

[Primary Care]

Emerging Supplements in Sports

Bryan C. Mason, MD,*† and Mark E. Lavallee, MD‡

Context: Nutritional supplements advertised as ergogenic are commonly used by athletes at all levels. Health care professionals have an opportunity and responsibility to counsel athletes concerning the safety and efficacy of supplements on the market.

Evidence Acquisition: An Internet search of common fitness and bodybuilding sites was performed to identify supplement promotions. A search of MEDLINE (2000–August, 2011) was performed using the most commonly identified supplements, including glutamine, choline, methoxyisoflavone, quercetin, zinc/magnesium aspartate, and nitric oxide. The search terms *supplement*, *ergogenic aid*, and *performance* were also used.

Results: Six common and newer supplements were identified, including glutamine, choline, methoxyisoflavone, quercetin, zinc/magnesium aspartate, and nitric oxide.

Conclusions: Controlled studies have not determined the effects of these supplements on performance in athletes. Scientific evidence is not available to support the use of these supplements for performance enhancement.

Keywords: supplements; sports; performance enhancement

In today's highly competitive world of sports, some athletes look to supplements as a way to get an edge on the competition. Athletes of all ages and abilities are using dietary supplements to improve their performance.^{1,30,32} According to a survey by the Blue Cross Blue Shield Association's Healthy Competition Foundation, nearly 1 million American adolescents have taken a performance-enhancing substance.³² A 2001 study of high school football and volleyball players from northern Iowa reported that 49 of 902 athletes (5%) were using supplements.²⁴ Among National Collegiate Athletic Association athletes, 29% reported nutritional supplement use.¹⁹ Additionally, a study of Olympic athletes showed that over 70% of those in the Athens Summer Olympic Games reported supplement use.³⁴

Since the Dietary Supplement Health and Education Act of 1994, supplement sales have been on the rise. The annual sale of all nutritional supplements in the United States exceeds \$20 billion.¹ Athletes are constantly bombarded with advertisements claiming dramatic improvements in strength, speed, and/or endurance.^{30,32} Health care professionals should counsel athletes, both elite and recreational, concerning the safety and efficacy of supplements on the market. This can be a difficult task because of the lack of quality data. A study by Green et al analyzed the contents of 12 different supplements and found that 11 contained less than the stated amount, 1 had 177% of the stated amount, 2 contained none of the stated ingredients, and 1 contained 10 mg of testosterone.¹⁸

Risks must be taken into account when counseling on potential supplement use. It is also important to note that of the 6 supplements presented in this article, the only one with a potential reported side effect was at a dose used for supplementation with a nitric oxide precursor, NO-Xplode. This side effect, presented as a single case report, by no means establishes causation.

Most national federations and professional leagues, including the International Olympic Committee, do not have approved supplement lists. The World Anti-Doping Agency and the US Anti-Doping Agency do not recommend supplements as safe. Professional leagues, including the National Football League, Major League Baseball, and others, have contracted NSF International (<http://www.nsf-sport.com>) to certify supplements. This certification process is only for the presence (or, more accurately, the absence) of banned substances and does not certify effectiveness.

Glutamine, choline, methoxyisoflavone, quercetin, zinc/magnesium aspartate, and nitric oxide and nitric oxide precursors are all commonly advertised as ergogenic aids (Table 1). This review relied on 2 sources: the International Society of Sports Nutrition's 2010 review and the Australian Institute of Sport's (AIS's) online supplement guide.^{4,21} There are currently no similar groups in the United States.

The AIS Sports Supplement Program was established to provide AIS athletes with sound information on the safety and legality of supplements. It categorizes supplements into 1 of 4

From the †Memorial Hospital, South Bend, Indiana, and ‡Memorial Sports Medicine Institute, South Bend, Indiana

*Address correspondence to Bryan C. Mason, MD, Memorial Hospital, 714 North Michigan Street, South Bend, IN 46601 (e-mail: bmason2@memorialsb.org).

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Table 1. Summary of Emerging Supplements.

Study	Dose	Duration	Performance Measure	Significant Benefit
Glutamine				
Candow et al ⁹	0.9 mg/kg of lean body mass per day	6 wk	Muscle performance, body composition, muscle protein degradation	No
Choline				
Spector et al ³³	2.43 g	1 h before exercise	Fatigue time, work performed	No
Warber et al ³⁵	8.425 g	Before and midway through exercise	Run time to exhaustion, squat test (both following 4 h of strenuous exercise)	No
Duester et al ¹⁵	50 mg/kg	Before exercise	Manual dexterity, handgrip strength, lower body strength and coordination, upper body strength, reaction time, logical reasoning, visual vigilance, serial addition and subtraction, working memory, spatial memory, decoding	No
Methoxyisoflavone				
Wilborn et al ³⁸	800 mg/d	8 wk	Bench press, leg press, peak sprint power	No
Quercetin				
Abby et al ²	500 mg twice per day	7 d	Repeat sprint exercise	No
Bigleman et al ⁶	1000 mg/d	42-54 d during training	Energy and fatigue	No
Davis et al ¹²	500 mg twice per day	7 d	VO ₂ max, ride time to fatigue (cycling)	Yes
Cheuvront et al ¹¹	2000 mg	Immediately before exercise	Work performed, pacing strategy	No
Ganio et al ¹⁶	1000 mg/d	5 d	VO ₂ max	No
Konrad et al ²⁰	1000 mg/d	15 min before exercise	Immune/inflammatory markers	No
Nieman et al ²⁷	1000 mg/d	7 d	Treadmill endurance	No
Quindry et al ³¹	250 mg 4 times per day	3 wk before and during event	Ultramarathon race performance	No
Zinc/magnesium aspartate				
Brilla and Conte ⁸	30 mg of zinc and 450 mg of magnesium aspartate	7 wk	Torque and power of quadriceps and hamstrings	Yes
Wilborn et al ³⁷	30 mg of zinc and 450 mg of magnesium aspartate	8 wk	Bench press, leg press, cycling anaerobic capacity	No
Nitric oxide and precursors				
Bailey et al ⁵	6 g of L-arginine	1 hr before exercise	VO ₂ max and cycle time to fatigue	Yes
Bloomer et al ⁷	Glycine propionyl-L-carnitine, 4.5 g	30-60 min before exercise	Muscular power and endurance	No

categories: group A, supported for use by athletes; group B, considered for provision to AIS athletes only under a research protocol; group C, little proof of beneficial effects; and group D, not to be used by AIS athletes.⁴

GLUTAMINE

Glutamine, a nonessential amino acid, has many functions in the human body, including protein synthesis, and is an important energy source for cells of the immune system.^{21,39} Glutamine supplementation by athletes is an attempt to maintain immunity and guard against the immunosuppression that occurs with strenuous training.²⁶ It may improve muscle glycogen synthesis and muscle protein levels.^{4,36} Low glutamine levels have been implicated in overtraining syndrome.²⁸ Glutamine supplementation may improve glucose utilization postworkout and increase growth hormone levels.¹⁷ However studies have not shown beneficial effect on muscle repair or muscle soreness.¹⁷ A placebo-controlled study of 31 untrained individuals on a resistance training program was based on glutamine use (0.9 g/kg of lean tissue mass per day) for 6 weeks. Muscle performance, body composition, and muscle protein degradation were not significantly affected with glutamine supplementation.⁹ The International Society of Sports Nutrition lists glutamine as not effective for muscle building and performance enhancement.²¹

Immune suppression and a decrease in glutamine levels have been found in athletes undergoing intense physical training.¹⁷ The data are mixed, but overall there is no convincing evidence that glutamine supplementation can affect exercise-related immunosuppression.¹⁷ However, glutamine supplementation may decrease infections, length of stay, and mortality in critical care settings.³⁶ In athletes, a decrease in upper respiratory infections was found the week following a marathon or ultramarathon competition (2 doses of 5 mg, 2 hours apart, posttrace). Significant side effects have not been reported with doses of 0.1 to 0.6 mg/kg in clinical trials.^{3,17}

The AIS gives glutamine a group B recommendation; however, it is still under review.⁴ Glutamine may yet play a role in illness prevention.

CHOLINE

Choline is designated as an essential nutrient by the Institute of Medicine.⁴⁰ It is synthesized by the body and is in many common foods (eg, eggs, peanuts, dairy products). Choline is a precursor for acetylcholine, a neurotransmitter for muscle contraction.⁴⁰ It has a complex role in normal healthy function.⁴⁰ Low plasma levels have been found in endurance athletes; supplementation may decrease fatigue during exercise.¹⁰ It may also improve cognitive function.¹⁵ There is significant variation in individual dietary needs.⁴⁰

Placebo-controlled trials have not shown increases in anaerobic nor aerobic activity performance with choline supplementation.^{10,33,35} A double-blind crossover study of 20 male cyclists found no benefit in fatigue time or work

performed with a 2.43-g choline supplementation 1 hour before exercise.³³ A double-blind crossover study of 14 individuals found no performance enhancement in run time to exhaustion and squat test with an 8.425-g choline supplementation before and midway through the exercise.³⁵ A third double-blind crossover study found no improvement in cognitive or physical performance in military recruits.¹⁵ Outcome measures included manual dexterity, handgrip strength, lower body strength and coordination, and upper body strength. Cognitive outcomes included choice reaction time, logical reasoning, visual vigilance, serial addition and subtraction, working memory, spatial memory, and decoding.¹⁵

Choline can transport fat in and out of cells, and it potentially increases lipolysis.⁴⁰ It has also been promoted as a weight loss supplement; there are no human trials to support this claim. According to the International Society of Sports Nutrition review, it is unknown if phosphatidylcholine is an effective weight loss supplement.¹⁶

Common dosing levels in the above trials ranged between a single 2.43-g dose before exercise to 8.425 g before and during exercise. Side effects were mostly minor and included gastrointestinal upset and fishy body odor. Supplementation should be avoided in those athletes with gout.¹⁰

METHOXYISOFLAVONE

Methoxyisoflavone is a flavanoid, a naturally occurring phytoestrogen found in soy beans. The 2 common forms of methoxyisoflavones are 5-methyl-7-methoxyisoflavone (methoxyisoflavone) and 7-isopropoxyisoflavone (ipriflavone).²² These compounds may improve bone mineral density, reduce hot flash symptoms, improve cognitive function, and decrease cholesterol.²⁵ There is an anabolic effect in animals with isoflavone supplementation.^{21,38} However, there is a paucity of data to support these claims in humans.²⁵

The performance-enhancing effect of methoxyisoflavone (800 mg per day) in resistance training was studied in males over an 8-week period. Compared with placebo, methoxyisoflavone did not enhance performance or yield a significant increase in lean body mass.³⁸ No side effects were reported. The International Society of Sports Nutrition classifies isoflavones as not effective as a muscle-building supplement.²¹ Soy and isoflavones may pose a risk to women at high risk for breast cancer or with estrogen-sensitive breast cancer.²⁵ However, current scientific data suggest that these compounds are safe in this regard.²⁵

QUERCETIN

Quercetin is a natural flavonoid in many foods, including apples, cranberries, blueberries, and onions. Quercetin may have many beneficial biological properties—anti-inflammatory, anticarcinogenic, cardioprotective, and neuroprotective.¹³ There is also considerable interest in quercetin's potential as an ergogenic aid. Quercetin may enhance performance through a caffeine-like psychostimulant effect, or it may enhance mitochondrial biogenesis.¹³

Caffeine enhances endurance and anaerobic exercise capacity through its affinity for the adenosine A₁ receptor.³ Flavonoids, including quercetin, also bind to the adenosine A₁ receptor producing ergogenic effects similar to those of caffeine.²

Mice treated with quercetin increased their exercise tolerance, voluntary wheel-running activity, and markers of mitochondrial biogenesis (peroxisome proliferator-activated receptor-coactivator, sirtuin 1, mitochondrial DNA, and cytochrome C).¹⁴

In human studies, quercetin supplementation (500 mg twice daily for 7 days) increased exercise endurance (VO₂ max and ride-to-fatigue time).¹² Total work performed during a cycling time trial under heat stress (40°C) did not improve with 2000 mg of quercetin immediately before exercise.¹¹ In a study of antioxidant properties of quercetin in ultramarathon participants, no effect was found in race performance (250 mg of quercetin 4 times per day for 3 weeks before and during the race).³¹ In addition, 1000 mg a day of quercetin did not improve repeat sprint performance, markers of postexercise inflammation, VO₂ max, or measures of energy and fatigue.^{2,6,16,20} Small improvement in treadmill performance (12-minute time trials) was found in untrained males with the 1000-mg dose.²⁷ Side effects were not reported with the commonly used doses of 1000 to 2000 mg per day.

ZINC/MAGNESIUM ASPARTATE

Deficiencies of zinc and magnesium aspartate decrease testosterone and insulin-like growth factor.²¹ Zinc and magnesium supplementation has had variable results.^{8,37} College football players taking 450 mg of magnesium aspartate and 30 mg of zinc over a 7-week period demonstrated a significant increase in quadriceps and hamstrings torque and power measurements and increased concentrations of total testosterone, free testosterone, and insulin-like growth factor.⁸ However, 42 resistance-trained males who received 450 mg of magnesium aspartate and 30 mg of zinc saw no significant ergogenic effect (anabolic and catabolic hormone, bench press, leg press, or cycling anaerobic capacity) after 8 weeks of supplementation.³⁷ No significant side effects were experienced at this dose.^{8,37} The International Society of Sports Nutrition reports that it is not known if zinc/magnesium aspartate is effective in muscle building.²¹ The AIS lists zinc/magnesium aspartate as a group C supplement (ie, clear proof of beneficial effects is lacking).⁴

NITRIC OXIDE AND PRECURSORS

Nitric oxide is a vasodilator.²⁹ Clinically, medications that increase circulating nitric oxide are mainstays in the treatment of sexual dysfunction and myocardial ischemia.²⁹ Elite athletes have used sildenafil for its vasodilatory and performance-enhancing effects.²⁹ There was an increase in athlete queries to a drug database about these products from 2006 to 2008.²⁹ There is some evidence that it improves cardiac parameters and performance in hypoxic environments (ie, altitude).²² However, in a cycling trial at low to moderate altitude, sildenafil (50 mg) did not improve performance.²²

No studies were found on nitric oxide. Nitric oxide precursors contain L-arginine, which may increase circulating levels of nitric oxide and enhance performance by increasing blood flow.⁵ Six grams of L-arginine did extend time to exhaustion in a small placebo-controlled trial (n = 9).⁵ Another precursor, glycine propionyl-L-carnitine, did not improve endurance or strength when taken before exercise.⁷ Although the risk of significant side effects appears to be small, nitric oxide precursor supplementation may cause hypotension.²⁹ Additionally, Magee et al reported bowel ischemic colitis in a 42-year-old man taking a nitric oxide precursor.²³ The AIS lists nitric oxide stimulators as lacking proof of beneficial effects.⁴

CONCLUSIONS

None of the supplements in this review clearly and consistently enhance performance. Studies on the ergogenic effects of supplements are limited; studies on potential side effects of supplements are rare.

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