A practitioner's guide to

sports supplements

Fullscript

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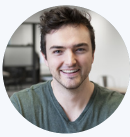

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Preface

Fullscript's Integrative Medical Advisory team (IMAT) develops comprehensive educational resources using an evidence-informed approach. This guide includes a selection of evidence-based ingredients that practitioners can reference and use as a foundation when developing individualized sport nutrition recommendations. As a means of determining the ingredients included, we followed the IMAT evidence-based decision support (EBDS) rating scale to discern the rigor of evidence supporting a specific nutrient's therapeutic effect.

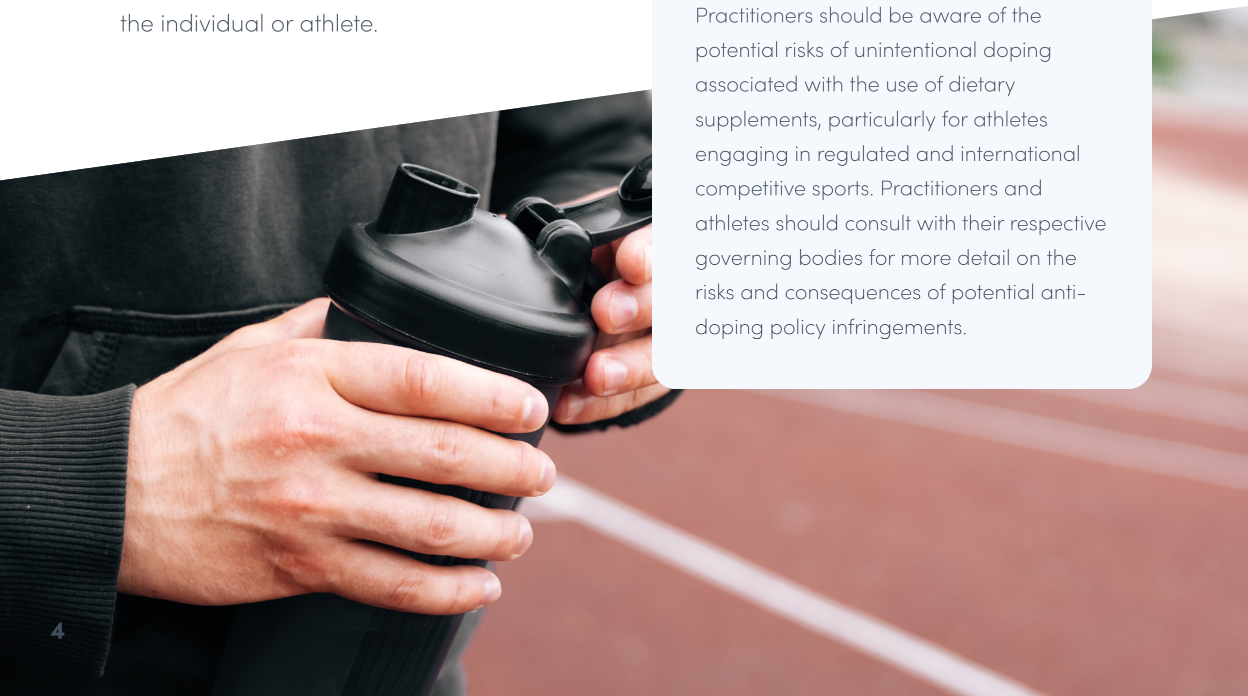
The ingredients included in this guide are based on a review of existing clinical research, with a priority placed on systematic reviews and meta-analyses, classified as A in the rating scale. Practitioner discretion is highly advised, as ingredients can vary in safety and effectiveness and depending on the needs of the individual or athlete.

Class	Type	Studies
A	Systematic review or meta-analysis of human trials	N/A
B	Human RDBPC	≥2 studies and/or 1 study with ≥50 studies
C	Human RDBPC or RCT	1 study <50 subjects
D	Human trials or in vivo animal trials	N/A

For further information on Fullscript's research methods, please refer to the full rating scale available at https://fullscript.com/blog/evidence-based-decision-support.

Disclaimer

Practitioners should be aware of the potential risks of unintentional doping associated with the use of dietary supplements, particularly for athletes engaging in regulated and international competitive sports. Practitioners and athletes should consult with their respective governing bodies for more detail on the risks and consequences of potential anti-doping policy infringements.



Introduction

Whether an individual visits a pharmacy, grocery store, or online nutrition or supplement retailer, they would be likely to encounter some kind of sports nutrition product. This is not surprising given that global consumer trends have shifted towards a more health conscious culture and that the adoption of active and healthy lifestyles are closely linked with physical activity and nutrition. (Arenas-Jal 2019)

In 2020, the global sport nutrition market was valued at **US$ 16.59 to 17.00 billion** and was projected to grow to **US$ 31.00 to 33.03 billion** by 2027 to 2028. (Grand View Research 2021) (Polaris 2021) North America has been the largest contributor to the industry, accounting for more than 61% of the market share as of 2019. (Grand View Research 2021)

Due to the increasing number of individuals seeking vegetarian or vegan options, products containing plant-based ingredients is one of the fastest growing segments in the sports nutrition industry. (Grand View Research 2021)(Research and Markets 2021) Though whey protein remains the most popular source of sport supplement protein, (Arenas-Jal 2019) it is derived from milk and not an appropriate source of protein for those following vegan diets. Rising sales of protein products formulated from soy, rice, pea, spirulina, pumpkin seed, hemp, and wheat drove the market value of the plant-based protein industry from **US$ 4.18 billion** in 2017 to **US$ 5.9 billion** in 2019, a value expected to reach **US$ 8.4 billion** by 2025. (Grand View Research 2019) Particular interest in using clean-labeled dietary supplements to improve sports performance, optimize weight loss, and support general wellness is also currently on the rise. (Arenas-Jal 2019)

As individuals have more information than ever at their fingertips to actively engage in healthy lifestyles, consumers may also turn to sports nutrition products in order to support their athletic and lifestyle goals. This clinical guide to sports supplements is intended to provide practitioners with a practical overview of:

- The sports nutrition industry
- Dietary considerations for athletes, including macronutrient and caloric requirements
- Evidence-based sport supplement ingredients
- Quality considerations, including dietary supplement regulations, third-party certifications, and anti-doping policies

An industry overview

Sports nutrition products are typically categorized as sports drinks, foods, or supplements. (Polaris Market Research 2021) (Research and Markets 2021) These terms are often used interchangeably (e.g., sport gels, electrolyte drinks, or protein powders may be called "supplements" or "sports foods"), though there are differences between how these products are regulated. While the specific regulatory details are beyond the scope of this guide, we have provided some basic definitions below.

Briefly, sports foods and drinks are products that can be consumed like any other food but have been formulated and marketed as a more convenient way to nutritionally prepare for a bout of physical activity or replace nutrients post-exercise. These kinds of products can include items such as sports drinks (e.g., Gatorade, Powerade, or depending on who you ask, energy drinks like RedBull), gels, meal replacements, protein powders, sports bars, and even high-protein-containing dessert products such as cookies. (Garthe 2018)(Maughan 2018)

In contrast, as per U.S. Food and Drug Administration (FDA) regulations, sports supplements (or any other dietary supplement) cannot be marketed as a food or as a replacement for a conventional meal or diet. They can be found in many formats, including **tablets, capsules, softgels, gelcaps, powders, liquids, and bars.** Sports supplements can also be formulated to contain single- or multi-ingredient formulations, such as vitamins, minerals, botanicals, amino acids, probiotics, enzymes, glandulars, concentrates, metabolites, constituents, and extracts. (FDA 2021)
Like sports foods and drinks, sports supplements are perhaps most commonly thought of as products that can be used to nutritionally prepare for or recover from a bout of exercise, build lean mass, lose weight, or improve athletic performance (i.e., ergogenic aids). Though ergogenic aids have been most consistently defined by their ability to improve performance, some experts classify them more broadly as substances that also enhance recovery or help prevent injury. (Kerksick 2018)

Who uses sport nutrition products and why?

The use of sports nutrition products, which has extended beyond the "traditional" sports nutrition market primarily dedicated to bodybuilders and other athletes, now caters to a broader audience including elite and amateur athletes, as well as individuals who may use sports products to support active lifestyles.

Popular online sports supplement retailers now include numerous product categories, such as **general wellness, immune health, gastrointestinal support, mental health and focus, sleep, and joint health.** This widened offering of products now also contributes to the sports nutrition industry's continued projected growth.

The sports nutrition industry's targeting of broader wellness categories is not surprising given that approximately half of all U.S. adults report using some kind of dietary supplement. (Bailey 2013)(Kantor 2016) Though this data does not indicate whether these individuals are using sport supplements specifically, another study in college students showed that the top reasons for using dietary supplements included supporting general wellness (73%), acquiring energy (29%), increasing muscle strength (20%), and enhancing performance (19%), (Lieberman 2015) indicating that a large portion of individuals also purchase supplements that are traditionally used in the sports setting.

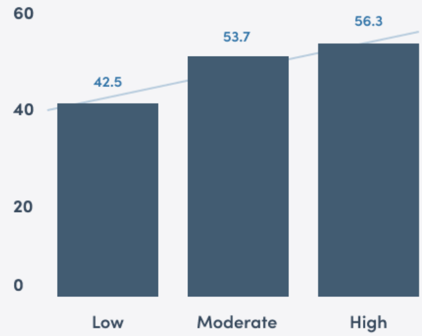
Industry reports commonly cite that the growth of the sports nutrition industry is largely attributable to consumers' increased awareness of the importance of physical activity, the desire to stay fit, and the desire to reduce the incidence of lifestyle-related diseases, coupled with increasing engagement with the fitness industry. (Polaris Market Research 2021)(Research and Markets 2021)

For example, the International Health Racquet and Sportsclub Association estimated that in the United States alone, 71.5 million individuals used health clubs (i.e., gyms, fitness centers) in 2018 (approximately nine million more than in 2017) by visiting at least one of the **39,570 clubs** (~1,100 more clubs than the previous year). (Rodriguez 2019) The number of health clubs continued to grow to **41,370 in 2019.** (Gough 2020)

Simultaneously, engagement in some form of physical activity continues to rise. The Physical Activity Council has estimated that **~75.6%** of the U.S. population (ages 6+) engages in some form of physical activity, which has increased by **2.7%** since 2015. (Physical Activity Council 2021)

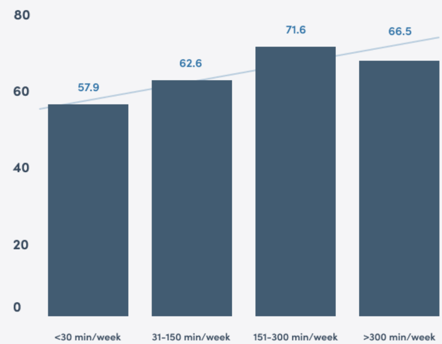
As shown in Figures 1 and 2, supplement use tends to increase with an individual's physical activity levels. A greater percentage of U.S. adults self-reporting moderate and high levels of physical activity also report using supplements more often than individuals who report lower levels. (Bailey 2013)

Figure 1: Prevalence of supplement use by self-reported exercise levels



Similar trends have been shown in college students; the use of any dietary supplement was associated with an increased duration of physical activity per week. (Lieberman 2015)

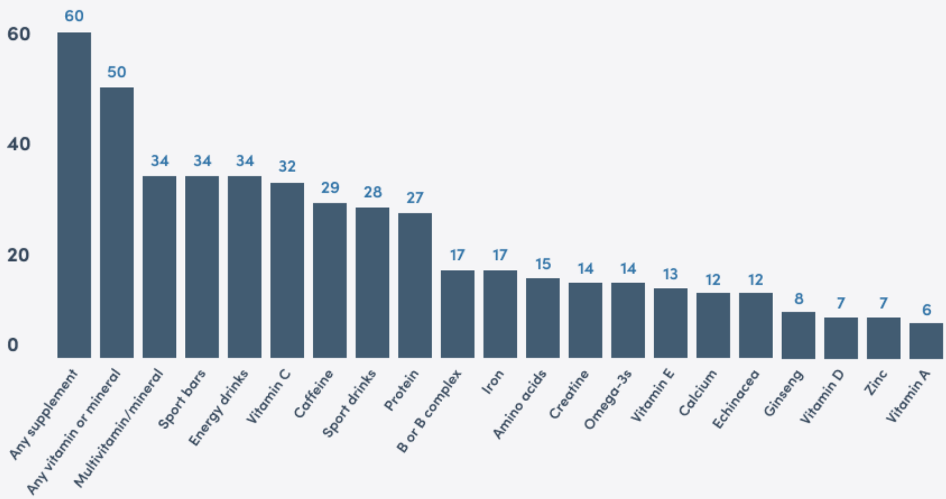
Figure 2: Percentage of college students reporting use of any supplement stratified by exercise level



The prevalence of dietary supplement use may also be higher in athletes. Compared to approximately 50% in the general population, (Bailey 2013)(Kantor 2016) a meta-analysis has indicated that approximately 60% of athletes (of any level) and up to 70% of elite athletes use dietary supplements. (Knapik 2016)

Figure 3 provides prevalence rates for the use of various dietary supplement types in elite and non-elite athletes. (Knapik 2016)
With such an increase in the interest and availability of sports nutrition support, it's important for the practitioner and general consumers to have a good understanding of an athlete's needs and the evidence available to support individual ingredients.

Figure 3: Prevalence of supplement use by athletes



Macronutrient requirements for athletes

An active athlete has different nutritional requirements when compared to the average sedentary individual. Notably, there are important differences in the requirements for both macronutrients and calories.

Macronutrients

Macronutrients, specifically carbohydrates, fats, and proteins, are the predominant sources of calories that fuel the body. The recommended intake of carbohydrates, fats, and proteins to prevent chronic disease varies across the globe. Major health organizations from the United States and Canada as well as the World Health Organization (WHO) have published optimal macronutrient distribution targets for the average adult, as shown in Table 1.

Table 1: Optimal macronutrient distribution targets

Source	Carbohydrates (%)	Protein (%)	Fat (%)
United States (Institute of Medicine 2002)	45–65	10–35	20–35
Canada (Health Canada 2006)	45–65	10–35	20–35
World Health Organization (World Health Organ Tech Rep Ser 2003)	55–75	10–15	15–30

Compared to the average sedentary adult, the average athlete's recovery and performance generally benefits from higher intakes of carbohydrate and protein, with similar or slightly higher levels of fat. (Kerksick 2018)

A recent review has shown that many athletes are not consuming adequate energy and carbohydrate levels recommended by experts from sports nutrition organizations (e.g., the International Olympic Committee, the International Society of Sports Nutrition, the American College of Sports Medicine). Tailored approaches to meet goals and sport-specific demands are therefore recommended. (Jenner 2019)

Carbohydrates

At rest, blood glucose that is not immediately needed is typically stored in muscle tissue and the liver as glycogen, and glucose consumed in excess can be converted to lipids and stored as fat. (Slavin 2014) Glycogen is the most readily available source of glucose and is broken down to meet the homeostatic demands of regulating blood sugar as well as for immediate fuel for muscles undergoing movement.

Did you know?

The average individual stores 500 g of glycogen in skeletal muscle and 80 g in the liver. While this constitutes only approximately 4% of the body's total glycogen content, these limited stores are the primary energy source for moderate to intense exercise. (Murray 2018)

During exercise, glycogen stores are broken down to produce glucose in order to meet energy (ATP) demands required to complete movement.

For example, this may occur during:

- Endurance exercise (e.g., jogging at 65–80% VO2max)
- Resistance exercise (e.g., weight lifting at 3–4 sets of 6–20 reps)
- High-intensity exercises (e.g., multiple 30-second sprints) (Kerksick 2017)(Murray 2018)

Recommended intake of carbohydrates

The Institute of Medicine has set the recommended dietary intake of carbohydrates at 130 g per day for a sedentary individual. (Institute of Medicine 2002) However, carbohydrate intake should be adjusted to an athlete's activity level, with common targets for daily consumption summarized in Table 2.

Table 2: Carbohydrate intake targets to meet the demands of increasing exercise volume

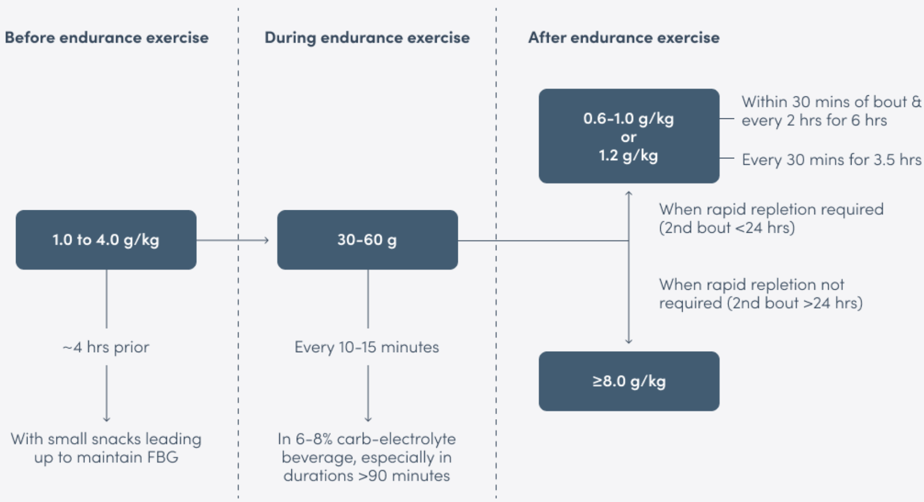
Daily exercise volume	Carbohydrate targets (g/kg/day)
<1 hour per day	3–5
1 hour per day	5–7
1-3 hours per day	6–10
>3 hours per day	8–12

(Burke 2011)

Carbohydrate intake and performance

In order to maximize endurance exercise performance, a higher consumption of carbohydrates is recommended to saturate glycogen stores. (Murray 2018) During endurance training (>70% VO2max; >60 to 70 minutes), carbohydrate supplementation can improve performance and is important for glycogen optimization, sparing, and repletion. (Kerksick 2017) Figure 4 provides dosing recommendations to meet these goals.

Figure 4: Recommended carbohydrate intake before, during, and after endurance exercise to optimize performance



Despite the glycogen-depleting effects of resistance-based exercise, there is little to no evidence to support the use of carbohydrate supplements to improve performance during resistance training. (Kerksick 2017) For more detailed information on potential applications of carbohydrate during resistance training, please refer to the "Considerations during exercise" section of this guide.

Protein

Proteins are made up of amino acids, which are required for virtually all functions as they make up the body's cellular machinery. There are a total of 20 amino acids, nine of which are considered essential (the body does not synthesize these proteins and they need to be ingested).

The nine essential amino acids (EAA) are:

- Histidine
- Isoleucine
- Leucine
- Lysine
- Methionine
- Phenylalanine
- Threonine
- Tryptophan
- Valine (Lopez 2021)

Recommended intake of protein

The Recommended Daily Allowance for protein is 0.8 g/kg of body weight per day for the average individual, but this level may be insufficient for a training athlete, (Jäger 2017) who are known to have a higher risk of protein malnutrition. (Kerksick 2018) A minimum daily intake of 1.4 to 2 g/kg of body weight per day is recommended to meet the needs of most athletes. (Jäger 2017) However, athletes who are trying to restrict energy intake and maintain fat-free mass may benefit from an intake up to 2.4 g/kg of body weight per day. (Burke, 2019)

In order to maximize muscle protein synthesis (MPS) and performance, an athlete may need to divide their protein intake throughout the day, with 20 to 40 g servings ingested approximately every three hours depending on an individual's body weight. (Kersick 2017) This strategy can help achieve the target intake of 1.4 to 2 g/kg of body weight per day by simplifying intake instructions. For example, a 90 kg athlete (with a target intake of 180 g of protein per day) could consume five meals/snacks per day, each containing 36 g of protein.

By clustering protein intake around the athlete's training schedule with meals or protein supplements (as a matter of convenience), it may be possible to mitigate protein imbalance prior to exercise, reducing muscle protein breakdown during exercise, and take advantage of the state of increased anabolic activity observed within the first few hours after exercise. (Jäger 2017)(Kersick 2017)

In general, protein supplementation provides a number of benefits, including improved muscle mass and strength gains post exercise (with resistance training, in particular), reduced loss of lean mass during periods of hypocaloric intake (e.g., when dieting to lose weight), and increased fat loss. (Jäger 2017)

Protein supplement considerations

A number of types of protein supplements are available, including **whey (concentrate, isolate, and hydrolysate), casein, soy, rice, hemp, and pea protein**, to name a few popular choices. Whey protein is the most commonly used protein supplement on the market due to its high-quality protein content (based on essential amino acid content) and its relatively quick digestion speed.

Three key considerations when choosing a protein powder:

1. Dietary restrictions
2. Protein quality & composition
3. Digestion & absorption speed

1. Dietary restrictions

Individuals and athletes may have different dietary preferences and restrictions that should be taken into consideration before choosing a protein supplement, as supplements can be manufactured from a variety of sources. For instance, products derived from animals (e.g., whey or casein) would not be appropriate for an athlete following a vegan diet. Athletes may also have allergies or intolerances (e.g., soy, dairy) that may prevent them from taking certain types of protein.

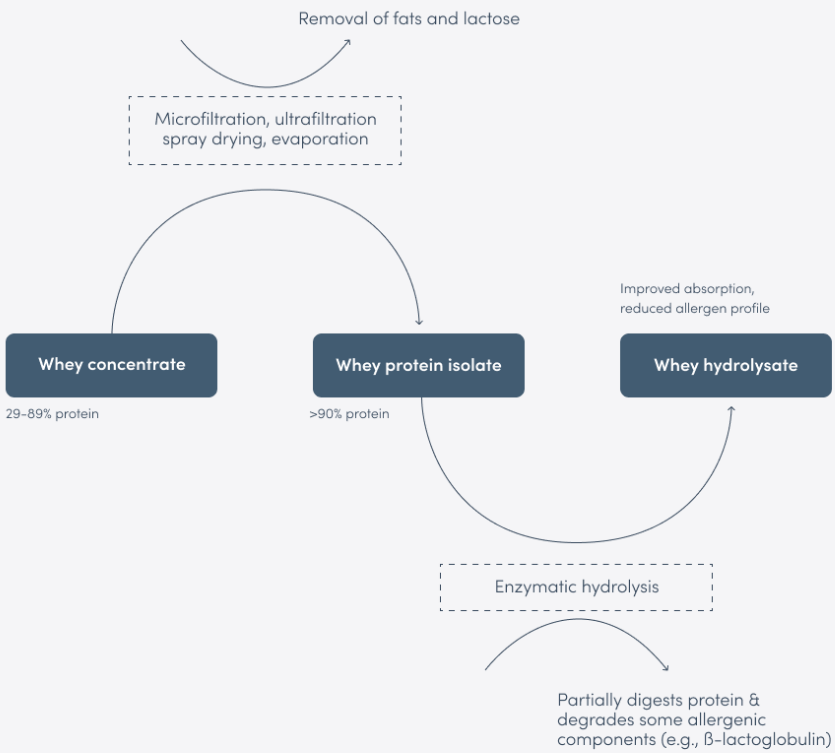
If there are no dietary restrictions to consider, whey protein may be the best choice because of its relatively high-protein quality and digestion speed. It is also important to note that various forms of whey protein (the most widely available protein type on the market) have different properties based on their degree of refinement. For instance, lactose, a commonly untolerated sugar found in milk products, is found in greater amounts in whey concentrates compared to isolates or hydrolysates, and therefore, an athlete may be inclined to use a more refined form of whey protein if they have a lactose intolerance. Note that despite its reduced lactose content, whey and casein proteins are derived from milk and are not suitable for those following a vegan diet.

As with most supplements, typically the more refinement a whey protein undergoes, the higher the cost of the end product itself. Hydrolysis of whey or soy-based proteins has been shown to more quickly increase amino acid availability (Morifuji 2010) and enhance muscular recovery post exercise than its non-hydrolysated counterparts, (Buckley 2010) though some studies do not support these results.

Figure 5 shows the process for producing whey-based proteins. As native whey proteins undergo concentration, isolation, and hydrolysation, three major alterations occur:

1. The relative amount of protein contained in the product increases as fats and carbohydrates are removed.
2. The amount of lactose reduces, which can help to reduce bloating or other gastrointestinal issues for lactose intolerant individuals.
3. The absorbability of protein increases, while the presence of allergenic compounds decreases. (Huecker 2019)(Jäger 2017)(Patel 2015)

Figure 5: The refinement of whey proteins



The removal of fats and carbohydrates may also be particularly important for an individual trying to lose weight by limiting the caloric composition of the protein supplement overall.

2. Protein quality and composition

The quality of a protein supplement relates to the completeness of its amino acid profile and its digestibility score. (Huecker 2019)(Jäger 2017) (Marinangeli 2017)

In general, complete proteins are obtained from animal-based protein sources, such as whey, and are thereby considered to possess greater "protein efficiency." On average, research demonstrates that animal-based proteins possess higher percentages of EAAs (37%) than vegetable-based proteins (26%). (Gorissen 2018) Vegetable proteins are often lacking in at least one EAA, which can lead to less MPS following exercise than observed with animal-based proteins. (Jäger 2017) For instance, whey protein typically contains approximately 12.5% leucine, while casein (~8.5%), rice (~8%), and soy (~7.5%) have relatively lower amounts, (Witard 2016) but compositions can vary slightly.

The branched-chain amino acids (BCAAs) isoleucine, leucine, and valine are the EAAs with the greatest role in stimulating MPS, with leucine being most important on its own. However, a balanced EAA profile is considered most beneficial to stimulate overall MPS. (Jäger 2017)

Table 3 provides amounts of protein needed to be ingested from various sources in order to match the leucine content of 25 g of whey protein (~11% leucine), which has been consistently shown to induce MPS. (Gorissen 2018) This table provides a practical way to recommend alternative protein sources to athletes or patients for which whey or casein proteins may not be a favorable option. The table also provides a summary of the Digestible Indispensable Amino Acid Score (DIAAS). DIAAS scores >100 indicate that the protein source is not limited by an amino acid and can meet recommended daily amino acid requirements. The greater the DIAAS score, the higher the quality of the protein.

Table 3: Quality and EAA content of various protein sources

Source	EAAs of total protein	Amount of protein needed to consume 10.9 g of EAAs	Amount of protein needed to consume 2.7 g of leucine	DIAAS score
Whey	43%	25 g	25 g	106
Casein	34%	32 g	34 g	137
Egg	32%	34 g	39 g	111
Pea	30%	37 g	38 g	83
Whey	28%	39 g	37 g	56
Casein	27%	40 g	40 g	103
Egg	23%	48 g	54 g	56

(Gorissen 2018)(Herreman 2020)

3. Digestion and absorption speed

When selecting a protein supplement, the relative absorption speed of the protein should be considered. For instance, one of the main differences between whey and casein proteins is that whey is water soluble and is quickly digested, while casein is not water soluble and is digested more slowly. (Jäger 2017) This may lead to differences in the speed of EAA availability between protein types and potential outcomes. For instance, within three hours, leucine levels were 200% higher in a whey protein group compared to casein (matched for EAA content), and MPS induced by whey protein at rest and after exercise was respectively 93% and 122% higher than the casein group. (Tang 2009) Bodybuilders using whey protein also have been shown to increase their muscle mass by an additional 4.2 kg over ten weeks compared to bodybuilders using casein, (Cribb 2006) potentially indicating an advantage of faster absorbing proteins.

The timing of ingestion may also be a relevant factor to consider when comparing whey and casein. For instance, there are multiple studies that show that consuming 30 to 40 g of casein approximately 30 minutes prior to sleep can improve MPS without reducing fat oxidation, (Jäger 2017) potentially leading to greater reliance on fat as a fuel source than would be observed with a more quickly absorbed whey protein. It has been proposed that whey protein may lead to a more pronounced insulin response, leading to a greater reliance on carbohydrate metabolism than with casein. (Madzima 2014) Similarly, casein has been shown to reduce whole body protein breakdown (by 34%) and demonstrated a lower leucine oxidation over seven hours compared to whey protein, despite the latter having greater protein synthesis (37% higher). (Boirie 1997) Ultimately, these findings suggest that to reduce muscle protein wasting that may occur over long periods of time without consuming a meal (e.g., overnight or during a fast), casein may be more beneficial than whey. Further supporting this hypothesis, greater reductions in fat mass and increases in lean mass were observed in individuals undergoing a resistance training program combined with a hypocaloric diet when using casein compared to whey protein. (Demling 2000)

The speed of absorption may also be an important consideration for vegetable-based proteins. For instance, supplementation with soy protein, a relatively quickly digested protein, increased MPS to a similar extent as whey protein but to a greater extent than casein (64% and 69% at rest and following exercise, respectively). (Tang 2009) Overall, no significant difference has been observed in strength, lean body mass gains, or protein synthesis between whey and soy protein supplementation (particularly if doses are matched for leucine content) when engaging in resistance training regimens. (Churchward-Venne 2019) (Lynch 2020)(Messina 2018) In comparison, a rice protein isolate with moderate to slow absorption increased leucine levels to a lesser total extent than whey protein, (Purpura 2014) but it provided equivalent benefits to recovery, lean mass gain, and fat loss. (Joy 2013)

Key considerations for selecting a protein supplement:

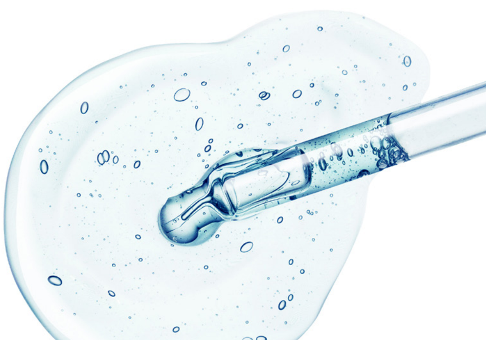
- Determine how much protein the individual needs by goals and weight.
- Select a protein source based on any dietary restrictions and preferences.
- Select a fast- or slow-acting protein based on goals, ingestion timing, and other dietary considerations.
- Match protein doses (particularly for leucine levels).

Collagen supplementation

One of the largest growing protein supplement categories is the collagen peptides category. Despite its popularity, collagen is considered an incomplete protein due to its lack of the amino acid tryptophan (Paul 2019) and its lower levels of leucine, isoleucine, and valine compared to whey proteins. (Alcock 2019) This may provide a potential explanation for collagen's lower efficacy on MPS compared to whey. Compared to dose-matched (30 g) whey protein, collagen peptides were less effective in improving MPS in older populations, (Oikawa 2020)(Oikawa 2018) but were slightly more effective than 15 g of whey protein to improve body composition in middle-aged, untrained men. (Zdzieblik 2021)

Though there is limited to no research on using collagen proteins to improve body composition and performance in athletes, in general populations, collagen peptide supplementation of 15 g per day when paired with resistance training can improve lean body mass, reduce fat mass, and improve strength in pre-menopausal women, (Jendricke 2019) young recreationally active (Kirmse 2019)(Oertzen-Hagemann 2019) and middle-aged untrained men, (Zdzieblik 2021) and older men with sarcopenia (Zdzieblik 2015) compared to placebo.

Overall, collagen supplementation may be less suited to improve MPS than whey protein, but it may be useful for other applications, such as improving post-exercise recovery and addressing joint pain. For instance, one study showed that collagen and whey protein intake both improved recovery from resistance and aerobic exercise to a similar extent. (Rindom 2016) Other studies show improvements in activity-related joint pain compared with placebo when ingesting 5 to 10 g per day over 12 to 24 weeks in athletes. (Clark 2008)(Zdzieblik 2017) Furthermore, tendon and ligament repair may be improved with collagen supplementation of 5 to 15 g per day over three to six months. (Dressler 2018)(Praet 2019)(Shaw 2017)



Fats

Recommended fat intake

Generally, the maintenance of approximately 30% of calories (20 to 35%) from fat is recommended for most athletes, which should consist of less than 10% from saturated fat and contain higher amounts of polyunsaturated fats and essential fatty acids. (Bytomski 2018)(Jenner 2019)(Thomas 2016) Fat intakes above 35% of the total caloric intake may reduce carbohydrate or protein consumption (to the detriment of recovery and performance) and/or cause weight gain if an athlete regularly consumes excess calories.

Adequate fat intake is also important; if fat intake makes up less than 10 to 20% of an individual's caloric intake, testosterone levels may begin to drop. (Kerksick 2018)(Whittaker 2021) If an athlete enters a state of overtraining, this may also reduce testosterone levels, and low testosterone levels may contribute to a loss of MPS and performance. (Fry 1998)(Pasiakos 2019) In such circumstances, ensuring adequate fat intake will help maintain testosterone levels. Additionally, long-term low-fat diets may begin to deplete fat-soluble vitamins and other important nutrients like omega-3 (n-3) fatty acids. (Thomas 2016) Omega-3 fatty acids also have potential positive effects on reducing inflammatory markers and improving recovery in athletes. (Lewis 2020)

If a change in body composition is desired, it has been recommended that fat intake alteration is ideally completed in an athlete's off season and under the supervision of a health practitioner specialized in sports to monitor safety and performance metrics. (American Dietetic Association 2009)

Performance and body composition

Research has examined the use of high-fat diets as a means to shift an individual's metabolic activity to more heavily rely on fat as a fuel source, ultimately sparing glycogen stores to prolong a sustained degree of performance. Athletes who are fat adapted (consuming <10% of their calories from carbohydrates) metabolize fat at a rate of 1.2 to 1.5 g per minute of progressively intense activity of 65% VO2max, covering required energy costs without needing exogenous carbohydrates. In contrast, athletes who are not fat adapted may require 90 to 105 g of carbohydrates per hour to fuel and maintain performance at a similar energy-expending rate. (Bytomski 2018)(Noakes 2014)

The use of the ketogenic diet to help athletes become fat adapted to improve athletic performance is considered controversial. The keto diet restricts carbohydrate intake to ~10% of an individual's caloric intake, predominantly replaced by increasing fat intake to 60 to 80% of caloric intake. This may help to spare glycogen and muscle proteins by utilizing ketones as an alternative energy source. (Aragon 2017)(Kang 2020) The upregulation of fat oxidation is mechanistically proposed to help reduce body weight by improving lipolysis, (Vitale 2019) even in states where calories are not restricted. (Kang 2020)

Overall, despite any body composition benefits, it appears that the ketogenic diet neither boosts nor deteriorates performance in endurance- or strength-based exercise. (Murphy 2021) Despite a reduced reliance on glycogen as a fuel source, the overarching pool of glycogen from which to pull during exercise may be reduced as a whole when following a ketogenic diet, which potentially limits improvements in performance, particularly during more intense exercise that relies on glycogen versus moderate- to light-intensity exercise, during which fat acts as the primary energy substrate. (Kang 2020)

Fat supplement considerations

Three lipid-based dietary ingredients including carnitine, conjugated linoleic acid (CLA), and medium chain triglycerides (MCTs) have been widely used to manipulate fat metabolism and improve performance; however, there is a lack of evidence to consistently demonstrate beneficial results.

L-carnitine is used to transport long-chain fatty acids into the mitochondria for metabolism; however, studies examining the effects of supplemental L-carnitine inconsistently show improvements in lipid metabolism and performance enhancement. (Kerksick 2018) (Sawicka 2020)

Overall, animal studies have shown strong benefits of CLA supplementation for improving body composition, but most trials in humans show no benefit to body composition or performance, (Kerksick 2018) despite potential benefits for general health such as reduced inflammation (Baghi 2016) and testosterone biosynthesis. (Vitale 2019)

MCTs can immediately enter the mitochondria for metabolism, which has led to interest in their use as an energy source during exercise. (Vitale 2019) However, there remains little to no evidence to support an ergogenic effect of MCTs. (Kerksick 2018)

Caloric requirements for athletes

A calorie is a unit of energy derived from macronutrients. 1g of carbohydrate and 1g of protein both contain roughly four calories, while 1g of fat contains nine calories. (Institute of Medicine 2002) The average female and male require 2,000 and 2,500 calories per day, respectively. (Institute of Medicine 2002) More accurate individual caloric requirements can be established by calculating resting metabolic rate (RMR) using a number of metabolic equations. The Mifflin-St Jeor equation has been shown to be one of the most reliable equations with the smallest degree of error, which may predict caloric intake within 10% accuracy. (Frankenfield 2005)

The Mifflin-St Jeor equation is as follows:
Males: RMR = 9.99 x weight (kg) + 6.25 x height (cm) - 4.92 x age + 5
Females: RMR = 9.99 x weight (kg) + 6.25 x height (cm) - 4.92 x age - 161
(Frankenfield 2005)

Physical activity level must then be taken into account, multiplying RMR by 1.4 to 1.69 for individuals who are sedentary or engaging in light-volume activity, a factor of 1.7 to 1.99 for individuals participating in moderate-volume activity (e.g., fitness classes, weight lifting, running, or cycling), or 2.0 to 2.4 for endurance or elite athletes. (Bytomski 2018) This yields an athlete's estimated Total Daily Energy Requirement (TDEE).

Table 4: Estimation of caloric needs based on training volume status

Training volume	Example of volume	Expected additional calorie expenditure per day (kcal/day)
Low	30-40 minutes per day 3x per week	200-400
Moderate	2-3 hours per day 5-6x per week	1,200-3,600
High	3-6 hours per day 5-6x per week	1,800-7,200
Elite	Variable	6,000-12,000

Beyond RMR, a number of other methods exist to more precisely gauge caloric expenditure (i.e., how many calories one burns during exercise and non-exercise activities). The gold standard for measuring overall caloric expenditure is the Doubly Labeled Water (DLW) method; (Johansson 2007) however, this method is often cost prohibitive and requires the services of an appropriate laboratory. As an alternative, the use of a heart rate monitor and accelerometer may closely replicate the findings of the DLW method. (Johansson 2007) Therefore, heart rate monitors and accelerometers may provide practitioners and their athletes with a realistic and accurate method for determining caloric expenditure and specific daily targets.

Ultimately, an athlete's caloric goals should be in line with their body weight goals. These goals may vary widely based on the specific sport or activity in which they are engaging and any weight requirements for the sport. (Garte 2011)

While there are technically 3,500 calories in a pound of fat, (Institute of Medicine 2002) a caloric deficit or surplus of 500 calories per day does not always yield a loss or gain of 1 lb per week as caloric restriction may slow one's metabolism (i.e., TDEE) to a variable degree, and caloric excess increases one's metabolism to a variable degree. (Aragon 2017) However, resistance training and maintaining adequate protein intake can help to minimize the drop in metabolism that is associated with caloric deficit. (Aragon 2017)

The magnitude of caloric deficit needed for weight loss may be proportional to an athlete's fat mass. (Nackers 2010) As they get leaner, smaller caloric deficits tend to promote better retention of lean mass. (Nackers 2010) Losing 0.5 to 1.0% of body weight per week (roughly 1 lb per week, depending on body weight) may be appropriate for leaner individuals. (Garthe 2011) (Helms 2014)

Considerations during exercise

A number of considerations related to the intake of fluids, electrolytes, carbohydrates, and proteins are provided below.

Fluids and electrolytes

Fluid and electrolyte intake are important considerations during exercise as the body can lose 10 to 81 oz (0.3 to 2.4 L) of water per hour. This varies based on environment, sex, body size, and length of activity. (Thomas 2016) Sodium, the most abundant electrolyte, may be lost at a rate of approximately 1,000 mg per 34 oz (1 L) of sweat depending on environmental conditions. (Casa 2019) As 51 oz (1.5 L) of fluid may be lost before thirst is perceived, (Herring 2013) thirst may not act as a good initial gauge to signal the need for fluid intake. Instead, athletes should generally proactively consume 6 to 12 oz (177 to 355 mL) of water every 15 to 30 minutes during exercise. (Bytomski 2018). A typical sports drink with a 6 to 8% carbohydrate-electrolyte solution (i.e., 6 to 12 fl oz) every ten to 15 minutes should adequately replace electrolyte losses during exercise. (Casa 2019)

Carbohydrates and protein

Carbohydrate and protein supplements are also popularly used during workouts. It appears that the use of either carbohydrate or protein supplements may be most effectively applied in endurance or resistance training, respectively.

During extended (>60 minutes) and high-intensity exercise (over 70% VO2 max), 30 to 60 g of 6 to 8% carbohydrate-electrolyte solution (i.e., 6 to 12 fl oz) every ten to 15 minutes helps to maintain fluid regulation and may mitigate glycogen depletion, which may therefore improve endurance performance. (Kerksick 2017) While some studies show that the provision of 1 g/kg of body weight of a carbohydrate supplement immediately prior to resistance exercise and 0.3 g/kg every ten minutes during exercise may spare glycogen, it does not seem to improve performance. (Haff 2000) It is possible, however, that resistance-based exercise performance may only be improved when providing a carbohydrate supplement to athletes who are already glycogen depleted. For instance, a 1.2 g/kg of body weight carbohydrate supplement protocol improved exercise performance in athletes who had undertaken a glycogen depleting exercise prior to resistance training, (Oliver 2016) while 0.3 g/kg of body weight improved performance only during the second bout of resistance training in the same day. (Haff 1999)

The benefit of providing protein during endurance exercise is less well established compared to carbohydrate supplementation. Several trials in endurance athletes (e.g., athletes completing approximately two hours of cycling to exhaustion) have noted improvements in performance, reductions in muscle damage, and/or improvements in glycogen replenishment when protein is added to the carbohydrate drink (4:1 ratio of carbohydrates to protein) versus carbohydrates alone. (Ivy 2003)(Saunders 2004)(Saunders 2007) However, other trials showed that when carbohydrate intake is high enough (over 1.2 g/kg of body weight per hour), the addition of protein may not improve glycogen repletion. (Howarth 2009)(Jentjens 1985)

Protein supplementation may be more important than carbohydrate supplementation during resistance training as MPS, hypertrophy, and strength tend to be similarly improved by protein supplementation alone compared to protein supplementation with carbohydrate. (Cribb 2006)(Power 2009)(Staples 2011) However, a 2013 review suggests that intra-workout protein and protein timing in a given day may have minimal effects on MPS. (Schoenfeld 2013) Rather, the overall daily dose of protein may be the most important factor. Overall, suggesting that an athlete consume a dose of protein within a workout (or immediately before or after) can strategically help an athlete achieve their protein target (e.g., ~2 g/kg of body weight).

Popular sport supplement ingredients

Many dietary supplements have been popularly marketed to improve sports performance; however, only a few key ingredients have strong evidence to support these claims. Table 5 provides an overview of some of the ingredients that have supportive research.

Practitioners should be aware that based on an ingredient's mechanism of action, a performance-enhancing effect may be observed for a certain type of exercise (e.g., aerobic), but these effects may not necessarily translate to another form (e.g., anaerobic). Additionally, some of the included ingredients may provide other benefits such as to enhance recovery or reduce pain, but they may not directly improve performance. For more detail on the ingredients found in Table 5, please refer to the subsequent ingredient summary sections.

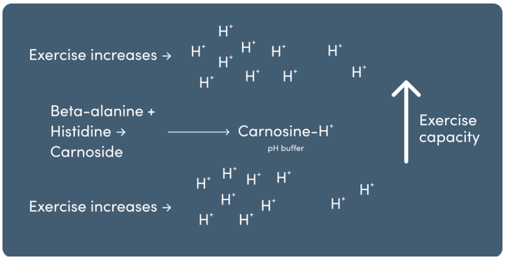
Table 5: Overview of popular ingredients in sports supplements

Ingredient	Main effects	Dose
Performance		
Beta-alanine	↑ anaerobic performance particularly within 30-second to 4-minute ranges	2 g 2-3x per day
Caffeine	↑ athletic performance ↑ aerobic performance ↑ anaerobic performance ↓ ratings of perceived exertion	3-6 mg/kg, 1 hour before exercise
Carbohydrate beverage	↑ aerobic performance via glycogen sparing for sustained ATP	6-12 oz of 6-8% carbohydrate beverage every 10-15 minutes during exercise
Citrulline malate & L-arginine	↑ anaerobic performance ↓ ratings of perceived exertion ↑ aerobic performance ↑ anaerobic performance	6-12 g, 1 hour before exercise 10-12 g, 1 hour before exercise
Creatine	↑ anaerobic performance and strength, especially for bouts of exertion 10 seconds-2 minutes	Initiation: 5 g, 4x per day for 5-7 days Maintenance: 3-5 g per day
Magnesium	↑ anaerobic performance	300-500 mg
Omega-3 fatty acids	↓ reaction time ↑ mood	3 g EPA+DHA in 2:1 ratio
Taurine	↑ aerobic performance	1-3 g, 1 hour before exercise

Body composition		
Whey protein	↑ muscle protein synthesis ↓ fat mass	20–40 g
HMB	↑ muscle mass in untrained athletes	1 g, 3x per day
Recovery and pain		
BCAAs	↓ post-exercise muscle soreness and oxidative damage	200 mg/kg, in a 2–3:1:1 ratio leucine:isoleucine:valine
Citrulline malate	↓ post-exercise muscle soreness	6–12 g, 1 hour before exercise
Curcumin	↓ exercise-related joint pain and improved recovery	180 mg Theracurmin® / 500 mg Meriva®
Magnesium	↓ inflammation and migraine headaches	300–500 mg
Omega-3 fatty acids	↓ post-exercise muscle soreness	3 g EPA+DHA in 2:1 ratio
Collagen	↓ exercise-related joint pain ↑ tendon & ligament repair	5–15 g per day
Immune support		
Vitamin C	↓ common cold risk, severity, and duration	1,000 mg per day
Vitamin D	↓ common cold risk	400–1,000 IU per day, though athletes may need 4,000–10,000 IU
Zinc	↓ common cold severity and duration	25 mg within 24 hours of onset, 2x per day for 6 days

Beta-alanine

Beta-alanine is a non-proteinogenic amino acid produced in the liver that can be found in poultry, fish, and red meat. It is commonly used to improve shorter bouts of high-intensity exercise by acting as a substrate to carnosine, an acid-buffering agent. (Ojeda 2020) (Trexler 2015)



Beta-alanine is the rate-limiting ingredient to form carnosine, which is particularly used in anaerobic metabolism that acts as a pH buffer, reducing acid (H+) buildup produced during high-intensity exercise when lactic acid dissociates to lactate. H+ buildup potentially leads to muscle fatigue by interfering with phosphocreatine resynthesis, muscle contraction, and glycolysis. (Hobson 2012)(Ojeda 2020) Therefore, reducing H+ may improve an individual's capacity to exercise. Beta-alanine supplementation can increase muscular carnosine levels by 23 to 28%. (Hoffman 2018) Its effects are primarily related to reducing muscle fatigue. (Zanella 2017)

Dosing and frequency

- 2 g 2-3 times per day for a minimum of 2-4 weeks to untrained or trained athletes (Trexler 2015)(Zanella 2017)

Effects on anaerobic performance

- Improves high-intensity anaerobic performance (Quesnele 2014) up to 3% (ranging up to 10%) compared to placebo with a small effect (ES = 0.374) (Hobson 2012)
  - 2x more effective for improving exercise capacity measures (e.g., time to exhaustion at max intensity exercise) than performance measures (e.g., time to a fixed endpoint such as a 400 m race), (Saunders 2017)
  - Effects were similar between trained and untrained individuals (Saunders 2017)
- Most effective for exercise bouts of 0.5-4 minutes, with positive but attenuating effects up to ten minutes (Hobson 2012) (Saunders 2017)
- Trivial effects were reported on reducing lactate concentrations and ratings of perceived exertion, as well as improving VO2max (Ojeda 2020)

Side effects

Supplementation can cause harmless sensations of tingling or prickling (~9x vs. placebo). (Dolan 2019) Side effects can be reduced when using smaller divided doses (0.8 to 1.6 g every three to four hours) and with sustained-release formulations. (Hobson 2012)(Saunders 2017) Tingling typically disappears within one to 1.5 hours. (Hoffman 2018)

Caffeine

Caffeine is one of the most widely used ingredients to boost both physical and mental performance, and it is widely available in capsule or tablet supplement form as well as a variety of products including coffee, tea, energy drinks, and pre-workout supplements. Caffeine appears to be equally and near perfectly (100%) absorbed across populations, (Guest 2021) but may affect individuals differently due to individual genetic variations in the CYP1A2 metabolic enzyme, primarily responsible for metabolizing caffeine, leading to either prolonged or reduced caffeine exposure. (Yang 2010)

Caffeine may produce its effects through a number of mechanisms. A previous popular hypothesis was that caffeine enhances free-fatty acid oxidation, which could spare glycogen stores and ultimately improve performance, but this has since been disproven. Now, the proposed mechanisms mainly centre on caffeine's ability to reduce the rate of perceived exertion (RPE) and muscular pain as well as increase muscular contraction force particularly via interaction with the central nervous system. By antagonizing adenosine receptors, caffeine may reduce the calming effects of adenosine. It may also mitigate pain perception, as well as increase neurotransmission (serotonin, dopamine, acetylcholine, norepinephrine, and glutamate) and rates of motor neuron action. While caffeine has been primarily shown to provide benefits for endurance sports, there may also be benefits for strength and power-based exercise. However, with all three forms of exercise, a balance between the stimulatory effects and the potential adverse effects, which may mitigate performance improvements, needs to be established with the individual. (Guest 2021)

Dosing and frequency

- 3-6 mg/kg body weight to trained or untrained individuals approximately 60 minutes before exercise performance (Ganio 2009)(Guest 2021)(Polito 2016)(Southward 2018)

Note: WADA has removed caffeine as a controlled substance but still monitors upper urinary limits of 12 μg/ml, which occurs with ingestion of ~10 mg/kg body weight (this is 3x more than the amount of caffeine need to improve performance). The NCAA allows upper limits of 15 μg/ml. (Guest 2021)

Effects on athletic performance

- Improved performance in any exercise modality by an average of 11%, potentially mediated by a reduced RPE of 5.6% compared to placebo (Doherty 2005)
- Regardless of exercise type, the benefits of caffeine appear to be most beneficial when the athlete is beginning to fatigue. (Guest 2021)

Effects on aerobic performance

- Improved cardiovascular endurance performance ~3% (small effect; 0.22)(Ganio 2009)(Southward 2018) and time trials ~2% (small effect; 0.28-0.45)(Ganio 2009)(Goncalves 2017)(Southward 2018)
    - The longer the endurance event, the greater the effect size, but this can range widely between athletes (i.e., -3-15.9%). (Shen 2019)

Effects on anaerobic exercise performance

- Improved muscular endurance with a small effect by ~18% (SMD = 0.27–0.38) (Polito 2016) (Warren 2010) and strength with a small effect of ~5–7% (SMD = 0.16–0.37)(Grgic 2019)(Grgic 2018)(Warren 2010)
  - Effects on strength may be attributed to increased muscle activation (Warren 2010)
- Improved muscular power with a small effect as measured by improved jump heights (SMD = 0.17–0.29), (Grgic 2018) sprints (SMD = 0.14–0.16), time to complete agility tests (SMD = 0.41), (Salinero 2019) or Wingate tests (SMD = 0.18–0.27; ~3–4%) (Grgic 2018)

Side effects

When consumed in daily amounts of up to 300 mg in pregnant women or 400 mg in healthy adults, there does not appear to be a risk of significant health effects. Similar safety profiles exist for children and adolescents consuming 2.5 mg/kg body weight per day. However, doses of 10 g can be lethal to an adult. (Wikoff 2017) Nonetheless, the most commonly reported dose-dependent adverse effects of caffeine include insomnia, feelings of restlessness or anxiety, tachycardia, and headaches. (Guest 2021)

Citrulline and arginine

Several kinds of supplements are marketed to improve aerobic and anaerobic performance by increasing nitric oxide (NO) synthesis. Two predominant NO precursor ingredients are L-arginine and L-citrulline, which have received much attention for their potential to improve aerobic and anaerobic performance. (Gonzalez 2020) L-arginine is a non-essential amino acid found in seafood, watermelon, nuts, seeds, algae, meat, and rice and soy proteins. Daily consumption typically ranges between 4 to 5 g per day. (Bescos 2012) Arginine can also be endogenously produced by L-citrulline (~80% conversion), another non-essential amino acid, whose name comes from the latin word for watermelon, *Citrullus*. Citrulline is commonly found in watermelon, other melons, and cucumber. (Bescos 2012) (Gonzalez 2020) Ingestion of L-citrulline may potentially yield greater NO production than observed with L-arginine, as it may not undergo the same extent of intestinal and hepatic metabolism. (Gonzalez 2020) Once absorbed, L-citrulline is converted to L-arginine, which is subsequently used to synthesize NO. (Speer 2020) L-citrulline and L-arginine's most commonly known mechanism of action relates to the vasodilatory effects of increased NO production (with inconsistent evidence), (Gonzalez 2020) but NO may also upregulate angiogenesis, mitochondrial respiration and biogenesis, and glucose and calcium regulation, potentially leading to improved muscular contraction, fatigue resistance, and exercise performance. (Jones 2014)(Jones 2018) Ultimately, increased NO availability from L-citrulline or L-arginine supplementation may improve muscular contraction, fatigue resistance, and exercise performance. (Jones 2014)(Jones 2018)

Dosing and frequency

L-arginine:

- Acute: 10-12 g ingested 1-1.5 hours before exercise
- Chronic: 1.5-2 g per day for at least 4-7 weeks (aerobic), or 10-12 g per day for at least eight weeks (anaerobic) (Viribay 2020)

L-citrulline:

- Acute: 6-12 g ingested 40-60 minutes before exercise (Trexler 2019)(Varvik 2021)
- Chronic: 6-12 g (most frequently 8 g as citrulline malate; 2:1 ratio of citrulline to malate produces 3-6 g of L-citrulline) per day for at least seven days ingested 1-1.5 hours before exercise (Gonzalez 2020)(Rhim 2020)

Effects on aerobic and anaerobic performance

- L-arginine has been shown to improve aerobic performance with a large effect (SMD = 0.84) and anaerobic performance with small effect. (SMD = 0.24). (Viribay 2020)
    - However, a body of evidence does not support oral ingestion of L-arginine for a performance benefit, especially when compared to L-citrulline. (Brooks 2016) (Gonzalez 2020)(Ojeda 2019)
- L-citrulline produced a small effect (SMD = 0.2) on anaerobic high-intensity exercise (e.g., resistance training or sprints of 30 seconds or less) in healthy adults. (Trexler 2019)

- L-citrulline increased the number of performed reps (by ~3 or ~6%) during strength training. (Varvik 2021)
- L-citrulline malate may reduce the rate of perceived exertion with a moderate effect (SMD = 0.44). (Rhim 2020)
- L-citrulline may provide benefits to muscle mass, strength, and physical performance (walking speed), particularly when paired with exercise in older populations. (Aubertin-Leheudre 2020)

Effects on exercise recovery

- L-citrulline may reduce muscle soreness between 24-48 hours post exercise with large effects (SMD = 0.99 and 1.06, respectively). No significant effect on blood lactate levels was observed. (Rhim 2020)
- Systematic reviews indicate that L-citrulline can provide benefits to exercise performance via reductions in perceived rate of exertion, muscle soreness, and blood lactate levels. (Gonzalez 2020)(Ojeda 2019)

Side effects

Most studies do not report adverse effects, and L-citrulline is well tolerated. Up to a 15 g dose of L-citrulline can be ingested without inducing side effects, though individual studies have reported that approximately 15% of users may experience gastrointestinal discomfort. (Gonzalez 2020)(Rhim 2020) L-arginine may be ingested in doses up to 20 g per day without serious adverse effects. (McNeal 2016) Please note that L-arginine may reduce blood pressure, (Dong 2011) and caution is advised for those already taking anti-hypertensive medication.

Creatine

Creatine is a nitrogenous compound found in skeletal muscle and used for short-term energy production. Creatine is found in the body in quantities between 120 to 140 g in the average 70 kg person, (Bemben 2005) and between 1 to 3 g per day are eliminated from the body. (Kreider 2017) Approximately half of excreted creatine is replenished via diet and half is resynthesized. (Brosnan 2016) 1 lb of uncooked beef or salmon may contain 1 to 2 g of creatine. (Balsom 1994) The liver and kidneys synthesize creatine from arginine and glycine using S-adenosylmethionine. Approximately two-thirds of intramuscular creatine is phosphocreatine (PCr), with the remaining third being free creatine (Kreider 2017). PCr and creatine stores may be increased by creatine supplementation by 10 to 40% and 10 to 30%, respectively. (Butts 2018)

By boosting creatine and PCr stores, creatine supplementation can improve the rate of adenosine triphosphate (ATP) production as PCr is rapidly rephosphorylated from adenosine diphosphate (ADP) to ATP by the Cr kinase reaction during repeated muscle contraction. Skeletal muscle cells store enough ATP and PCr for ten seconds of high-intensity activity. (Butts 2018) Creatine also shortens relaxation time during intermittent maximal isometric contraction by increasing calcium uptake by the sarcoplasmic reticulum. (Bemben 2005)

Dosing and frequency

- Loading phase of 0.3 g/kg body weight or 5 g four times daily for 5-7 days, followed by a maintenance phase of 3-5 g per day ongoing (Kreider 2017)
- Alternatively, 3 g per day ongoing; however, ergogenic effects may not manifest until towards the end of the first 28 days (Kreider 2017)

Effects on anaerobic performance

- Generally, high-intensity and/or repetitive exercise performance is increased by 10-20%. (Kreider 2017)
- Meta-analyses on both upper (Lanhers 2017) and lower (Lanhers 2015) limb performance showed small strength benefits (effect size = 0.235-0.317), with the largest being on the pectoralis major and minor for the bench press (5.3%). (Lanhers 2017)
- Effective for bouts of exertion 1-10 seconds long, with rest periods of 30 seconds to five minutes; (Bemben 2005)(Butts 2018) also helpful for continuous bouts of exertion between ten seconds and two minutes. (Bemben 2005)

- Likely no differences in effect size based on age, sex, and training status (Lanhers 2017)
- Also note that there is insufficient evidence to suggest that other forms of creatine (beyond creatine monohydrate, such as creatine HCl) have superior absorption of effectiveness (Jäger 2011)

Side effects

Robust evidence shows a small increase in body mass (possibly due to increased water retention from hyper-hydration of the muscle) (Kreider 2017) following creatine supplementation during the loading phase (0.26 kg), which tends to disappear during the maintenance phase. (Branch 2003) Despite this mass gain, there is no high-quality evidence supporting the ergolytic effects of creatine even in endurance athletes, which may be attributed to creatine's other benefits (e.g., muscle hydration, heat tolerance, enhanced recovery) (Kreider 2017). One of the longest studies of high-dose creatine supplementation (up to 30 g per day for five years) has shown no detrimental effects in healthy individuals. (Bender 2016) Additionally, there is no compelling evidence that creatine supplementation negatively affects kidney function in healthy or clinical populations. (Kreider 2017)

Taurine

The sulfur-containing amino acid taurine is a popular ingredient in energy drinks. It is a major amino acid in mammals, comprising 50 to 60% of the free amino acid pool, and is readily found in meat and seafood. (Huxtable 1992) Taurine is derived from methionine and cysteine (Sankararaman 2018) and is dependent on enzymes such as methyl-tetrahydrofolate reductase (MTHFR) for its synthesis. (Thirupathi 2020) Taurine may improve handling of calcium in the sarcoplasmic reticulum in both cardiac and skeletal muscle cells. (Dutka 2014) It may also assist with ATP turnover by stabilizing the mitochondrial matrix via its antioxidative properties. (Hansen 2006) Additionally, taurine may increase lipolysis and decrease the contribution of glycolytic mechanisms, thereby improving metabolic efficiency in endurance exercise. (De Carvalho 2018) Taurine is quickly absorbed, and blood levels return to baseline within six to eight hours after ingestion. (Ghandforoush-Sattari 2010)

Dosing and frequency

- 1-3 g once per day, (Kurtz 2021)(Waldron 2018) with an upper limit of 10 g (Shao 2008)

Effects on aerobic exercise and performance

- A meta-analysis examining exercise performance found a small benefit (Hedges' g = 0.40) of 1-6 g on endurance exercise performance, with no benefit on time trial speed and a borderline lack of benefit on sprint performance. (Waldron 2018)

    - One of the trials with a higher effect size found an 8.1% increase in time to exhaustion on treadmill running at 75% VO2max; however, this trial only included six subjects. (Lee 2003)
- A meta-analysis on the effects of taurine combined with caffeine (a combination often found in commercial energy drinks) found that higher doses of taurine in the range examined (0.07–3.1 g) tended to demonstrate stronger performance effects. (Souza 2017)
    - Both endurance and strength exercise performance was significantly improved.
    - There was no significant difference in sprinting performance.
- A 2021 systematic review found 1–3 g had the strongest effects on aerobic endurance exercise, with mixed results for reducing muscle soreness and improving strength and anaerobic exercise performance. (Kurtz 2021)

Side effects

As taurine is an amino acid, regular ingestion on training and non-training days or seasons shows no ill effects. (De Luca 2015) On its own (as opposed to in combination with caffeine in energy drinks), it is unlikely to have any negative effects. (Gurley 2014)

Branched-chain amino acids

BCAAs include the three essential amino acids leucine, isoleucine, and valine, which are involved in MPS. BCAAs are some of the few amino acids metabolized in skeletal muscle (as opposed to the liver). (Fouré 2017) Marketing-driven performance-enhancing claims of BCAAs center on maximizing anabolism and minimizing catabolism from exercise. (Wolfe 2017) BCAAs and especially leucine have been reported to activate mTOR, thereby promoting MPS, (Fouré 2017) though there is controversy around these claims. (Wolfe 2017) Beyond their musculoskeletal effects, BCAAs may also promote and maintain higher levels of glutamine, which may reduce the immune suppression observed after the end of exercise. (Cruzat 2014)

Dosing and frequency

- ~200 mg/kg per day (i.e., 14 g for a 70 kg individual) for 3-10 days (Fouré 2017)
- 2-3:1:1 ratio of leucine:isoleucine:valine (Salinas-Garcia 2014)

Effects on MPS

- Increasing leucine through BCAA supplementation may be an important factor in increasing MPS; (Jäger 2017) however, a higher total dose of all essential amino acids may better sustain increased rates of MPS. (Churchward-Venne 2012)
- The availability of other EAAs may be the rate limiting step for accelerated MPS, (Wolfe 2017) as several trials have reported decreases, rather than increases, in MPS after supplementation of BCAAs; (Wolfe 2017) this has led to doubts of the claim that BCAA supplementation increases MPS.
- One trial aimed to determine why BCAAs may be ineffective for MPS stimulation using two groups. Both groups were given 6 g of whey protein and 5 g of leucine. The second group was also given a BCAA supplement. The first group was found to have the highest MPS, possibly due to oversaturation of the BCAA transporters with isoleucine and valine, reducing the amount of leucine able to be transported into the cell and, therefore, MPS. (Churchward-Venne 2014)

Effects on recovery

- BCAAs have been postulated to improve recovery since they have been shown to reduce markers of oxidative damage and muscle soreness.
    - A 2017 systematic review found that BCAA supplementation may reduce skeletal muscle damage markers when muscle damage was low-to-moderate, the BCAA daily intake was high (over 200 mg/kg body weight) and prolonged (greater than ten days), and the BCAAs were taken prior to exercise. (Fouré 2017)
    - A 2021 meta-analysis showed that BCAA supplementation reduced creatinine kinase levels but not plasma lactate dehydrogenase, two markers indicative of muscle damage and soreness, after resistance exercise in trained males. (Khemtong 2021)

- BCAAs may reduce delayed-onset muscle soreness with a moderate effect (effect size = 0.73), particularly within 48 hours post exercise, according to a 2019 meta-analysis. (Fedewa 2019)

- Even though BCAAs tend to improve oxidative damage and muscle soreness as noted above, most research shows no effect on performance explicitly; BCAAs failed to improve measures of aerobic performance and strength, running times in a marathon, (Areces 2014) and vertical jump distance. (Howatson 2012)

Side effects

No adverse effects of BCAA supplementation were noted, (Fouré 2017) (Wolfe 2017) which is consistent with the fact that BCAAs are simply a small source of protein in the diet.

Beta-hydroxy-beta-methylbutyrate

Beta-hydroxy-beta-methylbutyrate (HMB) is a metabolite of the BCAA leucine. Leucine has been studied for its role as a stimulator of MPS and blocker of protein breakdown. (Wilson 2013) Leucine acts to prevent breakdown of protein maximally at concentrations ten to 20 times the concentration of leucine that maximally stimulates MPS, so it has been hypothesized that a metabolite of leucine may be more likely to be involved with maximizing the inhibition of protein breakdown. (Wilson 2013) HMB has shown promise in decreasing skeletal muscle degradation both in vitro and in vivo (Eley 2007)(Holecek 2009). Though HMB can be acquired from protein ingestion, in order to yield 3 g of HMB, one would need to consume approximately 600 g of high-quality protein (yielding approximately 60 g of leucine). (Wilson 2013) Thus, to most efficiently capitalize on HMB's potential benefits for blocking muscle protein degradation, supplementation with isolated HMB may be more convenient.

HMB may have several mechanisms of action as it may decrease inflammatory markers (i.e., TNF-a and IL-6), (Vandenburgh 2009) stimulate mTOR, (Pimentel 2011) increase expression of IGF-1, (Townsend 2015) and increase growth hormone production. (Gerlinger-Romero 2011) There are mixed results as to whether or not HMB ultimately improves MPS or performance markers, however. (Kerksick 2018) In addition, HMB has other metabolic functions, as it may metabolize carbohydrates and fats. (Bruckbauer 2012)(Sun 2009)

Dosing and frequency

- 3 g per day orally for 3–12 weeks (Kerksick 2018) may benefit untrained and elderly subjects.
  - 3 g appears to have additional benefit compared to 1.5 g, while 6 g does not appear to have any additional benefit. (Gallagher 2000)

- Optimal results may be achieved when taken as 1 g three times per day. (Vukovich 2001)

Effects on body composition

- Increased muscle mass among untrained and elderly subjects by an additional 0.5-1 kg versus controls (Kerksick 2018)
- Trained athletes supplementing with HMB may have reductions in fat mass, (Durkalec-Michalski 2015)(Durkalec-Michalski 2016)(Durkalec-Michalski 2017) though there are mixed results on whether trained athletes tend to gain muscle mass. (Kerksick 2018) Longer training periods (over six weeks) and periodization may increase the likelihood of lean mass gain. (Wilson 2013)

Effects on strength

- A 2018 meta-analysis on trained athletes showed a lack of an effect of HMB on bench press strength, leg press strength, body mass, fat-free mass, and fat mass. (Sanchez-Martinez 2018)
- A 2019 meta-analysis on untrained subjects aged 50-80 only showed a small borderline statistically significant effect on handgrip strength (ES=0.19, p=0.06), with no effects found on leg strength, muscle mass, or fat mass. (Courel-Ibáñez 2019)

Side effects

Doses up to 6 g per day have been well tolerated with no adverse effects. (Wilson 2013)(Gallagher 2000)

Epigallocatechin-3-gallate

Epigallocatechin-3-gallate (EGCG) is the major polyphenol and catechin in green tea (*Camellia sinensis*) leaves (Kapoor 2017) and has been found to improve endurance capacity and fat oxidation in rodent studies. (Murase 2005) The catechin EGCG is thought to stimulate fat oxidation by directly inhibiting catechol-O-methyltransferase, a norepinephrine-degrading enzyme. An ensuing increased concentration of catecholamines is believed to increase fatty acid mobilization and oxidation. (Jeukendrup 2011) Therefore, the majority of the research focusing on the benefits of EGCG in athletes tends to be on improving fat metabolism to increase aerobic performance, though these effects tend to be non-significant in humans. (Kapoor 2017)

Dosing and frequency

- 300 mg per day (Camfield 2014)

Effects on fat metabolism and aerobic performance

- A 2017 meta-analysis of EGCG on energy expenditure (EE) and fat oxidation (FO) showed a moderate acceleration of EE (300 mg), with no significant improvement of FO. (Kapoor 2017)
- Fat and glycogen oxidation rates did not differ with 270 mg of EGCG vs. placebo in cyclists and led to no improvements in aerobic performance over three different bouts of ~two hours of ~60% VO2max cycling. (Dean 2009)

Effects on weight loss and hunger

- A 2018 meta-analysis of green tea showed no significant effect on the hunger hormones leptin and ghrelin. (Haghighatdoost 2018)
- A 2009 meta-analysis of green tea on weight loss and weight maintenance showed a small (~ 1.31kg) effect of catechins such as EGCG. However, this was only seen in those who had habitual caffeine intake (>300 mg per day) and Asian ethnicity. (Hursel 2009)

Effects on resistance training

- 900 mg EGCG did not improve markers of skeletal muscle damage compared to placebo in subjects undergoing unaccustomed lower body resistance training. (Kerksick 2013)

Effects on cognition

- A 2016 meta-analysis of cognitive function and mood showed that EGCG failed to affect alertness ratings or improve rapid visual information processing, but may moderately increase calmness (300 mg), though there is limited data of EGCG use in isolation. (Camfield 2014)

Side effects

No consistent side effects of EGCG are noted at daily doses of 300 mg. (Hill 2007) Doses of up to 900 mg for 14 days showed no adverse outcomes. (Kerksick 2013) EGCG supplements may contain caffeine, however, which may have adverse effects if dosed above 400 mg per day in healthy adults. (Wikoff 2017)

Additional supplement considerations for athletes

As previously mentioned, many other dietary supplements are marketed to athletes for purposes that extend beyond the classic ergogenic aid definitions. Examples include supplements that help to reduce pain and inflammation or support immune function. A few ingredients with these applications in the athlete population are detailed below.

Pain and inflammation

During and especially after athletic activity, the body has a number of responses in order to help it recover and adapt. Many of these responses involve some level of local inflammation and muscle soreness that peaks within 24 to 48 hours after the exercise (i.e., DOMS). These processes may contribute to various functional deficits such as reduced strength and/or range of motion. (Davis 2007) Ingredients such as curcumin, omega-3 fatty acids, and magnesium are all gaining in popularity for their possible effects on reducing post-exercise pain and inflammation.

Curcumin

Curcumin is the main polyphenol found in turmeric (*Curcuma longa*), a yellow-colored herb from the ginger (Zingiberaceae) family. In addition to its anti-inflammatory properties, it may also have benefits for cardiovascular health, (Li 2020) gastrointestinal health, (Ghosh 2018) and psychological stress during training. (Suhett 2021)

Curcumin may improve athletic performance by reducing inflammation, (Davis 2007) supporting mitochondrial biogenesis, (Hamadie 2015) and reducing oxidative stress (Kawanishi 2013)

The evidence that curcumin is a good anti-inflammatory supplement for athletes is strong; two recent systematic reviews showed that curcumin reduced inflammatory markers (TNF-α, IL-6, IL-8, and IL-10), decreased pain and muscle damage (creatinine kinase levels), and led to superior recovery and muscle performance (i.e., quicker reduction of DOMS scores and subsequent restoration of muscle strength) in athletes. (Fang 2020)(Suhett 2021)

Dosing for curcumin supplementation for athletes varies widely based on the specific product extracts, ranging from 180 mg per day of Theracurmin® to 500 mg per day of Meriva® to 6,000 mg of less common formulations. (Suhett 2021) Curcumin is recognized by the U.S. Food and Drug Administration as "Generally Recognized as Safe." (Gupta 2013). A 2016 meta analysis examined the use of curcumin supplementation for pain relief and reported the following side effects in eight randomized controlled trials: gastrointestinal disturbances (dyspepsia, abdominal pain/distention, nausea/vomiting, loose stool), fever, pitting edema, and throat infection. All side effects were reported as mild, and none were responsible for withdrawal from the studies. (Sahebkar 2016)

Omega-3 fatty acids

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are the most important primary long-chain polyunsaturated omega-3 fatty acids found in fish oil. (Calder 2018) EPA may have anti-inflammatory effects through inhibition of cyclooxygenase-2 expression and metabolism of arachidonic acid. (Calder 2017) EPA and DHA are precursors to the "5-series" leukotrienes, protectins, and maresins, each of which possess unique anti-inflammatory actions. (Calder 2017) They may also improve nitric oxide production (Walser 2008) and lipid peroxidation. (Lewis 2020)

Dosing for EPA and/or DHA in athletes ranges up to 5 g each, with doses around 3 g and ratios of EPA to DHA of 2:1 tending to have more favourable results. (Ochi 2018) A 2020 review found that trials with positive outcomes such as improved recovery, reduced injury risk, and reduced illness risk tended to have a dose of over 2 g EPA+DHA, a duration over eight weeks, and study populations of untrained (vs. trained) participants. (Thielecke 2020) A 2020 systematic review of studies in athletes also showed that four out of the five included RCTs demonstrated consistent benefit of fish oil supplementation for reducing the inflammatory markers IL-6 and TNF-a, muscle soreness, and creatine kinase levels. Mixed results were noted on anaerobic endurance and sport performance. Improvements were noted in VO2 max in cyclists, yet no improvements were observed in endurance performance (time trials) or muscle force.

EPA and DHA might decrease post-exercise muscle soreness and improve range of motion. A systematic review noted a reduction of delayed onset muscle soreness in six of 12 trials and a lessened range of motion deficit after exercise in three of five trials. They also found interesting findings worthy of further exploration, including lessened muscle strength deficit after exercise in two of six trials and a reduction of swelling in the muscle in one of five trials. Results were mixed but generally found no effect on MPS. (Ochi 2018)

Supplementary n-3 fatty acids appear to have a low risk of adverse effects, as only one of five randomized controlled trials in a systematic review (Lewis 2020) reported adverse effects, noting poor palatability, gastrointestinal distress, and nausea in 10% of participants. (Oliver 2016) High n-3 consumption may prolong bleeding time; (Meydani 1991) however, the FDA has recognized that intakes of up to 3 g per day of omega-3 fatty acids is generally recognized as safe in humans, even with regards to claims on bleeding tendencies. (US FDA 2004)

Magnesium

Magnesium is an essential micronutrient and a cofactor for over 325 enzymatic reactions involved in cellular metabolism. (Newhouse 2000) Major dietary sources of magnesium are leafy green vegetables, seafood, nuts, and seeds. (Newhouse 2000) It has important roles in protein synthesis, cellular energy production and storage, and cell growth and reproduction. (NIH 2015)(Volpe 2015) Due to these roles, it has been proposed that magnesium may improve fitness in athletes.

Athletes may be at greater risk of magnesium deficiency. Approximately 60% of athletes were reported to consume less magnesium than the estimated average requirement, (Wierniuk 2013) compared to about 20% of the general population averages, (DiNicolantonio 2018) which may be a result of magnesium depletions associated with higher intensity exercise. (Molina-López, 2012)

Overall, the benefits of magnesium supplementation for athletes yields mixed results. However, a 2019 systematic review found beneficial effects of magnesium supplementation on strength measures (e.g., standing long jump and one-repetition maximums) and exercise-induced inflammation, DNA damage, cortisol and immunological blood markers when provided in doses of 300 to 500 mg per day. (Heffernan 2019) Long-term (over seven weeks) magnesium supplementation failed to consistently show beneficial effects in athletic populations, except in improving training-induced adaptive responses in young untrained athletes. (Heffernan 2019) Magnesium has been examined in non-athletes for other pain- and inflammatory-related conditions such as muscle cramps and migraine headaches. Magnesium supplementation has been shown to effectively reduce migraine intensity and frequency. (Veronese 2020) The evidence for prophylactic magnesium supplementation for leg cramps is weak, (Garrison 2012) though the studied populations were primarily older adults and pregnant women, so further research in athletes is warranted.

Adverse effects of magnesium supplementation are not commonly noted in research; (Newhouse 2000) however, the Lowest Observed Adverse Effect Level set by the Institute of Medicine for magnesium supplementation is 360 mg per day. Doses at or above this dose were noted to potentially contribute to diarrhea via an osmotic effect. (IOM 1997)

Immune support

Exercise may have adverse impacts on immune function, (Gleeson 2013) such as increasing the risk of upper respiratory tract infections (URTI) such as the common cold, (Simpson 2015) which may disrupt training and cause underperformance and even withdrawal from competition. (Gleeson 2015) Therefore, supplements commonly marketed to improve immune function may be worth consideration in athletic populations. Identified below are immune supplements with pertinent evidence for athletes, though there are many other herbs and nutrients that have immune benefit claims.

Zinc

Zinc is an essential trace mineral that has several functions in energy metabolism and antioxidation. (Chu 2018) The highest dietary sources of zinc include seafood and meat. (NIH 2021) Zinc is widely noted for its role in the immune system and also plays a role in supporting the cardiovascular system, (Chu 2018) testosterone levels, and muscular strength. (Kerksick 2018) Zinc has been found to be metabolically depleted by exercise (Chu 2016) and sweating. (DeRuisseau 2002) Athletes have been shown to have low levels of serum zinc, even though their intake is generally higher than controls. (Chu 2018)

A 2011 Cochrane review found that zinc reduced the duration and severity of the common cold when supplemented within 24 hours of onset in the general population. (Singh 2011) In athletes, 25 mg of zinc supplementation (and 2.5 mg copper) twice per day blunted the surge in oxidant and immune markers post exercise for high-intensity exercise (i.e., 75% of VO2max until exhaustion over hours) compared to a placebo. (Singh 1994)

Zinc supplementation may be unpalatable (if given as lozenges) and/or may result in nausea. (Singh 2011) The Tolerable Upper Intake Level (UL) set by the National Institutes of Health for zinc is 40 mg per day for adults. (NIH 2021) Prolonged intake above this level may increase the risk of adverse health effects such as low copper status, altered iron function, reduced immune function, and reduced high-density lipoprotein. (Hooper 1980)

Vitamin C

Vitamin C is a water-soluble micronutrient that is found in high concentrations in colorful fruits and vegetables. (Senturk 2005) It primarily acts as an antioxidant that counteracts reactive oxygen species (ROS) and supports immune function. (Gleeson 2015) Vitamin C is involved in collagen synthesis. (DePhillipo 2018) It may also reduce cortisol and act as an anti-inflammatory, as it reduces IL-6. (Gleeson 2015)

The recommended intake of vitamin C is 75 and 90 mg per day for females and males, respectively. (NIH 2021) This recommendation is based on the needs of non-active individuals, and may not be appropriate for athletes. Vitamin C intake closer to 200 mg is likely to maintain vitamin C concentrations in immune cells, which may maximize its functions as stated above. (Levine 1999) In order to decrease ROS, even higher intakes between 200 to 1,000 mg may be required. (Braakhuis 2012)

It should be noted, however, that sports performance may be impaired with excessive vitamin C intake. A 2012 review noted impaired performance when intakes were over 1,000 mg. This may have been due to an overt reduction in ROS, preventing the mitochondrial biogenesis-signalling function of ROS in muscle cells, leading to reduced mitochondrial metabolism and, therefore, athletic performance. (Braakhuis 2012)

Overall, if vitamin C supplementation is excessive and a subject does not have significant sources of oxidation from exercise stress or other stress, vitamin C supplementation may reduce their exercise-related training adaptations (i.e., performance). (Merry 2016) There is no convincing evidence demonstrating that vitamin C supplementation improves exercise-training adaptations, (Merry 2016) nor improves muscle strength and function in general. (Dutra 2020)(Higgins 2020)

However, vitamin C's beneficial effects on the immune system may help prevent interruptions in training caused by being sick. As such, the provision of vitamin C to support an athlete's immune system may be an important consideration to maintain strict training schedules. A Cochrane meta-analysis on prophylactic daily doses of vitamin C above 200 mg found a borderline lack of benefit (RR=0.97; 95% confidence interval [CI] 0.94 to 1.00) in general community trials (n=10,708) for reducing incidence of the common cold, whereas trials of vitamin C supplementation involving marathon runners, skiers, and soldiers on subarctic exercises (n=598) yielded a reduced incidence of the common cold by half (RR=0.48, 95% CI 0.35 to 0.64). Furthermore, in general community trials, both common cold duration (8%) and severity was significantly reduced. (Douglas 2007)

The UL set by the National Institutes of Health for vitamin C is 2,000 mg per day. The most common adverse effects of vitamin C include diarrhea, nausea, abdominal cramps, and other gastrointestinal disturbances from an osmotic effect due to unabsorbed vitamin C. (NIH 2021)

Vitamin D

Vitamin D is an essential fat-soluble vitamin and hormone that has two different forms: vitamin D2 (ergocalciferol; from plants) and vitamin D3 (cholecalciferol; from cold-water fish and sunlight). (Thacher 2011) In addition to regulating bone development and growth via increased absorption of calcium, (Thacher 2011) vitamin D metabolites regulate immune function and protein synthesis. (Ceglia 2009) (Heaney 2008)

There is mixed evidence with regards to vitamin D's effect on athletic performance. Three different meta-analyses from 2017 through 2019 had different results. Chiang et al found that doses of vitamin D3 (D2 was ineffective) ranging from 2,000 to 5,000 IU per day reliably improved strength measures, such as one-repetition max on bench press, squat, and leg press compared to placebo, with effect sizes ranging from 1.4 to 19%. Supplementation generally raised athletes' vitamin D blood levels to 40 ng/mL. (Chiang 2017) In comparison, Farrokhyar et al found no significant effect on strength or performance, though they did note potential relation to increased injuries with lower vitamin D blood levels. (Farrokhyar 2017) Finally, Han et al also found no significant effect on strength or performance, though quadriceps strength improved with a very large effect (SMD=2.14;

95% CI=0.59-4.87), although not statistically significant (p=0.12). (Han 2019)

With regards to effects on the immune system, a 2021 meta-analysis of non-athletes examined 1,528 articles for 46 eligible randomized controlled trials (sample size of 75,541) and concluded that vitamin D, given at a daily dose between 400 to 1,000 IU, safely reduced the risk of acute respiratory infections (ARIs) by 8%. (Jolliffe 2021) Grant et al examined athletes and noted reductions of ARIs when they were able to achieve blood levels over 40 ng/mL; however, higher vitamin D intakes were required (4,000 to 10,000 IU per day, depending on body size, skin pigmentation, and other personal factors) in order to achieve these levels compared to sedentary individuals. (Grant 2020)

Vitamin D typically has few adverse effects, with the most severe being hypercalcemia. (Grant 2020) However, in a study involving 20,308 measurements of vitamin D blood levels over ten years, only one clinical case of toxicity was associated with hypercalcemia and that subject had a blood level of 364 ng/mL. She was reported as taking 50,000 IU of vitamin D and 3,000 mg of calcium, one to four times per day for over three months. (Dudenkov 2015)

Quality considerations for sports supplements

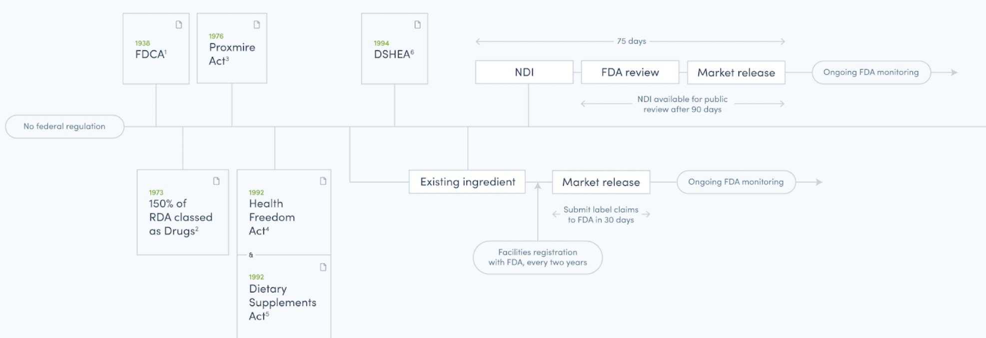
One of the most controversial topics in sports nutrition is related to the safety and transparency of using supplements, particularly in regulated high-performance sports. The dietary supplement industry has been criticized for a lack of regulatory control over products that are available on the market, particularly in the United States. (Marcus 2016)

The regulatory environment

On a high level, the FDA regulates dietary supplements under the Dietary Supplement Health and Education Act of 1994 (DSHEA). This legislation requires supplement companies to ensure the safety, efficacy, and transparency in the labeling and marketing of their products, but it does not require that companies acquire FDA approval prior to market release unless the product contains a new dietary ingredient (NDI) not previously available on the market before 1994. (FDA 2021)

Ingredient approval process

An overview of the approval process in the United States for both existing ingredients and new dietary ingredients (NDI).



1 Supplements are classified as drugs 2 Supplements containing 150% RDA classified as drugs 3 No limit to RDA on supplements – classified as food additives and subject to pre-market approval if not GRAS 4 Herbs as supplements
5 1-year moratorium on nutrient content, health and label claims 6 Supplements classified under foods – ingredients exisiting in food systems grandfathered into market without need for premarket approval, NDIs require approval

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The post-market regulatory environment has been widely criticized as being insufficient for ensuring that dietary supplement companies are held to high-quality standards prior to market release. As a result, consumers may be exposed to supplements that are cross-contaminated (intentionally or not) with ingredients or metabolites that are not listed on product labels or may not accurately reflect the strength of the ingredients within the supplements. (Walpurgis 2020) In a global context, it has been estimated that between 14 to 18% of dietary supplements are adulterated (Eichner 2016) (i.e., products may contain a lack of the ingredients specified on the label or may contain alternative ingredients not specified on the label). (Cohen 2018)

The sports nutrition segment may be under particular scrutiny due to high-profile stories in the media of elite athletes being disqualified from competition and the revokal of athletic accolades and corporate sponsorships due to positive doping tests caused by contaminated dietary supplements. (Chan 2016)(Maughan 2018)(Walpurgis 2020) Whether or not individuals are exposed to contaminated or mislabelled supplements or athletes are found guilty of (un)intentional doping, a lack of education of dietary supplement regulations may contribute to issues of product safety and potentially adverse effects.

U.S. consumers are often not aware that supplements do not need to be approved by the FDA, that they do not need to have been tested for safety, efficacy, and identity, and that known adverse effects are not required to be detailed to the consumers prior to market release. (Dodge 2016) It also appears that U.S. athletes may be most frequently acquiring information about dietary supplements from a number of sources, particularly coaches and trainers (50%) or friends and family (31%), and it is less common for practitioners to be utilized as a primary source of information. (Denham 2017)

Acquiring education about dietary supplements from reputable and knowledgeable sources and advocating for increased industry transparency is thus crucial for the safe and efficacious use of sports supplements. In fact, industry reports highlight that there is a growing awareness of the importance of label transparency and engagement with third-party certification companies to provide continued value to dietary supplement consumers. (Grand View Research 2020) Additionally, 88% of consumers have indicated that they would be willing to pay more for supplements from more transparent companies, (Pure Branding Report 2018) thus carving out a possibility for distinction between brands that offer products that are third-party certified.

How to read a supplement label

Supplement Facts
Serving Size 2 Capsules
Servings Per Container 30

	Amount Per Serving	% Daily Value
Vitamin C	500mg	834%*
Zinc	20mg	199%*
Beta Glucans	300mg	†
Echinachea purpurea Standardized to 4% alkylamides (4 mg)	100mg	†
Proprietary blend	500mg	
Echinacea angustifolia (leaf)		†
Allium sativum (bulb)		†
Withania somnifera (root)		†
Ganoderma lucidum (aerial parts)		†
Rhodiola rosea (root)		†
Andrographis paniculata (aerial parts)		†

* Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

The "Supplement Facts" title is an indicator that the product is marketed for sale in the U.S. and is an FDA standard.

The serving size, and sometimes the number of servings per container, will be included to help you compare more easily between products.

Make sure the serving sizes match when comparing supplements to get an accurate comparison between the products.

Vitamins and minerals will always show the dose in both weight and % daily value to help you understand how you're hitting your dietary requirements.

Many supplements will have doses that exceed the recommended daily value.

Dietary supplement ingredients that are not vitamins or minerals will not have a % daily value as they are not essential ingredients in the diet.

Dietary supplements are regulated by the FDA, and all labels must follow a consistent format to make it easier for consumers to understand supplements. There are some tricks to understanding dietary supplement labels well, so be sure to pay attention to the following points when you're evaluating your supplements.

Supplement Facts

Serving Size 2 Capsules
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Withania somnifera (root)		†
Ganoderma lucidum (aerial parts)		†
Rhodiola rosea (root)		†
Andrographis paniculata (aerial parts)		†

* Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

Herbs will sometimes have additional information listed in the supplement facts panel. You might see ratio numbers (i.e. 4:1) that designate how much raw material of the herb (fresh or dried herb) went into making the supplement version of the herb.

Herbs might have a standardization amount that corresponds to how much of an active ingredient is present in the herbal supplement. The dose of the active ingredient is often listed, but not always.

Proprietary blends are common in dietary supplements. Only the total amount of the proprietary blend in a serving needs to be listed on a supplement, which means that you don't get all of the information about every ingredient that is in the blend.

Ingredients in a proprietary blend are listed in order from most to least. This is similar to how food ingredients are listed on nutrition facts panels that you find on prepared foods.

The daily value percent is established against a 2,000 calorie diet. While this is the standard calorie amount across most labels, it's always important to scale your requirements based on the calorie intake that you need to reach your health goals.

Third-party certifications

Third-party certifications provide dietary supplement companies with a means to improve industry transparency and ensure product quality. For more detailed information on supplement quality, please refer to Fullscript's supplement quality resources.

Certification companies can provide independent audits of facilities, ingredient identity, and manufacturing processes, as well as ensure that additional product claims such as vegan, organic, and gluten-free are verified. Though there are many third-party certifications available, there are a few key certifications of importance within the context of sport, including:

- NSF Certified for Sport®
- Informed Sport®
- BSCG Certified Drug Free®

These organizations are particularly attuned to the regulations and doping standards set by various regulatory sporting bodies such as the World Anti-Doping Association (WADA). It is important to note that supplements that do not possess these third-party seals can still be of high quality and may not contain any contaminants or banned substances prohibited for high-level sport. However, in cases in which sports supplements are used, it may be recommended to select products with these third-party certifications, particularly for athletes competing in sport. Though other third-party certifications may test for contaminants and provide overall indication of manufacturing quality, they may not directly test for substances prohibited by sporting regulatory bodies such as WADA.

NSF Certified for Sport®

The NSF Certified for Sport® certification is perhaps the most well-known and officially-recognized sport certification in the industry and by regulatory sporting bodies, respectively. Without going into detail into quality standards, the NSF certification process entails some of the following:

- Good Manufacturing Practice (GMP) registration
- Annual product identity testing
- Banned substance testing for 280 substances banned in sport (NSF 2021)

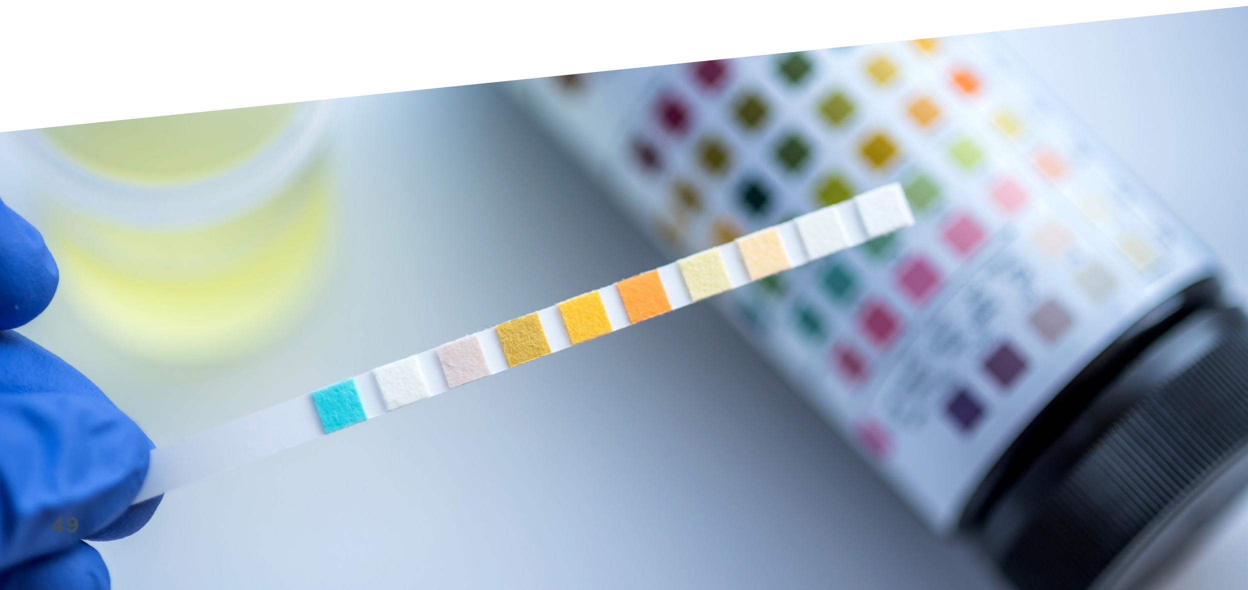
Certified products will appear in the Certified for Sport Database and will provide details related to the product specifications as well as the individual product lot numbers that have been certified. The Certification also provides this information via an app, where product labels can be scanned to verify if they are in the Safe for Sport database.

Informed Sport®

The Informed Sport® certification provides services similar to those offered by NSF Certified for Sport in that the companies applying for or maintaining certification undergo manufacturing and standards audits and every batch of each product, including the same products with multiple flavors, are tested for substances banned in sport. Post-market testing is also conducted, during which the Informed Sport® team purchases products available from distributors to carry out random, blinded batch testing. (Informed Sport 2021) The organization also offers sister certifications such as Informed Choice®, which is similar to Informed Sport®, but testing is less frequent. The Informed Sport® brand also provides similar database searches and product label scanning features within their app.

Banned Substances and Control Group (BSCG) Drug Free®

The BSCG Drug Free® certification is another well-known seal within the sports supplement community that tests for approximately 500 banned sport substances and other illicit drugs not included by other certifications. (BSCG 2021) Similar to the other two certifications, the BSCG also provides a searchable database where users can search by brand name, product name, or lot number in order to verify whether their dietary supplement has been analyzed to be free of banned substances. (BSCG-Database 2021)



Anti-doping considerations

Practitioners seeking to support their clients with sports nutrition should be aware of their client's level of competition and have a general understanding of anti-doping policies in the sporting landscape. This knowledge can guide selection of dietary supplements, used for sports performance or otherwise, appropriate for each individual client.

WORLD ANTI-DOPING AGENCY
play true

The World Anti-Doping Agency (WADA) is one of the leading organizations concerned with anti-doping regulation in sport. Founded in 1999 and headquartered in Montreal, Canada, WADA engages in activities related to upholding international compliance with fair play codes. (WADA 2021) A key service that WADA provides is a database of substances that are banned in and out of competition, specifically during competition, and in various sports. It is important to reiterate that while not all sporting levels of competition follow WADA regulation, WADA provides the gold standard for anti-doping policies. Violation of anti-doping policies can occur accidentally through use of dietary supplements and may ultimately lead to an athlete's disqualification from competition.

An international study funded by WADA showed that approximately 15% of non-hormonal supplements available on the global market in 2003 were found to contain unlabelled anabolic androgenic steroids. (Geyer 2004) Importantly, this steroid contamination prevalence has been found to have decreased to 0.7% (4 of 597 dietary supplements) when the study was repeated and published in 2015, (Geyer 2015) potentially highlighting an overall reduced risk of dietary supplement-related doping violations due to improved quality standards. However, high-level athletes should still be cautious and refer to the third-party certification programs for further guidance on safer products that are free from banned substances.

Though a list of specific banned substances will not be detailed here, high-level examples include:

- Activin receptor IIB inhibitors
- Anabolic androgenic steroids (e.g., androstenediol, testosterone, trenbolone, etc.) or other anabolic agents (e.g., selective androgen receptor modulators (SARMs))
- Anti-estrogenic substances (e.g., tamoxifen)
- Aromatase inhibitors
- Beta-2 agonists
- Cannabinoids (exception of cannabidiol (CBD))
- Diuretics and masking agents (e.g., desmopressin)
- Erythropoietins or substances affecting erythropoiesis
- Glucocorticoids (e.g., prednisone)
- Growth factors and modulators (e.g., insulin-like growth factor, vascular endothelial growth factor)
- Metabolic modulators (e.g., AMPK activators, insulin or insulin mimetics)

- Narcotics (e.g., morphine)
- Peptide hormones and metabolites (e.g., growth hormone)
- Stimulants (non-specified; e.g., amfetamine)
- Stimulants (specified; e.g., ephedrine or epinephrine with max allowable urine concentrations)

The full list of banned substances can be found on WADA's website. It is important to note that some ingredients like DHEA or 7-keto-DHEA that are regularly found in dietary supplements are explicitly banned by WADA.

It is also important to note that many natural ingredients or metabolites possess properties that act in similar manners to banned drugs. WADA's use of language such as "including, but not limited to" or "and other substances with a similar chemical structure or similar biological effect(s)" may indicate that certain natural ingredients fall within the sphere of banned substances. (Catlin 2020)

For instance, there more than 300 compounds found in natural sources that can act as aromatase inhibitors (inhibitors of estrogen production), such as *Vitis L. species* (grape), *Agaricus bisporus* (white button mushrooms), *Brassaiopsis glomerulata* (Blume), *Garcinia mangostana L.* (mangosteen), and various flavonoids. (Balunas 2008) In theory, WADA's regulatory language may thus classify these ingredients as banned substances, regardless of whether these compounds provide enough of an ergogenic effect.

In the case of the adenosine monophosphate-activated protein kinase (AMPK) activator category, the language does not clearly state "including, but not limited to" or "and other substances with a similar chemical structure or similar biological effect(s)" and thus leaves the classification of these substances up for interpretation (except for the two specific examples: AICAR and SR9009). (Catlin 2020) There are more than 100 natural ingredients that may possess AMPK-activating properties, including berberine, cordycepin (mushrooms), quercetin (all botanicals), resveratrol (grapes and red wine), curcumin, EGCG, green tea extract and theaflavins (all from green tea), gingerols (ginger), ginsenosides (ginseng), licorice, parthenolide (feverfew), salicylic acid (willow bark), salidroside (rhodiola), and indole-3 carbinol and DIM (cruciferous vegetables), to name a few of the more well-known compounds. (Arkwright 2015)(Hardie 2016) Whether these natural ingredients will be banned from sport in the future is not currently known.

Natural ingredients that have been found to contain currently banned stimulants include geranium oil (contains DMAA), bael trees (aegeline), dendrobium orchid (NADEP), *Acacia rigidula* (BMPEA and NN-DMPAA), Pouchong tea (DMBA, AMP, or AMP citrate), orange peel (oxilofrine), and bitter orange (p-Hydroxyephedrine octopamine). (Mathews 2018)

It should also be noted that WADA publishes a monitoring program that highlights ingredients that are not currently on the banned substances list but are being actively watched to uncover patterns that may lead to unfair sport. Of note from the 2021 watch list, an anabolic agent called ecdysterone, a naturally occurring hormone known as "insect hormone," is currently being monitored.

(WADA 2021) Ecdysterone is an anabolic agent that can be found in plants, perhaps most notoriously known for providing the popular cartoon character, Popeye, his strength due to his large consumption of spinach. Though spinach contains relatively low amounts of this phytohormone, spinach extracts and other dietary supplements containing certain botanicals such as *Cyanotis arachnoidea* continue to be used to improve sport performance. (Hunyadi 2016)

Practitioners providing sport nutrition counselling to their patients should thus be aware of the WADA watchlist as well as that certain botanical or "natural" products have the potential to lead to doping violations. This reinforces the need for practitioners working with high-level athletes to recommend products that have been third-party verified by organizations such as NSF Certified for Sport, Informed Sport, or BCSG to most effectively reduce the likelihood of doping violations.

Consider	Avoid
Starting with diet first 👍👍👍	Non-certified products 👎
3rd-party certified for sport 👍👍	Proprietary blends 👎👎
3rd-party certified 👍	FDA's tainted products list 👎👎👎

Conclusion

As the sports nutrition industry continues to grow, practitioners may begin to receive more inquiries about sport-related products from their clients or patients. Practitioners seeking to provide sport nutrition advice should understand the unique requirements of each person, from the active individual to the elite athlete.

These needs include factors such as macronutrient and caloric intakes as well as various sports supplement products that may be beneficial for improving performance, body composition, recovery from exercise, and immune and general wellness. Practitioners should also be familiar with the dietary supplement regulatory environment and other aspects related to supplement quality including available third-party certifications.

As a whole, it is important to remember that there are many sports nutrition supplements on the market that are purported to provide a variety of benefits to athletes, even when data on efficacy and safety in athletes are lacking. Before recommending a sports supplement to any individual, practitioners may utilize evidence-based approaches including determining the goals of the individual athlete, the type of sport or exercise in which they are competing, and whether there are ingredients that are supported by research that can help to safely achieve the desired results under the context of ethical sport.

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