Sports Supplements: What's New, What's Effective, and What's the Risk?

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2019 Primary Care Sports Medicine Course

Disclosures

- I have no relevant relationships to disclose or conflicts of interest to declare

Objectives

- Discuss common sports supplementation physiological mechanisms ergogenic effects on exercises
- Discuss common side effects of supplemental use

What is a supplement?

- A dietary supplement is a commercially available product that is consumed as an addition to the usual diet and includes vitamins, minerals, herbs (botanicals), amino acids, and a variety of other products.
- Dietary supplements used for exercise and athletic performance come in a variety of forms, including tablets, capsules, liquids, powders, and bars.

Regulation

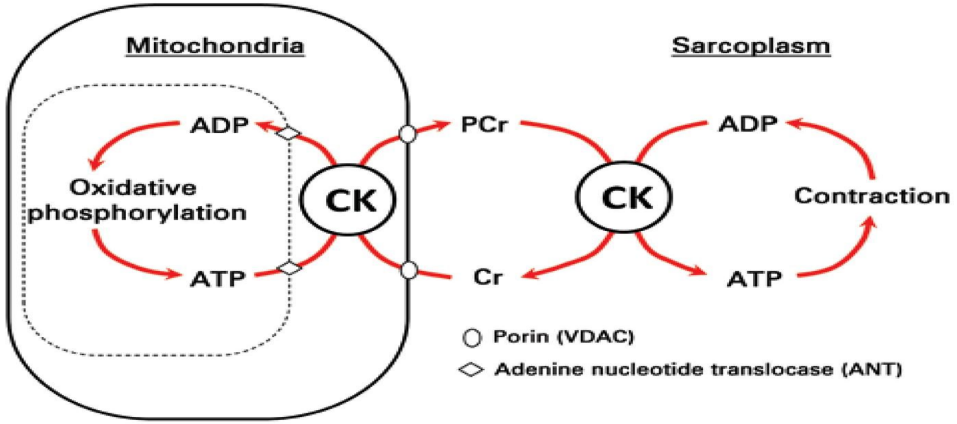
- Congress passed the Dietary Supplement Health and Education Act of 1994 (DSHEA), placing dietary supplements in a special category of foods
- The law defines a dietary supplement as a product that is intended to supplement the diet and contains a dietary ingredient.
    - By definition, dietary ingredients in these products may include vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, and glandular extracts.
- In the United States, dietary supplements are classified as food products, not drugs, and there is generally no mandate to register products with the FDA or obtain FDA approval before producing or selling supplements to consumers.
    - However, if a dietary supplement manufacturer is making a claim about their product, the company must submit the claims to FDA within 30 days of marketing the product.

Regulation

- In 2007, President Bush signed into law the Dietary Supplement and Nonprescription Drug Consumer Protection Act, which established the first mandatory Adverse Event Reporting (AER)
    - A Serious Adverse event is an event that results in:
        - death
        - a life-threatening experience
        - inpatient hospitalization
        - a persistent or significant disability or incapacity
        - a congenital anomaly or birth defect;
        - OR requires a medical or surgical intervention to prevent an outcome

Creatine

- Creatine is likely the most popular nutritional supplement used for performance enhancement
- Naturally occuring in the body and synthesized from glycine, arginine and methionine in the liver, kidney and pancreas
- Approximately 95% of creatine is stored in skeletal muscle in free and phosphorylated forms.
- It is not prohibited by WADA and has been shown to be effective at improving training and performance of short-duration, high-intensity exercise.
- Creatine is available in a wide range of commercial products, primarily as a powder
- Metabolized creatine is converted into the waste product creatinine, which is eliminated from the body through the kidneys.



ADP: adenosine diphosphate; CK: creatinine kinase; PCr: phosphocreatine; ATP: adenosine triphosphate; Cr: free creatinine

Physiological effects

- 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

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

Safety

- Studies have found no consistent set of side effects from creatine use, except that it often leads to weight gain,
- 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
- Overall, Creatine is considered safe for short-term use by healthy adults
- Anecdotal reactions to creatine use include:
    - nausea
    - diarrhea and related gastrointestinal distress
    - muscle cramps
    - heat intolerance

Safety

- Kidney function?
  - Although some have claimed that creatine can adversely affect kidney function, limited published evidence and wide experience with this supplement suggest that this is not true in patients with normal baseline renal function
- In fact, creatine may be beneficial when exercising in hot, humid conditions, as the increased body water appears to aid thermoregulation, reduce heart rate, and reduce sweating
- The potential long-term consequences of creatine supplementation are unknown,
- The American College of Sports Medicine (ACSM) recommends it be used only by physically mature, well-developed athletes and it is not recommended for adolescent athletes.

Implications for use

- The Academy of Nutrition and Dietetics (AND), the Dietitians of Canada (DoC), and the American College of Sports Medicine (ACSM) advise that creatine enhances performance of cycles of high-intensity exercise followed by short recovery periods and improves training capacity
- In its position statement, International Society of Sports Nutrition (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
- 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

BCAA

- Consist of leucine, valine, and isoleucine
- They cannot be synthesized in the body
- Mainly found in large amounts via red meat and dairy products
- Vegetarians can obtain sufficient amounts if they eat an adequate amount and appropriate mix of legumes, nuts, grains, and seeds daily.
- BCAAs are metabolized in the muscle during exercise in the mitochondria, which helps to provide energy during exercise

Proposed Mechanism of Action

- During prolonged exercise there is a rise in the breakdown of BCAA in muscle tissue and increased levels of free fatty acids in the blood.
- FFA compete with tryptophan for binding sites on plasma albumin, displacing tryptophan and increasing its blood levels
- With this increase, tryptophan and BCAA compete for transporters at the BBB, leading to an increase in levels of tryptophan crossing
- If tryptophan increases this leads to increased serotonin levels and contributes to possible limited mental and physical performance
- Its hypothesized that increased BCAA supplementation, decreases tryptophan levels and causes increased mental and physical performance

Photo

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
- 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
- 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
- Several studies have reported reductions in muscle soreness after both acute and chronic supplementation, but this is probably most prominent in untrained individuals

Safety

- Up to 20 g/day BCAA supplements in divided doses appear to be safe for up to 6 weeks
- 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)
- No known reported adverse effects

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 essential amino acids—automatically increases consumption of BCAAs

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
- The body also synthesizes arginine (from citrulline), mainly in the kidneys

Proposed MOA

- Some experts suggest that taking arginine in supplement form enhances exercise and athletic performance in several ways:
  - Arginine can be converted to nitric oxide, which acts as a potent vasodilator that can increase blood flow and the delivery of oxygen and nutrients to skeletal muscle
  - Removal of metabolic waste products due to increased vasodilation
  - Can serve as a precursor for the synthesis of creatine
  - 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 2-10 g as a single dose or 20 g/day divided into 3 doses have little to no effect on performance in either anaerobic or aerobic exercise
- A 2016 review article 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 and elite level athletes.
    - 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

Efficacy

- 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 or raise HGH and IGF-1 secretion
    - Even raised HGH secretion, however, might not translate into more blood flow into muscle or greater protein synthesis
    - Little evidence shows supplemental arginine by itself increases muscle creatine concentrations or is superior or complementary to direct consumption of creatine

Safety

- Most study results suggest that up to 9 g/day arginine for several days or weeks is safe and well tolerate
- 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
- The safety of taking high-dose arginine supplements for more than 3 months is not known

Implications for use

- Arginine ability to enhance strength, improve exercise or athletic performance, or promote muscular recovery after exercise has little scientific support

Antioxidants

- Consist of supplement that include but no limited to Vitamin C, Vitamin E and coenzyme Q10(CoQ10)
- Could be used to reduce this free-radical formation, which minimizes:
    - minimizing skeletal muscle damage
    - inflammation
    - fatigue
    - promoting recovery

Proposed Mechanism of Action

- 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

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 aged 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

Efficacy

- 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
- Another study randomly assigned 18 young men aged 20 to 34 years to receive 120 mg/day CoQ10 for 22 days or a placebo
    - 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.

Efficacy

- 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.
- 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

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.
- 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.
- Potential adverse effects of excess vitamin C are:
    - diarrhea, nausea, abdominal cramps, and other gastrointestinal disturbances.
- Potential adverse effects of excess vitamin E are:
    - increases the risks of hemorrhagic effects and if taken over several years, prostate cancer
- Potential adverse effects of excess CoQ10 are mild but can include:
    - fatigue, insomnia, rashes, nausea, upper abdominal pain, heartburn, sensitivity to light, irritability, dizziness, and headaches

Beet root 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, which is a potent vasodilator that can increase blood flow and the delivery of oxygen and nutrients to skeletal muscle.
  - 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
- Beetroot is available as a juice or juice concentrate and in powdered form; the amount of nitrate can vary considerably among products.

Efficacy

- 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
- Performance benefits are more likely in recreationally active non-athletes than elite athletes
- There has been little study of the effects of beetroot on anaerobic performance, such as high-volume resistance exercise with many repetitions
- 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

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.
- Although not a safety concern, beetroot consumption can color the urine pink or red due to the excretion of red pigments in the beets

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 they improve endurance exercise performance in recreational athletes.
- 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.
- 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, which provides up to 682 mg of nitrate, depending on the product

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.
- Glutamine is a key molecule in metabolism and energy production, and it contributes nitrogen for many critical biochemical reactions

Efficacy

Few studies have examined the effect of glutamine supplementation alone as an ergogenic aid

- One study randomized 31 male and female weight lifters 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
    - 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

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

Implications for use

- The research to date does not support taking glutamine alone to improve exercise and athletic performance

Sodium Bicarbonate

- 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
- 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
- Reviewers of these studies generally agree that taking about 300 mg/kg body weight sodium bicarbonate might provide a minor to moderate performance benefit
- 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.

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
- 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
- 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
- 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

Tart or Sour Cherry

- 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
    - hyperventilation trauma from endurance activities
- 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

- Study results vary, but the benefits appear to include more rapid recovery of strength and/or lower perceived muscle soreness
- 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)
    - 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.

Efficacy

- 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)
    - 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.

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.

References

http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1679-45082014000100024 photo creatine