Anabolic-androgenic steroids (AASs) have been used by athletes for decades to increase lean body mass, strength, and overall athletic performance. The legal issues and dangers associated with AASs, however, have resulted in a reluctance to use them by many athletes and a search for a more natural method for improving performance. This has led to an increase in the popularity of nutritional supplements marketed as ergogenic aids. Because they are considered natural and are available without a prescription, there is a misconception that these supplements are all healthy and safe, which is not always true. Although there are numerous supplements currently marketed as ergogenic aids, the more popular ones are those containing creatine, ephedra, and AAS precursors.

**Creatine**

The use of creatine (Cr) as a performance enhancer was first popularized after the 1992 Olympic Games in Barcelona, and testimonies by Mark McGuire and many other professional athletes helped make it extremely popular in the United States and Canada. Approximately 95% of the body’s Cr pool is found in skeletal muscle, with 60% of that in the form of phosphocreatine (PCr). Cr plays a primary role in the phosphagen energy system; PCr is the primary substrate for adenosine-triphosphate (ATP) resynthesis. The theory behind its use is similar to that of carbohydrate loading; increased muscle Cr and PCr content would conceivably enhance the capacity of the phosphagen energy system, providing greater resistance to fatigue, and improve performance. This has been partially supported; several reports indicate that muscle Cr and PCr can be elevated when a normal diet is supplemented with oral Cr. Its efficacy as a performance enhancer, however, remains in question.
being the more popular theories. Because the weight gain is observed over a short period of time, it cannot be explained by protein synthesis alone. Thus, water retention is a more likely cause. This theory has been supported because increases in both total body water and intracellular water volumes have been observed after supplementation.15,16 There is also evidence, however, supporting the theory of increased protein synthesis after increases in muscle Cr.17

At this time, the efficacy of Cr as a performance enhancer remains inconclusive. There are a number of factors that can affect the potential for performance improvements, such as the type of training and performance testing, training level, diet, and initial Cr levels. To achieve a performance effect from supplementation, one must first experience an increase in muscle Cr levels when it is ingested. As mentioned previously, this has been shown to occur,1,4 but a large amount of variability has been observed regarding the change in muscle Cr after supplementation.15,18 This might explain why some individuals do not experience an ergonomic effect.3,13,14 It has been reported that 20–30% of those ingesting Cr do not respond, meaning they experienced less than a 10-mmol/kg increase in the muscle concentration.18 It has also been reported that only 20% of individuals achieved concentrations of approximately 150–160 mmol/kg after supplementation.15 This concentration is considered the upper limit of muscle Cr stores, although some individuals have been observed to achieve higher levels.1,2

Side Effects

There have been numerous anecdotal reports of muscle cramping, spasm, strains, gastrointestinal distress, kidney dysfunction, and heat illness associated with Cr supplementation. Many of these are based on isolated cases. At this time, however, the only side effect directly associated with supplementation is weight gain.5,7,9,11,14-16 Creatine use over the past decade has been so high that an obvious causal relationship would have been noted if serious side effects were actually associated with it, but this has not occurred. In fact, a number of studies have specifically investigated the occurrence of side effects.19-22 The general conclusion from these studies was that Cr is not associated with any negative side effects. Thus, a causal relationship between Cr supplementation and negative side effects cannot be established at this time.

### Ephedra

The ephedra plant species, collectively known by their Chinese name ma-huang, have two primary active ingredients, ephedrine and pseudoephedrine.23-25 Ephedrine and pseudoephedrine are classified as sympathomimetic alkaloids because they directly stimulate the sympathetic nervous system. They are structurally similar to amphetamines and have direct alpha- and beta-agonistic properties, as well as catecholamine-releasing actions.24,26 These alkaloids also function as indirect adrenoreceptor agonists, because they augment the availability and action of norepinephrine in the brain and in the heart.24-27 Unlike pseudoephedrine, however, ephedrine also mediates its effects via circulating epinephrine.27,28 Based on these properties, ephedra is currently marketed as a central-nervous-system (CNS) stimulant and a thermogenic and lipolytic agent.

### Ergogenic Effects

Interest in ephedra supplementation originated from early reports of enhanced thermogenesis and lipolysis after ephedrine ingestion.29-30 These were clinical trials involving subjects seeking treatment for obesity, however, so it is likely that the participants were deficient in metabolic rate or fat metabolism. Although the research concerning ephedrine and performance in an athletic population is limited, most of it does not support ergonomic claims.31-33 Ephedrine ingestion has failed to improve muscle strength, endurance, and power; lung function; reaction time; hand-eye coordination; anaerobic capacity; speed; cardiopulmonary endurance; ratings of perceived exertion; and recovery.32 Similar observations have been made after pseudoephedrine ingestion; a single 120-mg dose had no effect on 40-km cycling time, maximal muscle force, or muscle endurance during repeated isometric contractions.31 Likewise, pseudoephedrine ingestion has also failed to improve VO2, time to exhaustion, and ratings of perceived exertion in comparison with placebo conditions during exercise.33,34

It is quite common to find products combining ephedra with garana or other sources of caffeine. The primary reason for combining the two drugs is to potentiate the effects of the ephedrine.28 Ephedrine exerts its thermogenic effects via catecholamine release. Increased catecholamine levels after ephedrine
ingestion are subject to negative feedback systems, which function to inhibit catecholamine release and actions. Caffeine interferes with this negative-feedback mechanism, thus potentiating the effects of ephedrine. This theory has been supported; the combination of caffeine and ephedrine has been shown to significantly increase cycling time to exhaustion by 64% and 58% over placebo conditions, whereas caffeine and ephedrine each on its own failed to provide such an effect. The authors attributed the improvement to CNS stimulation because no changes were observed for VO$_2$, carbon-dioxide production, or fat oxidation. Nonetheless, one would have to double the serving size of typical sports supplements containing both ephedrine and caffeine to achieve the doses used in these two studies. More recently, a similar combination of ephedrine (75 mg) and caffeine (375 mg) was shown to significantly improve running times during a Canadian Forces Warrior Test by 5%. It is important to note that negative side effects were commonly observed during these investigations, as well as others involving both healthy and obese individuals.

**Side Effects**

The spectrum of negative side effects associated with the use of ephedrine-containing products cannot be overlooked. Although it is likely that the side effects in many cases are the result of misuse, they have also been regularly observed in participants in clinical trials in which the dosages were controlled. Some of the minor side effects associated with ephedrine include headache, restlessness, tremors, palpitations, insomnia, and anxiety. Increases in both heart rate and blood pressure are also commonly observed after ephedrine ingestion. Although these effects are not serious in most users, the consequences can be severe in those with underlying heart disease, hypertension, or diabetes and those sensitive to ephedrine. The more serious side effects include severe hypertension, seizures, arrhythmias, hepatitis, psychosis, stroke, myocardial injury, and intracranial hemorrhage. Although few in number, cases of fatal intoxication after ephedrine ingestion have been reported. The cardiovascular and CNS-stimulant effects predominate in instances of ephedrine overdose, with the more common causes of death being myocardial infarction and cerebrovascular accident.

**AAS Precursors**

Dehydroepiandrosterone (DHEA), androstenedione (A’dione), and androstenediol (A’diol) are androgenic hormones produced primarily by the adrenal glands and gonads. Although they have little inherent androgenic activity on their own, they act as precursors in the endogenous production of testosterone and estrogen in the gonads and peripheral tissues. Approximately 95% of the circulating testosterone in an adult male is derived from testicular secretion, while the remaining 5% arises from the peripheral conversion of precursors. In women, circulating levels of testosterone are derived about equally from direct gonadal secretion and peripheral precursor conversion. As mentioned previously, testosterone production is not the only pathway for these precursors—testosterone and A’dione can also be converted to estradiol and estrone.

**Ergogenic Effects**

Increased levels of testosterone have been shown to increase protein synthesis, muscle strength, and lean body mass. Thus, the role of DHEA and A’dione as testosterone precursors has created interest in their potential as ergogenic aids. At this time, however, there is no scientific support for this theory—both A’dione and DHEA ingestion have failed to increase protein synthesis. Likewise, 8 weeks of A’dione supplementation (300 mg/day) and resistance training failed to increase muscle-fiber cross-sectional area when compared with placebo ingestion and training. This combination has also failed to promote changes in strength or lean body mass. Significant increases in A’dione were observed in two of the previously mentioned studies, whereas no changes were observed in testosterone. This suggests that exogenous DHEA and A’dione must first be converted to testosterone to achieve an anabolic effect.

Early research involving precursor supplementation and testosterone levels provided positive results, as increases in testosterone were observed. These changes were only observed in older women, however, and were not associated with any change in lean body mass. More recently, when young healthy men were investigated, the results are not as positive. Significant elevations in serum A’dione have been observed after acute ingestion of either DHEA or A’dione, whereas no.
changes in testosterone occurred. In contrast, higher dosages than those previously used have been shown to significantly increase testosterone levels. In one of those studies, acute testosterone levels in a group of young men ingesting 300 mg were significantly greater than in those ingesting 100 mg and those in a control group, whereas no differences were observed between the 100-mg and control groups. It was suggested that only higher dosages can increase testosterone, because a significant portion of the ingested A’dione is reduced and conjugated by the liver before it can reach peripheral testosterone-converting tissues.

**Side Effects**

Significant reductions in serum high-density lipoprotein (HDL) cholesterol have been observed after A’dione and DHEA supplementation. These changes have also been observed after AAS injection and have been associated with the development of cardiovascular disease. It has been previously reported that A’dione and A’diol ingestion can adversely affect HDL cholesterol levels, LDL-to-HDL cholesterol ratio, and risk of coronary heart disease. Thus, it is very possible that long-term supplementation could have serious side effects similar to those associated with AAS use. These side effects include liver dysfunction, cardiovascular disease, suppressed testosterone production, testicular atrophy, acne, male-pattern baldness, and aggressive behavior. If A’dione and DHEA are taken before puberty, a premature closing the epiphysis and stunted growth could occur. In women, increases in androgen concentrations could cause lowered voice pitch, hirsutism (changes in hair-growth patterns, including facial hair), increased abdominal fat accumulation, and general virilization. In young men, both acute and chronic increases in estradiol have been observed after high- and low-dose A’dione supplementation. It is very possible that the increases in estrogen concentrations experienced by men could have feminizing effects, including gynecomastia.

**Conclusion**

Whenever an athlete is considering using a nutritional supplement, three questions must be asked: Is it legal, is it safe, and does it work? At this time, Cr can be legally sold over the counter (OTC) in Canada, but AAS precursors cannot. Ephedra products can only be sold as decongestants/expectorants and only at a recommended dose of 8 mg. Ephedra is not legal for sale in weight-loss products or mixed with caffeine. In the United States, the Dietary Supplement Health and Education Act of 1994 allowed products containing creatine, ephedra, and AAS precursors to be legally sold OTC as natural supplements. Some of these products have come under heavy scrutiny, however, jeopardizing their classification as supplements and OTC availability. In December 2003, the Food and Drug Administration announced that it was banning ephedra because of associated health risks. The law required a phase-in period—the sale of ephedra products officially became illegal in April 2004. It is important to note that this law only bans the sale of ephedra. It does not make it illegal to possess or use the supplement. Nonetheless, the International Olympic Committee (IOC), National Collegiate Athletic Association (NCAA), Canadian Interuniversity Sport (CIS), Canadian Colleges Athletic Association (CCAA), and the National Football League (NFL) have all banned the use of ephedrine and ephedrine alkaloids. Likewise, these organizations have all banned the use of AAS precursors. Unlike ephedra, these products remain for sale OTC. The Anabolic Steroid Control Act of 1990 defines anabolic steroid as any drug or hormonal substance chemically and pharmacologically related to testosterone that promotes muscle growth. Under that act, testosterone and anabolic steroids are classified as Schedule III drugs and cannot be sold OTC or possessed without a prescription. Although DHEA, A’dione, and A’diol are structurally and pharmacologically related to testosterone, they have not been proven to promote muscle growth and are, therefore, not classified as Schedule III drugs. In 2003, however, a bill (cited as the Anabolic Steroid Control Act of 2003) was introduced to Congress that would amend the Controlled Substances Act and allow the attorney general to schedule AAS precursors. If this becomes law, any AAS precursors that are scheduled will no longer be available for sale OTC. Furthermore, it will be illegal to possess them without a prescription. It is very possible that this will become law, because the bill is supported by the American Medical Association, American College of Sports Medicine, American Academy of Pediatrics, National Athletic Trainers’
Association, NCAA, and NFL. Unlike AAS precursors and ephedrine, Cr is not banned by any of the associations governing athletic competition. It is interesting to note that the Canadian Football League has not banned any nutritional supplement and does not test its players for any illegal substances.

Unfortunately, the term natural supplement implies that a product is safe, but this is not always true. Although there are numerous anecdotal reports of negative side effects associated with Cr use, the only clinically documented side effect is weight gain, and at this time, a causal relationship between Cr and other side effects cannot be concluded. Thus, it appears that Cr can be used safely. The dangers associated with the immediate and prolonged use of ephedrine, however, are well documented, and numerous studies provide evidence of the possible dangers associated with AAS-precursor supplementation. Thus, it appears that the risks far outweigh any possible benefits they might provide.

A primary concern is that manufacturers are not required to list the ingredients on the labels of natural supplements, so consumers do not always know the true contents of such products. An analysis of one product found it to contain 45 mg of ephedrine and 20 mg of caffeine in a single tablet, despite the fact that Chinese ginseng was listed as the only ingredient. In it was also labeled as having "no side effects" and instructed users to take five tablets, which represents a total ephedrine dosage of approximately 11 times the usual recommended OTC dosage. Similar observations have been made with AAS-precursor products. In an analysis of 12 brands of AAS precursors, one brand contained 77% more than the amount stated on the label, and the other 11 tested contained less. In a similar study of nine different brands, six contained less than 90% of the amount stated on the label, one contained no A’dione, and one was actually found to contain 10 mg of testosterone. Furthermore, in the same study, 20 out of 24 men ingesting either 100 or 300 mg of A’dione would have tested positive for the banned steroid nandrolone based on levels of 19-norandrosterone (a metabolite of nandrolone) found in the urine.

Unfortunately, it is common practice for supplement manufacturers to take results from deficiency studies and generalize them to young, healthy, athletic individuals when advertising their products. Those of us in the research community know that this cannot and should not be done. Although not all studies are in agreement, there is scientific support for Cr as a performance enhancer. Although ephedrine appears to be an effective CNS stimulant with thermogenic and lipolytic effects, its ergogenic advantages are highly debatable. Likewise, there is no scientific support for the ergogenic or anabolic use of steroid precursors at this time. It is important that athletes understand that the key to performance is a well-developed training program and a healthy diet. As allied health professionals, it is important that athletic trainers and therapists be able to educate athletes regarding the efficacy and safety of nutritional supplements so they can continue to train in a safe and healthy manner.

References


Michael Powers is an assistant professor and coordinator of clinical education in the graduate athletic training program at Shenandoah University. He is a NATA-certified athletic trainer and an NSCA-certified strength and conditioning specialist.