ExerciseAndAthleticPerformance-HealthProfessional

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Dietary Supplements for Exercise and Athletic Performance  
Fact Sheet for Health Professionals  
  
This is a fact sheet intended for health professionals. For a general overview, see our consumer fact sheet.  
  
Introduction  
This fact sheet provides an overview of selected ingredients in dietary supplements designed or claimed to enhance exercise and athletic performance. Manufacturers and sellers promote these products, sometimes referred to as ergogenic aids, by claiming that they improve strength or endurance, increase exercise efficiency, achieve a performance goal more quickly, and increase tolerance for more intense training. These effects are the main focus of this fact sheet. Some people also use ergogenic aids to prepare the body for exercise, reduce the chance of injury during training, and enhance recovery from exercise [1,2].  
  
Dietary supplements to enhance exercise and athletic performance come in a variety of forms, including tablets, capsules, liquids, powders, and bars. Many of these products contain numerous ingredients in varied combinations and amounts. Among the more common ingredients are amino acids, protein, creatine, and caffeine. According to one estimate, retail sales of the category of sports nutrition supplements totaled $5.67 billion in 2016, or 13.8% of $41.16 billion total sales for dietary supplements and related nutrition products for that year [3].  
  
Several surveys have indicated the extent of dietary supplement use for bodybuilding and to enhance exercise and athletic performance:  
  
International surveys found that two-thirds of 3,887 adult and adolescent elite track and field athletes participating in world-championship competitions took one or more dietary supplements containing such ingredients as vitamins, minerals, creatine, caffeine, and amino acids [4]. Supplement use increased with age and was significantly more common among women than men.  
A survey of 1,248 students age 16 years or older in five U.S. colleges and universities in 2009 2010 found that 66% reported use of any dietary supplement. The reasons for use included enhanced muscle strength (20% of users), performance enhancement (19% of users), and increased endurance (7% of users) [5]. Products taken for these purposes included protein, amino acids, herbal supplements, caffeine, creatine, and combination products.  
In a national survey of about 21,000 U.S. college athletes, respondents reported taking protein products (41.7%), energy drinks and shots (28.6%), creatine (14.0%), amino acids (12.1%), multivitamins with caffeine (5.7%), beta-hydroxy-beta-methylbutyrate (HMB; 0.2%), dehydroepiandrosterone (DHEA; 0.1%), and an unspecified mix of testosterone boosters (1.6%) [6]. Men were much more likely to take performance-enhancing products than women, except for energy drinks and shots. Among the sports with the highest percentage of users of performance-enhancing products were ice hockey, wrestling, and baseball among the men and volleyball, swimming, and ice hockey among the women.  
In a review of studies on adolescent use of performance-enhancing substances, the American Academy of Pediatrics concluded that protein, creatine, and caffeine were the most commonly used ingredients and that use increased with age [7]. Although athletes used these ingredients more than nonathletes, teenagers not involved in organized athletic activities often took them to enhance their appearance.  
A survey of 106,698 U.S. military personnel in 2007 2008 found that 22.8% of the men and 5.3% of the women reported using bodybuilding supplements, such as creatine and amino acids, and 40.5% of the men and 35.5% of the women reported using energy supplements that might contain caffeine and/or energy-enhancing herbs [8]. Use of these products was positively associated with deployment to combat situations, being younger than 29 years, being physically active, and reporting 5 or fewer hours of sleep a night.  
It is difficult to make generalizations about the extent of dietary supplement use by athletes because the studies on this topic are heterogeneous. However, the data suggest that [9]:  
  
A larger proportion of athletes than the general U.S. population takes dietary supplements.  
Elite athletes (e.g., professional athletes and those who compete on a national or international level) use dietary supplements more often than their nonelite counterparts.  
The supplements used by male and female athletes are similar, except that a larger proportion of women use iron and a larger proportion of men take vitamin E, protein, and creatine.  
For any individual to physically perform at his or her best, a nutritionally adequate diet and sufficient hydration are critical. The Dietary Guidelines for Americans [10] and MyPlate [11] recommend such an eating plan for everyone. Athletes require adequate daily amounts of calories, fluids, carbohydrates (to maintain blood glucose levels and replace muscle glycogen; typically 1.4 to 4.5 g/lb body weight [3 to 10 g/kg body weight]), protein (0.55 to 0.9 g/lb body weight [1.2 to 2.0 g/kg body weight]), fat (20% to 35% of total calories), and vitamins and minerals [12].  
  
A few dietary supplements might enhance performance only when they add to, but do not substitute for, this dietary foundation. Athletes engaging in endurance activities lasting more than an hour or performed in extreme environments (e.g., hot temperatures or high altitudes) might need to replace lost fluids and electrolytes and consume additional carbohydrates for energy. Even with proper nutritional preparation, the results of taking any dietary supplement(s) for exercise and athletic performance vary by level of training; the nature, intensity, and duration of the activity; and the environmental conditions [13].  
  
Sellers claim that dozens of ingredients in dietary supplements can enhance exercise and athletic performance. Well-trained elite and recreational athletes might use products containing one or more of these ingredients to train harder, improve performance, and achieve a competitive edge. However, the National Athletic Trainers Association acknowledges in a position statement that because the outcomes of studies of various performance-enhancing substances are often equivocal, using these substances can be controversial and confusing [14].  
  
Most studies to assess the potential value and safety of supplements to enhance exercise and athletic performance include only conditioned athletes. Therefore, it is often not clear whether the supplements discussed in this fact sheet may be of value to recreational exercisers or individuals who engage in athletic activity only occasionally. In addition, much of the research on these supplements involves young adults (more often male than female) and not adolescents who may also use them against the advice of pediatric and high-school professional associations [7,15]. The quality of many studies is limited by their small samples and short durations, use of performance tests that do not simulate real-world conditions or are unreliable or irrelevant, and poor control of confounding variables [12]. Furthermore, the benefits and risks shown for the supplements might not apply to the supplement s use to enhance types of physical performance not assessed in the studies. In most cases, additional research is needed to fully understand the efficacy and safety of particular ingredients.  
  
Selected Ingredients in Dietary Supplements for Exercise and Athletic Performance  
Many exercise and athletic-performance dietary supplements in the marketplace contain multiple ingredients (especially those marketed for muscle growth and strength). However, much of the research has focused only on single ingredients. One, therefore, cannot know or predict the effects and safety of combinations in these multi-ingredient products unless clinical trials have investigated that particular combination. Furthermore, the amounts of these ingredients vary widely among products. In some cases, the products contain proprietary blends of ingredients listed in order by weight, but labels do not provide the amount of each ingredient in the blend. Manufacturers and sellers of dietary supplements for exercise and athletic performance rarely fund or conduct scientific research on their proprietary products of a caliber that reputable biomedical journals require for publication.  
  
In the text below, each ingredient s section begins with an introduction, followed by a summary of the scientific evidence of that ingredient s efficacy and safety. Each section concludes with information and advice from expert sources, when available, on use of the ingredient as an ergogenic aid.  
  
Antioxidants (vitamin C, vitamin E, and coenzyme Q10)  
Exercise increases the body s consumption of oxygen and induces oxidative stress, leading to the production of reactive oxygen and nitrogen species (i.e., free radicals) and the creation of more oxidized molecules in various tissues, including muscle. In theory, free radicals could impair exercise performance by impeding muscles ability to produce force, thereby accelerating muscle damage and fatigue and producing inflammation and soreness [16-18]. Some researchers have suggested that supplements containing antioxidants, such as vitamins C and E and coenzyme Q10 (CoQ10), could reduce this free-radical formation, thereby minimizing skeletal muscle damage and fatigue and promoting recovery [19].  
  
Efficacy  
Studies suggest that the use of large doses of antioxidant supplements, especially vitamins C and E, may actually reduce rather than promote some of the beneficial effects of exercise. One study, for example, randomly assigned 54 healthy Norwegian men and women age 20 30 years, most of whom were recreational exercisers, to receive 1,000 mg vitamin C and 235 mg (about 520 IU) vitamin E as DL-alpha-tocopherol or a placebo daily for 11 weeks while engaging in an endurance training program consisting mostly of running. Compared with placebo, the supplements had no effect on maximal oxygen consumption (VO2max, a measure of aerobic fitness and endurance capacity) or running performance. However, they significantly lowered levels of biochemical markers related to mitochondrial creation and exercise-induced cell signaling, thereby diminishing the desirable training-induced adaptations within skeletal muscle [20]. The same research group conducted another trial using the same doses of vitamins C and E in 32 young men and women who followed a strength-training program for 10 weeks. Compared with placebo, the supplements did not affect muscle growth, but they significantly reduced the gain in arm strength as measured by biceps curls and blunted cellular signaling pathways linked to muscle hypertrophy [21]. Another study randomly assigned 18 young men age 20 to 34 years to receive 120 mg/day CoQ10 for 22 days or a placebo [22]. After 7 days of high-intensity cycling sprints, the CoQ10 group had, on average, a significantly smaller improvement in mean power output than the placebo group, suggesting a poorer adaptation to training.  
  
The preponderance of research to date suggests that exercise-induced reactive oxygen species and nitric oxide are beneficial. These free radicals induce adaptive changes in muscle that lead to greater production of mitochondria and hypertrophy of myofibers [17,21,23,24]. Exposure of cells to high concentrations of various antioxidant supplements (of which vitamins C and/or E have the most evidence) appears to blunt or block cell signaling and thereby inhibit some favorable physiological and physical adaptations to exercise. However, these adaptations might not prevent improvements in VO2max or endurance performance [25].  
  
Safety  
Studies on the safety of vitamins C, E, and other antioxidant supplements taken during exercise show no evidence of adverse effects, aside from potentially reducing some of the benefits of exercise, but such studies have only lasted a few weeks or months. The Tolerable Upper Intake Level (UL) of vitamin C that the Food and Nutrition Board established as the maximum amount associated with little or no risk of adverse health effects is 1,800 mg/day for adolescents and 2,000 mg/day for adults [26]. These amounts are substantially higher than the doses that studies have typically used for exercise and athletic performance. The UL of vitamin E, at 800 mg/day for adolescents and 1,000 mg/day (1,100 1,500 IU) for adults, is likewise higher than the dose that these studies typically used [26].  
  
Among the potential adverse effects of excess vitamin C are diarrhea, nausea, abdominal cramps, and other gastrointestinal disturbances. The intake of excessive amounts of vitamin E increases the risks of hemorrhagic effects. Moreover, results from a large clinical trial show that vitamin E supplements, even at doses below the UL (400 IU/day taken for several years), might increase men s risk of prostate cancer [27]. The side effects of CoQ10 are mild and can include fatigue, insomnia, rashes, nausea, upper abdominal pain, heartburn, sensitivity to light, irritability, dizziness, and headaches [28].  
  
Implications for use  
Little research supports the use as ergogenic aids of antioxidant supplements containing greater amounts than those available from a nutritionally adequate diet [19,25]. In fact, they can adversely affect some measures of exercise and athletic performance. The Australian Institute of Sport, part of the government of Australia, does not recommend supplementation with vitamins C and E by athletes, except when they use these products as part of a research protocol or with proper monitoring [29].  
  
More information on vitamin C and vitamin E is available in the Office of Dietary Supplements (ODS) health professional fact sheets on these nutrients.  
  
Arginine  
L-arginine is an amino acid found in many protein-containing foods, especially animal products and nuts. The typical dietary intake is 4 5 grams/day [30]. The body also synthesizes arginine (from citrulline), mainly in the kidneys.  
  
Some experts suggest that taking arginine in supplement form enhances exercise and athletic performance in several ways [30-32]. First, some arginine is converted to nitric oxide, a potent vasodilator that can increase blood flow and the delivery of oxygen and nutrients to skeletal muscle. Second, increased vasodilation can speed up the removal of metabolic waste products related to muscle fatigue, such as lactate and ammonia, that the body produces during exercise. Third, arginine serves as a precursor for the synthesis of creatine, which helps supply muscle with energy for short-term, intense activity. Fourth, arginine may increase the secretion of human growth hormone (HGH), which in turn increases insulin-like growth factor-1 (IGF-1) levels, both of which stimulate muscle growth.  
  
Efficacy  
The research to support supplemental arginine as a performance enhancer is limited and conflicting. Overall, it suggests that doses of 2 20 g/day arginine have little to no effect on performance in either anaerobic or aerobic exercise [30,31]. Furthermore, arginine typically had no effect on nitric oxide concentration, blood flow, or exercise metabolites (e.g., lactate and ammonia), especially when well-trained athletes including cyclists, tennis players, and judo practitioners took the supplement for 1 28 days [30]. A recent review assessed 54 clinical studies examining the effects of arginine supplementation on strength performance, endurance, muscle blood volume and flow, cardiorespiratory measures, and nitric oxide production in healthy, active adults. The authors concluded that supplemental arginine (either alone or, more commonly, in combination with other ingredients, such as branched-chain amino acids [BCAAs] and lysine) provided little or no enhancement of athletic performance and did not improve recovery from exhaustion [33]. Most of the studies included few participants, primarily young men age 18 25 years (only four studies included women), and lasted only 4 8 weeks (with none lasting 3 months or longer). In the 18 studies that compared arginine alone with a placebo, the most common doses were 2 10 g/day as a single dose and up to 20 g/day divided into three doses.  
  
Research on the ability of supplemental arginine to raise HGH and IGF-1 serum concentrations also has had conflicting findings. Depending on the study (and therefore participants age, fitness level, and use of other supplements as well as the nature and duration of the exercise), extra arginine might either reduce HGH secretion [34] or raise HGH and IGF-1 secretion [35]. Even raised HGH secretion, however, might not translate into more blood flow into muscle or greater protein synthesis [31]. Little evidence shows supplemental arginine by itself increases muscle creatine concentrations or is superior or complementary to direct consumption of creatine [30].  
  
Safety  
Most study results suggest that up to 9 g/day arginine for several days or weeks is safe and well tolerated. At doses of 9 30 g/day, the most commonly reported adverse reactions are gastrointestinal discomfort, such as diarrhea and nausea, and slightly reduced blood pressure [33,36,37]. The safety of taking high-dose arginine supplements for more than 3 months is not known [33].  
  
Implications for use  
Arginine supplementation s ability to enhance strength, improve exercise or athletic performance, or promote muscular recovery after exercise has little scientific support [30-33,38,39].  
  
Beetroot or beet juice  
Beets are one of the richest food sources of inorganic nitrate. Ingested nitrate might enhance exercise and athletic performance in several ways, primarily through its conversion into nitric oxide in the body. Nitric acid is a potent vasodilator that can increase blood flow and the delivery of oxygen and nutrients to skeletal muscle. Ingested nitrate might also enhance performance by dilating blood vessels in exercising muscle when oxygen levels decline, thereby increasing oxygen and nutrient delivery, reducing the oxygen cost of submaximal exercise, attenuating the adenosine triphosphate (ATP)-creatine phosphate energy system s cost associated with skeletal muscle force production, and improving oxidative phosphorylation in mitochondria [40,41]. Beetroot is available as a juice or juice concentrate and in powdered form; the amount of nitrate can vary considerably among products.  
  
Efficacy  
A growing number of clinical trials investigating beetroot juice or concentrate as an ergogenic aid have been published since 2007. Beetroot has generally improved performance and endurance to different extents compared with placebo among runners, swimmers, rowers, and cyclists in time trials and time-to-exhaustion tests, but not in all studies [40,41-45]. Performance benefits are more likely in recreationally active nonathletes than elite athletes [42,46]. One study in 10 recreationally active, young male cyclists suggested a dose-response relationship [47]. Although consuming beetroot juice concentrate on each of 4 days to supply 4.2 mmol nitrate (70 ml) provided no performance benefits compared with placebo, larger amounts of juice supplying 8.4 mmol nitrate (140 ml) did. However, consumption of even more beetroot juice supplying 16.8 mmol nitrate (280 ml) produced no further performance benefits. There has been little study of the effects of beetroot on anaerobic performance, such as high-volume resistance exercise with many repetitions [40].  
  
More research is needed to clarify the potential benefits of nitrate supplementation from beetroot juice on exercise and athletic performance and to determine the best doses and dosing protocols [48]. No research has assessed longer term supplementation with beetroot-derived nitrate beyond several weeks as an ergogenic aid.  
  
Safety  
Studies have not identified any safety concerns with the consumption of beetroot juice in moderate amounts (about 2 cups/day) for several weeks. The amount of nitrate that this amount of juice provides is less than half the total nitrate consumption from a diet rich in vegetables and fruits [49]. Although not a safety concern, beetroot consumption can color the urine pink or red due to the excretion of red pigments in the beets [50].  
  
Implications for use  
In a position statement, the Academy of Nutrition and Dietetics (AND), the Dietitians of Canada (DoC), and the American College of Sports Medicine (ACSM) state that nitrate sources, such as beetroot juice, enhance exercise tolerance and economy and they improve endurance exercise performance in recreational athletes [12]. The Australian Institute of Sport supports the use of beetroot juice for improving sports performance in suitable athletic competitions under the direction of an expert in sports medicine, but it notes that more research might be required to understand how the supplement should be used for best results [29].  
  
Most studies have used 500 ml/day (about 2 cups) of beetroot juice taken once (about 2.5 to 3 hours before exercise) or daily for up to 15 days [40]. This amount of juice provides about 5 11 mmol (or 310 682 mg) nitrate, depending on the product [41]. Potential benefits persist for up to 24 hours after ingestion [40]. The labels on beetroot juice and concentrate usually indicate that these products are foods and not dietary supplements. Some dietary supplements contain beetroot powder in varying amounts, but studies have not assessed whether these are viable alternatives to beetroot juice or beetroot-juice concentrate.  
  
Beta-alanine  
Beta-alanine, a type of amino acid that the body does not incorporate into proteins, is the rate-limiting precursor to the synthesis of carnosine a dipeptide of histidine and beta-alanine in skeletal muscle. Carnosine helps buffer changes in muscle pH from the anaerobic glycolysis that provides energy during high-intensity exercise but results in the buildup of hydrogen ions as lactic acid accumulates and dissociates to form lactate, leading to reduced force and to fatigue [51]. More carnosine in muscle leads to greater potential attenuation of exercise-induced reductions in pH, which could enhance performance of intense activities of short to moderate duration, such as rowing and swimming [52].  
  
Beta-alanine is produced in the liver, and relatively small amounts are present in animal-based foods such as meat, poultry, and fish. Estimated dietary intakes range from none in vegans to about 1 g/day in heavy meat eaters [52]. Carnosine is present in animal-based foods, such as beef and pork. However, oral consumption of carnosine is an inefficient method of increasing muscle carnosine concentrations because the dipeptide is digested into its constituent amino acids. Consumption of beta-alanine, in contrast, reliably increases the amount of carnosine in the body. Four to six grams of beta-alanine for 10 weeks, for example, can increase muscle carnosine levels by up to 80%, especially in trained athletes, although the magnitude of response differs widely [53,54]. For example, in one study of young, physically active but untrained adult men who took 4.8 g/day beta-alanine for 5 6 weeks, the percent increase in muscle carnosine content after 9 weeks of follow-up ranged from 2% to 69% [55]. Among the low responders, the duration of the washout period when beta alanine concentrations returned to baseline values was less than half that for the high responders (6 weeks vs. 15 weeks).  
  
Efficacy  
Studies have evaluated beta-alanine as a potential ergogenic aid with a variety of participants, exercise and activity protocols, and dosing regimens. Some studies suggest that beta-alanine consumption could provide small performance benefits in competitive events requiring high-intensity effort over a short period, such as rowing, swimming, and team sports (e.g., hockey and football) that involve repeated sprints and intermittent activity [52]. Other studies have found no such benefits [53]. Evidence is conflicting on whether beta-alanine consumption improves performance in endurance activities, such as cycling [53,56]. Experts have not reached consensus on whether beta-alanine consumption primarily benefits trained athletes or recreationally active individuals [53,57]. Studies provide little consistent evidence of a relationship between the dose of beta-alanine and performance effect [51,58].  
  
The authors of a Department of Defense-sponsored review concluded that the limited evidence from 20 human trials did not support consumption of beta-alanine (alone or in combination products) by active adults to enhance athletic performance or improve recovery from exercise-related exhaustion [59]. Most of the studies in this review included young men age 18 25 years who took 1.6 6.4 g/day beta-alanine supplements (in two to four separate servings) over 4 8 weeks. In contrast, the International Society of Sports Nutrition (ISSN) concluded from its literature review that beta-alanine supplements (4 6 g/day consumed for at least 2 4 weeks) can improve high-intensity exercise performance that lasts more than 60 seconds, especially in time-to-exhaustion tasks [54]. However, performance benefits are more modest in exercise tests lasting more than 4 minutes because aerobic metabolic pathways increasingly meet energy demands. The ISSN called for more research to determine whether beta-alanine increases the strength and muscle mass that regular resistance exercise, such as weightlifting, can produce.  
  
The authors of the most recent review of studies on beta-alanine s effects on exercise concluded that supplementation has a statistically significant and positive effect on performance (including in both isolated-limb and whole-body exercises), especially in protocols lasting 30 seconds to 10 minutes [58]. However, this review also highlighted the fact that small studies of short duration using varied exercise and supplement protocols dominate this scientific literature. The 40 placebo-controlled studies reviewed, for example, employed 65 exercise protocols and 70 exercise measures in a total of 1,461 participants. Furthermore, the total dose of beta-alanine that participants consumed ranged from 84 to 414 g in studies lasting 28 90 days.  
  
Safety  
Beta-alanine supplementation appears to be safe at 1.6 6.4 g/day for up to 8 weeks [54]. Some evidence does show, however, that consuming a conventional dose of beta-alanine of at least 800 mg or exceeding 10 mg/kg body mass can provoke moderate to severe paresthesia [54,59]. This tingling, prickling, or burning sensation is common in the face, neck, back of the hands, and upper trunk and typically lasts 60 90 minutes but is not a painful, serious, or harmful reaction. Use of divided doses or a sustained-release form of the supplement can attenuate paresthesia resulting from beta-alanine consumption [52,54]. Some research has also found that beta-alanine supplements can produce pruritus (itchy skin), but the authors do not indicate the severity of this effect [59]. There are no safety data on use of the supplement for more than 1 year [54,60].  
  
Implications for use  
There is insufficient expert consensus on the value of taking beta-alanine to enhance performance in intense, short-term activities or its safety, particularly when users take it regularly for at least several months. In a position statement, the AND, DoC, and ACSM advise that beta-alanine supplementation might improve training capacity and does enhance performance, especially of high-intensity exercise lasting 60 240 seconds, that acid-base disturbances resulting from increased anaerobic glycolysis would otherwise impair [12]. In its position statement, the ISSN concludes that beta-alanine supplementation improves exercise performance and attenuates neuromuscular fatigue [54]. The Australian Institute of Sport supports the use of beta-alanine for improving sports performance in suitable athletic competitions under the direction of an expert in sports medicine, but it notes that more research might be required to understand how the supplement should be used for best results [29].  
  
For healthy individuals willing to use beta-alanine supplements, the ISSN recommends a daily loading dose of 4 to 6 g/day in divided doses of 2 g or less for at least 2 weeks. The society states that benefits increase after 4 weeks, when muscle carnosine concentrations rise by 40% 60% [54]. It advises users to take beta-alanine supplements with meals to augment muscle carnosine levels and to use divided lower doses or take a sustained-release form if paresthesia occurs.  
  
Beta-hydroxy-beta-methylbutyrate  
HMB is a metabolite of the branched-chain amino acid leucine. About 5% of the body s leucine is converted into HMB, which is then converted in the liver to a precursor (known as beta-hydroxy-beta-methylglutaryl coenzyme A) needed for cholesterol biosynthesis [61]. Some experts hypothesize that skeletal muscle cells that become stressed and damaged from exercise require an exogenous source of the coenzyme for synthesis of cholesterol in their cellular membranes to restore structure and function [62,63]. Experts also believe that the conversion of leucine to HMB activates muscle protein synthesis and reduces protein breakdown [63]. Supplementation is the only practical way to obtain 3 g/day HMB because one would otherwise need to consume more than 600 g/day of high-quality protein (from 5 lb of beef tenderloin, for example) to obtain enough leucine (60 g) for conversion into HMB [63].  
  
Efficacy  
Although studies have investigated HMB for two decades, they have used substantially different periods of supplementation (1 day to 6 weeks) and daily doses (1.5 to 6 g; most commonly 3 g based on evidence that this dose provides equivalent results to 6 g and better results than 1.5 g) [61,63,64]. Studies also used participants of different ages (19 to 50 years), training status (e.g., untrained or trained athletes), training protocols (e.g., with machines or free weights), training duration (10 days to 12 weeks), consumption of other supplements (such as creatine), and other factors. It is therefore difficult to predict what, if any, benefits an exercising individual might experience from consuming HMB.  
  
There is general agreement that HMB helps speed up recovery from exercise of sufficient amount and intensity to induce skeletal muscle damage [63,65]. Therefore, trained athletes must exert themselves more than untrained individuals to potentially benefit from using the supplement. Some studies suggest that HMB use has additional benefits, including an ability to enhance strength, power, skeletal muscle hypertrophy, and aerobic performance in both trained and untrained people [63].  
  
Safety  
A review of safety data from nine studies found that users tolerate HMB well, and it is safe at daily intakes of 3 g for 3 to 8 weeks in younger (ages 18 47 years) and older (ages 62 81) adults of both sexes who do or do not exercise [66]. Assessments of blood chemistry, hematology, and emotional affect found no adverse effects. Another study randomized 37 untrained males age 18 29 years participating in a resistance training program to take either no HMB or about 3 6 g/day HMB [62]. Use of HMB did not alter or adversely affect any measured hematologic, hepatic, or renal-function parameters in these young men. Although 3 g/day HMB appears to be safe for short-term use in adults, its safety profile (and efficacy) has not been studied in adolescents [63].  
  
Implications for use  
There is no expert consensus on the value of taking HMB for several months or longer or its safety. HMB is not on a list of evidence-based ergogenic aids issued by the AND, DoC, and the ACSM [12]. The Australian Institute of Sport does not recommend HMB supplementation by athletes, except as part of a research protocol or with proper monitoring [29]. However, the ISSN notes that HMB can enhance recovery by reducing exercise-induced skeletal muscle damage in both trained and untrained individuals [63].  
  
HMB is available in two forms: as a mono-hydrated calcium salt (HMB-Ca) and a calcium-free form (HMB-free acid [HMB-FA]). HMB-Ca is approximately 13% calcium by weight, and a daily dose of 3 g/day adds about 400 mg calcium to the diet [66]. Those who wish to limit their calcium intake can use HMB-FA [63]. Although the latter form appears to have a faster and greater effect based on its ability to raise HMB plasma levels, more studies are needed to compare the effects of HMB-Ca with those of HMB-FA [63].  
  
The ISSN recommends that healthy adults interested in using HMB supplements take 1 2 g HMB-Ca 60 to 120 minutes before exercise or 1 2 g HMB-FA 30 to 60 minutes before exercise [63]. It also suggests that supplement users ideally consume 3 g/day HMB (in three equal servings of 1 g) for at least 2 weeks before high-intensity exercise to optimize HMB s protective effects on muscle.  
  
Betaine  
Betaine, also known as trimethylglycine, is found in foods such as beets, spinach, and whole-grain breads. Average daily intakes of betaine range from 100 to 300 mg/day [67]. The mechanisms by which betaine might enhance exercise and athletic performance are not known, but many are hypothesized. For example, betaine might increase the biosynthesis of creatine, levels of blood nitric acid, and/or the water retention of cells [68].  
  
Efficacy  
A limited number of small studies in men have assessed betaine in supplemental form as a potential ergogenic aid. These studies, which typically examined strength- and power-based performance in bodybuilders and, occasionally, cyclists, provided conflicting results, and performance improvements tended to be modest [68-71]. The typical dose of betaine that studies used ranged from 2 to 5 g/day [71] for up to 15 days.  
  
Safety  
The several small studies of athletes described in the previous paragraph who took betaine supplements for up to several weeks found no side effects or safety concerns. However, research has not adequately evaluated the safety of betaine.  
  
Implications for use  
More research on betaine supplementation to enhance various types of performance, training protocols, and exercise during specific sports is needed before any recommendations for its use can be made [71].  
  
Branched-chain amino acids  
Three essential amino acids (EAAs) leucine, isoleucine, and valine are the branched-chain amino acids (BCAAs), whose name reflects their chemical structure. BCAAs make up approximately 25% of the amino acids in foods containing complete proteins (including all EAAs) [72]; most of these foods are animal products, such as meat, poultry, fish, eggs, and milk (see section on protein). BCAAs comprise about 14% 18% of the amino acids in human skeletal muscle proteins [73]. Unlike other EAAs, the BCAAs can be metabolized by mitochondria in skeletal muscle to provide energy during exercise [74,75]. The BCAAs, especially leucine, might also stimulate protein synthesis in exercised muscle [72,76].  
  
Efficacy  
The limited research on the potential ergogenic effects of the BCAAs has found little evidence to date that supplements of these amino acids improve performance in endurance-related aerobic events [75]. The BCAAs might delay feelings of fatigue or help maintain mental focus by competing with the amino acid tryptophan (a precursor of the neurotransmitter serotonin that regulates mood and sleep) for entry into the brain, but this effect has not been well studied [72,74,75]. The results of several short-term studies lasting about 3 to 6 weeks suggest that about 10 14 g/day supplemental BCAAs might enhance gains in muscle mass and strength during training [1]. Overall, however, studies to date provide inconsistent evidence of the ability of BCAAs to stimulate muscle protein synthesis beyond the capacity of sufficient dietary amounts of any high-quality protein to perform this function [76]. Furthermore, it is not clear from existing research whether consumption of protein and BCAAs before versus after a workout affects their ability to maximize muscle protein synthesis and reduce protein catabolism [12,77-79].  
  
Safety  
Up to 20 g/day BCAA supplements in divided doses appear to be safe [75]. For leucine alone, studies suggest an upper safe limit of intake of 500 mg/kg per day in healthy young and elderly men, or about 38 g/day for a man weighing 75 kg (165 lb) [80-82].  
  
Implications for use  
Studies have not consistently shown that taking supplements of BCAAs or any of their three constituent amino acids singly enhances exercise and athletic performance, builds muscle mass, or aids in recovery from exercise. Consuming animal foods containing complete proteins or a combination of plant-based foods with complementary proteins that together provide all EAAs automatically increases consumption of BCAAs (see section on protein). This is also true of consuming protein powders made from complete proteins, especially whey, which has more leucine than either casein or soy [78].  
  
Caffeine  
Caffeine is a methylated xanthine naturally found in variable amounts in coffee; tea; cacao pods (the source of chocolate); and other herbal/botanical sources, such as guarana, kola (or cola) nut, and yerba mate. Caffeine stimulates the central nervous system, muscles, and other organs such as the heart by binding to adenosine receptors on cells, thereby blocking the activity of adenosine, a neuromodulator with sedative-like properties [83,84]. In this way, caffeine enhances arousal, increases vigor, and reduces fatigue [13,85,86]. Caffeine also appears to reduce perceived pain and exertion [13,85]. During the early stages of endurance exercise, caffeine might mobilize free fatty acids as a source of energy and spare muscle glycogen [38].  
  
Caffeine is commonly used in energy drinks and shots touted for their performance-enhancement effects [87,88]. It is also found in energy gels containing carbohydrates and electrolytes as well as in anhydrous caffeine-only pills.  
  
Efficacy  
Many studies have shown that caffeine might enhance performance in athletes when they ingest about 2 6 mg/kg body weight before exercise by improving endurance, strength, and power in high-intensity team sports activities [13,85,89,90]. For an individual weighing 154 pounds (70 kg), this dose is equivalent to 210 420 mg caffeine. Taking more, however, is unlikely to improve performance further and increases the risk of side effects.  
  
A review of the literature found that caffeine intake affected sport-specific performance (e.g., running, cycling, swimming, and rowing), as measured in time trials. Although 30 of the 33 trials showed positive improvements in performance, the improvements were not statistically significant in half of them [85]. In these studies, performance improvement ranged from a decrease of 0.7% to an increase of 17.3%, suggesting that the caffeine was very helpful to some participants but slightly impaired performance in others. Factors such as the timing of ingestion, caffeine intake mode or form, and habituation to caffeine could also have accounted for the varied effects on performance.  
  
Caffeine supplementation is more likely to help with endurance-type activities (such as running) and activities of long duration with intermittent activity (such as soccer) than more anaerobic, short-term bouts of intense exercise (such as sprinting or lifting weights) [91]. Some evidence suggests that caffeine is more likely to improve performance in people who are not habituated to it [85]. Limiting caffeine intake to 50 mg/day or abstaining from caffeine for 2 7 days before taking it for an athletic event might maximize any ergogenic effect. However, other evidence shows no habituation effect of caffeine consumption on performance [92].  
  
Safety  
Heavy caffeine use (500 mg/day or more) might diminish rather than enhance physical performance and could also disturb sleep and cause irritability and anxiety [93]. Other adverse effects of caffeine include insomnia, restlessness, nausea, vomiting, tachycardia, and arrhythmia [94-97]. Caffeine does not induce diuresis or increase sweat loss during exercise and therefore does not reduce fluid balance in the body that would adversely affect performance [13,90,98].  
  
For healthy adults, the U.S. Food and Drug Administration (FDA) states that 400 mg/day caffeine does not usually have dangerous adverse effects [99]. The American Medical Association recommends that adults limit their intake of caffeine to 500 mg/day and that adolescents consume no more than 100 mg/day [100]. The American Academy of Pediatrics warns that caffeine-containing energy drinks in particular have no place in the diets of children or adolescents and are not suitable for use during routine physical activity [101].  
  
Pure powdered caffeine is available as a dietary supplement and is very potent. A single tablespoon contains 10 g caffeine, and an acute oral dose of 10 to 14 g caffeine (approximately 150 200 mg/kg) can be fatal [91]. Furthermore, combining caffeine with other stimulants could increase the potential for adverse effects [94]. At least two young men have died as a result of taking an unknown amount of pure powdered caffeine [102].  
  
Implications for use  
Caffeine is easily and rapidly absorbed, even from the buccal membranes in the mouth, and is distributed throughout the body and brain. It reaches peak concentrations in the blood within 45 minutes of consumption and has a half-life of about 4 5 hours [83]. For a potential benefit to athletic performance, users should consume caffeine 15 to 60 minutes before exercise [13,85]. Consumption of caffeine with fluid during exercise of long duration might extend any performance improvements [85].  
  
In a position statement, the AND, DoC, and ACSM state that caffeine supplementation reduces perceived fatigue and enables users to sustain exercise at the desired intensity longer [12]. The U.S. Department of Defense states that caffeine supplementation at 2 6 mg/kg body weight is linked to enhanced physical performance and the effects of smaller doses usually last longer and are greater in people who do not usually consume caffeine [89]. It adds that caffeine could reduce perceived exertion when exercise lasts longer. In a position statement, the ISSN describes caffeine as effective in trained athletes for improving sports performance and notes that supplementation with about 3 6 mg/kg has an ergogenic effect on sustained maximal endurance exercise but not necessarily on strength-power performance [13]. The Australian Institute of Sport supports the use of caffeine for improving sports performance in suitable athletic competitions under the direction of an expert in sports medicine, but it notes that more research might be required to understand how caffeine should be used for best results [29].  
  
The International Olympic Committee considers caffeine to be a controlled or restricted substance; Olympic athletes may consume it until urinary concentrations exceed 12 mcg/ml [103]. The National Collegiate Athletic Association prohibits use of caffeine from any source in amounts that would lead to urine concentrations exceeding 15 mcg/ml [104,105]. (Consuming about 500 mg caffeine produces a urinary caffeine concentration of 15 mcg/ml within 2 3 hours [106].) The World Anti-Doping Agency does not prohibit or limit caffeine use [107].  
  
Citrulline  
L-citrulline is a nonessential amino acid produced in the body, mainly from glutamine, and obtained from the diet. Watermelon is the best-known source; 1 cup diced seedless watermelon has about 365 mg citrulline [108]. About 80% of the body s citrulline is converted in the kidneys into arginine, another amino acid (see section on arginine) [30]. The subsequent conversion of arginine to nitric oxide, a potent dilator of blood vessels, might be the mechanism by which citrulline could serve as an ergogenic aid. In fact, consumption of citrulline might be a more efficient way to raise blood arginine levels than consumption of arginine because more citrulline is absorbed from the gut than arginine.  
  
Most studies have used citrulline malate, a combination of citrulline with malic acid (a constituent in many fruits that is also produced endogenously), because malate, an intermediate in the Krebs cycle, might enhance energy production [30].  
  
Efficacy  
The research to support supplemental citrulline as an ergogenic aid is limited and conflicting at best. The few published studies have had heterogeneous designs and ranged in duration from 1 to 16 days. As an example, in one randomized controlled study with a crossover design, 41 healthy male weightlifters age 22 37 years consumed 8 g citrulline malate or a placebo 1 hour before completing barbell bench presses to exhaustion [109]. Overall, participants could complete significantly more repetitions when taking the supplement and reported significantly less muscle soreness 1 and 2 days after the test. Another study that randomized 17 young healthy men and women to take citrulline without malate (either 3 g before testing or 9 g over 24 hours) or a placebo found that participants using the citrulline did not perform as well as those taking the placebo on an incremental treadmill test to exhaustion [110]. Although citrulline supplementation might increase plasma levels of nitric oxide metabolites, such a response has not been directly related to any improvement in athletic performance [30].  
  
Safety  
Studies have not adequately assessed the safety of citrulline, particularly when users take it in supplemental form for months at a time. In the study of weight lifters described above, 6 of the 41 participants reported stomach discomfort after taking the supplement [109]. Additional short-term studies in which supplemental citrulline was provided to nonathletes at up to 6 g/day for 4 weeks and 1.35 g/day for 6 weeks found no adverse effects [111].  
  
Implications for use  
The research to date does not provide strong support for taking citrulline or citrulline malate to enhance exercise or athletic performance [30]. Whether athletes in specific sports or activities might benefit from taking supplemental citrulline remains to be determined [109].  
  
Dietary supplements that contain citrulline provide either citrulline or citrulline malate. Citrulline malate is 56.64% citrulline by weight so, for example, 1 g citrulline malate provides 566 mg of citrulline. Sellers of some citrulline malate dietary supplements claim that they provide a higher percentage of citrulline (with labels listing, for example, citrulline malate 2:1 or tri-citrulline malate), but studies have not determined whether these supplements are superior to standard citrulline or citrulline malate supplements.  
  
Creatine  
Creatine is one of the most thoroughly studied and widely used dietary supplements to enhance exercise and sports performance [112]. Creatine is produced endogenously and obtained from the diet in small amounts. It helps generate ATP and thereby supplies the muscles with energy, particularly for short-term events [113]. Creatine might improve muscle performance in four ways: by increasing stores of phosphocreatine used to generate ATP at the beginning of intense exercise, accelerating the re-synthesis of phosphocreatine after exercise, depressing the degradation of adenine nucleotides and the accumulation of lactate, and/or enhancing glycogen storage in skeletal muscles [113].  
  
The liver and kidneys synthesize about 1 g/day creatine from the amino acids glycine, arginine, and methionine [114]. Animal-based foods, such as beef (2 g/lb), pork (2.3 g/lb), and salmon (2 g/lb), also contain creatine. A person weighing 154 pounds has about 120 g creatine and phosphocreatine in his or her body, almost all in the skeletal and cardiac muscles [112]. However, it is only when users consume much greater amounts of creatine over time as a dietary supplement that it could have ergogenic effects. Metabolized creatine is converted into the waste product creatinine, which is eliminated from the body through the kidneys.  
  
Efficacy  
Studies in both laboratory and sports settings have found that short-term creatine supplementation (for 5 to 7 days) in both men and women often significantly increases strength (e.g., for bench presses) and power (e.g., for cycling), work involving multiple sets of maximal effort muscle contractions, and sprinting and soccer performance [112,115]. In one example, a study randomized 14 healthy, resistance-trained men (age 19 29 years) to receive 25 g creatine monohydrate or a placebo for 6 7 days [116]. Participants taking the supplement had significant improvements in peak power output during all five sets of jump squats and in repetitions during all five sets of bench presses on three occasions. In another study, 18 well-trained male sprinters age 18 24 years received either 20 g/day creatine or a placebo for 5 days [117]. Compared with those taking the placebo, participants taking the creatine improved their performance in both 100-meter sprints and six intermittent 60-m sprints.  
  
Supplementation with creatine over weeks or months helps training adaptations to structured, increased workloads over time. For example, in a randomized study of 14 female collegiate soccer players during the off-season, those who received creatine (15 g/day for 1 week and then 5 g/day for 12 weeks) had significantly greater increases in muscle strength, as measured by bench press and full-squat maximal strength testing, but not lean tissue compared with participants who took a placebo [118].  
  
Individuals have varied responses to creatine supplementation, based on factors such as diet and the relative percentages of various muscle fiber types [114,119]. Vegetarians, for example, with their lower muscle creatine content, might have greater responses to supplementation than meat eaters. Overall, creatine enhances performance during repeated short bursts of high-intensity, intermittent activity, such as sprinting and weight lifting, where energy for this predominantly anaerobic exercise comes mainly from the ATP-creatine phosphate energy system [38,114].  
  
Creatine supplementation seems to be of little value for endurance sports, such as distance running or swimming, that do not depend on the short-term ATP-creatine phosphate system to provide short-term energy, and it leads to weight gain that might impede performance in such sports [113,114]. Furthermore, in predominantly aerobic exercise lasting more than 150 seconds, the body relies on oxidative phosphorylation as the primary energy source, a metabolic pathway that does not require creatine [114].  
  
Safety  
Studies have found no consistent set of side effects from creatine use, except that it often leads to weight gain, because it increases water retention and possibly stimulates muscle protein synthesis [112,113]. Several studies have found that supplemental creatine monohydrate, when used for a strength-training program, can lead to a 1 2 kg increase in total body weight in a month [73].  
  
Creatine is considered safe for short-term use by healthy adults [12,112,113,114]. In addition, evidence shows that use of the product for several years is safe [112,120-122]. Anecdotal reactions to creatine use include nausea, diarrhea and related gastrointestinal distress, muscle cramps, and heat intolerance. Creatine supplementation may reduce the range of motion of various parts of the body (such as the shoulders, ankles, and lower legs) and lead to muscle stiffness and resistance to stretching [114]. Adequate hydration while taking creatine might minimize these uncommon risks [113].  
  
Implications for use  
In a position statement, the AND, DoC, and ACSM advise that creatine enhances performance of cycles of high-intensity exercise followed by short recovery periods and improves training capacity [12]. In its position statement, the ISSN states that creatine monohydrate is the most effective nutritional supplement currently available for enhancing capacity for high-intensity exercise and lean body mass during exercise [112]. The ISSN contends that athletes who supplement with creatine have a lower incidence of injuries and exercise-related side effects compared to those who do not take creatine [112]. The Australian Institute of Sport supports the use of creatine for improving sports performance in suitable athletic competitions under the direction of an expert in sports medicine, but it notes that more research might be required to understand how the supplement should be used for best results [29].  
  
A typical protocol for creatine supplementation in adults, regardless of sex or body size, consists of a loading phase for 5 7 days, when users consume 20 g/day creatine monohydrate in four portions of 5 g, followed by a maintenance phase of 3 5 g/day [112-114]. In some studies, the loading dose is based on body weight (e.g., 0.3 g/kg) [114]. Another creatine supplementation protocol consists of taking single doses of about 3 6 g/day (0.03 0.1 g/kg body weight) for 3 to 4 weeks, without a loading phase, to produce ergogenic effects [112,114,119].  
  
Creatine monohydrate, which is 88% creatine by weight, is the most widely used and studied form [112,114,123]. Other, usually more expensive, forms of creatine (e.g., creatine ethyl ester, creatine alpha-ketoglutarate, and buffered forms of creatine) have not been proven to have superior ability to creatine monohydrate for enhancing muscle creatine levels, digestibility, product stability, or safety [73,112,123].  
  
Deer antler velvet  
Deer antler velvet consists of cartilage and epidermis from growing deer or elk antlers before ossification [124,125]. It is used as a general health aid in traditional Chinese medicine. Several growth factors have been detected in deer antler velvet, such as IGF-1, that could promote muscle tissue growth in a similar way to the quick growth of deer antlers.  
  
Efficacy  
Three randomized controlled trials in a total of 95 young and middle-age men and 21 young females provide virtually no evidence that deer antler velvet supplements improve aerobic or anaerobic performance, muscular strength, or endurance [125,126]. One of the trials randomized 38 active men age 19 24 years to take 300 mg/d of a deer-antler-velvet extract, 1.5 g/d of a deer-antler-velvet powder, or a placebo and begin a strength- and endurance-training program [126]. The supplements provided no significant ergogenic effects compared with placebo.  
  
Safety  
Studies have not adequately assessed the safety of deer antler velvet. The studies cited above found no side effects in participants taking deer-antler-velvet supplements. IGF-1 is available as a prescription medication, and its reported side effects include hypoglycemia, headache, edema, and joint pain [127]. An evaluation of six deer-antler-velvet dietary supplements that were commercially available in 2013 found that five of them contained no deer IGF-1, and four were adulterated with human IGF-1 [124]. Only one of the six supplements contained a low level of deer IGF-1.  
  
Implications for use  
The research to date does not support taking deer-antler-velvet supplements to enhance exercise or athletic performance. The National Collegiate Athletic Association [105] and the World Anti-Doping Agency [128] ban the use of IGF-1 and its analogues in athletic competition.  
  
Dehydroepiandrosterone  
DHEA is a steroid hormone secreted by the adrenal cortex. The body can convert DHEA to the male hormone testosterone; testosterone s intermediary, androstenedione; and the female hormone estradiol [129]. Testosterone is an anabolic steroid that promotes gains in muscle mass and strength when combined with resistance training [130].  
  
Efficacy  
The minimal research on DHEA s use to enhance exercise and athletic performance provides no evidence of benefit [129]. One study, for example, randomly assigned 40 male weightlifters (average age 48 years) to receive DHEA (100 mg/day), androstenedione (100 mg/day), or a placebo for 12 weeks while continuing their training programs. Compared to placebo, the DHEA and androstenedione produced no statistically significant increase in strength, aerobic capacity, lean body mass, or testosterone levels [131]. Another study randomly assigned 20 sedentary men 19 29 years of age to receive either 150 mg/day DHEA or a placebo for 6 of 8 weeks in combination with a resistance-training program. The supplement provided no benefits compared with placebo in increasing muscle strength, lean body mass, or testosterone concentrations [130].  
  
Safety  
Studies have not adequately assessed the safety of DHEA. The two short-term studies in men described above found no side effects from the DHEA; blood lipid levels and liver function remained normal. Other studies have found that in women, use of DHEA for months significantly raises serum testosterone but not estrogen levels, which can cause acne and growth of facial hair [129].  
  
Implications for use  
The research to date does not support taking DHEA supplements to enhance exercise or athletic performance. The National Collegiate Athletic Association and the World Anti-Doping Agency ban the use of DHEA [105,128].  
  
Ginseng  
Ginseng is a generic term for botanicals from the genus Panax. Some popular varieties are known as Chinese, Korean, American, and Japanese ginseng. Preparations made from ginseng roots have been used in traditional Chinese medicine for millennia as a tonic to improve stamina and vitality [132]. So-called Siberian or Russian ginseng (Eleutherococcus senticosus), although unrelated to Panax ginseng, has also been used in traditional Chinese medicine to combat fatigue and strengthen the immune system [133].  
  
Efficacy  
Numerous small studies, with and without placebo controls, have investigated Panax ginseng s potential to improve the physical performance of athletes, regular and occasional exercisers, and largely sedentary individuals. In almost all cases, the studies found that Panax ginseng in various doses and preparations had no ergogenic effect on such measures as peak power output, time to exhaustion, perceived exertion, recovery from intense activity, oxygen consumption, or heart rate [132,134-136].  
  
One review of studies of the effects of Siberian ginseng on endurance performance found that the five studies with the most rigorous research protocols (with a total of 55 men and 24 women) showed no effect of supplementation for up to 6 weeks on exercise performed for up to 120 minutes [133]. A subsequent randomized controlled trial using a crossover design with nine male college tennis players found that 800 mg/day Siberian ginseng (prepared from the root and rhizome) for 8 weeks significantly improved endurance in a cycling trial, elevated VO2max and heart rate, and increased fat oxidation [137].  
  
Safety  
Short-term Panax ginseng use appears to be safe; the most commonly reported adverse effects include headache, sleep disturbances, and gastrointestinal disorders [136]. Short-term Siberian ginseng use also appears to be safe. The studies cited above reported no adverse effects, although other reports of clinical trials have listed insomnia as a rare side effect [138].  
  
Implications for use  
The research to date provides little support for taking ginseng to enhance exercise or athletic performance [132,136].  
  
Glutamine  
Glutamine is the most abundant amino acid in muscle, blood, and the body s free-amino-acid pool. It is synthesized in the body primarily from the BCAAs, and an adult consumes about 3 6 g/day in protein-containing foods [139,140]. Glutamine is a key molecule in metabolism and energy production, and it contributes nitrogen for many critical biochemical reactions [141]. It is an EAA for critically ill patients when the body s need for glutamine exceeds its capacity to produce sufficient amounts.  
  
Efficacy  
Few studies have examined the effect of glutamine supplementation alone as an ergogenic aid [142]. One study randomized 31 male and female weightlifters to receive either glutamine (0.9 g/kg lean body mass, or almost 45 g/day) or placebo while completing a 6-week strength-training program. There were no significant differences between the two groups in measures of strength, torque, or lean tissue mass, demonstrating that glutamine had no effect on muscle performance, body composition, or muscle-protein degradation. Another study compared the effect of glutamine (four doses of 0.3 g/kg body weight over 3 days) or placebo in 16 young adult men and women on recovery from eccentric exercise consisting of unilateral knee extensions [143]. Supplementation with glutamine reduced the magnitude of strength loss, accelerated strength recovery, and diminished muscle soreness more quickly than placebo; these effects were more pronounced in the men. Some athletes use glutamine supplements in the hope that they will attenuate exercise-induced immune impairment and reduce their risk of developing upper respiratory tract infections. However, there is little research-based support for this benefit [140,141].  
  
Safety  
In the studies described above, the glutamine had no reported side effects. Many patients with serious catabolic illnesses, such as infections, intestinal diseases, and burns, take glutamine safely as part of their medical care. Daily oral doses ranging from 0.21 to 0.42 g/kg body weight glutamine (equivalent to 15 30 g/day in a person weighing 154 pounds) have provided no biochemical or clinical evidence of toxicity [139].  
  
Implications for use  
The research to date does not support taking glutamine alone to improve exercise and athletic performance [139,140].  
  
Iron  
Iron is an essential mineral and a structural component of hemoglobin, an erythrocyte protein that transfers oxygen from the lungs to the tissues, and myoglobin, a protein in muscles that provides them with oxygen. Iron is also necessary to metabolize substrates for energy as a component of cytochromes and to dehydrogenase enzymes involved in substrate oxidation [144]. Iron deficiency impairs oxygen-carrying capacity and muscle function, and it limits people s ability to exercise and be active [12,145]. Its detrimental effects can include fatigue and lethargy, lower aerobic capacity, and slower times in performance trials [146].  
  
Iron balance is an important consideration for athletes who must pay attention to both iron intakes and iron losses. Teenage girls and premenopausal women are at increased risk of obtaining insufficient amounts of iron from their diets. They require more iron than teenage boys and men because they lose considerable iron due to menstruation, and they might not eat sufficient amounts of iron-containing foods [147,148].  
  
Athletes of both sexes lose additional iron for several reasons [145,146,149,150]. Physical activity produces acute inflammation that reduces iron absorption from the gut and iron use via a peptide, hepcidin, that regulates iron homeostasis. Iron is also lost in sweat. The destruction of erythrocytes in the feet because of frequent striking on hard surfaces leads to foot-strike hemolysis. Also, use of anti-inflammatories and pain medications can lead to some blood loss from the gastrointestinal tract, thereby decreasing iron stores.  
  
The richest dietary sources of heme iron (which is highly bioavailable) include lean meats and seafood. Plant-based foods such as nuts, beans, vegetables, and fortified grain products contain nonheme iron, which is less bioavailable than heme iron.  
  
Efficacy  
Although iron deficiency anemia decreases work capacity, there is conflicting evidence on whether milder iron deficiency without anemia impairs sport and exercise performance [12,151,152]. One systematic review and meta-analysis to determine whether iron treatments (provided orally or by injection) improved iron status and aerobic capacity in iron-deficient but nonanemic endurance athletes identified 19 studies involving 80 men and 363 women with a mean age of 22 years. Iron treatments improved iron status as expected, but they did not guarantee improvement in aerobic capacity or indices of endurance performance [153]. Another systematic review and meta-analysis compared the effects of iron supplementation with no supplementation on exercise performance in women of reproductive age [149]. Most of the 24 studies identified were small (i.e., they randomly assigned fewer than 20 women to a treatment or control group) and had a risk of bias. Based on the limited data and heterogenicity of results, the study authors suggested that preventing and treating iron deficiency could improve the performance of female athletes in sports that require endurance, maximal power output, and strength.  
  
Safety  
Athletes can safely obtain recommended intakes of iron by consuming a healthy diet containing iron-rich foods and by taking an iron-containing dietary supplement as needed. High doses of iron may be prescribed for several weeks or months to treat iron deficiency, especially if anemia is present.  
  
The UL for iron is 45 mg/day for men and women age 14 and older and 40 mg/day for younger children [147]. Acute intakes of more than 20 mg/kg iron from supplements or medicines can lead to gastric upset, constipation, nausea, abdominal pain, vomiting, and fainting, especially if users do not consume food at the same time [147,150]. Individuals with hereditary hemochromatosis, which predisposes them to absorb excessive amounts of dietary and supplemental iron, have an increased risk of iron overload [154].  
  
Implications for use  
Correcting iron deficiency anemia improves work capacity, but there is conflicting evidence on whether milder iron deficiency without anemia impairs athletic performance. In a position statement, the AND, DoC, and ACSM do not recommend routine supplementation of iron except in response to a health care provider s instruction and note that such supplementation is only ergogenic if the individual has iron depletion [12]. Furthermore, they warn that iron supplementation can cause gastrointestinal side effects.  
  
The recommended dietary allowance (RDA) for iron is 11 mg for teenage boys and 15 mg for teenage girls [147]. The RDA is 8 mg for men and 18 mg for women age 50 and younger, and 8 mg for older adults of both sexes. Individuals who engage in intense exercise might require 30% to 70% more iron than moderately active and sedentary people [147]. Recommended intakes of iron for vegetarians and vegans are 1.8 times higher than for people who eat meat [147].  
  
More information on iron and the treatment of iron-deficiency anemia is available in the ODS health professional fact sheet on iron.  
  
Protein  
Protein is necessary to build, maintain, and repair muscle. Exercise increases intramuscular protein oxidation and breakdown, after which muscle-protein synthesis increases for up to a day or two [155]. Regular resistance exercise results in the accretion of myofibrillar protein (the predominant proteins in skeletal muscle) and an increase in skeletal muscle fiber size. Aerobic exercise leads to more modest protein accumulation in working muscle, primarily in the mitochondria, which enhances oxidative capacity (oxygen use) for future workouts [155,156].  
  
Athletes must consider both protein quality and quantity to meet their needs for the nutrient. They must obtain EAAs from the diet or from supplementation to support muscle growth, maintenance, and repair [155]. The nine EAAs are histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine. Most complete proteins (those that contain all EAAs) are composed of about 40% EAAs, so a meal or snack with 25 g total protein provides about 10 g EAAs.  
  
See other sections of this fact sheet for information on the amino acids arginine and glutamine as well as the BCAAs (leucine, isoleucine, and valine). The potential of these amino acids to enhance exercise and athletic performance is not related to their incorporation into proteins.  
  
Efficacy  
Adequate protein in the diet is required to provide the EAAs necessary for muscle-protein synthesis and to minimize muscle-protein breakdown. Dietary protein consumption increases the concentration of amino acids in the blood, which muscle cells then take up. Sufficient protein is necessary primarily to optimize the training response to, and the recovery period after, exercise [12,157].  
  
Muscle protein synthesis leading to increases in strength and muscle mass appears to be optimal with the consumption of high-quality protein (providing about 10 g EAAs) within 0 2 hours after exercise, in the early recovery phase [12]. However, a meta-analysis of randomized clinical trials found that ingesting protein within an hour before or after exercise does not significantly increase muscle strength or size or facilitate muscle repair or remodeling [77]. The period after exercise when protein intake reduces muscle protein breakdown, builds muscle, and increases mitochondrial proteins to enhance oxygen use by working muscles (the so-called window of anabolic opportunity) can last for up to 24 hours [79].  
  
Several studies in people engaged in resistance training show that consuming some protein before sleep can increase the rate of protein synthesis during the night and/or augment muscle mass and strength [79,158,159]. Participants in these studies consumed a bedtime drink containing 27.5 or 40 g of the milk protein casein, which increased circulating amino acid levels throughout the night. Some studies show increased muscle protein synthesis when plasma levels of amino acids are raised [76].  
  
Safety  
The Food and Nutrition Board has not set a UL for protein, noting that the risk of adverse effects from excess protein from food is very low [160]. However, it advises caution for those obtaining high protein intakes from foods and supplements because of the limited data on their potential adverse effects. High-protein diets (e.g., those providing two to three times the RDA of 0.8 g/kg/day for healthy adults and 0.85 g/kg/day for adolescents) do not appear to increase the risk of renal stones or dehydration; compromise renal function; reduce bone health; or, when consumed for several months, alter glomerular filtration rate or blood levels of lipids, glucose, creatine, or blood urea nitrogen [160-164]. Protein increases urinary calcium excretion, but this appears to have no consequence for long-term bone health [165] and, in any event, is easily compensated for by the consumption of slightly more calcium.  
  
Implications for use  
Many foods including meats, poultry, seafood, eggs, dairy products, beans, and nuts contain protein. Protein powders and drinks are also available, most of which contain whey, one of the complete proteins isolated from milk [166]. Digestion of casein, the main complete protein in milk, is slower than that of whey, so the release of amino acids from casein into the blood is slower [72]. Soy protein lacks the EAA methionine and might lose some cysteine and lysine in processing; rice protein lacks the EAA isoleucine [166]. Many protein supplements consist of a combination of these protein sources. All EAAs are necessary to stimulate muscle protein synthesis, so users should select singular or complementary protein sources accordingly. To maximize muscle adaptations to training, the AND, DoC, and ACSM recommend that athletes consume 0.3 g/kg body weight of high-quality protein (e.g., about 20 g for a person weighing 150 lb) 0 to 2 hours after exercise and then every 3 to 5 hours [12].  
  
Since the Food and Nutrition Board developed the RDA for protein, more recent data have suggested that athletes require a daily protein intake of 1.2 to 2.0 g/kg to support metabolic adaptations, muscle repair and remodeling, and protein turnover [12,167]. Athletes might benefit from even greater amounts for short periods of intense training or when they reduce their energy intake to improve physique or achieve a competition weight [12]. The 2007 2008 National Health and Nutrition Examination Survey (NHANES) showed that the average daily intake of protein by adult men is 100 g and by women is 69 g [168]. Athletes who require additional protein can obtain it by consuming more protein-containing foods and, if needed, protein supplements and protein-fortified food and beverage products.  
  
Quercetin  
Quercetin is a polyphenolic flavonol that is naturally present in a variety of fruits (such as apples), vegetables (such as onions), and beverages (such as wine and, especially, tea). An analysis of NHANES 1999 2002 data found that estimated daily total flavonol (including quercetin) consumption by adults averaged about 13 mg/day [169]. The mechanisms by which quercetin might enhance exercise and athletic performance when taken in much larger amounts are not known, but many have been hypothesized. For example, quercetin might increase the number of mitochondria in muscle, reduce oxidative stress, decrease inflammation, and improve endothelial function (blood flow) [170,171].  
  
Efficacy  
Numerous small studies have assessed quercetin in supplemental form as a potential ergogenic aid in young adult, mostly male, participants. These studies typically examined the endurance performance and VO2max of participants engaged in aerobic activities, such as running or cycling trials, who received either quercetin (most often 1,000 mg/day) or placebo for 1 to 8 weeks [170,172-175]. The effects of quercetin supplementation were inconsistent and varied by study, but they generally ranged from no ergogenic benefit to only a trivial or small improvement that might not be meaningful in real-world (in contrast to laboratory) exercise conditions [42,170,171,176].  
  
Safety  
The studies of trained athletes and untrained participants cited in the previous paragraph who took as much as 1,000 mg/day quercetin for up to 2 months found no side effects or safety concerns. The safety of longer term use of that amount of quercetin or more has not been studied. FDA considers up to 500 mg/serving quercetin to be generally recognized as safe (GRAS) as an ingredient in foods such as beverages, processed fruits and fruit juices, grain products, pastas, and soft candies [171,177].  
  
Implications for use  
More research, including larger clinical trials, on quercetin supplementation to improve aerobic capacity in trained athletes during specific sports and competitions is needed before any recommendations can be made [170].  
  
Ribose  
Ribose, a naturally occurring 5-carbon sugar synthesized by cells and found in some foods, is involved in the production of ATP [75]. The amount of ATP in muscle is limited, and it must continually be resynthesized. Therefore, theoretically, the more ribose in the body, the more potential ATP production [178].  
  
Efficacy  
The limited amount of research on ribose shows little if any benefit of doses ranging from 625 to 10,000 mg/day for up to 8 weeks for exercise capacity in both trained and untrained healthy adults [1,179].  
  
Safety  
The authors of the short-term studies investigating ribose as a potential ergogenic aid have not reported any safety concerns. No studies have assessed the safety of long-term ribose use as a dietary supplement.  
  
Implications for use  
Supplemental ribose does not appear to improve aerobic or anaerobic performance [1,75].  
  
Sodium bicarbonate  
Sodium bicarbonate is commonly known as baking soda. The consumption of several teaspoons of sodium bicarbonate over a short time temporarily increases blood pH by acting as a buffering agent. The precise mechanism by which this induced alkalosis leads to an ergogenic response to exercise is unclear. It is thought that bicarbonate loading enhances disposal of hydrogen ions that accumulate and efflux from working muscles as they generate energy in the form of ATP via anaerobic glycolysis from high-intensity exercise, thereby reducing the metabolic acidosis that contributes to fatigue [180,181]. As a result, supplementation with sodium bicarbonate might improve performance in short-term, intense exercises (e.g., sprinting and swimming) and in intermittently intense sports (e.g., boxing and tennis).  
  
Efficacy  
Many studies have assessed sodium bicarbonate as an ergogenic aid in swimmers, cyclists, rowers, boxers, tennis and rugby players, judo practitioners, and others [180-182]. These studies usually included a small number of participants who underwent one or more trials in a laboratory over several days.  
  
Because the research results are conflicting, the activities and individuals most likely to benefit from sodium bicarbonate supplementation in real-world conditions is not clear. Reviewers of these studies generally agree that taking about 300 mg/kg body weight sodium bicarbonate might provide a minor to moderate performance benefit in strenuous exercise over several minutes and in sports that involve intermittent, high-intensity activity [180-182]. However, individuals have varied responses to bicarbonate loading; the practice does not benefit some users, and it can worsen rather than enhance performance in others. Recreationally active individuals, in particular, might find the supplements to be ergogenic for one exercise session but not another. Many study findings suggest that supplementation with sodium bicarbonate is most likely to improve the performance of trained athletes [181,182].  
  
Safety  
The main side effect of sodium bicarbonate supplementation in gram quantities is gastrointestinal distress, including nausea, stomach pain, diarrhea, and vomiting. Supplement users can reduce or minimize this distress by consuming the total dose in smaller amounts multiple times over an hour with fluid and a snack of carbohydrate-rich food [180,183]. Sodium bicarbonate is 27.4% sodium by weight; 1 teaspoon (4.6 g) contains 1,259 mg sodium. A 70-kg individual ingesting a recommended dose of 300 mg/kg body weight would consume approximately 5,750 mg sodium. Such a large intake of sodium with fluid can lead to temporary hyperhydration, which could be useful in activities where large sweat losses might otherwise lead to significant fluid deficits. However, the slight increase in body weight from fluid retention might hinder performance in other sports [180]. Studies have not evaluated the safety (and effectiveness) of long-term use of sodium bicarbonate as an ergogenic aid over months or longer.  
  
Implications for use  
The amount of sodium bicarbonate in recommended servings of dietary supplements about 300 mg/kg body weight, or the equivalent of 4 5 teaspoons of baking soda for most individuals taken 1 2 hours before exercise in one or multiple doses as a pill or as a powder mixed with a flavored fluid is generally much less than the quantity that could enhance exercise and athletic performance. Many athletes find this amount of sodium bicarbonate powder dissolved in fluid to be unpalatably salty [180]. The Australian Institute of Sport supports the use of bicarbonate for improving sports performance in suitable athletic competitions under the direction of an expert in sports medicine, but it notes that more research might be required to understand how the supplement should be used for best results [29].  
  
Tart or sour cherry  
The Montmorency variety of tart or sour cherry (Prunus cerasus) contains anthocyanins and other polyphenolic phytochemicals, such as quercetin. Researchers hypothesize that these compounds have anti-inflammatory and antioxidant effects that might facilitate exercise recovery by reducing pain and inflammation, strength loss and muscle damage from intense activity, and hyperventilation trauma from endurance activities [184-187]. The labels on tart-cherry juice and concentrate products do not usually indicate that they are dietary supplements, although the labels on products containing encapsulated tart-cherry powder do.  
  
Efficacy  
Much of the limited research on use of tart cherry to enhance exercise and athletic performance involves short-term use of a tart-cherry product or placebo by young resistance-trained men for about a week before a test of strength (such as single-leg extensions or back squats); participants continue taking the supplements for about 2 days after the test. Study results vary, but the benefits appear to include more rapid recovery of strength and/or lower perceived muscle soreness [184,185,188]. One pilot study investigated the use of tart-cherry juice (472 ml/day; the equivalent of 100 120 whole cherries) or a placebo for a week before a marathon and 2 days afterward in 13 male and 7 female runners (age range 24 50 years) [186]. None of the participants who drank the juice experienced airway inflammation causing upper respiratory tract symptoms after the marathon (a common complaint in many marathon runners), but half of those drinking the placebo did. Another study compared a supplement containing 480 mg freeze-dried Montmorency tart-cherry-skin powder (CherryPURE) with a placebo in 18 male and 9 female endurance-trained runners and triathletes (age range 18 26 years) [189]. Participants took the supplements once a day for 10 days, including the day they ran a half-marathon, then for 2 days after the run. Participants taking the tart-cherry supplement averaged a statistically significant 13% shorter race finish time and had lower levels of blood markers of inflammation and muscle catabolism than the placebo takers, but perceptions of soreness of the quadriceps muscles did not differ significantly between the groups.  
  
Further research is needed to determine the value of tart-cherry products for enhancing performance and recovery from intense exercise or participation in sports especially when used on a regular basis and the amounts of supplement, juice, or concentrate needed to provide any benefits.  
  
Safety  
Studies have not identified any side effects of the fresh tart-cherry juice or concentrate or of supplements of dried tart-cherry-skin powder. However, they have not adequately assessed the safety of tart-cherry dietary supplements.  
  
Implications for use  
There is no expert consensus on the value of taking tart-cherry products to enhance exercise and athletic performance.  
  
Tribulus terrestris  
Tribulus terrestris (common names include bindii, goat s-head, bullhead, and tackweed), is a fruit-bearing plant that is most common in Africa, Asia, Australia, and Europe. It has been used since ancient times in Greece, China, and Asia to treat low libido and infertility [190]. Tribulus terrestris extracts contain many compounds, including steroidal saponins [191]. Some marketers claim that Tribulus terrestris enhances exercise and athletic performance by increasing serum concentrations of testosterone and luteinizing hormone, but studies have not adequately determined its potential mechanisms of action [192].  
  
Efficacy  
Only a few small, short-term clinical trials have investigated Tribulus terrestris as an ergogenic aid [192], and none since 2007. In one study, 10 mg/kg or 20 mg/kg Tribulus terrestris or a placebo taken for 4 weeks by men age 20 36 years did not raise levels of either hormone [193]. A study in 15 resistance-trained men found no differences among those taking 3.21 mg/kg Tribulus terrestris or placebo for 8 weeks in improvements in bench and leg press scores or in muscle mass [194]. In 22 elite male rugby players age 19.8 years, on average, who were randomly assigned to take 450 mg/day Tribulus terrestris or a placebo for 5 weeks, the supplement did not have a superior effect on strength or lean body mass [192].  
  
Safety  
The only toxicity studies of Tribulus terrestris were conducted in animals, where unspecified high intakes led to severe heart, liver, and kidney damage [190]. The clinical studies described above found no side effects of Tribulus terrestris. One case report involved an Iranian man with severe obesity, age 28, who consumed 2 L/day Tribulus terrestris water for 2 days before being hospitalized with seizures, severe weakness in the legs, malaise, and poor appetite [195]. Subsequent tests indicated hepatotoxicity, nephrotoxicity, and neurotoxicity. The man s condition improved after he discontinued the water, but the water was not tested to determine the presence or amount of Tribulus terrestris or any other potential toxin or contaminant.  
  
Implications for use  
The Australian Institute of Sport advises against the use of Tribulus terrestris by athletes, noting that this supplement and other claimed testosterone boosters are banned from athletic competitions or have a high risk of being contaminated with substances that, if ingested, could lead to positive drug-screening results [196].  
  
The published biomedical literature provides no support for the efficacy and insufficient support for the safety of Tribulus terrestris for enhancing exercise performance [190].  
  
Ingredients Banned from Dietary Supplements  
This section provides examples of ingredients that FDA currently prohibits in dietary supplements and that some consumers have used in the past as ergogenic aids, despite the lack of evidence supporting their use.  
  
Androstenedione  
Androstenedione is an anabolic steroid precursor, or prohormone, that the body converts to testosterone (which induces muscle growth) and estrogen [197]. Major League Baseball slugger Mark McGwire popularized androstenedione as an ergogenic aid in 1998 [198]. However, two randomized clinical trials found no performance benefits from androstenedione supplements. In one study, 10 healthy young men (age 19 29 years) took a single 100-mg dose of androstenedione. Another 20 were randomized to receive either 300 mg/day androstenedione or a placebo for 6 of 8 weeks while undergoing resistance-training and muscle-strengthening exercises [199]. The short-term or longer term use of the supplement did not affect serum testosterone concentrations, nor did it produce any significantly greater gains in resistance-training performance, muscle strength, or lean body mass. However, participants who took androstenedione for the 6 weeks experienced significant declines in their high-density lipoprotein (HDL) cholesterol levels and significant increases in serum estrogens. A similar study randomized 50 men (age 35 65 years) to take 200 mg/day androstenedione, 200 mg/day of the related androstenediol, or a placebo for 12 weeks while participating in a high-intensity resistance training program [200]. The supplements did not improve participants muscular strength or lean body mass compared with placebo, but they significantly decreased HDL cholesterol levels and raised levels of serum estrogens. Among participants taking the androstenedione, testosterone levels increased significantly by 16% after 1 month of use but declined to pretreatment levels by 12 weeks, in part due to downregulation of endogenous testosterone synthesis.  
  
In March 2004, FDA warned companies to cease distributing androstenedione-containing dietary supplements. The rationale was the lack of sufficient information to establish that such products could reasonably be expected to be safe and that FDA had never approved androstenedione as a new dietary ingredient permitted in supplements [197]. The U.S. Department of Justice classified androstenedione as a Schedule III controlled substance (defined as a drug with a moderate to low potential for physical and psychological dependence) in 2004 [201]. The National Collegiate Athletic Association, International Olympic Committee, and World Anti-Doping Agency ban the use of androstenedione [128,197].  
  
Dimethylamylamine  
Dimethylamylamine (DMAA) is a stimulant formerly included in some preworkout and other dietary supplements claimed to enhance exercise performance and build muscle. Studies have not evaluated DMAA in humans as a potential ergogenic aid. In 2013, FDA declared products containing this ingredient to be illegal after it received 86 reports of deaths and illnesses associated with dietary supplements containing DMAA. These reports described heart problems as well as nervous system and psychiatric disorders [202]. Furthermore, FDA had never approved DMAA as a new dietary ingredient that would reasonably be expected to be safe [202]. Although products marketed as dietary supplements containing DMAA are illegal in the United States, discontinued, reformulated, or even new products containing DMAA might still be found in the U.S. marketplace. The Department of Defense s Human Performance Resource Center maintains a list of currently available products that contain DMAA or are labeled as containing DMAA, 1-3-dimethylamylamine, or an equivalent chemical or marketing name (e.g., methylhexaneamine or geranium extract) [203].  
  
FDA also determined that dietary supplements containing 1,3-dimethybutylamine (DMBA), a stimulant chemically related to DMAA, are adulterated. As with DMAA, FDA had never approved this stimulant as a new dietary ingredient. The agency contended that there is no history of use or data offering sufficient assurance that this compound is not associated with a significant or unreasonable risk of illness or injury [204,205].  
  
Ephedra  
Ephedra (also known as ma huang), a plant native to China, contains ephedrine alkaloids, which are stimulant compounds; the primary alkaloid is ephedrine [206]. In the 1990s, ephedra frequently combined with caffeine was a popular ingredient in dietary supplements sold to enhance exercise and athletic performance and to promote weight loss.  
  
No studies have evaluated the use of ephedra dietary supplements, with or without caffeine, as ergogenic aids. Instead, available studies have used the related synthetic compound ephedrine together with caffeine and typically measured the effects 1 2 hours after a single dose [207,208]. These studies showed that the ephedrine caffeine combination produced a 20% 30% increase in power and endurance, but ephedrine alone had no significant effects on exercise-performance parameters, such as oxygen consumption or time to exhaustion [208]. No data show any sustained improvement in athletic performance over time with continued dosing of ephedrine with caffeine [207].  
  
Ephedra use has been associated with death and serious adverse effects, including nausea, vomiting, psychiatric symptoms (such as anxiety and mood change), hypertension, palpitations, stroke, seizures, and heart attack [206,207]. In 2004, FDA banned the sale of dietary supplements containing ephedrine alkaloids in the United States because they are associated with an unreasonable risk of illness or injury [207]. The World Anti-Doping Agency prohibits the use of ephedrine in amounts that lead to urine concentrations of ephedrine (or the related methylephedrine) exceeding 10 mcg/ml [107].  
  
Regulation of Dietary Supplements to Enhance Exercise and Athletic Performance  
FDA regulates dietary supplements for exercise and athletic performance in accordance with the Dietary Supplement Health and Education Act of 1994 [209]. Like other dietary supplements, exercise- and athletic-performance supplements differ from over-the-counter or prescription medications in that they do not require premarket review or approval by FDA. Supplement manufacturers are responsible for determining that their products are safe and their label claims are truthful and not misleading, although they are not required to provide this evidence to FDA before marketing their products. If FDA finds a supplement to be unsafe, it may remove the product from the market or ask the manufacturer to voluntarily recall the product. FDA and the Federal Trade Commission (FTC) may also take regulatory actions against manufacturers that make unsubstantiated physical-performance or other claims about their products.  
  
FDA permits dietary supplements to contain only dietary ingredients, such as vitamins, minerals, amino acids, herbs, and other botanicals. It does not permit these products to contain pharmaceutical ingredients, and manufacturers may not promote them to diagnose, treat, cure, or prevent any disease [209].  
  
For more information about dietary supplement regulation, see the ODS publication, Dietary Supplements: What You Need to Know.  
  
Safety Considerations  
Like all dietary supplements, supplements used to enhance exercise and athletic performance can have side effects and might interact with prescription and over-the-counter medications. In some cases, the active constituents of botanical or other ingredients promoted as ergogenic aids are unknown or uncharacterized. Furthermore, many such products contain multiple ingredients that have not been adequately tested in combination with one another. People interested in taking dietary supplements to enhance their exercise and athletic performance should talk with their health care providers about the use of these products.  
  
The Uniformed Services University and the U.S. Anti-Doping Agency maintain a list of products marketed as dietary supplements that contain stimulants, steroids, hormone-like ingredients, controlled substances, or unapproved drugs and that can have health risks for warfighters and others who take them for bodybuilding or other forms of physical performance [210].  
  
Fraudulent and adulterated products  
FDA requires the manufacture of dietary supplements to comply with quality standards that ensure that these products contain only the labeled ingredients and amounts and are free of undeclared substances and unsafe levels of contaminants [211]. However, FDA notes that products marketed as dietary supplements for bodybuilding are among those most often adulterated with undeclared or deceptively labeled ingredients, such as synthetic anabolic steroids or prescription medications [212]. As one example, some products sold for bodybuilding are adulterated with selective androgen receptor modulators; these synthetic drugs are designed to mimic the effects of testosterone [213]. Using such tainted products can cause health problems and lead to disqualification of athletes from competition if a drug test shows that they have consumed prohibited substances, even if they have done so unknowingly. FDA has warned against the use of any body-building products that claim to contain steroids or steroid-like substances [214]. It recommends that a user contact their health care provider if they experience symptoms possibly related to these products, especially nausea, weakness, fatigue, fever, abdominal pain, chest pain, shortness of breath, jaundice (yellowing of skin or whites of eyes), or brown or discolored urine.  
  
Some dietary-supplement firms have hired third-party certification companies to verify the identity and content of their supplements to enhance exercise and athletic performance, thus providing some extra, independent assurance that the products contain the labeled amounts of ingredients and are free of many banned substances and drugs. The major companies providing this certification service are NSF (nsf.org) through its Certified for Sport program, Informed-Choice (informed-choice.org), and the Banned Substances Control Group (bscg.org). The products that meet the requirements of these companies may carry the certifier s official logo and are listed on the certifier s website.  
  
Interactions with medications  
Some ingredients in dietary supplements used to enhance exercise and athletic performance can interact with certain medications. For example, intakes of large doses of antioxidant supplements, such as vitamins C and E, during cancer chemotherapy or radiotherapy could reduce the effectiveness of these therapies by inhibiting cellular oxidative damage in cancerous cells [215]. Ginseng can reduce the anticoagulant effects of the blood thinner warfarin (Coumadin or Jantoven) [216]. Iron supplements can reduce the bioavailability of levodopa (used to treat Parkinson s disease) and levothyroxine (Levothyroid, Levoxyl, Synthroid, and others, for hypothyroidism and goiter), so users should take iron supplements at a different time of the day than these two drugs [217,218]. Cimetidine (Tagamet HB, used to treat duodenal ulcers) can slow the rate of caffeine clearance from the body and thereby increase the risk of adverse effects from caffeine consumption [219].  
  
Individuals taking dietary supplements and medications on a regular basis should discuss the use of these products with their health care providers.  
  
Choosing a Sensible Approach to Enhance Exercise and Athletic Performance  
According to the AND, DoC, and ACSM, sound science supports the use of only a few dietary supplements whose labels claim ergogenic benefits [12]. These organizations add that the best way to use supplements is as additions to a carefully chosen diet, that dietary supplements rarely have ergogenic benefits when not used in these conditions, and that there is no justification for their use by young athletes. The National Federation of State High School Associations also expresses strong opposition to the use of supplements to enhance athletic performance by high school students [15]. The American Academy of Pediatrics adds that performance-enhancing substances do not result in significant improvements in most teenage athletes beyond those that can result from proper nutrition and training basics [7].  
  
Elite and recreational athletes perform at their best and recover most quickly when they consume a nutritionally adequate diet with sufficient fluids and when they have appropriate physical conditioning and proper training.  
  
For more information about building a healthy dietary pattern, refer to the Dietary Guidelines for Americansexternal link disclaimer [10] and the U.S. Department of Agriculture s MyPlateexternal link disclaimer [11]. The Dietary Guidelines for Americans describes a healthy dietary pattern as one that:  
  
Includes a variety of vegetables; fruits; grains (at least half whole grains); fat-free and low-fat milk, yogurt, and cheese; and oils  
Includes a variety of protein foods such as lean meats; poultry; eggs; seafood; beans, peas, and lentils; nuts and seeds; and soy products  
Limits foods and beverages higher in added sugars, saturated fat, and sodium  
Limits alcoholic beverages  
Stays within your daily calorie needs  
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