pay off in the long run (pun intended), for which a meta-analysis of 19 pertinent papers in endurance-trained participants reported significant long-term proadaptational effects on VO_2peak.[131] More specifically, the authors were able to demonstrate that more than a quarter of the benefits that the input studies observed in response to the chronic use of protein supplements were a direct result of the provision of extra protein. These benefits take time, though. Both the VO_2max increases and the improvements in time-trial performance, and the slightly but significantly larger increases in lean mass, were observed over the course of 4.5 and 24 weeks.

What's the optimal dose of (supplemental?) protein for endurance athletes?

In summary, both the short-term performance benefits of peri-workout protein supplements at doses of 0.4 g/kg, as well as their use as part of high(er) protein diets containing protein at 1.8 g/kg or more can accelerate the training progress of endurance athletes and eventually contribute to their competitive success. Moreover, the continuous provision of extra protein on a high-protein diet will help them to keep fasted plasma levels of free AA stable and thus provide the building blocks that are required to maintain a positive net protein balance in endurance athletes;[132] this might explain the often underappreciated increase in muscle protein synthesis that is often falsely thought of as beneficial only for sprinters, martial artists, bodybuilders, strength athletes, etc.

Warnings about *protein*

Unless a person has a preexisting condition that affects the liver or kidneys, the intakes suggested below will not harm these organs.[133]

How to take *protein*

In the United States, the Recommended Dietary Allowance (RDA) of 0.8 grams per kilogram of body weight (0.8 g/kg or 0.36 g/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.[134]

However, the current evidence suggests that this amount has been underestimated. Recent studies point to 1.0–1.2 g/kg as the minimum daily intake before the body starts downregulating important nonessential processes, from immune function to muscle protein synthesis.[135][136][137] Even a reanalysis of the data used to establish the above RDA suggests that the minimum daily protein intake should be at least 1.0 g/kg.[138]

But depending on their specific athletic goals, some people may need more protein.

In this guide, based on evidence for improving muscle gain, we suggest a minimum of 1.6 g/kg of body weight. This should provide most of the benefits of a higher protein intake. It’s possible that slightly greater gains could be obtained with a higher intake of up to 2.4 g/kg. Up to 3.3 g/kg may minimize fat gain while gaining muscle, which is a common desire of lifters.

As mentioned in the section on endurance, daily protein intake at 1.8 g/kg or more and peri-workout doses of 0.4 g/kg may help, but it’s important that this protein doesn’t replace carbohydrates.

💡 **Tip: Use our Protein Intake Calculator**

A person’s protein needs hinge on many factors — notably weight, health goals, and level of physical activity. Based on our research and the data that are input, we can calculate an optimal daily protein intake. Click on the image below to get started!

Carbohydrates

What makes *carbohydrates* a primary supplement

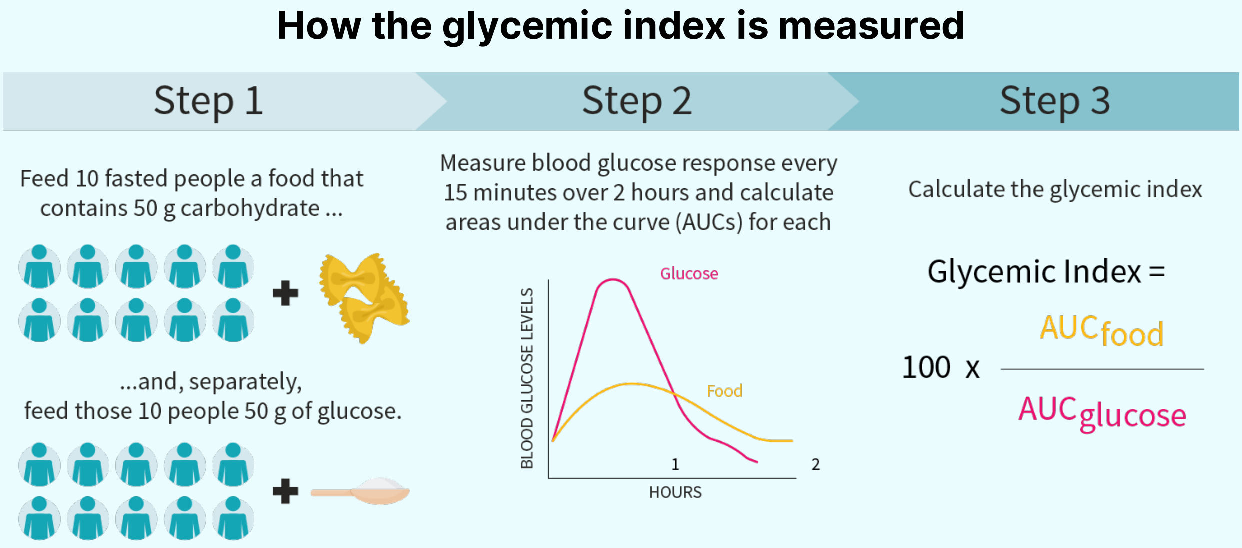
Carbohydrates are an athlete’s best friend. They are a primary source of fuel for skeletal muscles and the central nervous system and can support exercise over a large range of intensities due to their use in both anaerobic and aerobic pathways.[139] Whether it's continuous, moderate to high-intensity (65%–80% VO_2max) endurance exercise or a resistance training workout featuring multiple sets of 6–20 repetitions with maximal loads separated by brief rest intervals, the body relies extensively upon carbohydrates for energy. Notably, the depletion of carbohydrate stores (i.e., glycogen) during exercise is associated with fatigue, which manifests as reduced work output, impaired concentration, and increased perception of effort. As such, sufficient carbohydrate intake is of the utmost importance for individuals interested in peak physical performance. A substantial body of evidence demonstrates that strategies to enhance the availability of carbohydrates before, during, and after exercise improves performance across many different types of exercise.[139] However, in contrast to athletes who engage in frequent, rigorous training sessions, individuals who are engaged in a general fitness program don’t have to place too much thought into their daily carbohydrate intake because the average diet tends to provide a sufficient amount.

🔍 **Digging Deeper: Glycemic index vs. glycemic load**

The glycemic index was developed in the 1980s and was used to rank carbohydrates on a scale of 0 to 100 based on their ability to raise blood sugar after consumption.[140] To determine this ranking, fasted participants came to the lab and were fed a serving of food containing 50 grams of carbohydrates, and the greater and more prolonged the blood sugar response, the higher the GI rating. A high-GI food is typically characterized by rapid digestion and absorption into the bloodstream. High-GI foods are those with rankings greater than 70, moderate is 56 to 70, and low-

GI foods are those with rankings less than or equal to 55.

However, this model does not take into account the quantity of food consumed in a real life, free-living setting. The use of the *glycemic load* (GL) was meant to correct that problem. The glycemic load of a food considers both the glycemic index rating of the food and how much is consumed. So, GL = (glycemic index rating * grams of food consumed)/100. High-GL foods are those with values greater than 20, moderate GL is 11 to 19, and low GL is 1 to 10. Some foods, like watermelon, can have a very high GI (72). Once serving size is taken into account, the GL can be very low — in this case, a GL of 4 for watermelon. A table of calculated GIs and GLs can be found here.[141]



There are a few mechanisms that explain why carbohydrate supplementation during exercise improves performance: stimulation of the central nervous system during short-duration exercise, enhanced maintenance of blood glucose leading to increased carbohydrate burning by the working muscles, and offsetting glycogen utilization during prolonged exercise.

Most studies have used some form of continuous aerobic exercise to assess the effect on performance of carbohydrate intake during exercise. In these studies, it has been consistently shown that providing carbohydrate (230–350 mL of a 6%–8% carbohydrate solution) at regular intervals (10–15 mins) can improve performance.[142]

Although the effect is not as substantial as endurance exercise lasting more than 60 minutes, resistance exercise can deplete muscle glycogen by up to 40% depending on the intensity and duration of the workout.[143][144] The data are more limited and mixed regarding the acute (short-term) performance benefits of carbohydrate supplementation during a resistance training session, but it may be useful during high-volume sessions that include many sets to muscular failure and exceed 40 minutes in duration.[145] Ergogenic effects are also more likely if training takes place in the fasted state.

The quantity of carbohydrates that should be consumed during exercise (and whether they should be consumed at all) is largely determined by the duration of exercise because performance benefits become larger as glycogen becomes a more limiting factor. This is demonstrated by a review that reported that carbohydrate intake during endurance exercise lasting longer than 2 hours improved performance by 6.2% on average, whereas performance improvements were reduced to 4.9% and 2.6% in exercise durations of 1–2 hours and less than 1 hour, respectively.[146]

Warnings about *carbohydrates*

A central concern with preexercise carbohydrate feeding is *rebound hypoglycemia*, which has led to the common recommendation to avoid carbohydrates in the hour before exercise.

When carbohydrate is ingested, an insulin response is immediately triggered. Insulin facilitates glucose uptake, and when exercise is initiated in the presence of high insulin concentrations, muscle glucose uptake is further increased due to upregulation of GLUT-4 transporters. This leads to a rapid decrease in blood glucose concentrations in the first 15 minutes of exercise, and in some cases, hypoglycemia will develop in susceptible individuals.[147][148]

Despite the occurrence of this phenomenon in a number of athletes, the ergogenic effects of pre-exercise carbohydrate intake appear to outweigh the risks because almost all studies point toward unaltered or improved performance with preexercise carbohydrate ingestion.[149][150] Also, rebound hypoglycemia can be effectively negated by a proper warm-up and short rest period before exercise[151] or by shifting intake closer to the start of exercise (e.g., <10 min).[150]

Relatedly, there has been great interest in whether low *glycemic index* (GI) or high GI carbohydrates should be consumed in the preexercise meal due to their differential effects on postprandial (postmeal) glucose and insulin levels. Specifically, it's been hypothesized that low GI carbohydrates have superior effects on exercise performance due to decreased postprandial hyperglycemia and hyperinsulinemia following consumption, which leads to more stable blood glucose and a reduced risk of rebound hypoglycemia during exercise. Another potentially advantageous mechanism is increased fat oxidation during exercise.[152]

The available evidence suggests that there is no clear benefit of consuming low GI carbohydrates over high GI carbohydrates before exercise.[153][152] In spite of these findings, in situations where a preexercise meal must be consumed several hours before the start of exercise, or if carbohydrates are not available during exercise, low GI carbohydrates are theoretically useful.

How to take *carbohydrates*

Use the chart below to help choose a total daily carbohydrate intake according to activity levels and body weight (in kilograms or pounds).

Daily carbohydrate intake

INTENSITY	ACTIVITY	g/kg	g/lb
Low	Skill-based or general activities	3–5	1.4–2.3
Moderate	Exercise program (1 hr)	5–7	2.3–3.2
High	Endurance program (1–3 hr)	6–10	2.7–4.5
Very high	Extreme commitment (4–5+ hr)	8–12+	3.6–5.4+

Adapted from Thomas et al. *J Acad Nutr Diet.* 2016.[139]

Carbohydrate intake for various sports

SPORT	g/kg	g/lb
Ultramarathon	7–12	3.2–5.4

SPORT	g/kg	g/lb
Middle distance power sports (e.g., 800-meter run)	6–12*	3.8–5.45
"Stop and go" team sports (e.g., soccer, basketball)	5–7**	2.3–3.5
Heptathlon, decathlon	5–8	2.3–3.6
Strength sports (weightlifting, powerlifting)	4–7	1.8–3.2
Jumping, throwing, sprinting	3–6	1.4–2.7
Bodybuilding contest preparation	2–5***	0.9–2.3

Based on[154][155][156][157][158][98][159][160][161]. *Higher end of range during preseason, women generally on lower end of range. **Up to 10 g/kg/day during high volume preseason training, dependent on demands of sport and position. ***Approaching lower end of range as needed to reach desire stage condition.

Aside from simply eating enough carbohydrates each day, the timing of intake can further bolster acute performance and chronic training adaptations.

The primary goal of preexercise carbohydrate intake is to top off glycogen stores and ensure that adequate fuel is available to the muscle during exercise to optimize performance. To this point, the ergogenic effect of preexercise carbohydrate intake depends on prior glycogen stores. An individual with limited rest between training sessions (i.e., <8 hours) has much more to gain from a carbohydrate feeding before exercise than someone who has rested for multiple days while consuming a high-carbohydrate diet.[119]

Athletes can use the table below to optimize the timing of their carbohydrate intake. Other people can just remember the following sugar protocol: If you exercise for 45 minutes to 2 hours, aim for 30–60 grams per hour; if you exercise longer, aim for 60–90 grams per hour.

Carbohydrate intake timing

	SITUATION	TIME	CARBOHYDRATES
Before	Loading, if exercise duration will be >90 minutes	36–48 hr before the event	4.5–5.4 g/lb/day (10–12 g/kg/day)*
	Loading, if exercise duration will be <90 minutes	24 hr before the event	3.2–5.4 g/lb/day (7–12 g/kg/day)*
	Pre-event	1–4 hr before the event	0.5–1.8 g/lb (1–4 g/kg)**
During	Brief exercise	≤45 min	Unnecessary
	Sustained high-intensity exercise	45–75 min	Sugars: ≤30 g/hr
	Endurance exercise, including stop-and-start sports such as basketball, soccer, etc.	60–150 min	Sugars: 30–60 g/hr
	Ultra-endurance exercise	>150 min	Sugars: ≤90 g/hr
After	Speedy refueling	≤10 hr between two fuel-demanding sessions	0.5 g/lb/hr (1.0–1.2 g/kg/hr) for the first 4 hours then resume normal intake

	SITUATION	TIME	CARBOHYDRATES
	Typical refueling	>10 hr between two fuel-demanding sessions	0.5–0.7 g/lb (1.0–1.5 g/kg) over the first 30 minutes then resume normal intake

Adapted from.[139][162]*Select easily digestible “compact” sources that are low in fiber to minimize GI distress. **Select low glycemic index options if carbs cannot be consumed during exercise.

🔍 Digging Deeper: Carbohydrate mouth rinse

Carbohydrate feeding can improve performance during relatively short (approximately 1 hour) and intense exercise, although glycogen stores generally do not limit performance.[146]

Evidence suggests that when carbohydrate receptors in the mouth are stimulated by rinsing with a carbohydrate solution for 10 seconds and then spitting it out, brain areas responsible for reward and motor control are activated.[163] This can lead to increased motivation, reduced perception of effort, and increased corticomotor excitability during exercise.[164]

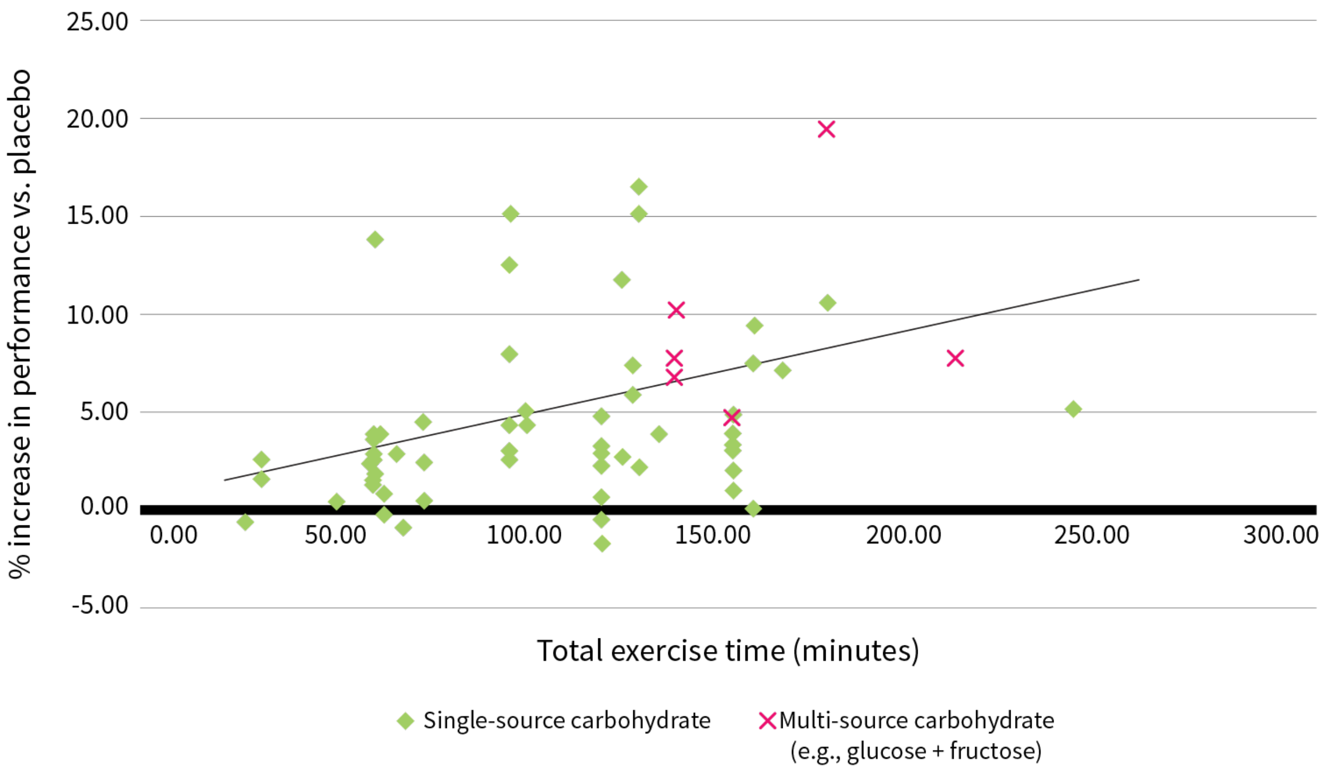
In recent years, several reviews on the topic suggest that a carbohydrate mouth rinse can improve power output during short-duration cycling exercise, but its ability to improve time trial performance has been inconsistent.[165][166][167] Also, a carbohydrate mouth rinse generally does not affect resistance exercise performance.[168][169][170][171][172][173][174][175] However, almost all of these studies have been conducted with a relatively low total workload, typically featuring a 1-repetition maximum test on bench press followed by a set to muscular failure with a low to moderate load (i.e., 40%–60% 1RM). Additionally, these interventions take place with high carbohydrate availability at the start of exercise.

Other research has displayed that a carbohydrate mouth rinse can improve performance during a whole-body resistance exercise workout when performed after an 8–11-hour overnight fast[176][83] or in a glycogen-lowered state.[177] Practically, these findings suggests that a carbohydrate mouth rinse could be a useful option to maintain or even increase exercise performance during a period of energy restriction.

As the duration of exercise increases, so does the recommended carbohydrate intake, and a dose-response relationship between carbohydrate ingestion and performance has been observed.[178] Even so, when ingesting glucose only, carbohydrate oxidation peaks at 1.0–1.1 grams per minute, thereby limiting further potential performance benefits from more carbohydrates. Furthermore, a large intake of carbohydrates during exercise can cause gastrointestinal distress, which typically worsens performance.

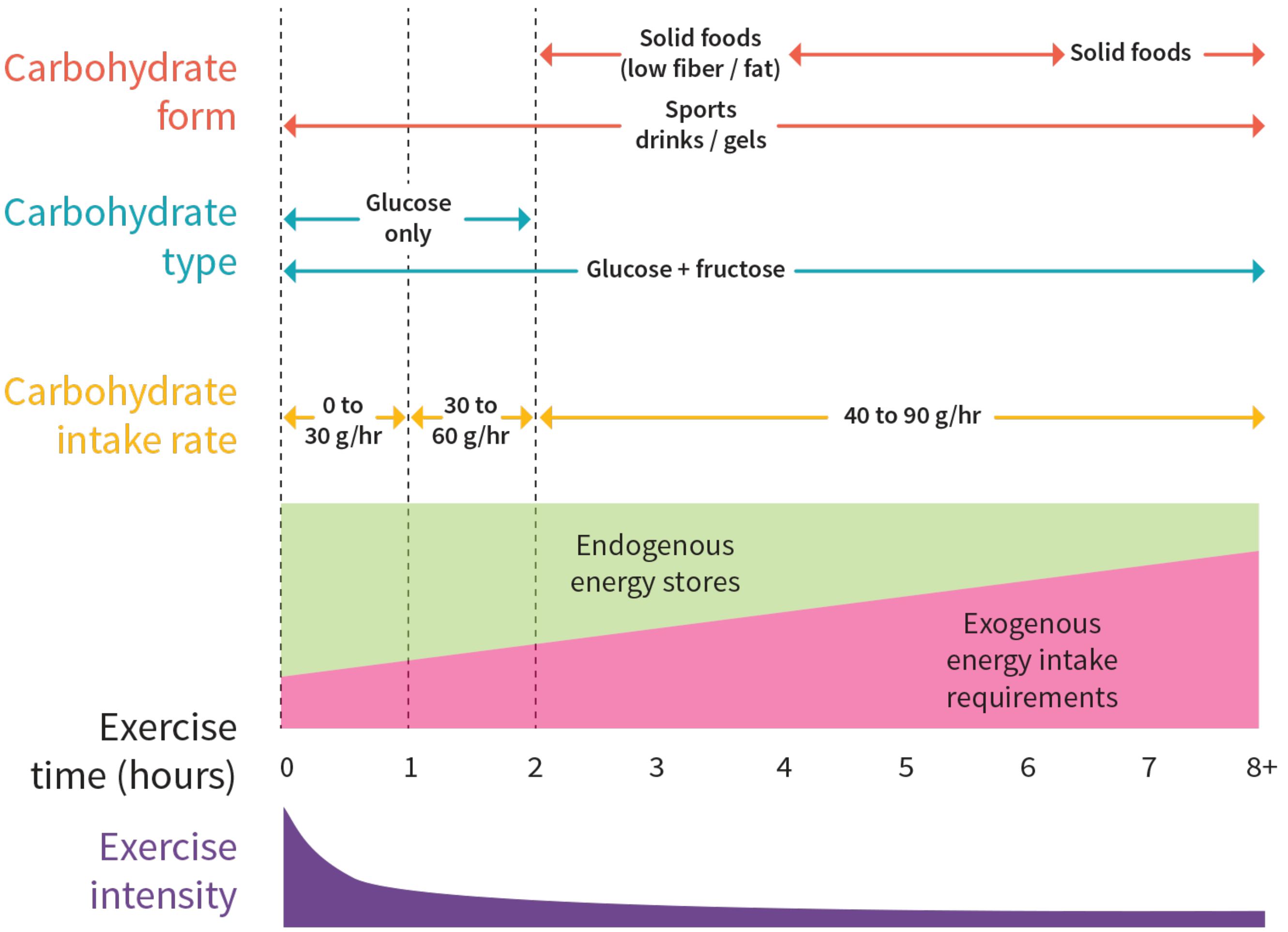
To overcome these issues, glucose can be coingested with fructose, which uses a different transport mechanism than glucose. Combining these sources results in an increased capacity to absorb carbohydrates[179][180] while minimizing gastrointestinal distress.[181][182]

Effect of carb type on endurance exercise performance



Adapted from Stellingwerff and Cox. *Appl Physiol Nutr Metab.* 2014.[146]

Summary recommendations for carb intake during endurance exercise



Adapted from Stellingwerff and Cox. *Appl Physiol Nutr Metab.* 2014.[146]

Glycogen restoration is the primary goal of postexercise carbohydrate intake, especially when there are multiple bouts of training or competition on the same day. Carbohydrate intake postexercise can also improve recovery by attenuating inflammatory signals and immune system disruption.[183] Glycogen restoration requires adequate carbohydrates and time because the rate of glycogen resynthesis is only about 5% per hour.[184] However, in situations where there are at least 24 hours of rest between exercise bouts, as long as the total intake of carbohydrates and calories is adequate, the sources of carbohydrate and timing of intake can be selected based on individual preferences.

For athletes in a hurry to replenish their glycogen stores, it's recommended to ingest 1.0–1.2 grams of carbohydrate per kilogram of body weight each hour (g/kg/hour) for the first 4 hours after exercise in frequent small feedings.[102] Within this paradigm, high-GI carbohydrates may be superior to low-GI carbohydrates for rapid glycogen synthesis due to production of a higher insulin response, but this isn't fully supported by the available evidence.[185][186] At the very least, high-GI carbohydrates tend to be easier to digest, which can make this speedy refueling strategy more manageable.

Other potential strategies revolve around supplementation. Short-term creatine loading (20 g/day) has been shown to enhance glycogen resynthesis by 82%, compared to placebo, at 24 hours after exercise.[63] Caffeine may also boost the rate of glycogen synthesis[187] and improve subsequent performance,[188] but the evidence is not unanimous, and there are practical concerns because caffeine ingestion is likely to disrupt sleep for people who exercise later in the day.

There has been great interest in the potential of coingesting protein with carbohydrates to enhance glycogen synthesis. This is due to research that has demonstrated a greater insulin response when protein is consumed alongside carbohydrates,[189] which should theoretically increase muscle glucose uptake. However, results from recent meta-analyses report that coingestion of protein and carbohydrates does not enhance glycogen synthesis compared to carbohydrates alone, and this finding holds true in situations of inadequate carbohydrate intake (<0.8 g/kg) as well.[190][191]

The following is a useful post- competition refueling strategy:[102]

- Consume carbohydrates as soon as possible after workout.
- Consume carbohydrates at 1.0–1.20 g/kg/hour for the first 4 hours following exercise in small frequent feedings.
- Consume moderate GI to high GI carbohydrates

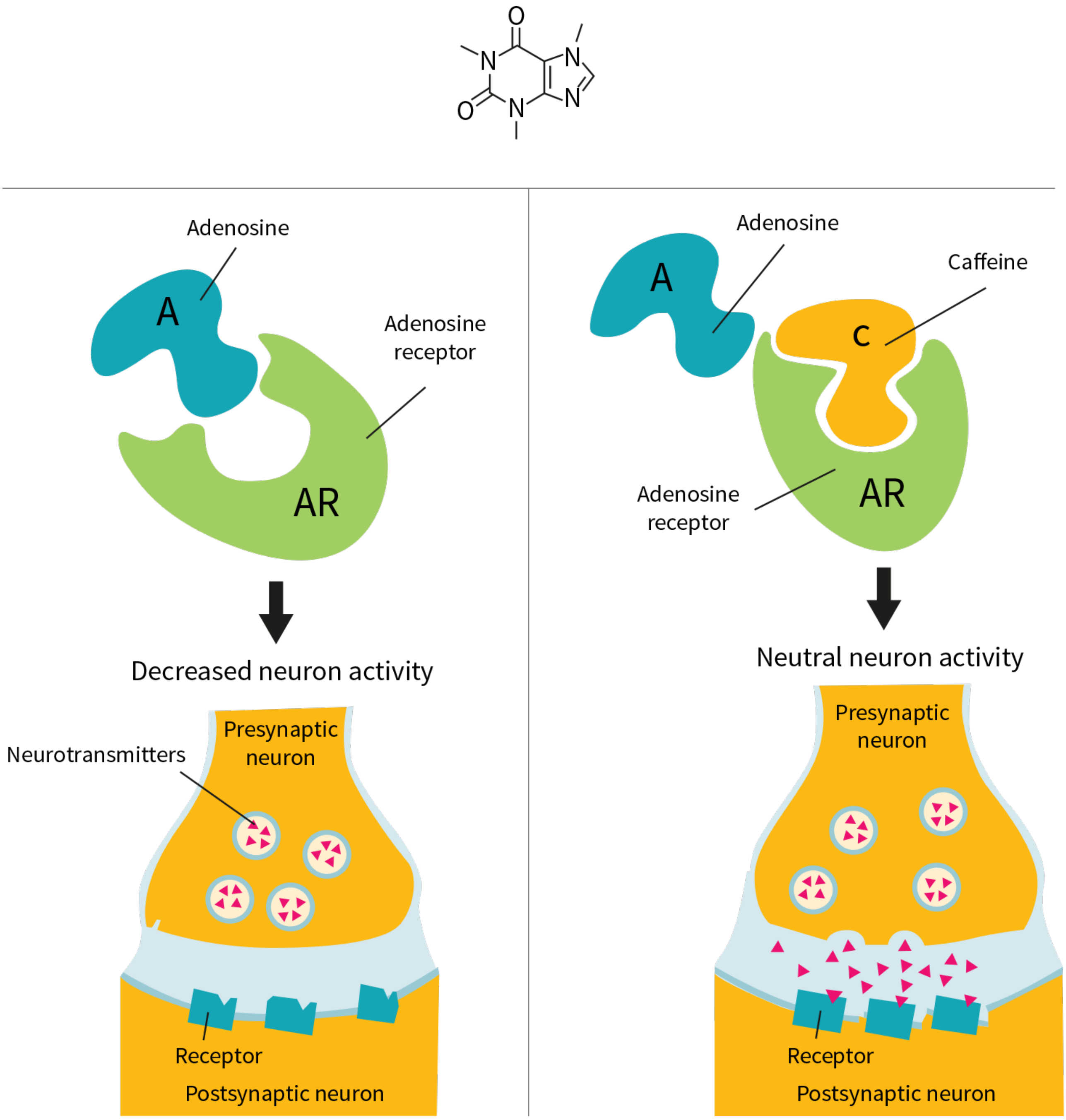
Caffeine

What makes *caffeine* a primary supplement

Caffeine exerts an ergogenic effect primarily by stimulating the central nervous system. Specifically, caffeine blocks certain adenosine receptors in the brain. Adenosine downregulates arousal and is associated with sensations of fatigue. It is known to inhibit the release of neurotransmitters such as dopamine, serotonin, acetylcholine, glutamate, and norepinephrine,[192] and to promote sleep.[193]

Caffeine, which has a similar molecular structure to adenosine, binds to adenosine receptors A_1 and A_{2A} after ingestion and opposes the effects of adenosine, leading to an increase in the concentrations of excitatory neurotransmitters. This generally results in a variety of positive outcomes that can enhance exercise performance, including improved wakefulness, alertness, focus, and vigilance,[194] as well as pain suppression[195][196] and reductions in perceived exertion.[197]

The mechanism of caffeine



Reference: Ferré. *J Neurochem*. 2008.[198]

Caffeine also seems to have direct effects on skeletal muscle. Caffeine increases motor unit recruitment and calcium release from the sarcoplasmic reticulum,[199][200] which may result in a more forceful muscular contraction.[201] Originally, it was proposed that caffeine enhanced endurance performance via enhanced free fatty acid oxidation and consequent glycogen sparing during exercise, but this theory has since been dismissed.[202]

Caffeine improves a wide variety of physical performance measures. For aerobic exercise, caffeine has been reported to improve time trial performance by 2.2%–2.9%[203][204], and the magnitude of effect may increase with the duration of exercise.[204] Caffeine has also been found to improve 2000-meter rowing ergometer time by 4.1 seconds while slightly boosting average power output.[205] Notably, these effects do not appear to be influenced by sex, age, training status, or dose of caffeine (at least when consumed within a range of 3–6 milligrams per kilogram of body mass, or mg/kg). Although these improvements may seem unsubstantial, an approximate 2% increase in performance during a half marathon is the difference between first and 97th place in a recent list of fastest half marathon times.[203]

Moving on to anaerobic performance, with a particular focus on strength and power to start, caffeine ingestion may increase mean and peak power output on the Wingate test by 3% and 4%, respectively.[206] Additionally, caffeine supplementation can increase vertical jump height during single and repeated jumps by 2%–4%[207][208] and throwing performance by 3.7%–6%.[209][210]

With regard to resistance exercise in particular, caffeine has a moderate effect on average and peak movement velocity, and this finding is consistent across loading zones (i.e., 25%–100% of *1-repetition maximum* (1RM)) and upper and lower body exercises.[211] Furthermore, caffeine has a trivial effect on 1RM strength,[212] which is more distinguishable on upper body exercises,[208][213] and a small effect on muscular endurance in both men and women.[213][214] Practically, caffeine ingestion tends to increase repetitions (reps) performed per set by 1–4 reps, and this has been observed in studies using loads in the range of 30%–85% of 1RM and protocols that feature single and multiple sets.[212]

Outside of the weight room, the effect of caffeine on sports-specific performance has also been examined. Caffeine has been shown to improve some parameters of combat sports[215] and team sports performance (i.e., time to complete agility tests, sprint performance, sport-specific endurance measured by different Yo–Yo tests).[207]

Overall, caffeine is one of the most extensively studied ergogenic aids in existence. Due to its potential to improve exercise performance in any athlete or physically active person, regardless of what they’re training for, it is classified as a primary supplement.

🔍 **Digging Deeper: How do caffeine's effects differ between individuals?**

In the face of a robust body of evidence supporting the ability of caffeine to improve various aspects of aerobic and anaerobic performance, it's critical to note that the response to caffeine is highly individual. For example, in a recent review on time trial performance, it was reported that the range of percent difference between the caffeine and placebo group was −3% to +15.9%.[204]

Interindividual differences in the response to caffeine may be partly due to variations in the *CYP1A2* gene and the *ADORA2A* gene. *Single nucleotide polymorphisms* (SNP) within the *CYP1A2* gene affect the speed at which caffeine is metabolized. Individuals with the AC or CC genotype (slow metabolizers) have an elevated risk of heart attack and hypertension with increasing caffeinated coffee consumption, whereas those with the AA genotype (fast metabolizers) do not.[216][217]

There is a growing body of evidence evaluating the influence of these differences on the ergogenic effect of caffeine, but the results are inconclusive. Most recently, a systematic review of 17 studies reported that only 4 studies showed a significant effect of genotype on caffeine's ergogenic effect. In each of these studies, trained participants were included, and the AA genotype experienced a greater improvement in performance than AC/CC.[218]

The *ADORA2A* gene codes for the A_{2A} adenosine receptor, which is one of two adenosine receptors that caffeine acts on. As such, it's believed that variations in this gene may impact the sensitivity to caffeine. Moreover, *ADORA2A* C allele carriers seem to have a higher habitual caffeine consumption compared to TT homozygotes.[219]

In a small pilot trial conducted in 2015, caffeine increased total work performed during a cycling time trial in TT carriers but only 1 participant in the CT/CC group.[220] In light of the possibility that carriers of the C allele are "nonresponders" to caffeine supplementation, researchers evaluated resistance exercise performance following caffeine ingestion in 20 C allele carriers. In contrast to the former study, caffeine was ergogenic for most outcomes.[221] Most recently, caffeine ingestion has been found to improve vertical jump height, sprint velocity, and ball throwing velocity in professional handball players[222] and increase total work performed in a 15-minute cycling time trial to a similar degree in TT and C allele carriers.[223]

🔍 **Digging Deeper: Tolerance and habituation to caffeine**

Another variable of interest that may impact the ergogenic (i.e., performance-enhancing) effect of caffeine is habituation. As previously mentioned, caffeine's ergogenic effect is mainly explained by antagonizing adenosine receptors in the brain. In animal models, long-term ingestion of caffeine is associated with an upregulation of adenosine receptors,[224][225] which has led to the idea that habitual caffeine intake may reduce the ergogenic effect of acute caffeine ingestion.[226] Does caffeine's ergogenic effect diminish over time with chronic use in humans?

There have been 2 studies that examined the time course of tolerance to caffeine. One trial had the participants ingest 3 mg of caffeine per kg of body weight for 20 consecutive days. It found that caffeine maintained its ergogenic effect during a 15-second Wingate test throughout the intervention period, but the magnitude of effect decreased from large to moderate.[227] Similarly, ingesting 1.5–3.0 mg of caffeine per kg of body weight per day for 28 days was found to significantly reduce its ergogenicity during a 30-minute cycling time trial, although performance was still greater with caffeine supplementation after habituation compared to the baseline placebo test (+3.8%).[228]

In addition, an early study reported that the magnitude of caffeine's ergogenic effect was reduced in habitual high consumers (≥300 mg/day) compared to low consumers (<50 mg/day) during a time-to-exhaustion test,[229] but the methods employed were of questionable quality — specifically, the method by which habitual caffeine intake was assessed and the exercise test used because time-to-exhaustion tests are known to have poor reliability due to high intraindividual variation in performance.[230] A more recent study, however, used a repeated sprint test and also found that the ergogenic effect of caffeine was diminished in high habitual caffeine users compared to low habitual users.[231]

Notwithstanding, many other acute trials featuring various forms of exercise tests have found contrasting results. In these studies, supplementation with caffeine enhanced vertical jump height,[232][209][233] cycling time trial performance,[234][235] muscular endurance,[232][233] medicine ball throw distance,[209] bench press velocity and power,[233] Wingate test performance,[233], and sprint time,[236] irrespective of whether the participants were low or high habitual caffeine consumers.

Ultimately, a 2022 meta-analysis of 59 randomized controlled trials concluded that habitual caffeine consumption does not influence the ergogenic effect of acute supplementation with caffeine,[237] meaning that even with daily caffeine consumption, ingesting some caffeine about an hour before exercise will still have a positive impact on performance in people who benefit from caffeine (which is not everyone). But could there be a way to enhance caffeine's ergogenicity in habitual consumers?

To maximize the ergogenic effect of caffeine, athletes and coaches have long recommended using a caffeine withdrawal period before important training sessions or competitions. However, the available evidence indicates that abstaining from caffeine for 24–96 hours does not enhance its ergogenicity.[237][238][239]

It's also been speculated that consuming a larger dose of caffeine than is typically consumed will maximize its ergogenicity,[240] but this doesn't appear to be the case, and supplementation with a higher or lower dose of caffeine than is typically consumed has been shown to produce a similar ergogenic effect in habitual consumers.[237]

Warnings about *caffeine*

Because a person can become *habituated* to caffeine when they become *tolerant* to some of its effects, if they stop taking caffeine, they can experience symptoms of withdrawal, such as fatigue, irritability, headaches, and — ironically — sleeplessness.

Caffeine may increase anxiety for people who are anxiety prone and may cause difficulty sleeping for some, especially when taken close to bedtime. However, the overall risk for anxiety and sleep difficulty for the general population, when doses are limited to 400 mg or less per day, is low.[241]

Of the other issues associated with caffeine, we can only mention a few. Caffeine interacts dangerously with several pharmaceuticals, notably tizanidine and a type of antidepressant called *monoamine oxidase inhibitors* (MAOIs). It 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.

Caffeine can also decrease blood lithium levels. Suddenly eliminating all caffeine from the diet may cause lithium levels to rise. People who are taking lithium medication should keep their day-to-day caffeine intake roughly the same.[242] A person who wished to stop taking caffeine should talk with their physician about using a slow weaning process.

Some people might already be consuming more caffeine than they think. When calculating daily intake, consider all beverages, foods, and supplements. Bear in mind that caffeine can be "hidden" in a product — for instance, if "guarana seeds" is listed on a label, remember that those are richer in caffeine than coffee seeds.

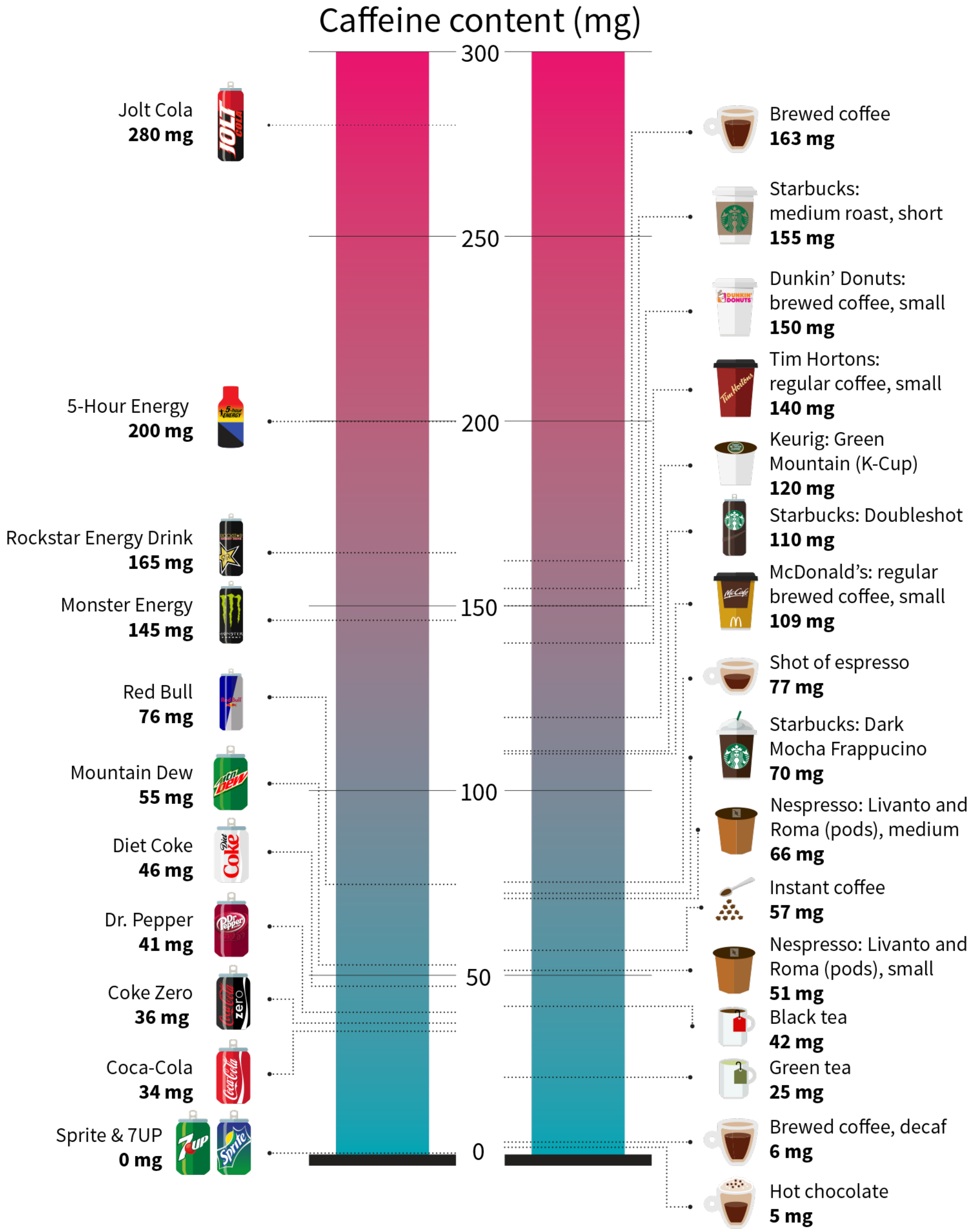
How to take caffeine

Caffeine has consistently been shown to improve exercise performance when consumed in doses of 3–6 milligrams per kilogram of body mass (mg/kg).[202] Very high doses of caffeine (e.g., ≥9 mg/kg) are associated with a high incidence of side effects and do not seem to be required to elicit an ergogenic effect. In the research setting, caffeine is most commonly consumed 60 minutes before exercise in the form of a capsule. Sixty minutes preexercise is believed to be the optimal timing of caffeine ingestion because this tends to correspond with peak plasma concentrations.[243] However, peak plasma concentrations have been reported to range from 30 to 120 minutes after caffeine ingestion.[202] The source of caffeine also influences when peak plasma concentrations occur.

For example, caffeine ingested in chewing gum is absorbed significantly faster than that taken in capsule form.[244][245] In accordance, studies have reported improved performance when caffeine gum is taken 5–10 minutes before exercise.[246][247] Similarly, although plasma caffeine concentrations have not been measured following the ingestion of caffeine gel, limited evidence suggests that consumption 10 minutes before exercise[248][249] is superior to 60 minutes before exercise.[250]

Another consideration when it comes to the source of caffeine, especially as it pertains to maximizing its ergogenic effect, is whether the dose of caffeine on the product label is what's actually being provided. Coffee is a notable offender in this regard. The caffeine content in coffee widely varies due to the plant variety, environmental growing conditions, and/or the brewing method used. For example, the caffeine content in coffees found in Austrian supermarkets and retail stores was found to range from 9 to 200 mg per 240 mL.[251] Additionally, in a study that evaluated the caffeine content of 20 different coffees available in coffee shops across the United States, it was reported that the amount of caffeine ranged from 76 to 112 mg per 240 mL. Moreover, the caffeine content of the same type of coffee purchased from the same stores on 6 separate occasions varied from 130 to 282 mg per 240 mL.[252]

Caffeine content of popular drinks



References: McCusker et al. *J Anal Toxicol.* 2006.[253] ● Desbrow et al. *Nutr Health.* 2019.[254] ● Ludwig et al. *Food Funct.* 2014.[255] ● Fox et al. *J Agric Food Chem.* 2013.[256] ● McCusker et al. *J Anal Toxicol.* 2003.[252] ● Angeloni et al. *Food Res Int.* 2019.[257]

Due to the likelihood that caffeine's ergogenicity is reduced with chronic use and that a higher-than-usual dose is needed to maximize its benefits (which can lead to side effects), it's been recommended to cease caffeine use for a short period before competition to resensitize to its physiological effects.[240] To date, there have only been 2 studies to assess the efficacy of this recommendation, and each reported that a 4-day withdrawal period did not augment caffeine's ergogenicity in high habitual consumers.[238][239] Considering the fact that withdrawal is also associated with a plethora of negative outcomes such as headache, irritability, fatigue, and muscle pain, it may be unwise to abstain from caffeine in the days leading up to competition.

For people who find that caffeine makes them jittery in an uncomfortable way, even with normal doses, taking 250 mg of theanine may help to reduce this effect.[258]

Secondary Supplements

BCAAs

What makes *BCAAs* a secondary option

Proteins are composed of amino acids, some that can be made by the body and others that cannot. The ones that need to be ingested, because the body cannot synthesize them, are called *essential amino acids* (EAAs). BCAAs are 3 of the 9 amino acids essential to humans, namely, isoleucine, leucine, and valine.

Because a person ingests BCAAs each time they ingest protein, supplementing with BCAAs in isolation is mostly redundant. For example, 100 grams of a whey protein concentrate can contain 11 grams of leucine, 6 grams of isoleucine, and 6 grams of valine, so 23 grams of BCAAs (the numbers vary between supplements).

Many studies have investigated the effects of supplemental BCAAs on exercise, and these effects have proved to be minimal when it comes to measures of physical performance.[259] Where BCAAs *may* be useful is in reducing muscle soreness and muscle damage due to exercise, which may improve performance in the case of frequent, intense exercise such as competitive sports.[260][261] However, these effects could also be expected from general protein supplements, and it's unclear whether BCAAs have any unique benefits in this regard.

On the whole, BCAAs have only two potential advantages over protein powders:

- *First,* they are less likely to cause cramping or nausea when consumed before exercise.
- *Second,* they are free from tryptophan (an amino acid that might promote exercise-related fatigue).

This is largely speculation, however.

Warnings about BCAAs

Adverse events reported during BCAA supplementation include nausea and vomiting, diarrhea, abdominal distension, abdominal pain, and hypertension.[262] However, it should be noted that none of these adverse events have been confirmed to be significantly greater than placebo, and larger and longer studies are needed to properly evaluate the safety of BCAAs.

BCAAs are structurally similar enough to tryptophan that they can compete for entrance into the blood-brain barrier.[263] Tryptophan is a precursor to serotonin, and excessive levels of BCAAs in the blood may reduce serotonin as well as catecholamines, as has been observed in animal studies.[263][264] This may produce anxiety-like behavior or low mood. Tryptophan is also a precursor of melatonin, so it's possible that a high dose of BCAAs in the evening could impair melatonin synthesis, though this is speculative.

🔍 **Digging Deeper: What's the relationship between BCAAs and diabetes?**

There is an ongoing debate about the role that BCAAs play in metabolic health. The first observation is that levels of BCAAs are elevated in people with insulin resistance and that there are some plausible mechanisms by which BCAAs could be involved in insulin resistance.[265] However, this could be a consequence of insulin resistance rather than a cause, and mechanistic roles may not equate to dietary relevance.

On the one hand, there seems to be some truth to the idea that obesity and insulin resistance may lead to an increase in circulating BCAAs, though this doesn't preclude a two-way effect. On the other hand, Mendelian randomization studies, which look for the association between a genetic variant and health outcomes, have found a positive correlation between genetically higher BCAAs and diabetes. Moreso, animal studies have found increases in insulin resistance during BCAA supplementation during obesogenic feeding, though not in cases of nonobesogenic diets. Yet another interesting observation is that a high BCAA intake led to hyperphagia in rats, but this effect was reversed by tryptophan supplementation. The most likely explanation was the aforementioned serotonin depletion because serotonin is an appetite suppressant.

A few observational studies have found a higher BCAA intake to be positively associated with the risk of diabetes, though these studies could easily be confounded.[266] However, a randomized controlled trial failed to find a statistically significant effect of a low-BCAA diet in participants with prediabetes and obesity, though it was a very short-term study and the low-BCAA group saw a modestly greater reduction (that wasn't statistically significant); it's possible that a longer study would have found a more convincing difference.[267] Another study used a generally protein-restricted diet (7%–9% protein) for 6 weeks and found a greater reduction in blood sugar and fat mass in the protein-restricted group.[268] However, it's difficult to rule out the influence of other dietary changes or even rule out the effects of restriction of other amino acids on gluconeogenesis or insulin resistance. Yet another short study found that a lower BCAA intake for 4 weeks coincided with reduced glycemia and insulin secretion during a mixed meal tolerance test.[269]

It is probably fair to say that a high intake of BCAAs may lead to a greater risk of insulin resistance for people at risk of diabetes and may be involved in overeating in some cases, which also ties into diabetes risk. It also may be true that very low BCAA intake may have a unique antidiabetic effect. However, it is still very unclear whether or not healthy and active people will be negatively affected by BCAA supplementation. Concomitant supplementation with tryptophan may be prudent, however.

How to take *BCAAs*

To supplement with BCAAs, take 10–20 grams before exercise, in water or a sugary drink. A ratio of 2:1:1 (leucine:isoleucine:valine) is often recommended based on 2 studies that actually used a 2.3:1:1.2 ratio. Both studies compared this 2.3:1:1.2 mix to a placebo (dextrin); different ratios were not compared, so the ideal ratio is unknown.

Taking tryptophan with BCAAs in proportion to the relative amount in dairy or meat protein may prevent serotonin depletion and its adverse effects mentioned above. This works out to roughly 66 mg of tryptophan per gram of BCAAs, based on data from chicken breast.

Citrulline

What makes *citrulline* a secondary option

Citrulline (or L-citrulline) is a nonessential amino acid found primarily in cucurbits such as watermelons, cucumbers, and other melons. Unlike arginine, ingested citrulline passes through the liver without being metabolized.[270] Instead, it is released into circulation and then converted by the kidneys into arginine. This means that supplementing with citrulline is a more effective way of raising blood arginine levels than supplementing with arginine. By increasing blood arginine levels,[271] supplementation with citrulline can boost *nitric oxide* (NO) production,[272] which may improve exercise performance via its potential effects on vasodilation,[273] mitochondrial respiration,[274] calcium handling,[275] and glucose uptake.[276] Additionally, citrulline can potentially improve exercise performance by promoting the clearance of ammonia during exercise (the build-up of which may promote muscle fatigue) through the urea cycle.[277] As a product of these effects (i.e., the clearance of ammonia and augmentation of blood flow), it's also speculated that citrulline could bolster acute recovery.

Citrulline is commonly supplemented in the form of *citrulline malate* (CitMal), which is a combination of L-citrulline and malate, an ionized form of malic acid. By mitigating the production of lactic acid and using it to form more pyruvate, malate may increase aerobic energy production and create more *adenosine triphosphate* (ATP),[278] thereby reducing muscle fatigue and improving muscle performance. However, although these mechanisms sound promising, there is an absence of direct evidence to support them. Furthermore, no study to date has directly compared L-citrulline and CitMal supplementation to determine whether the addition of malate provides further benefits to exercise performance.

The effects of citrulline supplementation have mainly been investigated in the context of anaerobic exercise performance in young, physically active adults. The available evidence demonstrates that citrulline has a consistent, small positive effect on muscular endurance.[279][280] A recent meta-analysis reported that citrulline supplementation increases the total number of repetitions performed to failure by about 3 extra repetitions across multiple sets.[281] Notably, 2 studies in this analysis used a German Volume Training protocol, comprising 10 sets of 10 repetitions for barbell curls and knee extensions, and both reported that citrulline had no effect.[282][283] However, each of the studies used a CitMal supplement that provided a 1.1:1 ratio of citrulline:malate, which is much lower than the recommended 2:1 ratio and consequently may have influenced the results.

In contrast, citrulline does not seem to affect muscular power or maximal strength.[279] These divergent results for muscular endurance and muscular power and maximal strength apply to older adults (ages 55+) as well.[284]

Outside of citrulline's direct effects on exercise performance, it may enhance training adaptations by improving recovery. The available evidence suggests that citrulline reduces the rating of perceived exertion immediately following exercise and the feeling of muscle soreness at 24 and 48 hours after exercise.[285] Even so, it does not appear to reduce blood lactate levels after exercise.[285] A potential caveat of this finding is that it's based on *acute* CitMal supplementation before *anaerobic* exercise. Acute citrulline supplementation has been shown to reduce lactate levels after a half-marathon.[286] Moreover, chronic citrulline supplementation (2–4 weeks) leads to reduced lactate levels after high-intensity exercise.[287][288]

Warnings about citrulline

Citrulline may interfere with the chemotherapy drug doxorubicin by preventing lipid peroxidation. It also seems to increase cellular uptake in some tissues and decrease cellular uptake in others,[289] although this is not clearly a bad or good thing. Citrulline supplementation could affect the cellular uptake of other drugs, which could potentially have negative side effects. This is highly speculative and without clear implications besides general caution.

Citrulline may reduce blood pressure,[290] and although its role in blood pressure regulation is as a nitric oxide precursor and not an inhibitor of signaling (such as ACE inhibitors), it could still potentially contribute to hypotension when combined with blood pressure medication.

How to take *citrulline*

In the research setting, CitMal is most frequently administered as a single acute dose of 8 grams (containing a 2:1 ratio of citrulline:malate) at 1 hour before exercise. It's worth highlighting that the supplement should contain a 2:1 ratio of citrulline:malate because recent evidence suggests that many popular supplement companies only provided a ratio of approximately 1.6:1.[283]

Another option is to supplement with L-citrulline in isolation at 1 hour before exercise, which (as previously alluded to) is likely to be as effective as CitMal based on the current evidence. The minimally effective dose of L-citrulline is reported to be 3 grams per day, and the maximum effective dose may be as high as 10–15 grams per day.[291] A dose-response study reported that peak citrulline levels occurred with a 15-gram dose, and citrulline levels were 28.4% higher compared to a 10-gram dose.[292]

It's possible to obtain an ergogenic dose of L-citrulline from fresh watermelon, but it's rather impractical because it would require consuming over a kilogram to reach the minimum effective dose.[293]

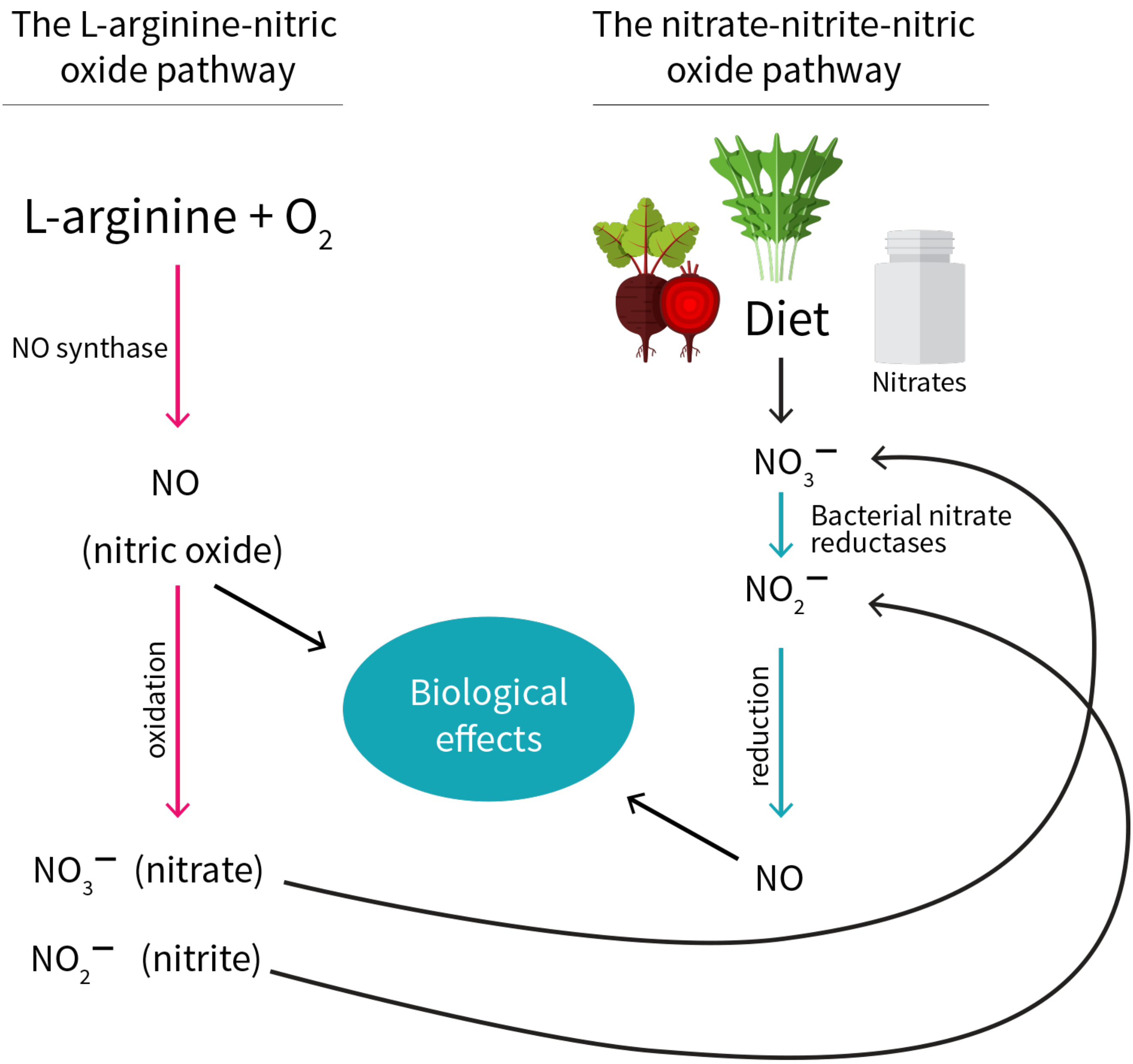
Interestingly, preliminary evidence suggests that the combined effect of citrulline and arginine could be more beneficial than a single dose of either amino acid alone. In a study in rats and rabbits, coingestion of citrulline and arginine caused a more rapid increase in plasma arginine levels and significantly greater increases in NO compared to either amino acid in isolation.[294] A combination of citrulline and arginine has been shown to more efficiently increase plasma arginine in humans as well,[295] which may be due to an inhibiting effect of citrulline on arginase, thus increasing the bioavailability of arginine.[296] One study in male soccer players found that ingesting 1.2 grams per day of both citrulline and arginine for 7 days significantly elevated plasma levels of arginine and NO and led to improved power, as well as reduced subjective perception of leg soreness and effort during exercise. Although it's still too early to recommend supplementing with these amino acids in combination, further research into their potentially synergistic effects is warranted.

Nitrates

What makes *nitrates* a secondary supplement

Nitrates can be found in different foods, notably beetroot and leafy green vegetables. Nitrates break down into nitrites, which circulate in the body and are turned into *nitric oxide* (NO) as needed. Elevated NO levels during exercise provide a variety of benefits.

How nitric oxide (NO) is made



Reference: Lundberg et al. *Cardiovasc Res.* 2011.[297]

Nitrates are postulated to enhance exercise performance by improving exercise efficiency — more specifically, a reduced ATP and phosphocreatine cost of muscle force production and oxygen cost of aerobic exercise, thereby permitting more work to be performed per unit of time for the same energy cost.[298][299][300][301]

Improved exercise efficiency should manifest as the ability to sustain the same work rate for longer, and as it turns out, a robust body of evidence supports this theory. Nitrate supplementation has consistently demonstrated a small positive effect on time to exhaustion and may attenuate reductions in maximal strength or power during fatigue index tasks.[302][303] These ergogenic effects have been observed across environments (i.e., normoxic vs. hypoxic) and different supplementation protocols, but only in moderately trained and untrained men. Generally, nitrate supplementation does not delay fatigue in elite athletes (VO_2max > 64.9 mL/kg/min) and women (based on a small body of evidence) or during low-intensity prolonged exercise (>15 minutes).[302] Additionally, nitrates have a small-to-medium effect on muscle power[304] but have largely failed to affect time trial performance.[302][303]

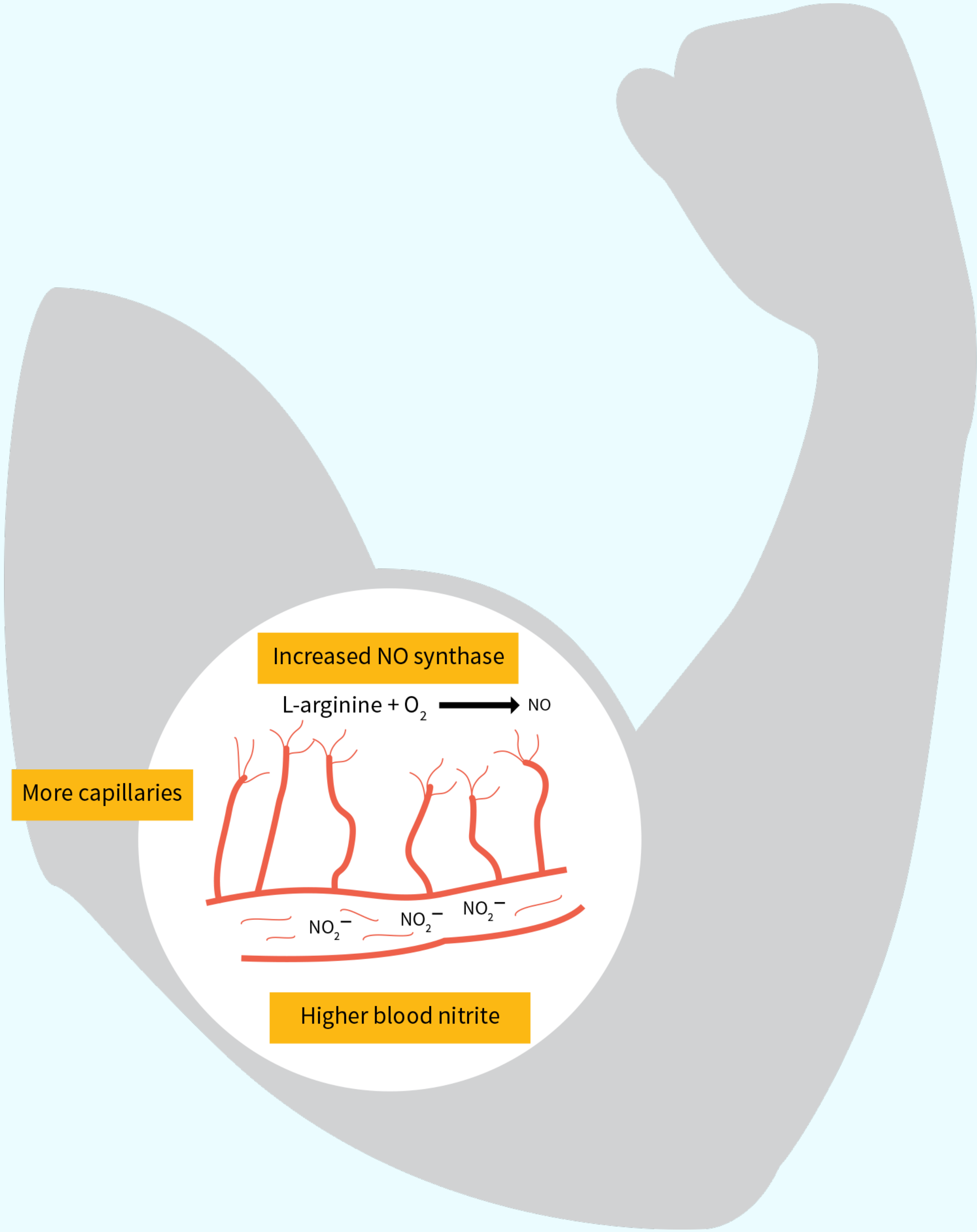
With regard to resistance exercise, nitrates have a larger effect on muscular endurance than muscular strength. A recent meta-analysis on the topic reported that, compared to placebo, nitrates may improve muscular strength by 4% and endurance by approximately 12% independent of training status, although it's debatable how well trained the participants characterized as "athletes" were.[305]

🔍 Digging Deeper: How training status interacts with nitrate's effects

In recent years, it has become increasingly apparent that highly trained athletes get little to no performance benefits from nitrate supplementation. More specifically, although moderately trained and untrained individuals experience a significant ergogenic effect, individuals with a VO_2max higher than 64.9 mL/kg/min do not.[302]

There are several reasons why this could be the case, with some shown in the figure below. One reason is that exercise improves the body's ability to make its own nitric oxide through higher plasma nitrite,[306] which is converted to nitric oxide in acidic and low-oxygen conditions, and increased nitric oxide synthase.[307] These two factors could make supplementing with nitrates less important. Athletic muscles also have more capillaries running through them so that they get relatively more blood,[308] and thus, there may not be much room for blood flow improvement via nitrate supplementation in well-trained individuals.

Why highly-trained people may not respond to nitrates



Reference: Jones. *Sports Med*. 2014.[309]

How to take *nitrates*

Nitrates do not exist as isolated dietary supplements, unfortunately, because of regulations against high quantities of sodium nitrate (a food additive frequently added to meat products). Instead, most studies use beetroot juice. Beetroot powder is also an option (one-eighth the weight of raw beetroot), but not in capsules because a person would need to take too many.

To achieve the maximal ergogenic effect, consume at least 5.1 mmol up to 25 mmol (378.2–1550 mg) of nitrate 2–3.5 hours before exercise.[302] Because the nitrate contents of beet-based sports supplements (juice, powder, concentrate) vary so greatly,[310] it's important to check the amount of nitrate that the product delivers per serving. Remember to follow these guidelines to find a quality supplement.

As it stands, there isn't strong evidence to suggest that chronic supplementation (15 days) is superior to acute (short-term) supplementation. However, the ergogenic potential of nitrate supplementation is largely dependent on the reduction of nitrate in saliva to nitrite by facultative anaerobic bacteria in the mouth, and the oral microbiome is exceptionally sensitive and modifiable. For example, antibacterial mouthwash disturbs the oral microbiome and blunts the increase in plasma nitrite concentrations following nitrate ingestion.[311] Evidence suggests that nitrate supplementation increases the abundance of nitrate-reducing bacteria, thereby leading to an enhanced ability to reduce ingested nitrate and subsequently greater plasma nitrite concentrations.[312][313] As such, it may be prudent to supplement with nitrate for several days before a performance test to maximize its effectiveness.

Nitrate-rich vegetables (mg per 100 gram)

NITRATE-RICH VEGETABLES	Nitrates (mg)	Total oxalate (mg)	Soluble oxalate (mg)	Vitamin K~1~ (μg)
Arugula/rocket	362.4	7.1	<0.5	108.6
Turnip greens	346.7	50	—	251
Dill	259	159	60	0
Collard greens	254.5	450	—	437.1
Spinach	248.5	656	542.6	482.9
Swiss chard	236.3	964	207.7	830
Turnips	217.4	210	—	0.1
Rhubarb	199.9	805	223	29.3
Beetroot	199.2	121	74.9	0.2
Celery	196.4	17.5	<0.5	29.3
Mustard greens	187.5	128.7	—	257.5
Radish	177.3	9.2	<0.5	1.3
Lettuce	168.9	13.6	<0.5	126.3
Watercress	164	10	<0.5	250
Bok choy	162	2	—	45.5
Kale	137.5	20	—	704.8
Parsley	130.47	136	76	1640

This table is composed of averages from multiple samples. Farming techniques, transport, storage conditions, and cooking methods can all greatly affect the actual nitrate and oxalate content of food.

References: Jackson et al. *Nutr Res Rev*. 2017.[314] ● Lidder and Webb. *Br J Clin Pharmacol*. 2013.[315] ● Griesenbeck et al. *Nutr J*. 2009.[316] ● Tamme et al. *Food Addit Contam*. 2006.[317] ● Siener et al. *Food Chem*. 2006. DOI:https://doi.org/10.1016/j.foodchem.2005.05.059 ● Hönow and Hesse. *Food Chem*. 2002. [318] ● Santamaria et al. *J. Sci. Food Agric*. 1999. [319] ● Dr. Duke's Phytochemical and Ethnobotanical databases ● FoodData Central

Vegetables sorted by nitrate content (mg per 100 grams)

NITRATE CONTENT	VEGETABLES
Very high (250+)	Arugula/rocket, collard greens, dill, turnip greens
High (100 to <250)	Beetroot, bok choy, celeriac, celery, kale, kohlrabi, lettuce, mustard greens, parsley, radish, rhubarb, spinach, swiss chard, turnip, watercress
Moderate (50 to <100)	Broccoli, cabbage, cauliflower, endive, savoy cabbage
Low (20 to <50)	Chicory, eggplant, fennel, green beans, green onion, leek, pumpkin/squash
Very low (<20)	Artichoke, asparagus, broad bean, brussels sprouts, carrot, cucumber, dry beans, garlic, lima beans, maize, mushroom, onion, peas, pepper, sweet potato, tomato, white potato

References: Jackson et al. *Nutr Res Rev.* 2017.[314] ● Hord et al. *Am J Clin Nutr.* 2009.[320] ● Jones. *Sports Med.* 2014.[309]

Warnings about *nitrates*

Nitrates are prevalent in many foods, and an intake above the acceptable daily intake is important to consider for safety measures. The acceptable daily intake set by the European Food Safety Authority of nitrates is 3.7 mg (or 0.06 mmol) per kilogram of bodyweight. [315] For example, a 50 kg person would have an acceptable daily intake of 185 mg of nitrates. However, this value was derived from animal studies in the 1960s that found that the highest tested dose had no adverse effects, so this is actually a lower bound for safe intake.

Although dosing can vary, nitrate toxicity may lead to an increased risk of methemoglobinemia, a disorder in which hemoglobin cannot transport oxygen.[321] However, this condition is rarely due to dietary nitrates; insead, it’s usually caused by drinking water contaminated with high levels of nitrates, and the disease is most often seen in infants and children.

Nitrates are reduced to nitrites, which eventually can form nitrosamines in the acidic environment of the stomach.[322] These nitrosamines have been studied and determined to have carcinogenic potential.[323] Nitrates have been particularly linked to an increased risk of thyroid cancers.[324] Therefore, it is important to consider the different dosages of nitrates available in different foods prior to consumption.

Nitrates tend to get most of the attention when it comes to the subject of processed red meat and colorectal cancer/other cancers, but vegetables with many higher nitrate levels aren't convincingly tied to carcinogenesis. Evidence suggests that the heme iron in meat acts as an important catalyst of nitrosamines formation when it reacts with nitrates and nitrites.[325] For this reason, it might be particularly harmful to consume a large amount of nitrates with red meat, though the presence of calcium salts, chlorophyll, vitamin C, and various polyphenols inhibit this reaction. On the one hand, the concurrent consumption of green vegetables and high calcium foods will likely mitigate this effect to some extent, but on the other hand, it is still unclear how much of these foods is needed to maximally inhibit the reaction, and it still may be prudent to treat processed meats as detrimental to gastrointestinal cancer risk regardless of precautions taken.

Beetroot juice is rich in inorganic nitrates and has been used as a supplement to reduce blood pressure in adults. However, the side effects of red urine and red stools can be seen with supplementation.[326]

Most vegetables that are rich in nitrates are also rich in oxalate, which can increase the risk of kidney stones. People who are already at an increased risk of forming kidney stones, as well as people with oxalosis or hyperoxaluria, should keep their oxalate intake to a minimum.

Other people need not ban all oxalate from their diet, but someone who consumes high amounts of nitrates (and the dosage range in this guide certainly qualifies) more than twice a week should favor oxalate-poor vegetables. If eating oxalate-rich foods on occasion, consider cooking them and/or pairing them with calcium-rich foods to reduce oxalate absorption.

Vegetables sorted by total oxalate content (mg per 100 grams)

OXALATE CONTENT	VEGETABLES
Very high (100+)	Beetroot, collard greens, dill, mustard greens, parsley, rhubarb, spinach, swiss chard, turnips
High (10 to <100)	Cauliflower, celery, kale, lettuce, turnip greens
Moderate (2 to <10)	Arugula/rocket, asparagus, carrot, radish, sweet potato, watercress
Low (<2)	Bok choy, cabbage, radicchio

Because glutathione may slow the rate of NO breakdown in the bloodstream, adding 200 mg of *N-acetylcysteine* (NAC) to nitrates might prove synergistic.

Sodium Bicarbonate

What makes *sodium bicarbonate* a secondary option

(This is the short version. For the long version, scroll down to the bottom of this entry and find the sidebar titled "A more detailed version") Sodium bicarbonate, aka NaHCO3 or baking soda, is a powerful alkaline pH buffer. In contrast to beta-alanine, which is also discussed in this supplement guide, sodium bicarbonate acts not within but outside of the cell. With 64% of the total buffering capacity, bicarbonate is the major acid buffer in our blood with health relevance way beyond the realms of optimal exercise performance.[327]

The bicarbonate buffer system

During periods of exercise, the body will produce greater amounts of hydrogen ions (H+), which is acidic and can decrease performance.

Sodium bicarbonate can buffer these acids by binding with them, which begins a process through which acidity can be decreased.

This acid buffering can prolong energy metabolism in the muscle cells during exercise, which can translate into a more sustained power output.

When consumed in high quantities of 200–600 mg per kg of body weight, bicarbonate can transiently increase an athlete's blood pH levels to supraphysiological levels. If the timing is right, these peak pH levels will occur slightly before an intense workout or competition and effectively buffer the hydrogen ions (H+) that are released during muscular contraction. Most of the research on sodium bicarbonate has been conducted in sports with a significant anaerobic contribution to energy metabolism. For athletes who compete in these sports, the previously described progressive decline in blood pH is regarded as a major obstacle to optimal performance. Classic examples are 800-meter runs, sprinting, high-intensity track or road cycling, boxing, wrestling, weightlifting, gymnastics, tennis, and team sports like basketball, lawn or ice hockey, lacrosse, football, or even soccer, where the H+ accumulation during the many intermittent sprints must not be overlooked as a contributor to the players' cumulative performance decline.

A recent meta-analysis pooled data from 10 pertinent studies with a total of 102 participants to assess the effects of sodium bicarbonate supplements on peak and mean power in Wingate or comparable high-intensity exercise tests.[328] The author's analysis of the data indicated that the benefits of sodium bicarbonate supplementation on mean power progressively increased from negligible effect sizes (standardized mean difference SMD, an effect size measure, of 0.09) on the second of several repeated tests, to potentially match-winning or race-winning medium-sized effects (SMD of 0.62) on the fourth of a set of repeated tests. Often, significant effects were only observed on the last of up to 4 high-intensity exercise tests. Mean power and peak power increases of 15% and 8%, respectively, have been reported on repeated bouts of high- intensity exercise.[329] These improvements also translate from the track, field, and even basketball court, where bicarbonate supplementation has been shown to significantly increase female basketball players' sprint performance in the final quarters of a 60-minute simulated basketball game.[330]

Although sodium bicarbonate's benefits on repeated sprint performance or similar glycolytic activities have a lot of scientific backup, its effects on muscle strength and endurance are less well established. In the latest available meta-analysis of 20 randomized controlled trials that looked at strength and endurance outcomes,[331] the authors confirmed beneficial effects on muscular endurance, albeit with an overall small effect size (SMD = 0.37) and absolute improvements that spanned a huge range from impressive (100% increases in time to fatigue in an isometric knee extension exercise test; 95 seconds vs. 40 seconds for placebo)[332] to statistically nonsignificant and practically irrelevant effects on calf muscle endurance.[333] Systematic differences between small (SMD = 0.31) and large muscle groups (SMD = 0.40) — or an effect of recovery status (rested vs. fatigued), supplement timing, and the bicarbonate concentration that the participants achieved immediately before the testing sessions — could not be detected in the meta-analysis.

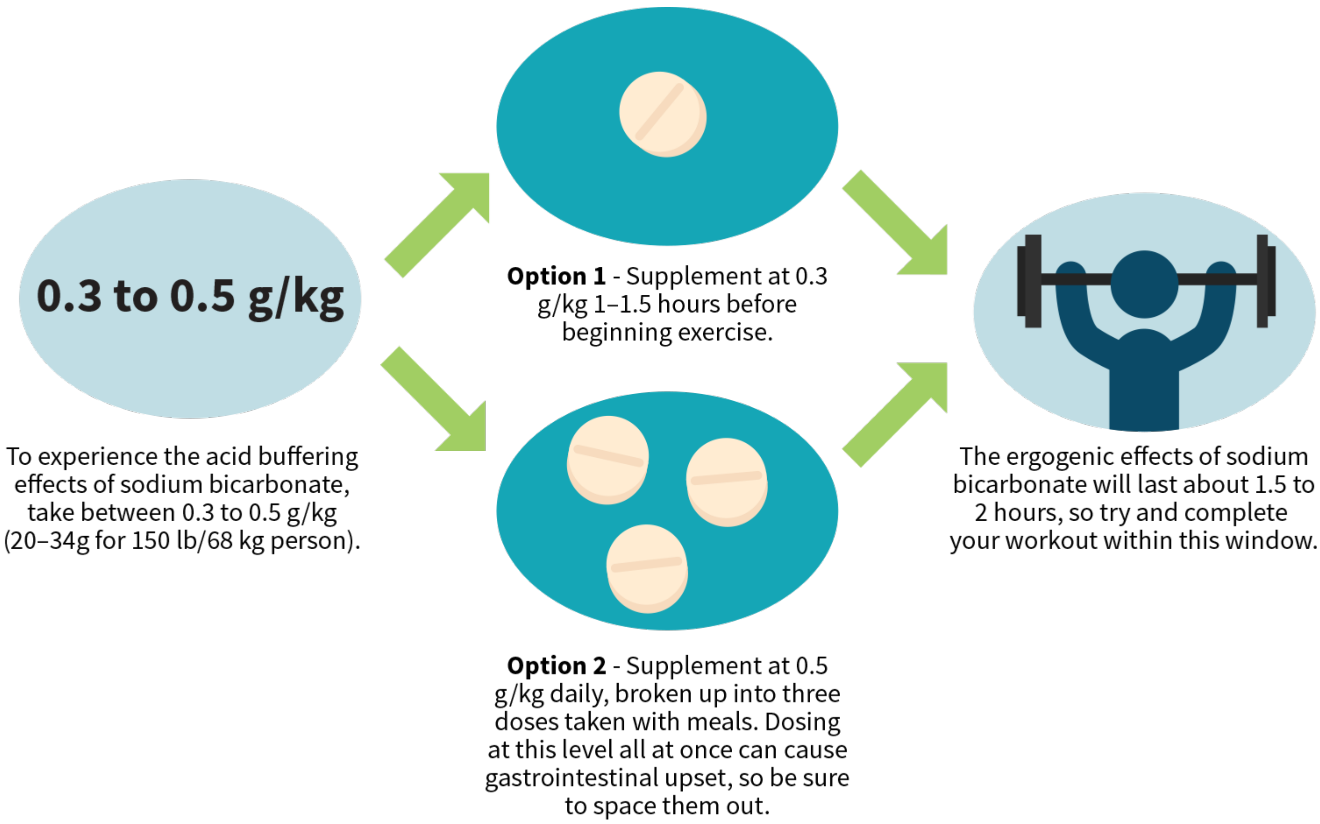
Unlike its previously discussed immediate effects on exercise performance, there's no research that properly investigates the potential long-term benefits (and risks) of chronic sodium bicarbonate supplementation. Based on the observation that resistance training volume is the major predictor of muscular hypertrophy,[334] being able to train at higher volumes for weeks and months should translate into greater gains in muscle size. However, until we have clinical studies lasting at least 6 to 8 weeks, the promise of accelerated muscle hypertrophy with chronic sodium bicarbonate supplementation is nothing but a viable research hypothesis.

Warnings about *sodium bicarbonate*

Gastrointestinal upset and diarrhea are the adverse events found with oral supplementation[331] and can sometimes limit the use of sodium bicarbonate. Individuals who experience GI upset with higher doses require coingestion of sodium bicarbonate with food or fluid to reduce such symptoms. Keep in mind that one dose can be 200% or more of the daily recommended sodium intake.

For doses of 0.3 grams per kilogram of body weight (g/kg), dividing the dose into 2 or 3 doses throughout the day and/or taking it with meals can ameliorate the nasty GI effects of acute high doses of sodium bicarbonate, though it ultimately depends on the individual's tolerance.[335] Alternatively, 0.2 g/kg might be a the sweet spot to avoid GI-related adverse effects and still experience some ergogenic benefits.

Possible sodium bicarbonate dosing strategies



Finally, it seems imperative to address an often-voiced concern about sodium bicarbonate supplementation: the significant contribution of sodium bicarbonate supplements to their users' 24-hour sodium consumption. An average dose of 25 grams of sodium bicarbonate contains 6.83 grams of sodium (27.3% of the total weight). This is significantly more than the WHO recommendation of 2 grams of sodium per day or less,[336] which is the equivalent of 5 grams of table salt (NaCl). Unlike table salt, sodium bicarbonate has been found to have no immediate effect on blood pressure in humans.[337] Potential adverse effects on blood pressure are thus unlikely, but neither prohypertensive effects nor critical mineral imbalances can be fully excluded in the absence of long-term studies investigating the effects of chronic high-dose sodium bicarbonate supplementation.

How to take sodium bicarbonate

The recommended dosages of sodium bicarbonate range from 200–300 mg per kg of body weight (mg/kg) to 500 mg/kg. There's insufficient evidence to support the notion that further dose escalation will provide additional benefits. Moreover, ample experimental evidence shows that even the lowest effective dose of 200–300 mg/kg of sodium bicarbonate can be hard to stomach for many people.

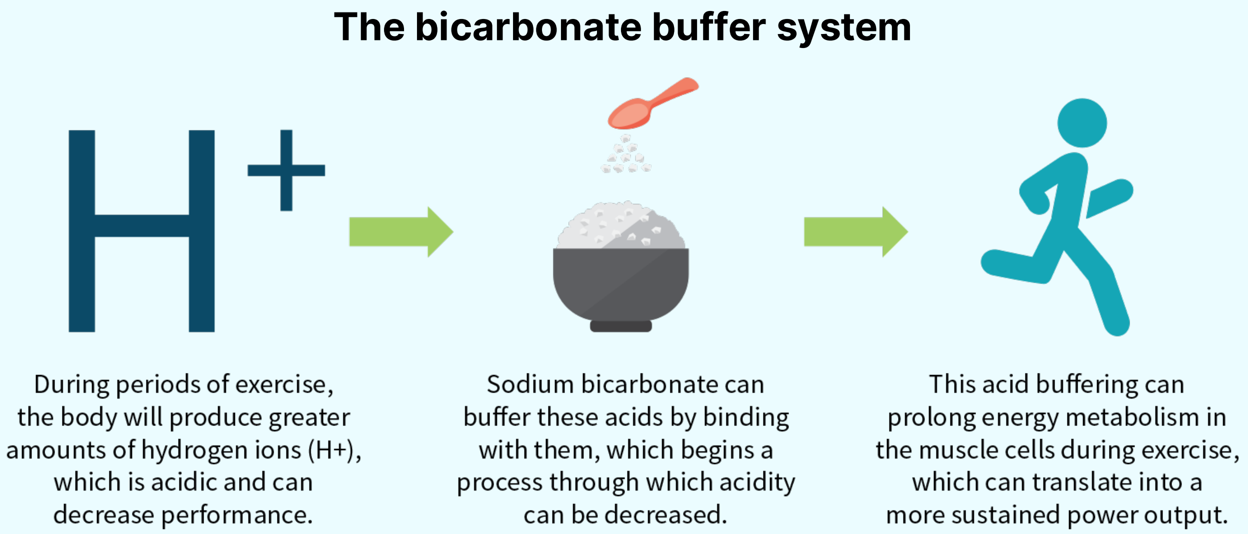
The exact time that it takes for blood bicarbonate levels to peak after the ingestion of sodium bicarbonate varies significantly between individuals. Studies suggest that most people will achieve maximum alkalosis (highest blood pH) 60–90 minutes after the ingestion of sodium bicarbonate in the form of a liquid solution or capsules. In this context, it may be worth mentioning that some people suggest shortening the timespan between supplementation and the onset of exercise to 45–60 minutes for longer bouts of anaerobic exercise (e.g., a road cycling event). However logical that may sound, convincing experimental data to support the superior efficacy of this practice does not exist.

To mitigate gastrointestinal side effects, researchers have begun to put the bicarbonate powder into gelatin capsules instead of dissolving it in water, as was done in earlier studies.[338] Another probably even more efficient strategy for minimizing adverse events is referred to as "serial loading" , which splits the total amount of sodium bicarbonate into several smaller servings that are consumed over hours or even days before an exercise test or competition, with or without meals.[339][340] All of these strategies seem to reduce the risk of diarrhea and other gastrointestinal side effects. Future head-to-head comparisons of selected administration patterns are necessary to determine which of them provides the greatest ergogenic effect and the lowest incidence of undesirable side effects.

As a supplement, any form of pure, food-grade sodium bicarbonate or baking soda can be used. Baking powder, on the other hand, contains comparatively small amounts of sodium bicarbonate and other ingredients and hence cannot be used as a replacement for baking soda.

Digging Deeper: A more detailed version

Sodium bicarbonate, NaHCO3, or baking soda is a powerful alkaline pH buffer. In contrast to beta-alanine, which is also discussed in this guide, sodium bicarbonate acts not within but outside of the cell. Bicarbonate is the major acid buffer in our blood and accounts for 64% of buffering capacity. It is one of the few dietary supplements that made the International Olympic Committee's (IOC) list of dietary supplements with "good evidence of benefits".[341][327]



When consumed in high quantities of 200–600 mg per kg of body weight, sodium bicarbonate can transiently increase an athlete's blood pH levels to supraphysiological levels. If the timing is right, these peak pH levels will occur slightly before an intense workout or competition. At this time, they will serve as an extended extracellular buffer for the proacidic protons (hydrogen or H+ ions) that are released during muscular contraction. Bicarbonate supplements can thus delay the decline in blood pH to a level that will negatively affect exercise performance and help athletes maintain optimal muscle function for longer time spans.

Most of the research on sodium bicarbonate has been conducted in sports with a significant anaerobic contribution to energy metabolism. For athletes who compete in these sports, the previously described progressive decline in blood pH is regarded as a major obstacle to optimal performance. Classic examples are 800-meter runs, sprinting, high-intensity track or road cycling, boxing, wrestling, weightlifting, gymnastics, tennis, and team sports like basketball, lawn or ice hockey, lacrosse, football, or even soccer, where the H+ accumulation during the many intermittent sprints must not be overlooked as a contributor to the players' cumulative performance decline.

To assess the efficacy of sodium bicarbonate as a buffer, researchers have used various testing regimens. In exercise research, the Wingate test and comparable “all-out” interval tests are probably the most commonly used surrogates to model the metabolic demands of the previously mentioned sports.[342] A meta-analysis pooled data from 10 pertinent studies with a total of 102 participants to assess the effects of sodium bicarbonate supplements on peak and mean power in Wingate or comparable high-intensity exercise tests.[328] The author's analysis of the data indicated that the benefits of sodium bicarbonate supplementation on mean power progressively increased from negligible effect sizes (SMD = 0.09) on the second of several repeated tests, to potentially match-winning or race-winning medium-sized effects (SMD = 0.62) on the fourth of several high-intensity exercise tests. To give an idea of what that means, let's look at a 2007 study by Zinner et al.,[329] in which sodium bicarbonate supplementation improved the participants' mean power in the fourth bout of a high-intensity exercise test by 15% and their peak power by approximately 8%.

If we assume that the findings from the short high-intensity exercise tests translate to actual sports performance (team sports, for example), this means that the potential benefits of bicarbonate supplements should increase with each intermittent sprint that a basketball or soccer player performs. And indeed, a 2014 paper from the Department of Kinesiology at Westmont College[330] reported a small but significant 3% improvement in basketball players' sprinting performance in the final quarter of a validated 60-minute basketball simulation test. In contrast, results from studies that used tests with lower amounts of accumulated anaerobic exercise volume were inconsistent, with no significant difference between studies using tests with total durations of less vs. more than 4 minutes.[343] In view of the low number of studies with longer total exercise durations (15 minutes) and thus more time spent exercising at pH-lowering anaerobic intensities, the notion that "the higher the volume, the greater the benefit of bicarbonate supplements" remains to be tested with proper scientific scrutiny.

Further research is also necessary to make definite statements about sodium bicarbonate's effect on muscle strength and endurance. In the latest available meta-analysis by Grgic et al., the authors' analysis of data from 20 studies exploring the effects of sodium bicarbonate on muscular endurance and/or muscular strength yielded divergent results.[331] Although the 13 datasets related to the effects of sodium bicarbonate supplementation on muscular endurance confirmed the existence of measurable, statistically significant benefits, the aggregated data from the 11 datasets related to muscle strength didn't confirm an ergogenic effect of bicarbonate supplementation.

With an effect size of SMD = 0.37, the overall effect on muscle endurance was “small”, and in the individual trials, the absolute and relative benefits varied largely, ranging from more than 100% increases in time to fatigue in an isometric knee extension exercise test (95 seconds vs. 40 seconds for placebo) to a negligible <1% (596 seconds vs. 592 seconds for placebo) effect on calf muscle endurance.[333][332] Although this example may suggest that larger muscle groups could benefit more, the previously cited meta-analysis refutes the existence of significant systematic differences between small (SMD = 0.31) and large muscle groups (SMD = 0.40). Recovery status (rested vs. fatigued), supplement timing, and the bicarbonate concentration that the subjects achieved immediately before the testing sessions didn't affect the effect sizes either.

Why is sodium bicarbonate not a “primary option” if it's endorsed by the IOC?

The effects of sodium bicarbonate are admittedly small in many sports. However, for elite athletes, those few seconds of faster running or longer time to fatigue can make the difference between bronze and gold medals. And for recreational athletes, training at slightly higher volumes and/or sustaining even slightly higher exercise intensities could make an important difference over time! Unfortunately, the lack of data on the long-term effects and benefits of chronic sodium bicarbonate supplementation is the second reason for ranking this supplement from the IOC's short list of dietary supplements with “good evidence of benefits” as a “secondary option”, along with reason number 3, the notoriously high risk of gastrointestinal side effects.[341]

A relevant reduction of gastrointestinal side effects like general gastric discomfort, bloating, and diarrhea seems to be achievable simply by using sodium bicarbonate in gelatin capsules instead of dissolving the powder in plain water or other liquids.[338] Another probably even more efficient strategy for minimizing adverse events is referred to as “serial loading” in which the total amount of sodium bicarbonate is split into 2 or 3 smaller servings that are consumed over hours or even days before an exercise test or competition. In a follow-up to the previously discussed basketball study,[340] for example, the participants received 3 doses of 33 mg/kg of sodium bicarbonate with breakfast, lunch, and dinner for 3 consecutive days (total dose per day of 400 mg/kg; additional doses were taken on the day of the test) before completing a simulated basketball match. With this study, the scientists were able to show that “serial loading” eliminates the risk of gastrointestinal side effects (none were reported by the participants) while still providing similar ergogenic effects as the bolus ingestion of the same amount of sodium bicarbonate in the study before. Whether the 3x3+1 day protocol in this study is the “optimal” way to use sodium bicarbonate is yet unknown, and in defense of classic bolus dosing, it should not go unsaid that 13 out of 20 studies included in the muscle strength and endurance meta-analysis by Grgic et al. [331] reported no adverse events, at all. The other 7 studies that made it into the meta-analysis reported mostly mild side effects.

In a guide intended to provide practical and relevant supplement advice to people who strive not only for transient improvements in exercise performance but also for increased muscle and strength gains over time, the lack of studies investigating the effects of chronic ingestion of sodium bicarbonate on these desirable outcomes may be even more relevant for our decision to rank sodium bicarbonate as a “secondary option”. In view of the proposed link between skeletal muscle hypertrophy and resistance training volume,[334] one could certainly argue that the increased volume load per session that a bodybuilder could (supposedly) sustain by using sodium bicarbonate supplements with every workout will contribute to increased gains in muscle size over time. However, studies that confirm this reasonable hypothesis have not yet been conducted yet.

Currently, sodium bicarbonate can be recommended for athletes who are competing in sports in which the practitioners accumulate significant volumes of anaerobic workload — anything from high-intensity road cycling to individual sports like tennis and team sports like basketball to boxing, martial arts and high-volume resistance training. Whether the benefits of supplementation will extend beyond immediate performance increases and augment or accelerate the adaptive response to exercise when bicarbonate is taken on every training day remains to be investigated in future studies.

Promising Supplements

Ashwagandha

What makes *ashwagandha* a promising option

Ashwagandha (*Withania somnifera*) is an Ayurvedic herb that belongs to the Solanaceae family. It's been used for millennia in traditional Indian medicine as a Rasayana (i.e., tonic) to increase energy, improve longevity, and prevent and treat a number of diseases.[344]

Ashwagandha is an adaptogen, and like rhodiola, is a potent anti-stress agent. Interest in ashwagandha also stems from its purported ability to reduce cortisol, boost testosterone,[345][346] and mitigate oxidative stress,[347][348] all of which may have a positive influence on exercise performance and recovery.

Concerning endurance exercise performance specifically, ashwagandha may also increase hemoglobin concentrations, leading to an improved capacity to transport oxygen to exercising muscles, and subsequently, an enhanced aerobic capacity.[348][349]

That said, the majority of studies have investigated the effect of ashwagandha on aerobic adaptations. One meta-analysis, which included 4 randomized controlled trials, reported a 3.0 mL/kg/min increase in VO_2max (95% CI: 0.18, 5.82), with greater improvements observed in athletes (i.e., elite cyclists and hockey players).[350] These data, plus 1 study, were also analyzed with different statistical methods in a more recent meta-analysis, and it reported a large effect on VO_2max.[351] In agreement, a newly published study conducted in healthy adults reported an increase in VO_2max from 40.22 to 46.82 mL/kg/min after 8 weeks of ashwagandha supplementation.[352] Ashwagandha has also been shown to improve 7.5 km time trial performance.[353]

Much less research has assessed the effect of ashwagandha on resistance exercise performance. Even so, the available evidence is compelling. Ashwagandha has been shown to significantly increase bench press *1-repetition maximum* (1RM) in 2 studies,[346][353] as well as 1RM leg extension and 1RM squat.[346][353] Notably, both trials also reported improvements in markers of muscle damage, including creatine kinase and perceived soreness.[346][353] However, it's worth mentioning that these studies were conducted in healthy untrained men, so it's unclear whether these effects would pertain to athletes and women.

The current body of evidence demonstrates a consistent positive effect of ashwagandha on VO_2max and muscular strength, but due to the magnitude of effect and the limited number of studies available (especially for resistance training), it's rated as a promising option.

Warnings about ashwagandha

Ashwagandha continues to show promising safety data. Mild side effects reported with the use of ashwagandha include drowsiness, upper *gastrointestinal* (GI) discomfort, dizziness, and loose stools.[354]

Because ashwagandha may increase testosterone levels,[355] people with hormone-sensitive prostate cancer should avoid it.

The herb's hormonal effects could raise concern about its use during pregnancy, but the research is mostly old, sparse, and unclear.[356] Given the lack of data, it's safest to avoid ashwagandha while pregnant or breastfeeding.

There have also been case reports illustrating ashwagandha's potential link to liver injury.[357] Ashwagandha should not be taken with benzodiazepines, anticonvulsants, or barbiturates, because all of these drugs have sedative properties, as does ashwagandha, and combining them can increase these effects.[354]

Herbs can be contaminated with arsenic, cadmium, and lead, and ashwagandha is no different.[358] It is vitally important to purchase supplements from a company that subjects their products to credible third-party testing for purity.

How to take *ashwagandha*

In the research, the most frequently used products are KSM-66 and Sensoril, and the most common dosing protocols are 300 or 500 mg taken twice per day (600–1000 mg total), with one dose ingested in the morning and the other before bed.

Tart Cherry

What makes *tart cherry* a promising option

Tart cherries (TC) contain high amounts of polyphenols (anthocyanins, in particular) that possess antioxidant and anti-inflammatory properties. As a consequence, TC may support muscle gain and exercise performance by optimizing recovery, so that the athlete can return to hard training faster and thus accumulate more volume.

Indeed, TC supplementation appears to reduce muscle soreness and inflammation (e.g., interleukin 6, C-reactive protein) and lead to faster recovery of muscle strength and power following different forms of exercise.[359] Notably, TC supplementation has been reported to have a medium effect on soreness following resistance exercise, a large effect on the recovery of jump height, and a large effect on C-reactive protein following endurance exercise.[359]

Additionally, TC supplementation has been shown to reduce some markers of oxidative stress in some instances,[360][361][362] but not others.[363][364][365] This body of evidence is severely limited by heterogeneity in the markers used to assess oxidative stress, in addition to the variety of exercise protocols used, which prevents the ability to draw meaningful conclusions.

While plausible, it's currently unclear whether the effects of TC supplementation augment muscle gain and exercise performance in the long term. Even so, it's clear that supplementation can improve recovery in the short term. Therefore, in scenarios in which an athlete needs to return to competition form as quickly as possible (e.g., two events in the same day) or is performing training that they are unaccustomed to (which generates a high degree of muscle damage), TC supplementation may be of benefit.

Warnings about tart cherry

One study found that roughly 6% of people who consumed tart cherry juice experienced diarrhea.[366]

How to take *tart cherry*

Take 8 to 12 ounces of TC juice (nonconcentrated) twice per day (16–24 ounces total) or 1 ounce of TC juice *concentrate* twice per day (2 ounces total). For the purpose of promoting maximal recovery after a competition, follow the aforementioned protocol at least 4 days before, the day of (with a dose taken 2 hours before the event), and 2 days following the competition.

Taurine

What makes *taurine* a promising option

Taurine is a sulfur-containing amino acid that received its name because it was first isolated from the bile of the ox and is otherwise known as *Bos taurus*. It accounts for 50%–60% of the free amino acid pool and is especially abundant in skeletal muscle.[367] More specifically, taurine concentrations are reported to be about 4 times higher in type I compared to type II muscle fibers.[368] Given taurine's ubiquitous presence in the body, its role in diverse metabolic and physiological processes is unsurprising. It's hypothesized that many of these functions could augment exercise performance, which has led to taurine becoming a staple ingredient in many popular energy drinks.

Taurine is thought to increase mitochondrial buffering capacity,[369] and some evidence suggests that it reduces lactate accumulation during exercise.[370] Correspondingly, impaired exercise capacity has been observed in rodents lacking the taurine transporter gene.[371] Taurine supplementation may also delay fatigue during exercise by increasing lipolysis (thus preserving muscle glycogen) and reducing oxidative stress.[370][372][373] Lastly, taurine assists sarcoplasmic reticulum calcium accumulation and release,[374][375] and as such, supplementation may improve force and power production by modulating skeletal muscle contractile function.

As a product of its prevalence in oxidative muscle fibers, most trials have assessed the effect of taurine on time to exhaustion, with inconsistent results. In the studies conducted in young, physically active individuals, about half have reported a positive effect,[376][377][378][379][380] whereas others found no difference in performance compared to placebo.[381][382][383][384] A meta-analysis published in 2018 reported that taurine had a small positive effect on time to exhaustion, although 2 of the included studies with relatively large effects were conducted in participants who were older adults with heart failure.[385]

Similarly, taurine's effect on time trial performance is unclear. Three trials administered an acute dose of taurine (1–1.66 grams) within 1–2 hours of exercise. One trial found a 1.7% improvement in performance,[386], and 2 others found no effect of taurine supplementation.[387][372] Notably, 1 of these studies featured 90 minutes of cycling at 65% VO_2max before the time trial, which likely influenced the results.[372]

With regard to anaerobic measures of performance, the effect of taurine on muscular power has been investigated in a few studies. Supplementing with 50 mg/kg of taurine at 1–1.5 hours before cycling sprints was found to improve mean and peak power.[388][378] However, no effect on power was observed when measured by vertical jump.[381] In one particularly intriguing trial that grouped participants by habitual caffeine consumption, taurine *reduced* power output during isokinetic and isometric knee extension exercise in noncaffeine consumers. In contrast, in caffeine consumers who were deprived of caffeine for 24 hours, taurine increased power during isokinetic knee extensions but did not affect performance during isometric knee extensions.[389]

The data concerning taurine's effects on recovery are mixed. Of the 3 studies that assessed the influence of taurine supplementation on *delayed onset muscle soreness* (DOMS) following eccentric exercise,[390][391][392] 2 reported a positive effect.[390][392] The ability of taurine to improve recovery may be explained by its ability to attenuate exercise-induced oxidative stress.[393][390][384]

Also, taurine supplementation was shown to result in faster recovery of concentric and isometric muscle strength in one study,[390] whereas another showed no effect on these parameters, but it did report a faster recovery of eccentric muscle strength at 48 hours.[394] These differences may be related to the dosing protocol. In the former study, taurine was supplemented for 14 days before and 7 days after eccentric exercise. In the latter study, taurine was only supplemented for 3 days after eccentric exercise. In conflict with the aforementioned findings, taurine does not appear to affect biochemical markers of muscle damage (e.g., creatine kinase).[391][392][394][382]

Overall, taurine has the potential to improve a variety of exercise performance measures. As it stands, taurine may prolong time to exhaustion, but it doesn't seem to improve time trial performance. Additionally, taurine supplementation could expedite recovery from exercise. Further research is needed to draw strong conclusions on the efficacy of taurine to improve exercise performance, but the available evidence suggests taurine is a promising option.

Warnings about taurine

Trials with taurine have found no convincing evidence of adverse events greater than those experienced with placebo. Adverse events associated with taurine, such as abnormal heartbeat and high blood pressure, are more likely due to other ingredients in energy drinks, such as high doses of caffeine.[395]

Taurine is generally well tolerated within the recommended dose range of up to 3 grams.[396] More research needs to be done to determine the maximum safe dose.[397]

Note that a lot of energy drinks contain approximately 750 mg of taurine per serving, so people who consume energy drinks should be sure to take this source into account.[397]

Taurine can reduce blood pressure, and so it's possible that it could lead to hypotension when combined with blood pressure medication. However, this is a speculative and not well-documented phenomenon.

How to take *taurine*

Taurine is effective in doses of 1–3 grams per day, and many studies have safely administered doses as high as 6 grams per day.[398] Plasma concentrations of taurine peak anywhere from 1 to 2.5 hours after ingestion (1.5 hours on average), with a faster time to peak when ingested on an empty stomach.[399] Therefore, taurine should be taken about 1.5 hours before exercise.

To improve performance, acute and chronic taurine supplementation appear to be equally effective. In terms of recovery outcomes, the available studies have generally had participants supplement with taurine multiple days before and after exercise. Furthermore, relatively larger doses have been used (approximately 6 g/day). It remains unclear whether taurine's effects differ in untrained vs. trained participants and whether its effects differ in women because very little research has been conducted in this population.

Unproven Supplements

Alpha-GPC

What makes *Alpha-GPC* an unproven option

Alpha-glycerylphosphorylcholine (Alpha-GPC) is a choline molecule bound to a glycerol molecule via a phosphate group. Once ingested, it is rapidly absorbed by the brain and has been shown to significantly increase plasma choline concentrations.[400] Interest in alpha-GPC as a supplement for muscle gain and exercise performance stems from it being a precursor to acetylcholine, a neurotransmitter that is responsible for the action potential that stimulates skeletal muscle to contract.[401]

Alpha-GPC supplementation has been shown to augment the synthesis and release of acetylcholine in rats,[402] and it's hypothesized that increased levels of acetylcholine could lead to a stronger signal for muscle contraction and thus enhance force production.

However, the small body of evidence available has shown meager results. Although alpha-GPC supplementation has been shown to improve vertical jump power,[403][404] only 1 of 2 studies supports its ability to improve isometric mid-thigh pull force,[405][403] and it has failed to increase upper body isometric force production.[405][403] One study suggests that alpha-GPC supplementation could increase bench press peak force, but it was a poster abstract that also reported no effect on bench press peak power or rate of force development, so the results should be interpreted with caution.[406]

Betaine

What makes *betaine* an unproven option

Betaine, also known as trimethylglycine, is the amino acid glycine with 3 methyl groups attached. It was first discovered in the juice of sugar beets in the 19th century and is a significant component of many other foods, including wheat, shellfish, and spinach.[407] Its main physiological roles are acting as a methyl donor for the transmethylation of homocysteine to methionine and as an osmolyte to protect cells against dehydration.[408]

Supplemental betaine has been shown to increase lean mass and decrease fat mass in animals, which has prompted interest in its use as a supplement for athletes.[409][410]

A couple of studies suggest that betaine may improve body composition in humans when combined with a training program,[411][412] but conflicting evidence is also available.[413][414] The same can be said for its effect on muscular endurance.[415][416][417]

In contrast, the totality of evidence suggests that betaine supplementation has no effect on measures of strength and power.[411][412][416][418][415][419][413]

Capsaicin

What makes *capsaicin* an unproven option

Capsaicin (CAP) is a natural substance found primarily in chili peppers and is responsible for the spicy taste. It is known to modulate the *transient receptor potential vanilloid-1* (TRPV1) channels in the mouth, stomach, and small intestine, which activates the sympathetic nervous system.

Mechanistic data suggests CAP may increase calcium release in the sarcoplasmic reticulum,[420] increase fatty acid oxidation and decrease glycogen utilization,[421][422][423] increase pain tolerance,[424] and increase the release of acetylcholine. In combination, these effects could improve performance by reducing muscular fatigue and enhancing force production during exercise.

The human evidence from investigating the effect of CAP supplementation on endurance exercise performance is mixed. CAP supplementation has been shown to improve 400-meter,[425] 1500-meter,[426], and 3000-meter running time-trial performance in physically active adults,[425], but not 10-kilometer running time-trial performance in amateur athletes.[427]

In terms of time to exhaustion, CAP supplementation did not have an effect on continuous high-intensity exercise,[428] but it increased time to exhaustion during high-intensity *intermittent* exercise.[429]

Another trial worth mentioning found no effect of 7 days of CAP supplementation on repeated sprint performance.[430] However, contrary to other studies, cayenne pepper was used to provide a large dose of CAP (25.8 mg/day). This resulted in all but 1 participant experiencing significant gastrointestinal distress, which may have influenced the results.

In sum, the potential of CAP as an ergogenic aid for endurance exercise may depend on the duration of exercise (e.g., 1500 meter or 10 km), the type of exercise (i.e., intermittent or continuous), and possibly the training status of the athlete. Currently, no strong conclusions can be drawn on the efficacy of CAP in improving endurance exercise performance.

There are also a small number of studies that investigated the effect of CAP on measures of resistance exercise performance. In 2 studies, CAP supplementation increased total weight lifted in the squat while reducing the rating of perceived exertion.[431][432] Other evidence suggested that CAP may have a small positive effect on quadriceps muscle strength.[433] A recent 6-week randomized controlled trial in untrained participants reported greater increases in fat-free mass and bench press strength with daily CAP supplementation.[433]

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Glutamine

What makes *glutamine* an unproven option

Glutamine is an amino acid that plays an important role in muscle cells. In fact, *in vitro* studies (studies done in a test tube or a cell culture dish) require the addition of glutamine to keep cells alive. When glutamine is added to muscle cells *in vitro*, protein synthesis increases.

One of glutamine's roles in the body is to help get leucine inside the cells. It does so by entering a cell on its own and then leaving it using a transporter that simultaneously pulls in leucine. Basically, when the cell kicks out glutamine, it brings in leucine. This process is necessary for the stimulation of *mammalian target of rapamycin* (mTOR), one of the main anabolic pathways of protein synthesis.[434]

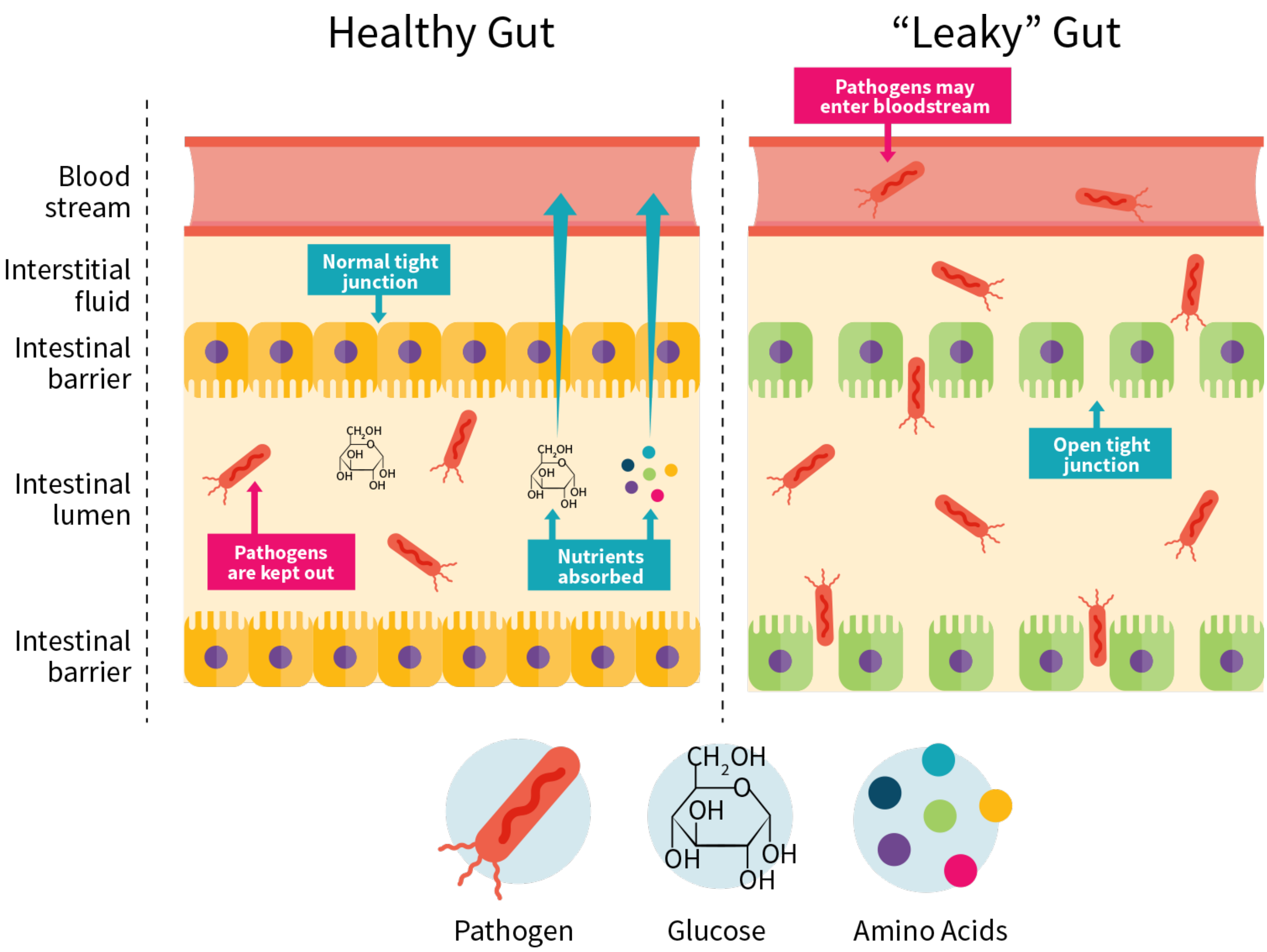
The prominent role played by glutamine in amino acid transport and protein synthesis brings up the question of whether glutamine supplementation can enhance muscle growth or exercise performance.

A few studies have investigated the effects of glutamine supplementation on body composition, and a meta-analysis of these studies found no benefit.[435] Even the study that used the highest dosage of 0.9 grams per kilogram of body weight per day (g/kg/day) in resistance-trained adults found no effect.[436] There may be a benefit to exercise recovery,[436] especially when glutamine is combined with leucine,[437] but more research is needed for confirmation.

Endurance athletes who train a lot may benefit in another way, though. Glutamine plays an important role in immune function (it is notably the primary fuel source of white blood cells).[438] After prolonged endurance exercise, plasma glutamine levels are reduced, which correlates with an increased risk of infection.[439] Glutamine supplementation may help prevent or lessen this increase.

Relatedly, prolonged endurance exercise is known to cause "leaky gut", a condition in which heat stress and reduced blood flow to the gastrointestinal tract cause intestinal cell damage.[440] This damage loosens tight junctions between cells, allowing for the absorption of things that are not supposed to pass through the intestinal barrier (e.g., proinflammatory endotoxins).

Healthy vs "leaky" gut



Glutamine supplementation reduces exercise-induced intestinal permeability and the resulting increase in serum endotoxin and inflammatory markers.[441][442] At least one study in participants with Crohn's disease (a type of inflammatory bowel disease) reported that glutamine and whey protein similarly reduce intestinal permeability and damage.[443] Note, however, that whey protein contains glutamic acid (aka glutamate), *not* glutamine, though your body can make the latter out of the former.

The data are promising, but more human clinical trials are needed to confirm this effect.

HMB

What makes *HMB* an unproven option

Beta-hydroxy-beta-methylbutyrate (HMB) is a metabolite of the amino acid leucine — a key initiator of muscle protein synthesis after feeding — which has sparked interest in HMB's potential as an ergogenic aid. In accordance with leucine's well-known function, research has demonstrated that HMB increases muscle protein synthesis.[444][445] It also uniquely decreases muscle protein breakdown,[444][445] which may be due to inhibition of the ubiquitin-proteasome proteolytic pathway, among other mechanisms.[446][447]

However, in contrast to these findings, HMB supplementation does not have a significant effect on muscle gain in untrained individuals or resistance-trained (>1 year of resistance training experience) and athletic populations.[448][449][450] Additionally, HMB has no effect on bench press strength or lower body strength in young, trained or untrained populations.[448][450]

Similarly, HMB supplementation has failed to boost muscle gain, muscle strength, and physical function in older adults (ages 50–80) when combined with exercise,[451][452] although it appears to have a positive effect on muscle mass in the absence of exercise in older adults.[452]

Where HMB may prove useful is in in conditions characterized by skeletal muscle weakness and a loss of muscle mass (e.g., cancer cachexia).[453] There is also reasonable evidence demonstrating that HMB reduces markers of muscle damage (i.e., creatine kinase, lactate dehydrogenase) after exercise when 3 grams per day are ingested for at least 6 weeks.[454] This effect is greater in untrained participants due to their greater levels of muscle damage than trained individuals following exercise.[449]

🔍 **Digging Deeper: HMB free acid vs. calcium HMB**

HMB supplements typically come in two forms: the calcium salt form, referred to as calcium HMB, and the HMB free acid form (HMB without the calcium salt attached).

Calcium HBM is the most commonly available (and studied) form. When timing HMB around a workout, it's important to know that calcium HMB is not absorbed as quickly or as well as HMB-FA.[455] It takes 1.5 to 2 or more hours before calcium HMB peaks in the bloodstream, compared to just 30 minutes with HMB-FA. The absorption of HMB-FA is also greater, resulting in almost twice the concentration in the bloodstream when comparing respective peaks. However, it is not yet known whether timing for either supplement form plays a critical role in its effect on exercise performance.

Maca

What makes *maca* an unproven option

Lepidium meyenii, also known as maca, is a plant in the *Brassicaceae* family. It has been cultivated and used by Andean people for over a thousand years in Peru as food and medicine. Maca was fed to Inca warriors for strength and resilience during battle, but it's been commonly used for its aphrodisiac properties.

Indeed, maca appears to improve sexual desire[456][457][458] and even some semen parameters (e.g., sperm count, sperm motility).[459][460] However, these effects are not due to modulations in hormones, and more specifically, maca does not increase testosterone. There is currently no clearly understood mechanism of action for these effects, which raises the following question: if maca doesn't boost testosterone, how might it benefit muscle gain and exercise performance?

Numerous bioactive compounds in maca (polysaccharides, in particular) have demonstrated the ability to enhance antioxidant enzyme activity and reduce fatigue.[461] In rodent studies, maca supplementation consistently decreases biochemical parameters related to fatigue (e.g., lactate dehydrogenase, blood urea nitrogen) and prolongs swimming time to exhaustion.[462][463][464][465] Additionally, it increases liver glycogen content, which is a very advantageous adaptation to bolster exercise capacity.[462][463][464]

Despite these impressive results in rodents, there is a lack of human trials investigating the effects of maca on exercise performance. In the sole study available, 14 days of maca supplementation improved 40-kilometer cycling time-trial performance in 8 trained male cyclists, but the improvement was not significantly different from placebo.[456] Due to the absence of human data to support the use of maca as an ergogenic aid, it is currently classified as an unproven option.

Rhodiola Rosea

What makes *Rhodiola rosea* an unproven option

Rhodiola rosea, also known as golden root, is a herb that grows in mountainous and arctic regions of Europe and Asia. It is classified as an adaptogen, a substance that increases resistance to a broad spectrum of stressors (e.g., physical, chemical, biological), thereby promoting adaptation and survival.[466] A sizable body of evidence supports the ability of rhodiola to significantly reduce the fatigue generated by stress and anxiety. The question is, does this anti-fatigue effect extend to exercise performance?

Preliminary evidence suggests there are multiple mechanisms by which rhodiola may increase exercise performance. Rhodiola has been shown to act as a *central nervous system* (CNS) stimulant in rats,[467] and other CNS stimulants such as caffeine are known to boost power output.[208] In another study, rhodiola prolonged swim time to exhaustion by 24.6% in mice, which appeared to be due to increased ATP content in mitochondria.[468] However, rhodiola has not been shown to enhance ATP turnover during or following exercise in humans.[469] It's also speculated that rhodiola could improve exercise performance by increasing endogenous opioid production, leading to decreased perception of effort at a given workload.[470][471][472]

Human trials investigating the effect of rhodiola supplementation on endurance exercise performance have typically used a cycle ergometer. In time-to-exhaustion tests, 4 weeks of daily rhodiola supplementation has failed to outperform placebo.[473][474][471] The same was found in a study that had participants perform a wrist flexion exercise to fatigue.[469] Interestingly, the sole positive result (i.e., rhodiola increased time-to-exhaustion) occurred with a single dose taken 1 hour before exercise.[471]

Similarly, rhodiola supplementation taken 1 hour before a 6-mile time trial slightly improved performance while decreasing the rating of perceived exertion,[475] but supplementing for 30 days before running a marathon had no effect.[476]

In terms of rhodiola's effect on measures of anaerobic performance, there is less data available, and each study assessed a different outcome. One study reported no effect on maximal isometric quadriceps strength,[471] while another reported an increase in bench press velocity.[477] Strikingly, rhodiola also decreased repetitions to failure across 3 sets of bench press in the latter.[477] Lastly, rhodiola was found to enhance mean power, mean peak power,and total work performed during repeated Wingate cycling tests.[478]

As it stands, rhodiola is not a convincing supplement for endurance or anaerobic athletes, and it appears that acute (1 hour before exercise) or short-term (≤3 days) supplementation is more efficacious than chronic supplementation.

Inadvisable Supplements

Arginine

What makes *arginine* an inadvisable option

Interest in the conditionally essential amino acid arginine (or L-arginine) stems from it being a precursor of *nitric oxide* (NO). It's postulated that arginine supplementation increases NO production and, subsequently, blood flow to active muscles. This in turn is expected to lead to higher nutrient and oxygen delivery during exercise, thus enhancing adaptations.

In opposition to this claim, a robust body of evidence indicates a limited systemic bioavailability of oral arginine for NO synthesis.[272] Arginine is largely absorbed by the intestines and liver and is mainly converted to ornithine and urea through first-pass metabolism.[479] It's been reported that 0.087% of 1.8 grams and 0.068% of 4.9 grams of arginine contribute to plasma NO.[480] Consequently, several studies have failed to show a significant effect of arginine supplementation on NO production in individuals without known health conditions.[481][482][483][484][485]

Arginine appears to be mainly degraded by the arginase enzyme and intestinal bacteria rather than the NO synthase enzyme, which effectively limits its accessibility for NO synthesis and shuttles it into other cellular pathways.[272] This fact makes arginine inferior to citrulline and nitrate as a NO booster.

The effect of arginine on exercise performance has been investigated in a multitude of contexts, with meager results. In terms of aerobic exercise, arginine has largely failed to prolong time to exhaustion,[486][487][296][488][489] but conflicting evidence is available in elite wrestlers[490] and untrained individuals.[491] Similarly, arginine has no effect on time trial performance at distances ranging from 5 km[492][493] to 16.1 km[494] and a full marathon.[495]

For anaerobic exercise, arginine supplementation does not improve peak power output during cycling,[483][496][296] peak torque during isokinetic elbow extensions,[497] or measures of strength and power in older women.[498][499] Two studies have examined the efficacy of L-arginine alpha-ketoglutarate to improve bench press 1-repetition maximum, and although an acute dose had no effect,[500] supplementing with 12 grams per day for 8 weeks led to superior strength increases compared to placebo.[488]

Similarly, arginine supplementation does not have any meaningful effect on total work completed across multiple sets of upper body and lower body resistance exercise[482][501][500][488] or repeated sprint performance.[483][496][502][503]. Lastly (and perhaps unsurprisingly), arginine does not improve performance during brief maximal efforts, regardless of whether it's a 200-meter swim,[504] 180-meter run,[492] or 60-second cycling trial.[296]

Choline

What makes *choline* an inadvisable option

Choline is an essential nutrient and has diverse functions related to cell membrane integrity, lipid transport, methyl-group metabolism, and brain development. It is also a precursor for acetylcholine — a neurotransmitter responsible for the action potential that stimulates skeletal muscle to contract — which has sparked interest in choline as an ergogenic aid.

Certain types of strenuous exercise can create a significant decrease in free (non-membrane-bound) plasma choline levels. For example, runners of the Boston Marathon showed a 40% drop in plasma choline levels.[505][506] An acute drop in choline during exercise is thought to inhibit optimal muscle performance by decreasing the amount of choline available for acetylcholine synthesis, thereby inhibiting excitation contraction coupling at the neuromuscular junction.[506] In support of this theory, weak evidence suggests that individuals whose choline levels dropped the least during a marathon also had the best finish time.[507] Similarly, it's believed that increased acetylcholine availability from choline supplementation could increase muscular contraction and delay muscular fatigue during exercise.

Of the available studies that have investigated the effect of choline supplementation before endurance exercise, all of them have failed to find an effect on time to exhaustion, rating of perceived exertion, and biochemical parameters, despite a significant increase in plasma choline concentrations from supplementation.[508][509][510]

However, each of these studies suffers from the same limitation: there was no significant change in plasma choline levels in the placebo group. As it stands, there is a single study abstract (the full paper was never published) that investigated the effect of choline supplementation during exercise that significantly reduced plasma choline levels. It claimed that ingesting 2.8 grams of choline citrate 1 hour prior to and at the 10-mile mark of a 20-mile run led to significantly faster finish times than placebo.

It may be the case that choline supplementation has a beneficial effect only in a very specific context and that it does not benefit long low-intensity exercise or brief high-intensity exercise because these activities do not deplete choline below baseline levels.[511] Nevertheless, until further research comes out to support this possibility, choline is classified as an inadvisable supplement

Fenugreek

What makes *fenugreek* an inadvisable option

Fenugreek (*Trigonella foenum-graecum*) is a popular herb that belongs to the *Fabaceae* family. It originates from India and Northern Africa and has a long history of folkloric uses, ranging from treating edema in the legs to stimulating lactation.[512]

Fenugreek is rich in steroidal saponins, including diosgenin, which serves as the starting material for many commercial steroids.[513] Interest in fenugreek as an ergogenic aid stems from its ability to increase testosterone,[514] which is purported to be mediated through inhibition of aromatase and 5-alpha reductase, thereby increasing total testosterone levels by blocking its conversion to estrogen and dihydrotestosterone.[515] Several studies have shown that the administration of testosterone derivatives increases muscle size and strength, including in younger men,[3] older men,[516] and those classified as hypogonadal.[517] Could fenugreek supplementation have similar effects?

The effects of fenugreek on exercise performance and muscle gain have been investigated solely in men and measures related to anaerobic performance. Fenugreek increased lean body mass in 2 studies,[518][519] but conflicting evidence is also available.[515] In another trial that combined fenugreek with creatine, lean body mass gains were superior to placebo but no different from creatine plus dextrose, indicating that the results were primarily due to creatine.[520]

Although fenugreek's potential to enhance body composition sparks interest, its effects on exercise performance have been disappointing. At large, fenugreek does not affect upper body or lower body muscular endurance.[520][521][518][515][519] It's also failed to increase bench press *1-repetition maximum* (1RM).[521][520][518][515][519]. Interestingly, fenugreek supplementation led to greater gains in leg press 1RM in 2 studies,[518][519] but 3 others did not find any difference compared to placebo.[521][520][515] Additionally, 3 studies measured mean and peak power using a Wingate test, and each found no effect on either outcome.[520][518][515]

Despite the pronounced effects of supraphysiological doses of exogenous testosterone on muscle strength and hypertrophy, elevations in the normal physiological range are unlikely to influence these outcomes.[522] Further evidence is needed to confirm the effects of fenugreek on body composition, especially in well-trained participants, but due to fenugreek's consistent inability to improve measures of anaerobic performance, it is currently classified as an inadvisable option.

Panax Ginseng

What makes *Panax ginseng* an inadvisable option

Panax ginseng is an adaptogenic herb that has been used for thousands of years to restore energy and enhance well-being in China.[523] Today, there is widespread interest in *Panax ginseng* due to its potential role in antioxidant activity, fatigue, diabetes management, immunomodulation, cardiovascular function, etc.[524][525][526] In fact, etymologically, the genus "Panax" means "panacea" or "all-healing."

Panax ginseng, which is grown in both China and Korea, is classified into two main types depending on how it is processed: white ginseng is harvested at 4–6 years old and is dried after peeling, whereas red ginseng is harvested at 6 years old and is *steamed*, then dried.[527] These differences influence the content of bioactive compounds, namely, ginsenosides (saponins), of which there are more than 30 different types, each with different pharmacological effects. Red ginseng contains the ginsenosides Rg3, Rg5, and Rk1, which are not found in white ginseng,[528] and this may at least partly explain its unique efficacy for treating erectile dysfunction.[529]

Akin to other adaptogens, interest in *Panax ginseng* mainly revolves around its antifatigue properties. Evidence in mice demonstrates that *Panax ginseng* prolongs endurance swimming time, decreases biomarkers of fatigue (e.g., ammonia, lactate), and increases antioxidant activity.[530] However, these results have not panned out in humans.

The effects of *Panax ginseng* on a variety of aerobic (i.e., VO_2max, heart rate, time-to-exhaustion) and anaerobic (i.e., peak power, mean power) measures have been investigated, and no significant effects have been reported.[531][532]

Regarding fatigue and recovery, the data are mixed on red ginseng's effect on antioxidant function (as measured by levels of superoxide dismutase and catalase), while the evidence leans towards red ginseng not affecting lactate levels.[531] In terms of subjective fatigue, a limited number of studies suggest that *Panax* *ginseng* can reduce fatigue when at least 1000 mg per day are taken for at least 6 weeks.[532]

With these findings in mind, it's worth mentioning that the vast majority of trials have been of low methodological quality, and most have not used products tested for purity with a standardized ginsenoside profile. Also, few trials have investigated the effects of *Panax ginseng* on anaerobic exercise performance and recovery.

A recent study, which used Korean ginseng with increased bioavailability (GINST15), reported a reduction in the rating of perceived exertion while performing a leg press workout that consisted of 5 sets of 12 repetitions at 70% of 1-repetition maximum.[533] A medium effect on muscle soreness at 24 hours postexercise was also observed, which is supported by a previous trial with GINST15 that found increased antioxidant activity following exercise and reduced creatine kinase levels at 24 hours postexercise.[534]

As it currently stands, *Panax ginseng* does not appear to have a worthwhile effect on exercise performance or recovery, but further high-quality trials are needed

Phosphatidic Acid

What makes *phosphatidic acid* an inadvisable option

Phosphatidic acid (PA) is a phospholipid consisting of a glycerol backbone with 2 fatty acid chains and a phosphate group. It is naturally found in the body's cell membranes, as well as in various foods (e.g., cabbage, tomatoes, cucumbers) in tiny amounts.[535]

Interest in PA emerged due to its role as a direct upstream regulator of *mammalian target of rapamycin* (mTOR), which is considered the master regulator of muscle protein synthesis and essentially mediates resistance training-induced muscle hypertrophy.[536][537]

Of the few studies that have investigated the effects of PA supplementation on muscle strength and hypertrophy, the results have been equivocal.[538][539][540] As it stands, only 1 study has reported a significant benefit of PA supplementation on muscle strength and hypertrophy.[541] In this trial, participants supplemented with 750 mg of soy-derived PA daily for 8 weeks.

Keep in mind that all muscle builders and exercise performance enhancers are overhyped to some extent. This is a lucrative market, so unsubstantiated claims are numerous. As a rule, avoid "proprietary blends" that can hide how much of each ingredient is actually delivered.

Tribulus Terrestris

What makes *Tribulus terrestris* an inadvisable option

Tribulus terrestris (TT) is a herb that belongs to the Zygophyllaceae family and has been traditionally used in Indian and Chinese medicine for many purposes, including as a diuretic and to treat eye problems and enhance libido. TT fruits generally contain polyphenolic compounds, alkaloids, and over 20 steroidal saponins — predominantly protodioscin, which is considered the main pharmacologically active steroidal saponin.[542] However, vast variation (i.e., different concentrations in compounds as well as the absence of some compounds) has been observed between samples, even ones collected from the same country.[543]

TT is marketed as a testosterone booster. Specifically, it's claimed to stimulate androgen receptors within the brain, which causes the posterior pituitary gland to secrete more luteinizing hormone, thus stimulating the testes to synthesize more testosterone.[544] Several rodent studies support that TT increases testosterone levels.[545] TT has also been reported to increase testosterone and dihydrotestosterone acutely in primates and with chronic supplementation in rabbits.[546] However, TT has largely failed to alter testosterone in humans, including healthy young and older men. [547][548][549][550][551] Regardless, what are the effects of TT on muscle gain and exercise performance?

In adolescents and young men (i.e., ages 16–22), TT has not been shown to have an effect on body composition,[552][548][549] strength,[548] or muscular endurance,[552] although it may slightly improve mean power as measured by the Wingate test.[549][553]

Notably, the effects of TT have only been investigated in well-trained participants, including recreational bodybuilders with an average body fat percentage of 12%, professional rugby players, and national second-level boxers. This is both a strength and a limitation of the available evidence. Concerning the latter, one could speculate that if TT does have a small effect on body composition, the interventions may have been too short (5–8 weeks) for measurable changes to manifest because these individuals were already lean and relatively muscular.

The current evidence does not support the utility of TT supplementation to augment muscle gain and exercise performance. However, its effects in untrained individuals and women are unclear, and further long-term studies are needed to confidently discern its effects.

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.

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] can differ in many respects, notably body fat).

Q. I have an iron stomach. I have never felt nauseous from supplements. Do I still need to take precautions to avoid gastrointestinal upset?

If you have never had any issues with nausea or vomiting, you may have an easier time ingesting large doses of certain supplements. Nevertheless, it is not a good idea to disregard the warnings on a product.

Q. Why do study results differ for a given ergogenic supplement?

One reason that sports supplements can show benefit in some studies but not others is because there are many different testing procedures that researchers can use to determine if there is an effect from the supplement trial.

For example, studies can test participants using a time-trial (covering a pre-set distance as quickly as possible), time to exhaustion (maintaining a pre-set pace for as long as possible), or repeated sprint tests (generating as much power as possible each time). Within these different protocols there is a lot of potential variability, like the distance of the time trials, the intensity for the time to exhaustion tests, or the number of repeated sprints to be measured, as well as rest time between efforts, whether the participants are recreational athletes or trained professionals, etc.

Underlying all of these variables are sex differences, as males and females can differ when it comes to fuel sources, metabolism, and specific adaptations to exercise. There are tons of ergogenic supplement trials enrolling only or mostly fit men: for muscle gain, fat loss, and exercise performance. The same is not true for fit females, which is a big issue for evidence applicability.

Q. How long does it take for caffeine tolerance to set in? And how long do I need to go without caffeine for this tolerance to fade away?

It varies, in both cases, depending notably on dosage (amount and frequency) and genetics. Some people become tolerant in days, others in weeks. Some people can reset their tolerance in a week, whereas others may need a couple of months.

In the end, you'll have to experiment to find what works for you. Should you wish to reset your tolerance, take at least two weeks off caffeine, then try a small dose (50–200 mg). If you find the stimulation acceptable, you can resume using caffeine more often; if you don't, take another week off, then try a small dose again.

Do not attempt to fight caffeine tolerance with higher and higher doses. It would be not only dangerous, but also counterproductive, as you'd soon reach an insurmountable tolerance — a tolerance no dose can overcome.

Q. Don't creatine and caffeine negate each other?

Although not all studies agree, a high dose of caffeine (5 mg per kilogram of body weight, so about 2.3 mg/lb) might partially negate the benefits of creatine, but only when both supplements are co-ingested during a creatine loading phase. This potential issue can be sidestepped by consuming your creatine and caffeine several hours apart or by skipping the optional creatine loading phase.

Q. Can I take caffeine without theanine, or vice versa?

Caffeine is an effective stimulant on its own. Adding theanine will enhance your focus. Theanine by itself provides no exercise-related benefit.

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.[554]

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.[555] You can see how it varies below.

Isoflavone content of common soy foods

Food category	Food	Milligrams of isoflavones per 100 g of food		
		Average	Minimum	Maximum
Traditional unfermented soy foods	Edamame	18	14	19
	Soybeans (boiled)	65	23	128
	Soybeans (raw)	155	10	440
	Soybean sprouts	34	0	107
	Soy milk (unsweetened)	11	1	31
	Soy nuts	148	2	202
	Tofu	30	3	142
Traditional fermented soy foods	Miso	41	3	100
	Miso soup	1.5	1.5	1.5
	Miso soup mix (powder)	70	54	126
	Natto	82	46	124
	Soy sauce	1	0	3
	Tempeh	61	7	179
Second-generation soy foods	Soy-based veggie “meats”	9	0	23
	Soy cheeses	26	3	59
	Soy yogurt	33	10	70
Soy flours and protein powders	Soy flour (defatted)	151	74	324
	Soy flour (full-fat)	165	130	260
	Soy infant formula (powder)	28	21	31
	Soy protein concentrate (alcohol wash)	12	2	32
	Soy protein concentrate (water wash)	95	61	167
	Soy protein isolate	91	46	200

Reference: USDA FoodData Central Databases. Accessed Jan 18, 2019

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.[556]
- Most studies that looked at protein intake and calcium excretion list dairy products as a protein source,[557] 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[558] and that high protein intake "promotes bone growth and retards bone loss whereas low-protein diet is associated with higher risk of hip fractures."[559] High-protein diets have also been shown to modestly suppress the decrease in bone mineral density caused by weight loss.[560]

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.[561] 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),[562] which promotes notably bone growth.[563]

All in all, current evidence suggests that *protein's effect on bones is either neutral or beneficial.*[561][564]

Q. Why do you have entries for BCAAs and HMB but not leucine?

BCAAs might alleviate cognitive fatigue when taken before a game, so they have a niche to fill. There is some evidence that HMB could be more anti-catabolic as the same amount of leucine when calories are restricted, in which case it would also have a niche to fill. With regard to anabolism, increasing your protein intake is more likely to help than leucine alone, so leucine doesn't really have a niche to fill.

Q. Since the body makes carnosine out of β-alanine and histidine, should I also supplement histidine?

It isn't necessary. If you consume enough protein, your muscles already have all the histidine they need to produce more carnosine.

Q. Still, why β-alanine? Wouldn't it be simpler to supplement carnosine directly?

Since carnosine simply gets broken down into β-alanine and histidine,[565] and since your muscles already have enough histidine, carnosine supplementation has no advantage over β-alanine supplementation[566] — especially since β-alanine is cheaper.

Q. Are sodium bicarbonate and β-alanine doing

the same thing or can they be used synergistically?

Sodium bicarbonate is primarily an extracellular buffer,[20] while carnosine is primarily intracellular. In one study, the combination of both β-alanine and sodium bicarbonate supplementation may exert a synergistic influence, alleviating muscle fatigue and improving performance more than when supplemented alone.[567]

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

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

Q. Can I get enough nitrates from fruit?

In short, no. Even “nitrate-rich” fruits, such as melons and strawberries, pale in comparison to most vegetables. Compare, for instance, 100 g of beetroot (199.2 mg of nitrates) with 100 g of melon (32.5 mg), strawberries (17.2 mg), banana (7.6 mg), apple (2 mg), or orange (0.9 mg).

Q. I’ve heard that I should “load” creatine. What does that mean?

Loading creatine means taking a high daily dose for a few days before moving down to a smaller maintenance dose, which can be taken indefinitely. This is not necessary for effective supplementation, however; benefits may be felt sooner through loading, but they normalize after a few weeks.

If you wish to load creatine, take 20–25 g/day for 7 days (splitting your daily intake into smaller doses, taking them with some food, and drinking more fluids may help prevent intestinal discomfort). Take 5 g/day thereafter.

Q. Creatine doesn’t seem to work for me. What should I do?

Some people are creatine nonresponders: the creatine they ingest largely fails to reach their muscles. Alternate forms of creatine, such as creatine ethyl-ester, have been marketed to nonresponders, but they lack scientific support. Currently, the best way to lessen creatine nonresponse is to take 5 grams twice a day, each time with protein and carbs, preferably close to a time of muscle contraction (i.e., before or after your workout).

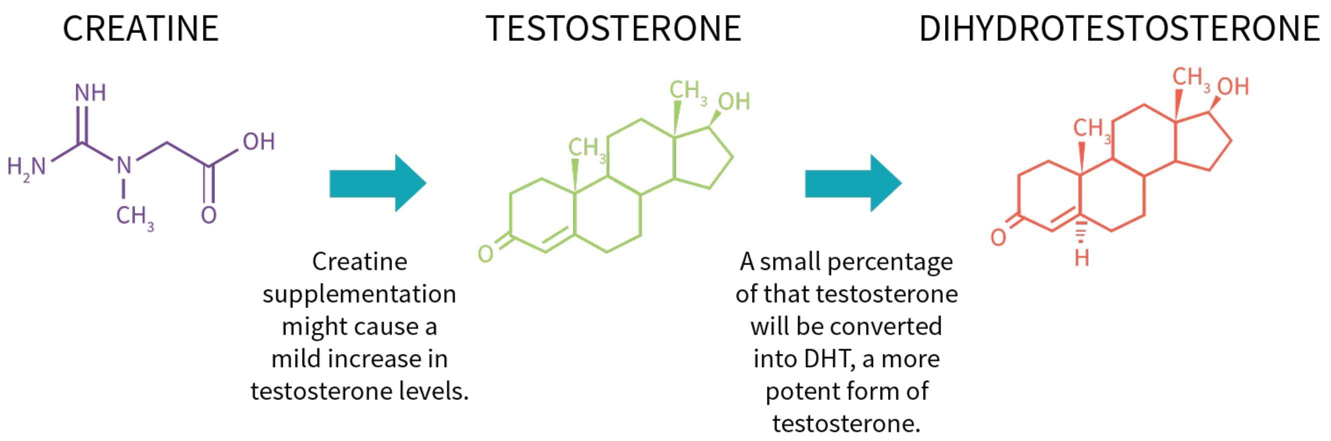
Note that even if supplemental creatine fails to enter your muscles it can still benefit you in other ways, such as by improving your body's methylation status (methylation being a way for your cells to help manage gene expression).

Q. Will creatine cause hair loss?

The idea that creatine *might* increase hair loss stems from a single randomized controlled trial (RCT) whose participants (20 healthy, young, male rugby players) saw a small but statistically significant increase in *dihydrotestosterone* (DHT) after supplementing with creatine for 21 days.[42] When DHT, a potent metabolite of testosterone, binds to DHT receptors on the hair follicles of the scalp, those follicles may shrink and stop producing hair.[568][569]

To date, this RCT is the only one to have tested creatine's effects on DHT. However, a number of RCTs have examined creatine's effects on testosterone. Out of 12 additional RCTs, two saw a significant increase in testosterone,[43][44] but 10 saw no effect.[42][79][45][46][47][48][49][50][51][570] Of those 12 RCTs, five also tested creatine's effects on free testosterone, the form that gets converted into DHT, and all saw no significant increases.[79][45][47][49][51]

A proposed mechanism behind creatine's effect on testosterone

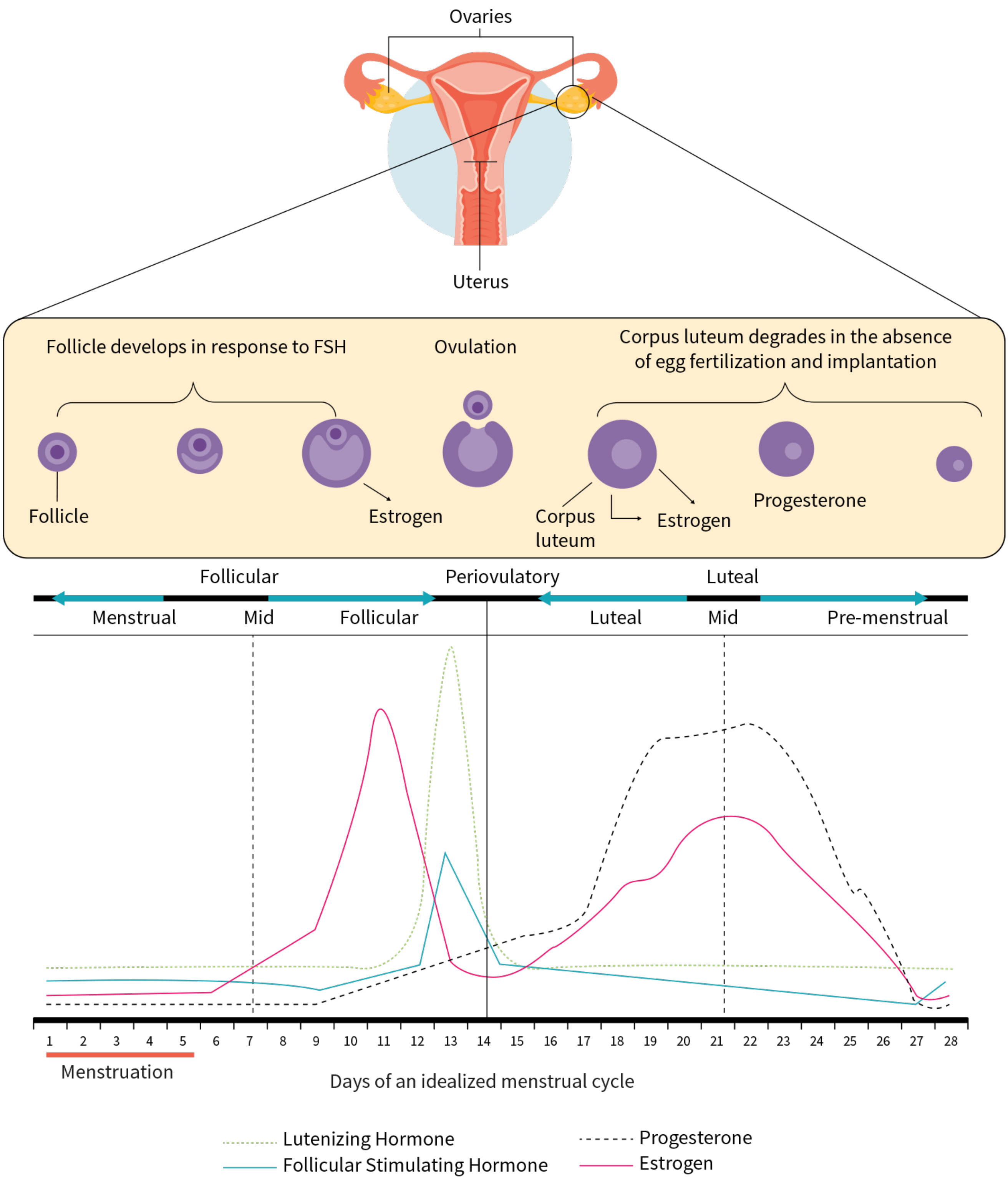


Creatine *could* nonsignificantly increase free testosterone yet significantly increase DHT (i.e., a small increase in free testosterone, which can convert into DHT, could lead to a much greater increase in total DHT). So while it's *technically* possible that creatine might have some effect on hair loss, current evidence and mechanistic data indicate it's quite unlikely.

Q. Does the menstrual cycle affect caffeine's performance-enhancing properties?

Caffeine is a popular ergogenic aid, the performance-enhancing effects of which have been confirmed in the scientific literature. However, the vast majority of the available trials have been conducted in males, with most of the interventions that have been conducted in females having tested the ergogenic properties of caffeine during the follicular phase of the menstrual cycle, which possibly minimized the potential effects of hormonal variations on a given studies performance outcomes (speed, strength, etc).

The menstrual cycle



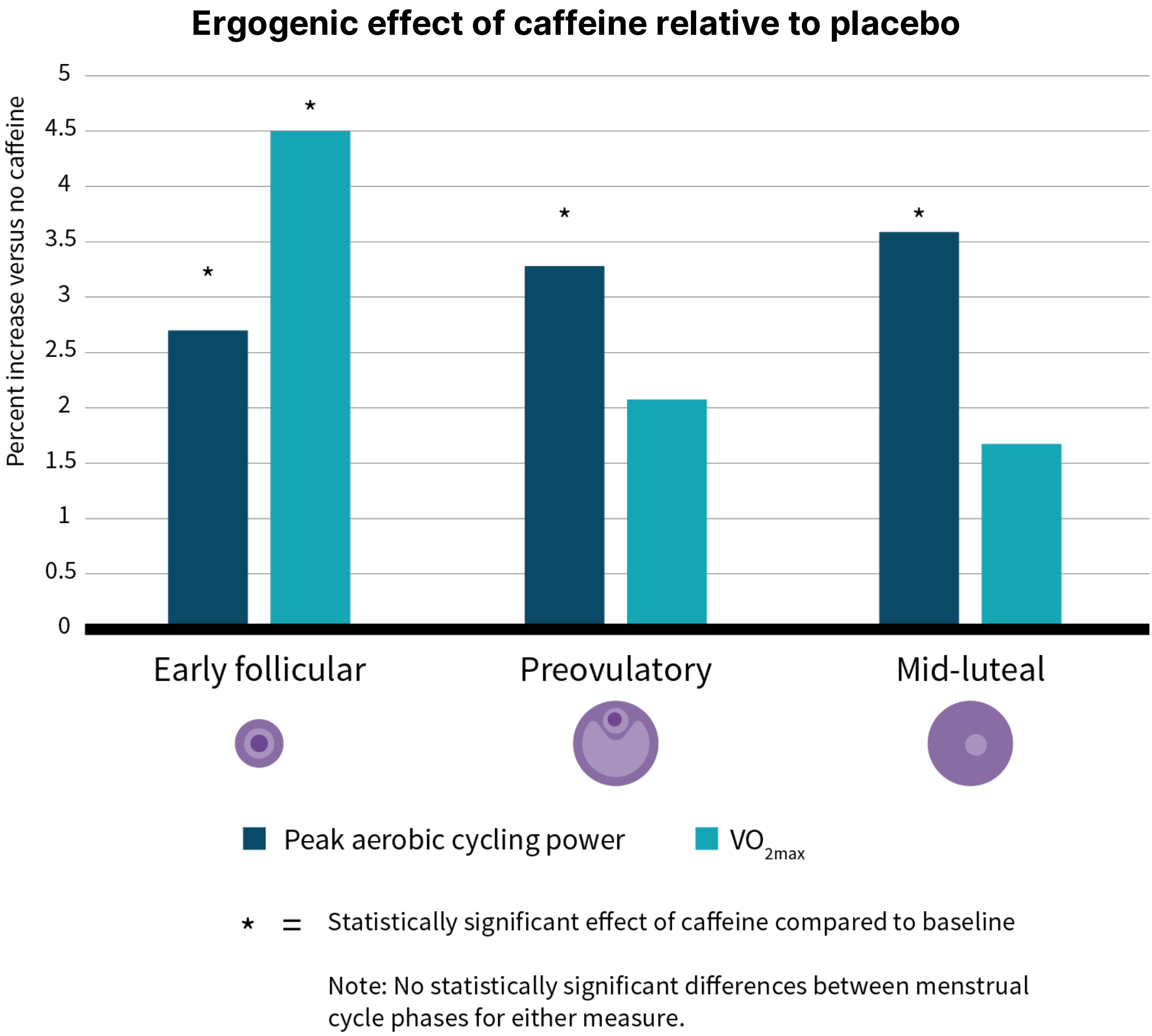
Adapted from Draper et al. *Sci Rep*. 2018.[571]

While the magnitude of the ergogenic effect of caffeine may potentially vary during the different phases of the menstrual cycle, only one study has examined this possibility. This clinical trial examined the ergogenic effects of caffeine ingestion in females during different phases of the menstrual cycle.[572]

In this four-week, double-blind, randomized, crossover trial, 13 well-trained young females ingested a capsule containing either caffeine (3 mg/kg of bodyweight, which was around 180 mg, in this case) or placebo 60 minutes before an exercise bout on two separate experimental trials in each of the following three phases of the menstrual cycle for a total of six identical experimental trials.

- Early follicular

- Preovulatory
- Mid-luteal



Q. How does resistance training affect testosterone levels?

In general, serum testosterone rises immediately following resistance training in males, but returns to baseline, or even below baseline, after about 30 minutes.[573] Several factors may affect the specific testosterone response to working out, however. For instance, high intensity or high volume alone isn't enough to induce a testosterone response. A response is induced by meeting a minimum threshold for both.

In females, some studies have also found short-term increases in serum testosterone, but others haven't, so the results are more equivocal.

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