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Dietary supplements for athletes: Emerging trends and recurring themes

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Dietary supplements for athletes: Emerging trends and recurring themes

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Abstract
Dietary supplements are widely used at all levels of sport. Changes in patterns of supplement use are taking place against a background of changes in the regulatory framework that governs the manufacture and distribution of supplements in the major markets. Market regulation is complicated by the increasing popularity of Internet sales. The need for quality control of products to ensure they contain the listed ingredients in the stated amount and to ensure the absence of potentially harmful substances is recognized. This latter category includes compounds prohibited under anti-doping regulations. Several certification programmes now provide testing facilities for manufacturers of both raw ingredients and end products to ensure the absence of prohibited substances. Athletes should carry out a cost–benefit analysis for any supplement they propose to use. For most supplements, the evidence is weak, or even completely absent. A few supplements, including caffeine, creatine, and bicarbonate, are supported by a strong research base. Difficulties arise when new evidence appears to support novel supplements: in recent years, β-alanine has become popular, and the use of nitrate and arginine is growing. Athletes seldom wait until there is convincing evidence of efficacy or of safety, but caution is necessary to minimize risk.

Keywords: Supplements, health, performance, creatine, nitrate

Supplement use
Assessing the prevalence of dietary supplement use by athletes is complicated by the various definitions of what constitutes a supplement. For most purposes, sports drinks, energy bars, gels, and other sports foods are excluded from the definition of supplements, although the use of these products is widespread in sport. Dietary supplements are used by a large proportion of the general population, and the available evidence suggests that the rate of use is even higher among athletes (Huang, Johnson, & Pipe, 2006). The pattern of use varies between sports and with the level of competition. Tscholl and colleagues (Tscholl, Alonso, Dolle, Junge, & Dvorak, 2010) reported a rate of use of 1.7 supplement products per athlete, on the basis of analysis of almost 4000 doping control declarations from elite track and field athletes, but noted that the final ranking in the championships was unrelated to the quantity of reported supplements taken. A similar analysis at the 2002 and 2006 FIFA World Cups revealed a rate of use of 1.3 supplements per player per match in 2006 compared with 0.7 supplements per player per match in 2002 (Tscholl, Junge, & Dvorak, 2008). Even among recreational gym users, a large survey revealed that 37% used one or more dietary supplements (Goston & Correia, 2010).

Most athletes are aware that the use of some supplements can bring benefits that include improved adaptations to training that lead to performance enhancement, and the potential for preservation of good health (Maughan, Depiesse, & Geyer, 2007). Surveys show that athletes have many reasons for using supplements and some of those most commonly cited are listed in Table I. A recent study of 310 male and female athletes competing in the track and field World Championships showed that 83% of males and 89% of females were using one or more dietary supplements (F. Depiesse, unpublished data). The reasons these athletes gave for using supplements were:

- to aid recovery from training: 71%
- for health: 52%
Table I. Categories of dietary supplements commonly used by athletes.

- Promote tissue growth, repair, and adaptation to training
- Promote fat loss
- Enhance energy supply (including muscle buffering)
- Promote immune function and resistance to illness/infection
- Central nervous system stimulant effects
- Promote joint health
- Promote general health
- Sports drinks, energy bars, etc.

- to improve performance: 46%
- to prevent or treat an illness: 40%
- to compensate for a poor diet: 29%

These reasons raise some questions. Dietary supplement manufacturers are not permitted to claim that supplements can prevent or treat illness unless there is valid proof of such an effect, and this is invariably absent. If an athlete is concerned about a poor diet, it makes more sense to improve the quality of the diet than to try to compensate for this by the use of supplements.

It is less clear, however, that athletes fully understand the limitations to the claims made for many of the supplements that they use. They are also likely to be unaware of the negative consequences that may arise from the use of some supplements or from the inappropriate use of supplements that may be helpful in some circumstances, but detrimental to performance in others (Braun et al., 2009).

Supplement regulation

Although there are undoubted benefits for some consumers of dietary supplements, there is also the potential for some negative outcomes. Regulation of the dietary supplements market varies greatly between countries, and Internet sales often mean that athletes have access to supplements of uncertain origin. Inevitably, the United States represents the largest market and the Dietary Supplements Health and Education Act of 1994 (DSHEA) passed by the US Congress has meant that nutritional supplements that do not claim to diagnose, prevent or cure disease are not subject to regulation by the Food and Drugs Administration (FDA) in the same way as food ingredients are not subject to the stringent regulations that are applied to the pharmaceutical industry. From this it follows that there is not the same requirement to prove product purity and claimed benefits or to show safety with acute or chronic administration. The DSHEA included a legal definition of a “new dietary ingredient” and a requirement that a notification of intention to market a new ingredient be made to the FDA before its use in dietary supplements. However, the very many dietary ingredients on sale at the time of the Act were exempted under a “grandfather” clause, even though there was little or no evidence as to the efficacy and safety of many of these compounds. Furthermore, many supplements contain a complex mixture of various substances, the interaction of which is entirely unknown.

It is well recognized that there are problems with the quality of some of the dietary supplements on sale, but the options open to those responsible for food safety are limited by the legislation that applies. The FDA has used its powers to prevent the marketing of a number of new ingredients (McGuffin & Young, 2004) and to recall products where there is evidence of harm or where there are infringements of labelling or other standards. The FDA can also encourage companies selling products that are deemed unsafe or inappropriate to undertake voluntary recalls of such products. There have also been a number of cases where the FDA has issued public warnings over the safety of supplements or where these products have been withdrawn from sale because of links to adverse health effects: these include a widespread ban on the use of the herb kava in 2003 (Nutraingredients, 2003) and an FDA warning on hydroxycut products in May 2009 because of a number of serious adverse effects on liver function, including one death (FDA, 2009). In September 2010, the manufacturers announced a voluntary nationwide recall of “Off Cycle II Hardcore”, a product containing 3,17-keto-etiocholtriene (an aromatase inhibitor), which was marketed as a dietary supplement (FDA, 2010). Although described by the manufacturers as a voluntary recall of the product, this was a direct response to notification by the FDA that this compound did not qualify as a new dietary ingredient.

It is not unusual to find cases of poor hygiene in the manufacture, storage, and provision of foodstuffs to the general public, so it should not be surprising that some dietary supplement manufacturers fail to follow good manufacturing practice. Some supplement products have been shown to contain impurities (lead, broken glass, animal faeces, etc.) because of poor quality control during manufacture or storage. The risk of gastrointestinal upset because of poor hygiene during the production and storage of products is a concern to athletes. At best, this may be nothing more than a minor inconvenience, but it may cause the athlete to miss a crucial competition. Recent reports have documented several cases of serious adverse effects on health resulting from the use of dietary supplements containing undeclared anabolic steroids, so it is clear that some products on the market remain unsafe (Krishnan, Feng, & Gordon, 2009).
Quality control

Where the content of active ingredients in a supplement is variable, this is likely to be due to poor quality control during the manufacturing process. There is also evidence, however, that some products do not contain an effective dose of expensive ingredients listed on the label, and in some cases the active ingredient is entirely absent and the product contains only inexpensive materials. Even relatively inexpensive ingredients may be absent or present in only trivial amounts, as reported by Harris and colleagues (Harris, Almada, Harris, Dunnett, & Hespel, 2004) in the case of a creatine product. This has been interpreted by some as a cost-saving exercise by manufacturers. A rather sophisticated chemical analysis is required to identify the contents of a supplement, so there is no way for athletes to know what is in any of these products.

Cost–benefit analysis

Athletes who take supplements often have no clear understanding of the potential effects of the supplements they are using, but it is clear that supplements should be used only after a careful cost–benefit analysis has been conducted. On one side of the balance are the rewards, the most obvious of which is an improved performance in sport, and on the other side lie the costs and the risks. For several of the supplements used by athletes, there is good evidence of a benefit for some athletes in some specific circumstances (Maughan et al., 2007). In addition, athletes may respond very differently to a given supplement, with some exhibiting a beneficial effect while others experience a negative effect on performance. Hence supplements are often used in an inappropriate way, and athletes conceivably may benefit from professional advice by a qualified sports dietician before using any supplements. Such advice, however, is not readily available to all athletes.

Vitamin and mineral supplements are generally perceived as being harmless, and the one-a-day multivitamin tablet is seen as an insurance policy “just in case”. Many herbal products are also used, even though there is little or no evidence to support their claimed benefits. The fact that most of these supplements enjoy only brief periods of popularity before disappearing from the marketplace suggests that any benefits perceived by athletes are not strong enough to warrant continued use or recommendation to friends and colleagues. Although these supplements are mostly benign, this is not always the case. Routine iron supplementation, for example, can do more harm than good, and the risk of iron toxicity is very real for some consumers (Papanikolaou & Pantopoulos, 2005). Mettler and Zimmermann (2010) assessed iron status in 170 recreational runners participating in the Zurich marathon, and found that functional iron deficiency was present in 5 (3.9%) and 11 (25.5%) male and female runners; however, iron overload was found in 19 of 127 (15.0%) men but only 2 of 43 women (4.7%).

Can a supplement cause a positive doping test?

The biggest concern for athletes who are liable to testing for the use of drugs that are prohibited in sport is the possibility that a supplement may contain something that will result in a positive doping test (Maughan, 2005). Recent evidence suggests that these concerns may apply to some foods as well as to supplements (Braun, Geyer, & Koehler, 2008). Only a very small number of individuals are tested for evidence of the use of doping agents, but these are invariably the most successful performers. For these athletes, a failed drugs test may mean the loss of medals won or records set, as well as temporary suspension from competition. It also leads to damage to the athlete’s reputation and perhaps to permanent loss of employment and income. Where there has been deliberate cheating, such penalties seem entirely appropriate, but it is undoubtedly true that some failed doping tests can be attributed to the innocent ingestion of dietary supplements. The strict liability principle applied by the World Anti-Doping Agency (WADA) does not distinguish between deliberate cheating and inadvertent doping, so athletes must accept personal responsibility for all supplements (and medications) that they use.

Many published studies show that contamination of dietary supplements with prohibited substances is common (Maughan, 2005). A wide range of stimulants, steroids, and other agents that are included on WADA’s prohibited list have been identified in otherwise innocuous supplements. These instances are quite distinct from the legitimate sale of some of these substances, as their presence is not declared on the product label; in some cases, these adulterated products are even labelled as being safe for use by athletes. In some but not all cases, the extraneous additions have actions that are linked to the intended use of the product. Thus anabolic agents have been found in supplements sold as muscle growth promoters, stimulants in herbal tonics, and anorectic agents in herbal weight loss supplements. These observations suggest that this is either a deliberate act to add active ingredients to otherwise ineffective products or that the managers have allowed some mixing of separate products at the manufacturing facility. This might occur in the preparation of the raw ingredients or in the formulation of the finished product. In some cases, the amount of supplement present may be high, even higher than the normal
therapeutic dose. Geyer and colleagues (Geyer, Bredehoft, Marek, Parr, & Schanzer, 2002) purchased a “body building” supplement in England and upon analysis found it to contain methandienone (commonly known as Dianabol) in an amount substantially higher than the therapeutic dose. This drug was present in high amounts, enough to have an anabolic effect, but also enough to produce serious side-effects, including liver toxicity and carcinogenicity. Unlike many of the earlier cases involving cases of steroids related to nandrolone and testosterone, these are not trivial levels of contamination, which raises the probability of deliberate adulteration of the product with the intention of producing a measurable effect on muscle strength and muscle mass. The prospect of adverse health effects at these high doses also raises real concerns.

Can you guarantee a supplement is safe?

In spite of these problems, it remains true that the majority of dietary supplements are safe and will not result in either health problems or violations of the doping code. It is equally true, however, that a problem remains in that a significant minority of the products on sale to athletes carry such risks. Many attempts are being made to address these problems, but there is not at present any way in which a particular product can be guaranteed to be free of any risks. This is in part due to the extremely small amounts of some substances that may cause a positive doping outcome. Ingestion of 19-norandrostenedione, a prohibited substance and precursor of nandrolone, will result in the appearance in the urine of 19-norandrosterone, the diagnostic metabolite. If the urinary concentration of 19-norandrosterone exceeds 2 ng · ml⁻¹, a doping offence is deemed to have occurred. The addition of as little as 2.5 μg of 19-norandrostenedione to a supplement can result in a urinary concentration of 19-norandrosterone in excess of this threshold in some, but not all, individuals (Watson, Judkins, Houghton, Russell, & Maughan, 2009). This effect is transient, and it can be seen from Figure 1 that even when a larger dose (10 μg) of steroid is administered, it is likely that only the first or second urine sample after ingestion will contain enough of the steroid metabolites to give a positive test: this means that an athlete who ingests this may or may not test positive, depending on when the sample is collected in relation to consumption of the supplement. The amount of steroid added is close to the limits of detection of the analytical methods currently applied to the analysis of dietary supplements, and there is no certainty that analysis of the finished product would have detected this.

The very small amounts of extraneous doping agents that have been reported to be present in many supplements – perhaps in as many as one in four of those selected for testing – will have no effect on physiological function, even though they may result in a positive doping test (Table II) (Geyer et al., 2004). In the absence of any physiological effect, there is no obvious reason for the deliberate addition of these compounds. It seems likely that their presence is due to accidental contamination at some stage of the manufacture, storage or distribution of

![Figure 1](image-url)

**Table II. Results of the analysis of dietary supplements for anabolic agents carried out for the International Olympic Committee by the Cologne Doping Laboratory (Geyer et al., 2004).**

<table>
<thead>
<tr>
<th>Country</th>
<th>No. tested</th>
<th>No. “positive”</th>
<th>Percent “positive”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Netherlands</td>
<td>31</td>
<td>8</td>
<td>25.8</td>
</tr>
<tr>
<td>Austria</td>
<td>22</td>
<td>5</td>
<td>22.7</td>
</tr>
<tr>
<td>UK</td>
<td>37</td>
<td>7</td>
<td>18.9</td>
</tr>
<tr>
<td>USA</td>
<td>240</td>
<td>45</td>
<td>18.8</td>
</tr>
<tr>
<td>Italy</td>
<td>35</td>
<td>5</td>
<td>14.3</td>
</tr>
<tr>
<td>Spain</td>
<td>29</td>
<td>4</td>
<td>13.8</td>
</tr>
<tr>
<td>Germany</td>
<td>129</td>
<td>15</td>
<td>11.6</td>
</tr>
<tr>
<td>Belgium</td>
<td>30</td>
<td>2</td>
<td>6.7</td>
</tr>
<tr>
<td>France</td>
<td>30</td>
<td>2</td>
<td>6.7</td>
</tr>
<tr>
<td>Norway</td>
<td>30</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>Switzerland</td>
<td>13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sweden</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hungary</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>634</strong></td>
<td><strong>94</strong></td>
<td><strong>14.8</strong></td>
</tr>
</tbody>
</table>

*Note: For each country where supplements were purchased, the table shows the number of samples tested, the number that contained prohibited steroids, and the fraction of the total this accounts for.*
the raw ingredients or of the finished product. This may be due to cross-contamination of production lines where prohibited substances are processed alongside dietary supplements or due to poor quality control in the production of raw ingredients.

Various efforts are being made to address the problems and to minimize the risk of inadvertent doping by athletes by identifying products that athletes may use with confidence. There can be no absolute guarantee that any product is entirely safe, but such programmes do help the athlete to manage the risk. Because of the strict liability principle that applies in doping cases, inadvertent ingestion of a prohibited substance through use of a contaminated dietary supplement does not absolve the athlete of guilt. Athletes contemplating the use of dietary supplements should consider very carefully whether the potential benefits outweigh the risks of a doping offence that might bring an end to their career.

Supplements that may benefit some athletes

Of the many hundreds or even thousands of supplements on sale to athletes, only a few are supported by strong evidence for positive effects on health or performance and by evidence of absence of harm (Table III). The picture, however, continues to evolve as new evidence emerges, and many supplements experience short periods of popularity before falling out of favour. The scientific evidence often appears to have little impact on sales, thus by implication there is little incentive for those selling supplements to support scientific evaluation of their products. Several reports, for example, have indicated that glucosamine and chondroitin have little or no positive effect on joint pain in arthritis (Sawitzke, Shi, & Finco, 2008; Wandel et al., 2010), yet sales continue to be strong.

For a few supplements, there is good evidence from several well-controlled laboratory studies and also positive responses from athletes. It is clearly impossible to provide an overview of the many hundreds of different supplements used by athletes, and we will focus on only two to highlight some of the issues involved: the use of creatine supplements, where the evidence base is strong, both from a physiological and a performance perspective, and where there is a relatively long history of use, and the use of nitrate and l-arginine, which is novel and where the evidence base is small but convincing.

Creatine supplements: Benefits and risks

Creatine monohydrate is one of the most popular dietary supplements among strength and power athletes and is also widely used in team sports. Although there are reports of sporadic use by athletes over many years, it has become popular only since about 1992. Creatine is a natural guanidine compound and is a normal component of the diet, occurring in relatively high amounts (3–7 g \( \text{kg}^{-1} \)) in skeletal muscle, so that meat and fish are the major dietary sources (Walker, 1979). Some of the body’s creatine content is hydrolysed to creatinine at a fairly constant rate and about 2 g is lost in the urine each day. This can be replaced from dietary sources or by

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Ergogenic effects</th>
<th>Underlying physiological effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkalinizing agents (sodium bicarbonate)</td>
<td>Improves anaerobic endurance performance</td>
<td>Increases pre-exercise pH</td>
</tr>
<tr>
<td>(sodium citrate)</td>
<td></td>
<td>Increases extracellular buffer capacity</td>
</tr>
<tr>
<td>l-Arginine</td>
<td>Improves aerobic endurance exercise performance</td>
<td>Increases plasma nitrite concentration</td>
</tr>
<tr>
<td>Beta-alanine</td>
<td>Improves aerobic and anaerobic endurance performance</td>
<td>Reduces oxygen consumption during submaximal exercise</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Improves endurance exercise performance</td>
<td>Increases muscle carnosine content</td>
</tr>
<tr>
<td></td>
<td>Improves reaction time</td>
<td>Improves intra-myocellular buffer capacity</td>
</tr>
<tr>
<td>Creatine</td>
<td>Improves performance in strength and power events</td>
<td>Reduces perception of fatigue</td>
</tr>
<tr>
<td></td>
<td>Improves intermittent sprint performance</td>
<td>Increases central drive by central adenosine receptor inhibition</td>
</tr>
<tr>
<td>Nitrate</td>
<td>Stimulates the effects of resistance training</td>
<td>Increases muscle free creatine and phosphorylcreatine content</td>
</tr>
<tr>
<td></td>
<td>Improves aerobic endurance exercise performance</td>
<td>Facilitates muscle relaxation</td>
</tr>
</tbody>
</table>

Note: The effects of water, electrolytes, carbohydrates, and protein/amino acid intake in exercise performance and training are addressed in other papers in this issue. Note that the number of published studies on the effects of L-arginine and nitrate is small, but the data seem convincing.
synthesis from amino acid precursors. A variety of synthetic creatine supplements have been developed, including creatine malate, creatine pyruvate, creatine citrate, creatine-magnesium chelate, creatine ethyl ester, and many more. Marketing claims for these compounds include better solubility and stability in solution, improved absorption and bioavailability, increased muscle uptake, and greater performance enhancement compared with creatine monohydrate. Where these alternatives have been investigated, however, no benefit has been reported (Spillane et al., 2009; Van Schuylenergh, Van Leemputte, & Hespel, 2003).

About two-thirds of the total muscle creatine content is in the form of creatine phosphate, or phosphorylcreatine, with the remainder present in equilibrium amounts as free creatine. The muscle phosphorylcreatine content is relatively high and is usually seen as a store of high-energy phosphates that serves to prevent large decreases in the cellular ATP, and corresponding increases in ADP when energy demand is high. The phosphorylcreatine–creatinine system also has an important role in acid–base balance during high-intensity exercise, as absorption of a proton during the creatine kinase reaction promotes activation of key enzymes in glycogenolysis (glycogen phosphorylase and phosphofructokinase) and buffers the hydrogen ions produced in glycolysis, thus delaying the development of intracellular acidosis.

There is now a very substantial body of evidence to support the view that supplementation of the diet with creatine monohydrate can increase the skeletal muscle creatine content (Harris, Soderlund, & Hultman, 1992), and improve performance and recovery during a variety of different exercise models (Bemben & Lamont, 2005). A classical creatine loading regimen consists of an initial loading phase of 15–20 g per day for 4–7 days followed by a maintenance dose of 2–5 g per day (Terjung et al., 2000). This contrasts with the typical daily intake from the diet for non-vegetarians of about 1 g per day, although some strength athletes who are focused on a high protein intake and achieve that by a high intake of animal protein sources may achieve high intakes from the diet. However, there are some data to indicate that the effects of creatine supplementation may fade during supplementation beyond 2 months (Derave, Eijnde, & Hespel, 2003). It is now known that insulin can stimulate short-term muscle creatine accumulation in humans above that seen with creatine alone (Steenge, Lambourne, Casey, MacDonald, & Greenhaff, 1998). Insulin infusion is clearly impractical, but combining 5 g of creatine with 95 g of simple carbohydrates has been shown to increase muscle creatine content to a greater extent than is seen with creatine alone (Green, Hultman, MacDonald, Sewell, & Greenhaff, 1996). Similar effects are seen when creatine is combined with mixtures of carbohydrate and protein or amino acids (Pittas, Hazell, Simpson, & Greenhaff, 2010).

Practically this indicates that creatine ingestion in conjunction with a meal containing carbohydrates and protein is more effective than ingestion on an empty stomach. Furthermore, exercise per se also promotes muscle creatine uptake during supplementation (Robinson, Sewell, Hultman, & Greenhaff, 1999).

Many different types of exercise performance have been studied, including strength, power, single and repeated sprints, and endurance, with exercise modes that include cycling, running, and swimming. It is well established that creatine supplementation can enhance power output during short maximal sprints (Terjung et al., 2000), and the effect may be even more evident when repeated sprints are performed with short recovery periods (Casey, Constantin-Teodosiu, Howell, Hultman, & Greenhaff, 1996; Greenhaff, Casey, Short, Harris, & Soderlund, 1993; Hespel et al., 2001; Vandenberghe et al., 1996, 1997; Van Leemputte, Vandenberghe, & Hespel, 1999). This effect is also observed in multiple-sprint endurance exercise events such as football and other team sports (Cox, Mujika, Tumilty, & Burke, 2002). Furthermore, several studies have shown that creatine supplementation can potentiate the gains in fat-free mass and muscle force and power output that accompany resistance training (Hespel et al., 2001; Kreider et al., 1998; Maganaris & Maughan, 1998; Vandenberghe et al., 1997; Volek et al., 1999). There is also some evidence that creatine supplementation can facilitate recovery of muscle volume and functional capacity following muscle atrophy induced by leg immobilization (Hespel et al., 2001). Given the high incidence of musculoskeletal injury and consequent muscle disuse atrophy in athletes, creatine supplementation may be a worthwhile option to enhance post-injury rehabilitation and thereby speed return to training and competition. The mechanism of actions for these effects on muscle mass is not entirely clear (Louis et al., 2003a, 2003b; Louis, Van Beneden, Dehoux, Thissen, & Francaux, 2004). The increased training load that can be sustained with creatine supplementation, however, may be responsible at least in part for improved muscle mass and function (Kreider, 2003).

Creatine has also been shown to have effects on muscle glycogen storage. This may be important because although creatine supplementation appears to have no effect on endurance performance, muscle glycogen availability is a principal determinant of endurance exercise performance, and its depletion corresponds with the development of muscle fatigue.
A short period of “carbohydrate loading” can supercompensate muscle glycogen stores by over 100% within 48–72 h (Bergström & Hultman, 1966). As a result, substantial improvements in subsequent endurance exercise performance (“time to fatigue”) of about 50% can be expected (Bergström et al., 1967). Supplementation with creatine in combination with a high-carbohydrate diet can augment post-exercise muscle glycogen storage during a conventional “carbohydrate loading” regimen in humans, and is of a magnitude that could be expected to produce a significant improvement in endurance exercise performance (~150 mmol · kg⁻¹ dry muscle; Robinson et al., 1999). However, it should be emphasized that there is no evidence that such a performance benefit will result from the addition of creatine to high-carbohydrate meals to acutely increase muscle glycogen content. In addition, the probable gain in body weight due to such a creatine plus carbohydrate loading regimen may be detrimental to performance in many endurance competitions.

The safety of creatine supplementation is frequently questioned, but those studies that have been conducted do not confirm any cause for concern. The increase in body mass that often accompanies creatine supplementation may be desirable for many athletes, but may be problematic for those in weight-category or weight-sensitive sports. According to a report from the French Agency for Food Safety (AFFSA, 2001), about one-third of the published studies show no significant variations in weight; the other two-thirds show increases of 0.8–2.9%, at the most, in body weight, achieved in the first few days, with no subsequent alteration. The news media contain frequent anecdotal reports of muscle cramps, and occasionally more severe dysfunction, that are ascribed to creatine supplementation, but these are usually found on later investigation to be without substance. There are also warnings of the dangers of renal and hepatic failure as a result of high-dose creatine supplementation, but those long-term studies that have been carried out do not confirm these concerns (Kreider et al., 2003). It is widely accepted that it would be wise for those with established renal disease or those at risk for renal dysfunction (diabetes, hypertension, impaired glomerular filtration rate) to avoid creatine supplementation.

The French Agency for Food Safety (AFFSA, 2001) issued an opinion on the use of creatine supplements that included a warning of the risk of mutagenic and carcinogenic effects. This report attracted much attention, but the dangers have not been supported by any subsequent research. There is potential for the presence of two compounds, dicyandiamide and dihydrotriazine, that may occur as by-products during the chemical synthesis from sarcosine and cyanamide. Both of these may be harmful to health, but in 2004 the European Food Safety Authority (EFSA) published an opinion on the use of creatine monohydrate as a food supplement and identified it as being safe within the dosage limits described here. It should be acknowledged that the safety and the regulatory status of the many different creatine derivatives that are currently on sale to athletes are unknown at the present time.

**Dietary nitrate**

Depending on the sports discipline, about 5–30% of the energy turnover during exercise is used to do useful work, with the remainder appearing directly as heat. Thus, even a small increase in the efficiency of muscle contraction may be of major significance for exercise performance. Increasing the efficiency of muscle contraction would allow a greater work output for the same oxygen cost. Athletes may experience a small increase in efficiency – as measured by a reduction in the oxygen cost of a standardized exercise task – in response to prolonged intensive training. Ingestion of large doses of nitrate (NO₃⁻, about 0.1 mmol of sodium nitrate per kilogram of body mass, or 300–400 mg per day), either in the form of pure sodium nitrate (Larsen, Ekblom, Sahlin, Lundberg, & Weitzberg, 2007; Larsen, Weitzberg, Lundberg, & Ekblom, 2010; Vanhatalo et al., 2010) or beetroot juice (Bailey et al., 2009; Bailey et al., 2010a) in young healthy individuals rapidly increases plasma nitrite (NO₂⁻) concentration about 2–3 fold, and this elevated nitrite concentration can be maintained for at least 2 weeks (Vanhatalo et al., 2010). Increased plasma nitrite stimulates the production of nitric oxide (NO). Nitric oxide is an important physiological signalling molecule that is implicated in, among other things, regulation of muscle blood flow and mitochondrial respiration. There is some interesting recent information to demonstrate that either acute or short-term ingestion of nitrate allows the same power output to be achieved with a lower rate of oxygen consumption. Thus, Larsen et al. (2007) found a significant reduction in the oxygen cost of submaximal cycling exercise, corresponding to an increase in mechanical efficiency, from 19.7 ± 1.6% to 21.1 ± 1.3%, due to oral intake of sodium nitrate. Recent evidence from the same laboratory has identified a mechanism for this effect by showing that nitrate supplementation reduced the expression of ATP/ADP translocase, a protein involved in proton conductance within the mitochondria (Larsen et al., 2011). This resulted in a better oxidative phosphorylation efficiency (P/O ratio) in isolated mitochondria. They also showed that the
improved mitochondrial P/O ratio correlated to the reduction in oxygen cost during exercise.

These effects on the mitochondria have implications for exercise performance, and dietary nitrate supplementation reduces maximal oxygen consumption while maintaining power output in maximal exercise (Larsen et al., 2010). Meanwhile, investigators in another laboratory reported the same effects could be achieved with dietary sources of nitrate. Volunteers were fed a placebo or 500 ml of beetroot juice (beetroot, spinach, and a few other vegetables have a high nitrate content) per day for 6 days, the beetroot juice providing 5.5 mmol of nitrate per day (Bailey et al., 2009). This study confirmed the reduction in the oxygen cost of submaximal exercise and also showed that during very intense exercise, the time to exhaustion was extended after ingestion of the beetroot juice (675 ± 203 s) relative to the placebo trial (583 ± 145 s). In a subsequent study, the same authors (Bailey et al., 2010a) showed that beetroot juice supplementation for 6 days attenuated the reduction in muscle phosphorylcreatine concentration during exercise and increased endurance time from 586 ± 80 s after placebo treatment to 734 ± 109 s. This was accompanied by an apparent reduction in the ATP cost of muscle force production. They have also shown (Lansley et al., 2011) that the effects of beetroot juice supplementation on blood pressure and the oxygen cost of walking and running were not observed when nitrate-depleted beetroot juice was given.

Another pathway to stimulate the production of nitric oxide is the stimulation of endogenous nitric oxide synthesis from L-arginine. Interestingly, a recent study showed acute high-dose L-arginine supplementation (3 days, 6 g per day) to yield similar effects on exercise-induced oxygen consumption as the ingestion of dietary nitrate (Bailey et al., 2010b).

The total number of studies showing performance benefits from nitrate supplementation is small and they have involved only a few participants, but the data look impressive. Concerns have been raised as to the safety of high doses of dietary nitrate and nitrite (Derave & Taes, 2009), echoing earlier concerns about a possible role in the development of cancers (Archer, 2002), but athletes have not awaited further studies to confirm the efficacy or safety of such supplements, and the use of beetroot juice is becoming increasingly popular in endurance events. Evidence is certainly increasing to indicate that nitrate is an essential component of the diet and has a range of beneficial effects on health (Archer, 2002; Gilchrist et al., 2010; McKnight et al., 1999). However, the dose–response curve is entirely unknown, and overdosing conceivably may be health damaging, as with all nutrients consumed in excess. Therefore, further studies are sure to follow rapidly and will either confirm or refute these findings with regard to both efficacy and safety.

Conclusions

The use of dietary supplements is widespread in sport, as it is in the general population. Athletes should be aware that few supplements can match the extravagant health and performance claims that are often made for them. A few supplements may have something to offer in terms of health protection or performance enhancement, but supplement use cannot compensate for poor food choices and an inadequate diet. The risk of an adverse outcome, especially a positive doping test, remains real, and the risks of supplement use must be balanced against the potential rewards.

References


