CHAPTER 16

Supplements and sports foods

LOUISE BURKE, MICHELLE CORT, GREG COX,
RUTH CRAWFORD, BEN DESBROW, LESLEY FARTHING,
MICHELLE MINEHAN, NIKKI SHAW AND OLIVIA WARNES

16.1 Introduction

Supplement use is a widespread and accepted practice by athletes, with a high prevalence of use and a large range of different types and brands of products. Such observations are illustrated by the results of a study of 77 elite Australian swimmers (Baylis et al. 2001), which found that 94% of the group reported the use of supplements in pill and powder form. When the use of specialised sports foods such as sports drinks was also taken into account, 99% of swimmers reported supplement use and a total of 207 different products was identified. According to other recent studies, supplement use is also widespread among athletes at high school and collegiate levels (Massad et al. 1995; Krumbach et al. 1999; Froiland et al. 2004).

16.2 Overview of supplements and sports foods

'Dietary supplements', 'nutritional ergogenic aids', 'sports supplements', 'sports foods' and 'therapeutic nutritional supplements'—these are some of the terms used to describe the range of products that collectively form the sports supplement industry. Just as there are a variety of names for these products, there are a variety of definitions or classification systems. Characteristics that can be used to categorise supplements include:

- function (for example, muscle building, immune boosting, fuel providing)
- form (for example, pills, powders, foods or drinks)

- availability (for example, over-the-counter, mail order, Internet, multi-level marketing), and
- scientific merit for claims (for example, well-supported, unsupported, undecided).

This last approach has been adopted recently by the Australian Institute of Sport (AIS) to guide the use of supplements by the athletes within its programs. The goal of this approach is to provide objective information to athletes, coaches and sports administrators regarding the likely efficacy of these products so that individuals can make informed decisions about their intended use. The specific details of the AIS Sports Supplement Program will be addressed later in this chapter.

For the purposes of this chapter we will discuss supplements and sports foods that meet one or more of the following definitions:

- They provide a convenient and practical means of meeting a known nutrient requirement to optimise daily training or competition performance (for example, a liquid meal supplement, sports drink, carbohydrate gel, sports bar).
- They contain nutrients in large quantities in order to treat a known nutritional deficiency (for example, an iron supplement).
- They contain nutrients or other components in amounts that directly enhance sports performance or maintain/restore health and immune function—scientifically supported or otherwise (for example, caffeine, creatine, glycerol, ginseng).

There is an ever-increasing range of supplements and sports foods that are easily accessible to athletes and coaches. It is of primary importance for the sports nutrition professional to have a thorough working knowledge of the various sports foods and supplements in order to provide sound advice about appropriate situations of use, possible benefits, potential side effects and risks associated with use.

16.2.1 Regulation of supplements and sports foods

The regulation of supplements and sports foods is a contentious area and encompasses issues of manufacture, labelling and marketing. In addition to the concerns of efficacy and safety faced by the general consumer, athletes are faced with the problem of contamination with prohibited substances, leading to a positive doping offence. There is no universal system of regulation of sports foods and supplements. Countries differ in their approach and practice of the regulation of sports foods and supplements, with some involving a single government body (such as the Food and Drug Administration—FDA—in the United States of America), while others fall under several government agencies (for example, Food Standards Australia and New Zealand for food-based products and Therapeutic Goods Administration for pill-based products in Australia).

Athletes need to have a global understanding of the regulation of dietary supplements, since regular travel and modern conveniences such as mail order and the Internet provide them with easy access to products that fall outside the scrutiny of their own country's system. Although it is outside the scope of this chapter to review the various regulatory issues in different countries, the important changes that can be attributed to the Dietary Supplement Health and Education Act of 1994 in the United States are worthy of special mention. This Act reduced the regulation of supplements and broadened the category to include new ingredients, such as herbal and botanical products, and constituents or metabolites of other dietary supplements. As a result, a new group of products flooded the US and international market: the 'pro-hormones' or compounds including androstenedione, DHEA, 19-norandrostenedione and other metabolites found in the steroid pathways that can be converted in the body to testosterone or the anabolic steroid nandrolone (Blue & Lombardo 1999). These products will be discussed later in the context of doping and inadvertent doping outcomes. The other important outcome of the 1994 Dietary Supplement Act was to shift responsibility from the supplement manufacturer to the FDA to enforce safety and claim guidelines. Since the passing of the Act, good manufacturing practice has not been enforced within the supplement industry, leaving non-compliant products or manufacturers to flourish unless there is specific intervention by the FDA.

Athletes and coaches often fail to understand that, in the absence or minimisation of rigorous government evaluation, the quality control of supplement manufacture is trusted to supplement companies. Large companies that produce conventional supplements such as vitamins and minerals, particularly to manufacturing standards used in the preparation of pharmaceutical products, are likely to achieve good quality control. This includes precision with ingredient levels and labelling, and avoidance of undeclared ingredients or contaminants. However, this does not appear to be true for all supplement types or manufacturers, with many examples of poor compliance with labelling laws (Gurley et al. 1998; Parasrampuria et al. 1998; Hahm et al. 1999) and the presence of contaminants and undeclared ingredients (see sections 16.3.4 and 16.3.5).

Although manufacturers are not meant to make unsupported claims about health or performance benefits elicited by supplements, product advertisements and testimonials show ample evidence that this aspect of supplement marketing is unregulated and exploited. For example, a survey of five issues of body-building magazines found 800 individual performance claims for 624 different products within advertisements (Grunewald & Bailey 1993). It is easy to see how enthusiastic and emotive claims provide a false sense of confidence about the products. Most consumers are unaware that the regulation of such advertising is generally not enforced. Therefore, athletes are likely to believe that claims about supplements are medically and scientifically supported, simply because they believe that untrue claims would not be allowed to exist.

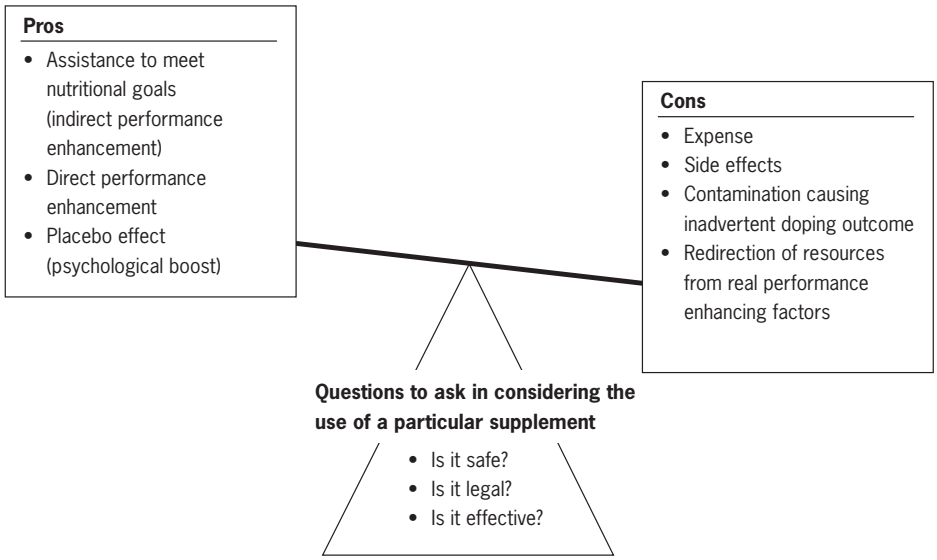

Figure 16.1 Issues to consider in the decision to take a supplement

16.3 The pros and cons of using supplements and sports foods

The decision by an athlete to use a supplement or sports food should be made after careful consideration of several issues. Figure 16.1 provides an overview of important questions that should be answered regarding the safety, efficacy and legality of any product. It also characterises the balance between the arguments for and against the use of the product. The potential for both positive and negative outcomes will now be discussed in greater detail.

16.3.1 *Pros—true performance benefits*

Some supplements and sports foods offer real advantages to athletic performance. Some products 'work' by producing a direct performance-enhancing (ergogenic) effect. Other products can be used by athletes to meet their nutrition goals and, as an indirect outcome, allow the athlete to achieve optimal performance. In some cases these effects are so well known and easily demonstrated that beneficial uses of sports foods or supplements are clear-cut. For example, there are many studies that support the benefits of consuming sports drinks to supply carbohydrate and fluid during exercise (see Coombes & Hamilton 2000). But even when indirect nutritional benefits or true ergogenic outcomes from supplement use are small, they are often worthwhile in the competitive world of sport (Hopkins et al. 1999). Of course, athletes need to be aware that it is the use of the product as much as the product itself that leads to the beneficial outcome. Therefore education about

specific situations and strategies for the use of supplements and sports foods is just as important as the formulation of the product.

16.3.2 Pros—the placebo effect

Even where a sports food does not produce a true physiological or ergogenic benefit, an athlete might attain some performance benefit because of a psychological boost or 'placebo' effect. The placebo effect describes a favourable outcome arising simply from an individual's belief that they have received a beneficial treatment. In a clinical environment, a placebo is often given in the form of a harmless but inactive substance or treatment that satisfies the patient's symbolic need to receive a 'therapy'. In a sports setting, an athlete who receives enthusiastic marketing material about a new supplement or hears glowing testimonials from other athletes who have used it is more likely to report a positive experience. Despite our belief that the placebo effect is real and potentially substantial, only a few studies have tried to document this effect in relation to sport. In one investigation, weightlifters who received saline injections that they believed to be anabolic steroids increased their gains in lean body mass (Ariel & Saville 1972). Another investigation in which athletes were given either a sports drink or a sweetened placebo during a 1-hour cycling time trial found that performance was affected by the information provided to the subjects (Clark et al. 2000). The placebo effect caused by thinking they were receiving a CHO drink allowed the subjects to achieve a small but worthwhile increase in performance of 4%. Being unsure of which treatment was being received increased the variability of performance, illustrating that the greatest benefits from supplement use occur when athletes are confident they are receiving a useful product.

Additional well-controlled studies are needed to better describe the potential size and duration of the placebo effect and whether it applies equally to all athletes and across all types of performance. In the meantime we can accept that the placebo effect exists and may explain, at least partially, why athletes report performance benefits after trying a new supplement or dietary treatment.

16.3.3 Cons—expense

An obvious issue with supplement use is the expense, which in extreme cases can equal or exceed the athlete's weekly food budget. Such extremes include the small number of athletes identified in many surveys (Baylis et al. 2001) who report a 'polypharmacy' approach to supplements, identifying long lists of products that often overlap in ingredients and claimed functions. However, even a targeted interest in a small number of supplements can be expensive: the cost of some individual products such as ribose or colostrum can exceed A$50 per week to achieve the manufacturer's recommended dose or the amounts found to have a true ergogenic outcome in scientific studies. The issue of expense is compounded for teams and sports programs that have to supply the needs of a group of athletes.

Expense must be carefully considered when there is little scientific evidence to support a product's claims of direct or indirect benefits to athletic performance. But even where benefits do exist, cost is an issue that athletes must acknowledge and prioritise appropriately within their total budget. Supplements or sports food generally provide nutrients or food constituents at a price that is considerably higher than that of everyday foods. At times, the expense of a supplement or sports food may be deemed money well spent, particularly when the product provides the most practical and palatable way to achieve a nutrition goal, or when the ergogenic benefits have been well documented. On other occasions the athlete may choose to limit the use of expensive products to the most important events or training periods. There are often lower-cost alternatives to some supplements and sports foods that the budget-conscious athlete can use on less critical occasions; for example, a fruit smoothie drink fortified with milk powder or a commercial liquid meal replacement product is a less expensive choice to supplement energy and protein intake than most protein-rich 'body builder' products.

16.3.4 Cons—side effects

Since most supplements are considered by regulatory bodies to be relatively safe, in many countries there are no official or mandatory accounting processes to document adverse side effects arising from the use of these products. Nevertheless, information from medical registers (Perharic et al. 1994; Kozyrskyj 1997; Shaw et al. 1997) shows that while the overall risk to public health from the use of supplements and herbal and traditional remedies is low, cases of toxicity and side effects include allergic reactions to some products (for example, royal jelly), overexposure as a result of self-medication and poisoning due to contaminants. During the 1980s, deaths and medical problems resulted from the use of tryptophan supplements (Roufs 1992); products containing Ephedra and caffeine are a more recent source of medical problems, sometimes causing deaths in susceptible individuals. Many reports call for better regulation and surveillance of supplements and herbal products, and increased awareness of potential hazards (Perharic et al. 1994; Kozyrskyj 1997; Shaw et al. 1997).

16.3.5 Cons—doping outcomes

A number of ingredients that may be found in supplements are considered prohibited substances by the codes of the World Anti-Doping Agency (WADA) and other sports bodies. These include pro-hormones (steroid-related compounds such as androstenedione, DHEA, 19-norandrostenedione) and stimulants such as ephedrine or related substances. Although the group of pro-hormone substances is not available for sale in Australia, they can be bought as over-the-counter products in countries such as the United States of America. Drug education programs highlight the need for athletes to read the labels of supplements and sports foods

carefully to ensure that they do not contain such banned substances. This is a responsibility that athletes must master to prevent inadvertent doping outcomes.

However, even when athletes take such precautions, inadvertent intake of banned substances from supplement products can still occur. This is because some supplements contain banned products without declaring them as ingredients; this is a result of contamination or poor labelling within lax manufacturing processes. The pro-hormone substances seem to provide the greatest risk of inadvertent consumption via supplement use, with a positive test for the steroid nandrolone being one of the possible outcomes. The most striking evidence of these problems was uncovered by a study carried out by a laboratory accredited by the International Olympic Committee (Geyer et al. 2004). This study analysed 634 supplements from 215 suppliers in 13 countries, with products being sourced from retail outlets (91%), the Internet (8%) and telephone sales. None of these supplements declared pro-hormones as ingredients, and came from both manufacturers who produced other supplements containing pro-hormones as well as companies who did not sell these products. Ninety-four of the supplements (15% of the sample) were found to contain hormones or pro-hormones that were not stated on the product label. A further 10% of samples provided technical difficulties in analysis such that the absence of hormones could not be guaranteed. Of the 'positive' supplements, 68% contained pro-hormones of testosterone, 7% contained pro-hormones of nandrolone, and 25% contained compounds related to both. Forty-nine of the supplements contained only one steroid, but 45 contained more than one, with eight products containing five or more different steroid products. According to the labels on the products, the countries of *manufacture* of all supplements containing steroids were the USA, the Netherlands, the UK, Italy and Germany; however, these products were *purchased* in other countries. In fact, 10–20% of products purchased in Spain and Austria were found to be contaminated. Just over 20% of the products made by companies selling pro-hormones were positive for undeclared pro-hormones, but 10% of products from companies that did not sell steroid-containing supplements were also positive. The brand names of the 'positive' products were not provided in the study, but included amino acid supplements, protein powders, and products containing creatine, carnitine, ribose, guarana, zinc, pyruvate, HMB, *Tribulus terristris*, herbal extracts and vitamins/minerals. It was noted that a positive urinary test for nandrolone metabolites occurs in the hours following uptake of as little of 1 μg of nandrolone pro-hormones. The positive supplements contained steroid concentrations ranging from 0.01 to 190 μg per gram of product.

This is a major area of concern for serious athletes who compete in competitions that apply anti-doping codes, since many of these codes place liability with the athlete for ingestion of banned substances, regardless of the circumstances and the source of ingestion. As such, full penalties can be expected for a positive doping test arising from the ingestion of a banned substance that is a contaminant or undeclared ingredient of a supplement. Further information on contamination of supplements can be found in reviews by Maughan (2005) and Burke (2006).

Athletes should make enquiries at the anti-doping agencies within their countries for advice on the specific risks identified with supplement use, and any initiatives to reduce this risk.

16.3.6 Cons—displacement of real priorities

A more subtle outcome of reliance on supplements is the displacement of the athlete's real priorities. Successful sports performance is the product of superior genetics, long-term training, optimal nutrition, adequate sleep and recovery, state-of-the-art equipment and a committed attitude. These factors cannot be replaced by the use of supplements, but often appear less exciting or more demanding than the enthusiastic and emotive claims made for many supplements and sports foods. Athletes can sometimes be side-tracked from the true elements of success in search of short-cuts from bottles and packets. Most sports dietitians are familiar with individual athletes who are reliant on supplements while failing to address some of the basic elements of good training and lifestyle.

16.3.7 Special issues for the young athletes and supplement use

Success in sports involves obtaining an 'edge' over the competition, and children and adolescents may be uniquely vulnerable to the lure of supplements. The pressure to 'win at all costs', extensive coverage in lay publications, and hype from manufacturers with exciting and emotive claims all play a role in the use of supplements by young athletes. The knowledge that famous athletes and other role models use or promote supplements and sports foods adds to the allure.

An array of ethical issues arises in the consideration of supplement use by young athletes, including all the factors previously outlined in this section. Displaced priorities and the failure to build a foundation of sound training, diet and recovery strategies are particularly important since a long-term career in sport is underpinned by such an investment. The lack of information about the long-term safety of ingesting various compounds on a growing or developing body is a special concern.

Various expert groups have made strong statements against the use of supplements by young athletes. The American Academy of Pediatrics policy statement on the use of performance enhancing substances (2005) condemns the use of ergogenic aids, including various dietary supplements, by children and adolescents. The American College of Sports Medicine recommends that creatine not be used by people under 18 years of age (American College of Sports Medicine 2000). These policies are based on the unknown but potentially adverse health consequences of some supplements and the implications of supplement use on the morals of a young athlete. Many people consider supplements to be an 'entry point' to the decision to take more serious compounds, including prohibited drugs.

16.4 Finding proof of the efficacy of supplements and sports foods

The process of substantiating the performance benefits or outcomes from supplement use is difficult. To various audiences, 'proof' comes in different forms, including testimonials from 'satisfied customers' and scientific theories that predict the outcome from the use of a product. On evaluation, however, these methods are flawed in their ability to provide definite support for the actions of a supplement. The scientific trial remains the best option for measuring the potential benefits of the use of a product. Nevertheless, the limitations of scientific studies need to be understood before a full interpretation of the results can be applied to real-life sport.

16.4.1 *Scientific theories*

The current focus of the sports supplement industry is on compounds and nutrients that act as cofactors, intermediary metabolites or stimulants of key reactions in exercise metabolism. The rationale behind supplementation is that if the system is 'supercharged' with additional amounts of these compounds, metabolic processes will proceed faster or for longer time, thus enhancing sports performance. The marketing of many contemporary supplements is accompanied by sophisticated descriptions of metabolic pathways and biochemical reactions, with claims that enhancement of these will lead to athletic success. In some cases, these descriptions are supplemented with data from studies on patients with an inherited deficiency of these compounds—these patients respond when supplementation is able to correct their deficiency.

To the scientist, a theory that links an increased level of a compound with performance enhancement may be a hypothesis that is worthy of testing, but it does not constitute proof for the idea. However, to the public, a hypothesis can be made to sound like a *fait accompli*, and athletes can be induced to buy products on the strength of a 'scientific breakthrough' that exists only on paper. In an era when sports scientists feel challenged by the apparent sophistication of the scientific theories presented by supplement companies, it is unlikely that athletes will possess sufficient scientific knowledge to be critical of these proposals.

While a 'supercharging' hypothesis may appear plausible at first glance, there are many reasons why it may not occur. Other issues to be considered include:

- Will oral ingestion of the compound increase concentrations at the sites that are critical?
- Does the present level of compound fall below the critical level for optimal metabolism?
- Is this reaction the rate-limiting step in metabolism or are other reactions setting the pace?

A scientific theory or hypothesis should be developed and fine-tuned before setting up a supplementation study. Since studies are expensive in time, money and resources, it is important that ideas that make it to trial are based on sound logic. But while a scientific theory should be developed in preparation for a study (or to explain the data collected in a study), it cannot be accepted as proof of the efficacy of a supplement until verified by actual research.

16.4.2 Anecdotal support

Testimonials provide a powerful force in the advertising and marketing of sports supplements, particularly in the case of products that target the body-building or resistance-training industry. This is also true of supplements sold through multi-level marketing schemes, where individual distributors are encouraged to have a 'personal story' of how the product has enhanced their life. Testimonials for supplements and sports foods highlight the successful health or performance outcomes that people have achieved, allegedly as a result of their use of a supplement product. Often famous athletes or media stars supply these testimonials, but sometimes they also feature the exploits of 'everyday' people. Although people sometimes receive payment for their testimonials, in other cases the endorsement for a supplement is provided by hearsay, observation or direct recommendation from a 'satisfied customer'. Successful athletes and teams are perpetually being asked to nominate the secrets of their success by peers, fans or the media. In the following reviews of well-known ergogenic aids, there are many examples where public interest in a product can be traced back to the recommendation or testimonial of a winning sportsperson.

It is hard for athletes to understand that success in sport results from a complicated and multi-factorial recipe, and that even the most successful athletes may not fully appreciate the factors behind their prowess. In many cases, it is likely that the athlete has succeeded without the effects of the supplements they are taking—and in some cases, perhaps, in spite of them! Unsupported beliefs and superstition are key reasons behind many decisions to use supplements. The idea that 'everyone is doing it' provides a powerful motivation to the athlete contemplating a new product. Sometimes, this manifests as a fear that 'others may have a winning edge that I don't have'. The *ad hoc* and undiscriminating patterns of supplement use reported by some athletes are testament to the power of 'word of mouth'.

Of course, the anecdotal experiences of athletes may be useful when considering the scientific investigation of a supplement. These experiences may support the case for expending resources on a study, or help in deciding on protocols for using a supplement or for measuring the outcomes. However, by itself, a self-reported experience provides very weak support for the benefits of a supplement. Many of the benefits perceived by athletes who try a new supplement result from the psychological boost or placebo effect that accompanies a new experience or special treatment.

16.4.3 The scientific trial

The scientific trial remains the 'gold standard' for investigating the effects of dietary supplements and nutritional ergogenic aids on sports performance. Scientists undertaking scientific trials should test the effects of the supplement in a context that simulates sports performance as closely as possible. Additional studies might be needed to elucidate the mechanisms by which these effects occur, but, overall, sports science research must be able to deliver answers to questions related to real-life sport.

It is beyond the scope of this chapter to fully explore the characteristics of good research design. However, there are many variables that interfere with the outcomes of research and need to be considered. Table 16.1 summarises the

Table 16.1 Factors in conducting research on supplements and sports foods

Factors to consider in designing a research protocol to select independent and dependent variables of importance

- Subject variables—age, gender, level of training, nutritional status
- Measurement variables—validity and reproducibility of techniques, costs, availability of equipment, subjective versus objective measures, application to the hypothesis being tested
- Study design—acute versus chronic supplementation, lab versus field, 'blinding' of subjects and researchers, crossover versus parallel group design, placebo control
- Supplementation protocols—timing and quantity of doses, duration of the supplementation period

Strategies to undertake to eliminate or standardise the variables that might otherwise confound the results of a supplement study

- Recruit well-trained athletes as the subject's level of training may alter the effect of the supplement and will affect the precision of measurement of performance.
- Incorporate the use of a placebo treatment to overcome the psychological effect of supplementation.
- Use repeated measures or 'crossover' design to increase statistical power; each subject acts as their own control by undertaking both treatment and placebo.
- Allow a suitable wash-out period between treatments.
- Randomly assign subjects to treatment and placebo groups and counter-balance the order of treatment.
- Employ a double-blind allocation of treatments to remove the subjective bias of both researcher and subjects.
- Standardise the pre-trial training and dietary status of subjects.
- Design the parallel conditions to mimic real-life practices of athletes.
- Choose measurement variables that are sufficiently reliable to allow changes due to the supplement to be detected, and that are applicable to the hypothesis being tested.
- Choose a performance test that is highly reliable and applicable to the real-life performances of athletes.
- Choose a supplementation protocol that maximises the likelihood of a positive outcome.
- Interpret the results in light of what is important to sports performance.

issues that need to be addressed to control for these variables, along with other issues to consider in designing trials to test the effects of supplements on sports performance. Several factors that are important to consider in the interpretation of results will now be discussed.

16.4.3.1 Are we testing the athlete's definition of improvement?

In the world of sport, the difference between winning and losing can be measured in hundredths of seconds and millimetres. To the athlete or coach, that hundredth of a second or millimetre seems a meaningful improvement in performance. This helps to explain why supplements that promise a performance boost are greeted with such enthusiasm—the chance of the tiniest improvement seems worth their investment. Unfortunately, the traditional framework of sports science research works on a different basis. The scientist aims to detect (declare statistically significant) an effect, with acceptably low rates for detection of non-existent effects (5%) and failed detection of a real effect (20%). Most scientific investigations of supplements are biased towards rejecting the hypothesis that the product enhances performance, due to small sample sizes and performance-testing protocols with low reliability. In effect, most intervention studies are able to detect only large differences in performance outcomes. Changes that are smaller than this large effect are declared to be 'not statistically significant' and are dismissed.

Hopkins and colleagues attempted to find some middle ground between what scientists and athletes consider significant (Hopkins et al. 1999). First, they established that an athlete's required improvement is *not* the tiny margin between the place-getters in a race (also known as between-athlete variation). Each athlete has their own day-to-day or event-to-event variability in performance, known as the within-athlete variation or coefficient of variation (CV) of performance. This variation would influence the outcome of an event if it were to be rerun without any intervention. By modelling the results of various sporting events in track and field, Hopkins suggested that 'worthwhile' changes to the outcome of most events require a performance change equal to ~0.4–0.7 times the CV of performance for that event. Note that this 'worthwhile' change does not *guarantee* that an athlete would win an event, but would make a reasonable change to an athlete's likelihood of winning—for example, improve the probability of winning, for an athlete who has a true probability of winning the race 20% of the time, to 30%. Across a range of track and field events, Hopkins noted that the CV of performance of top athletes was within the range of 0.5–5%, thus making performance changes of up to 3% important to detect (Hopkins et al. 1999).

Even though 'worthwhile' performance differences are larger than the tiny margins considered important by athletes, these changes are still outside the realms of detection for many of the studies commonly published in scientific

journals. As discussed by Hopkins et al. (1999), a change of 0.7 of the CV in a parameter requires a sample size of about 32 for detection in a crossover study in which every athlete receives an experimental and placebo treatment. For a parallel group designed study, 128 subjects would be needed. Such sample sizes are beyond the patience and resources of most sport scientists!

To bridge the gap between science and the athlete on the issue of a significant performance change, Hopkins proposed a new approach to reporting and interpreting the results of intervention studies (Hopkins et al. 1999). He suggested that outcomes should be as a per cent change in a measure of athletic performance—for example, a study may find a 1% enhancement in time, caused by a 0.8% improvement in mean power, as a result of the use of a supplement. The reporting of the 95% confidence limits for the outcome will provide the likely range of the true effect of the treatment on the average subject. For example, in our study, the 95% CI for the change in time might be −1% to +3%. This can then be interpreted in terms of the likely effect on athletes in an event. For example, the outcome in this study includes the possibility of a small decrement in performance as well as a substantial improvement in performance. Both possibilities could change the outcome of an event, and the athlete needs to consider the small risk of a negative outcome as well as the more likely chance of a noticeable improvement in finishing order. It is hoped that sports scientists will undertake such interpretations of the results of their studies.

16.4.3.2 Individual responses

Notwithstanding the general variability in performance, there is evidence that some treatments cause a range of different responses in individual athletes. In some cases, the same intervention can produce favourable responses in some individuals, neutral responses in others and, sometimes, detrimental outcomes to another group. For example, research has identified that some athletes are 'non-responders' to caffeine or creatine supplementation (Graham & Spriet 1991; Greenhaff et al. 1994). It is useful to have metabolic or other mechanistic data to substantiate real differences in response, and to differentiate these from the general variability of performance. For example, it has been shown that subjects whose muscle creatine levels did not increase by at least 20% as a result of creatine supplementation did not show the functional changes and performance enhancements seen by the rest of the experimental group (Greenhaff et al. 1994).

Studies employing simple group analysis and small sample sizes are not appropriate for situations in which there is true variability in the size and direction of the response to an intervention. Such studies will fail to detect a difference in performance, even though this is a real outcome for some subjects in the group. Ideally, studies employing large sample sizes and co-variate analysis should be used; this approach will allow real changes to be detected and may also identify

the characteristics of individuals which predict 'response' and 'non-response'. At present, such studies are rare.

16.5 The AIS Sports Supplement Program

In some cases, sporting organisations or institutions make policies or programs for supplement use on behalf of athletes within their care. This may range from a single sporting team, to an entire sports program such as that of the National Collegiate Athletics Association (Burke 2001). Since 2000, the Australian Institute of Sport (AIS) has implemented a supplement program for athletes within its funding program with the stated goals of:

- allowing its athletes to focus on the sound use of supplements and special sports foods as part of their special nutrition plans
- ensuring that supplements and sports foods are used correctly and appropriately to deliver maximum benefits to the immune system, recovery and performance
- giving its athletes the confidence that they receive 'cutting edge' advice and achieve 'state of the art' nutrition practices
- ensuring that supplement use does not lead to an inadvertent doping offence.

A key part of the AIS program is a ranking system for supplements and sports foods, based on a risk-to-benefit analysis of each product by a panel of experts in sports nutrition, medicine and science. This ranking system has four tiers, each of which has a prescribed level of use by AIS-funded athletes. Although the hierarchy of categories was developed for long-term use, there is a regular assessment of supplements and sports foods to ensure that they are placed in the category that best fits the available scientific evidence. The hierarchical system allows the program to avoid the 'black and white' assessment that any particular product works or fails to live up to claims. Rather, the available science is reviewed to place supplements into categories ranked from what is most likely to provide a benefit for little risk, to what provides least benefit and a definite risk. Table 16.2 provides a summary of the AIS supplement program at the time of publication. The remainder of this chapter provides a summary of the current scientific support for a range of products within the various supplement categories.

16.5.1 Supplements in Group A of the AIS Sports Supplement Program

According to the judgements of the expert panel of the AIS Sports Supplement Program, products listed in Group A have scientific support to show that they can be used within an athlete's nutritional plan to provide direct or indirect benefits to performance.

Table 16.2 Australian Institute Sport Supplement Program 2006 (see www.ais.org.au/nutrition)

Supplement category and explanation of use within the AIS supplement program	Products included in category
Group A: Approved supplements • Provide a useful and timely source of energy and nutrients in the athlete's diet, or • Have been shown in scientific trials to provide a performance benefit, when used according to a specific protocol in a specific situation in sport. *AIS Sports Supplement Panel position* We know that athletes and coaches are interested in using supplements to achieve optimal performance. Our supplement program aims to focus this interest on products and protocols that have documented benefits, by: • making these supplements available and accessible to the AIS athletes who will benefit from their appropriate use. In particular, to provide these supplements at no cost to AIS sports programs, through systems managed by appropriate sports science/medicine departments. Strategies to provide products range from individual 'prescription' of supplements requiring careful use (e.g. creatine) to creative programs that make valuable sports foods and everyday foods accessible to athletes in situations of nutritional need (e.g. post-exercise recovery bars) • providing education to athletes and coaches about the beneficial uses of these supplements/sports foods and their appropriate use, with the emphasis on state-of-the-art sports nutrition • ensuring that supplements/sports foods used by AIS athletes carry a minimal risk of doping safety problems.	• Sports drinks • Liquid meal supplements • Sports gels • Sports bars • Caffeine • Creatine • Bicarbonate • Anti-oxidants: vitamin C, vitamin E • Sick pack (zinc and vitamin C) • Multivitamin/mineral supplement • Iron supplement • Calcium supplement • Glycerol (for hyperhydration) • Electrolyte replacement
Group B: Supplements under consideration Supplements may be classified as belonging to Group B if they have no substantial proof of health or performance benefits, but: • remain of interest to AIS coaches or athletes • are too new to have received adequate scientific attention • have preliminary data that hint at possible benefits. *AIS Sports Supplement Panel position* These supplements can be used at the AIS under the auspices of a controlled scientific trial or a supervised therapeutic program.	• Echinacea • Glutamine • Hydroxymethylbutyrate (HMB) • Colostrum • Probiotics • Ribose

(*Cont.*)

Table 16.2 (*Continued*)

Supplement category and explanation of use within the AIS supplement program	Products included in category
Group C: Supplements that have no clear proof of beneficial effects This category contains the majority of supplements and sports products promoted to athletes. Supplements not specifically listed within this system probably belong here. These supplements, despite enjoying a cyclical pattern of popularity and widespread use, have not been proven to enhance sports performance or recovery. In some cases these supplements have been shown to impair sports performance or health, with a clear mechanism to explain these results. *AIS Sports Supplement Panel position* In the absence of proof of benefits, these supplements should not be provided to AIS athletes from AIS program budgets. If an individual athlete or coach wishes to use a supplement from this category, they may do so providing: • they are responsible for payment for this supplement • any sponsorship arrangements are within guidelines of AIS marketing • the supplement brand has been assessed for doping safety and considered 'low risk', and • the use is reported to an AIS sports dietitian or physician.	• Amino acids (these can be provided by everyday foods or sports foods in Group A) • Ginseng • Garlic • *Cordyceps* • Nitric oxide stimulators • Inosine • Coenzyme Q10 • Cytochrome C • Carnitine • Bee pollen • Gamma-oryzanol and ferulic acid • Chromium picolinate • Pyruvate • Vitamin B12 injections • Injectable forms of other vitamins • Oxygenated water • All supplements from network marketing companies • Most of the other supplements not listed in this system
Group D: Banned supplements These supplements are either directly banned by the WADA anti-doping code or provide a high risk of producing a positive doping outcome. *AIS Sports Supplement Panel position* These supplements should not be used by AIS athletes.	• Androstenedione • DHEA • 19-norandrostenedione and 19-norandrostenediol • *Tribulus terristris* and other herbal testosterone supplements • Ephedra • Strychnine

16

16.5.1.1 Sports foods and dietary supplements that achieve nutritional goals

Sports foods that provide a practical way to meet goals of sports nutrition are among the most valuable special products available to athletes. Table 16.3

summarises the major classes of sports foods together with the situations or goals of sports nutrition that they can be used to address. Substantiation for many of these nutrition goals is well accepted and often includes situations where a measurable enhancement of performance can be detected as a result of the correct use of the sports food. More detail about the uses of these products can be found in various chapters throughout this text (see Table 16.3 for cross-referencing).

Although most sports foods have specialised uses in sport, some products (for example, sports drinks) have crossed successfully into the general market. As long as consumers are prepared to pay the appropriate price for a niche product and sports nutrition messages are left intact, most sports nutrition experts are not unduly concerned by this outcome. In fact, there is some support for the use of products such as sports drinks by 'weekend warriors' and recreational exercisers, since the benefits of fluid intake and carbohydrate replacement during a workout are determined by the physiology of exercise rather than the calibre of the person who is exercising. In fact, most studies of sports drinks have been undertaken on moderately-to-well-trained performers rather than elite athletes; therefore, where evidence of a performance benefit does exist, it is directly relevant to these sub-elite populations.

Vitamin and mineral supplements that are used to correct or prevent a suboptimal nutrient status can also be considered as supplements that help an athlete achieve their nutritional goals. These include multivitamin, iron and calcium supplements used in specific situations or individuals (see Table 16.3).

16.5.1.2 Caffeine

Caffeine is a drug that enjoys social acceptance and widespread use around the world. This acceptance now includes its use in competitive sport following the removal of caffeine from the WADA list of prohibited substances in January 2004. Caffeine is the best known member of the methyl xanthines, a family of naturally occurring stimulants found in the leaves, nuts and seeds of a number of plants. Major dietary sources of caffeine such as tea, coffee, chocolate, cola and energy drinks typically provide 30–100 mg of caffeine per serve, whereas some non-prescriptive medications contain 100–200 mg of caffeine per tablet. The recent introduction of caffeine (or guarana) to 'energy drinks', confectionery and sports foods/supplements has increased the opportunities for athletes to consume caffeine, either as part of their everyday diet or for specific use as an ergogenic aid.

The complex range of actions of caffeine on the human body has been extensively researched (Tarnopolsky 1994; Spriet 1997; Graham 2001a, 2001b; Fredholm et al. 1999). Briefly, caffeine has several effects on skeletal muscle, involving calcium handling, sodium–potassium pump activity, elevation of cyclic-AMP and direct action on enzymes such as glycogen phosphorylase (see Chapter 1). Increased catecholamine action, and the direct effect of caffeine on cyclic-AMP, may both act to increase lipolysis in adipose and muscle tissue, causing

Table 16.3 Sports foods and dietary supplements used to meet nutritional goals

Supplement	Form	Composition	Sports-related use	Chapter
Sports drink	Powder or liquid	5–8% CHO	Optimum delivery of fluid + CHO during exercise	13
		10–25 mmol/L sodium	Post-exercise rehydration	14
		3–5 mmol/L potassium	Post-exercise refuelling	14
Sports gel	Gel 30–40g sachets or larger tubes	60–70% CHO (~25 g CHO per sachet)	Supplement high-CHO training diet	14
		Some contain MCTs or caffeine	Carbohydrate loading	12
			Post-exercise CHO recovery	14
			May be used during exercise when CHO needs exceed fluid requirements	13
Electrolyte replacement supplements	Powder sachets or tablets	≤2% CHO 57–60 mmol/L sodium 10–20 mmol/L potassium	Rapid and effective rehydration following dehydration undertaken for weight-making	7
			Replacement of large sodium losses during ultra-endurance activities	13
			Rapid and effective rehydration following moderate to large fluid and sodium deficits (e.g. post-exercise)	14
Liquid meal supplement	Powder (mix with water or milk) or liquid	1–1.5 kcal/mL 15–20% protein 50–70% CHO low to moderate fat vitamins/minerals: 500–1000 mL supplies RDI/RDAs	Supplement high energy/CHO/nutrient diet (especially during heavy training/competition or weight gain)	14

(*Cont.*)

Table 16.3 (*Continued*)

Supplement	Form	Composition	Sports-related use	Chapter
			Low-bulk meal replacement (especially pre-event meal)	12
			Post-exercise recovery—provides CHO, pro- and micronutrients	4, 14
			Portable nutrition for travelling athlete	23
Sports bar	Bar (50–60 g)	40–50 g CHO 5–10 g protein Usually low in fat and fibre Vitamins/minerals: 50–100% of RDA/RDIs May contain creatine, amino acids	CHO source during exercise	13
			Post-exercise recovery—provides CHO, protein and micronutrients	5, 14
			Supplements high energy/CHO/nutrient diet	14
			Portable nutrition (travelling)	23
Vitamin/mineral supplement	Capsule/tablet	Broad range 1–4 × RDI/RDAs of vitamins and minerals	Micronutrient support for low-energy or weight-loss diet	6
			Micronutrient support for restricted variety diets (e.g. vegetarian diet)	20
			Micronutrient support for unreliable food supply (e.g. travelling athlete)	23
			Heavy competition schedule where normal eating patterns may be disrupted	
Iron supplement	Capsule/tablet	Ferrous sulfate/gluconate/fumarate	Supervised management of iron deficiency (including treatment and prevention)	10
Calcium supplement	Tablet	Calcium carbonate/phosphate/lactate	Calcium supplementation in low-energy or low dairy food diet? Treatment/prevention of osteopenia	9

an increase in plasma free fatty acid concentrations and increased availability of intramuscular triglyceride. It has been proposed that an increased potential for fat oxidation during moderate-intensity exercise promotes glycogen sparing. However, studies have found this effect to be short-lived or confined to certain individuals, and are unable to explain the ergogenic effects seen with caffeine supplementation (for review, see section 15.8.1). Caffeine may also influence athletic performance via central nervous system effects, such as a reduced perception of effort or an enhanced recruitment of motor units. Breakdown products of caffeine such as paraxanthine and theophylline may also have actions within the body. Caffeine supplementation is a complex issue to investigate due to the difficulty in isolating individual effects of caffeine, and the potential for variability between subjects.

The effect of caffeine on exercise performance has received extensive scientific attention for almost a century (Rivers 1907), with recent excellent reviews including Spriet (1997), Graham (2001a, 2001b) and Doherty and Smith (2004, 2005). Due to the large volume and turnover of such research we will present our summary of the available peer-reviewed literature as a continually updated online publication at the following website (www.ais.org.au/nutrition). This resource includes a tabulation of the results of studies of caffeine supplementation and exercise/sports performance, divided according to the type of exercise task and the method of administration of caffeine administration. Some of the key information from this resource will now be presented to summarise our current knowledge of the effects of the quantity, timing and source of caffeine on exercise performance.

Caffeine dose

An obvious interest of athletes is to find the dose of caffeine that elicits the greatest benefit to their specific performance for the minimum level of risk or side effect. Unfortunately, it is difficult to conduct this analysis across all of the available literature due to the mixture of studies providing caffeine in absolute doses (for example, 250 mg caffeine) and relative doses (for example, 3 mg/kg body mass of caffeine) across populations of differing body sizes. When including studies using an absolute dose protocol in our tabulated summary of caffeine and exercise performance, we have tried to include an approximate value of the caffeine intake per kilogram of body mass. However, this figure is calculated from the mean weight of the subjects within that study so care should be taken with any interpretation.

Studies that have investigated a dose–response relationship with caffeine supplementation, by examining the performance outcomes following the intake of different doses of caffeine by the same subjects, have been isolated for specific comment (see Table 16.4). These include a number of brief high-intensity performance (<20 minutes) in relatively untrained (Dodd et al. 1991; Perkins et al. 1975) and trained subjects (Anderson et al. 2000; Bruce et al. 2000). In untrained

subjects, the data show that caffeine supplementation in any dose fails to provide a detectable change in exercise capacity. However, in the studies undertaken by trained subjects who were familiarised to the performance protocol (Anderson et al. 2000; Bruce et al. 2000), 6 and 9 mg/kg of caffeine had similarly positive effects on a time trial performance.

In events of slightly longer duration (~1 hour) the effects of caffeine supplementation appear more consistent. Similar benefits to endurance or performance were identified at caffeine doses of 5, 9 and 13 mg/kg (Pasman et al. 1995) and at 3 and 6 mg/kg (Graham & Spriet 1995). Kovacs and colleagues (1998) demonstrated a threshold of the performance benefits to a cycling time trial at a caffeine dose of 3.2 mg/kg dose (that is, no further benefit with 4.5 mg/kg). Whereas caffeine did not have a detectable benefit to the performance of a half-marathon in the heat at intakes of 5 or 7 mg/kg (Cohen et al. 1996), Cox and co-workers (2002) found that intakes of as little as 1–2 mg/kg caffeine enhanced the performance of a time trial at the end of 2 hours of cycling to the same degree as an intake of 6 mg/kg. In some trials (Graham & Spriet 1995), large amounts of caffeine (9 mg/kg) reduced endurance compared to smaller doses.

Overall, it appears that, for the performance of events lasting 1 hour or longer, benefits are seen at low doses of caffeine (1–3 mg/kg), and there do not seem to be further benefits at doses higher than this. Further research of this type is warranted so that athletes can identify the *smallest* dose of caffeine that produces a worthwhile benefit to their performance.

Timing of intake of caffeine

Caffeine is rapidly absorbed, reaching peak concentrations in the blood within 1 hour after ingestion (for a review of caffeine pharmacokinetics see Fredholm et al. 1999). This explains why the traditional approach to caffeine supplementation has been to consume the caffeine dose 1 hour prior to exercise. In the case of prolonged exercise (>60 minutes), this protocol of intake is often associated with a benefit to endurance or performance, whereas the effect on shorter term high-intensity exercise is less consistent (see the tables on caffeine supplementation at www.ais.org.au/nutrition). Whether this relates to the real outcome, the reliability of the exercise in allowing changes to performance to be detected, or the timing of the intake of caffeine is unknown.

Caffeine is slowly catabolised (half life 4–6 hours) and individuals maintain peak concentrations for 3–4 hours (Graham 2001a, 2001b). Studies have reported that the ergogenic benefits of caffeine may be sustained for up to 6 hours post-ingestion (Bell & McLellan 2002), even after a prior bout of exhaustive exercise (Bell & McLellan 2003).

Although early studies (Ivy et al. 1979) demonstrated the potential benefits of consuming caffeine both before and throughout an exercise task, it is only recently that there has been a renewed interest in investigating the effects of divided or progressive doses of caffeine during exercise (Kovacs et al. 1998;

Table 16.4 Dose–response studies of caffeine on exercise performance using placebo-controlled crossover design (for updates see www.ais.org.au/nutrition)

Reference	Exercise protocol	Subjects	Caffeine dose	Enhanced performance	Summary
Protocols >60 minutes exercise, caffeine taken 1 hour pre-exercise					
Cohen et al. (1996)	Running • half-marathon in hot conditions	5 male & 2 female trained runners	0, 5 and 9 mg/kg	No	No detectable effects on RPE or performance at either dose compared with placebo trial
Protocols >60-minute event, caffeine taken 1 hour pre-exercise and during exercise					
Cox et al. (2002)	Cycling • 2 hours (70% $VO_{2\ peak}$) + TT	Study A: 12 well-trained male cyclists/ triathletes Study B: 8 well-trained male cyclists/ triathletes	Study A: • placebo • 6 mg/kg 1 hour pre-exercise • 6 × 1 mg/kg @ 20-minute intervals during exercise • ∼1–2 g/kg caffeine @ 100–140 minutes of exercise (2 × 5 mL/kg Coca-cola) Study B: Double-blind placebo presentation of cola drinks • 6% CHO, no caffeine • 11% CHO, no caffeine • 6% CHO, 13 mg/100 mL caffeine • 11% CHO, 13 mg/100 mL caffeine	 Yes Yes Yes Yes Yes	6 mg/kg enhanced TT performance by ∼3% independently of timing of intake. Similar performance enhancement achieved by consumption of smaller dose of caffeine during last third of exercise protocol (e.g. when athlete is fatiguing). Study B confirmed findings of ergogenic benefits of 1–2 mg/kg caffeine, attributing most of the benefit of consuming Coca-cola late in exercise due to caffeine (13 mg/100 mL) rather than increased intake of CHO compared with sports drinks (11% versus 6%)

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

30–60-minute event, Caffeine taken 1 hour pre-exercise					
Pasman et al. (1995)	Cycling • 80% W_{max} to exhaustion	9 well-trained male cyclists	0, 5, 9 and 13 mg/kg	Yes	Time to exhaustion was 27% longer in caffeine trials. No greater gains with increasing caffeine doses. Large individual variation in urinary caffeine concentrations following the intake of a given dose of caffeine.
Graham and Spriet (1995)	Running • 85% $VO_{2\ max}$ to exhaustion	8 well-trained male runners	0, 3, 6, 9 mg/kg	Yes (3 AND 6 mg/kg only)	Endurance improved by ~22% with both 3 and 6 mg/kg but outcome with 9 mg/kg not significantly different to placebo. Highest dose of caffeine had the greatest effect on epinephrine and metabolites, yet had the least effect on performance.
30–60 minute event, caffeine intake before and during exercise					
Kovacs et al. (1998)	Cycling • ~60 minutes TT	15 well-trained male cyclists	0, 2.1, 3.2 and 4.5 mg/kg Doses divided between 75 min pre-exercise and 20 and 40 minutes during TT	Yes	Addition of caffeine to CHO/electrolyte drinks improved 60 minute TT performance at all levels of intake. Improvement with 3.2 and 4.5 mg/kg caffeine doses equal, and greater than improvement with 2.1 mg/kg. Urinary concentrations of caffeine remained below 12 μg/mL in all subjects at all doses.

(*Cont.*)

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.4 (*Continued*)

Reference	Exercise protocol	Subjects	Caffeine dose	Enhanced performance	Summary
~20-minute events, caffeine taken 1 hour pre-exercise (unless stated)					
McLellan and Bell (2004)	Cycling • 80% $VO_{2\ max}$ to exhaustion	9 male + 4 female untrained subjects; habitual caffeine users	Coffee consumed 1.5 hours prior to exercise + capsules 30 minutes later • Decaf coffee + placebo • Decaf coffee + caffeine (5 mg/kg) • Coffee (1.1 mg/kg) + caffeine (5 mg/kg) • Coffee (1.1 mg/kg) + caffeine (3 g/kg) • Coffee (1.1 mg/kg) + caffeine (7 mg/kg) • Brown water (placebo coffee) + caffeine (5 mg/kg)	Yes	Caffeine consistently extended time to fatigue (21.7 ± 8.1 minutes versus 27.0 ± 8.4 for placebo and caffeine respectively). Exercise capacity was improved regardless of caffeine dose, or whether trial was preceded by intake of coffee, decaffeinated coffee or placebo (brown water).
Dodd et al. (1991)	Cycling • Incremental test to exhaustion	17 moderately trained male subjects (8 caffeine naive and 9 habitual caffeine users)	0, 3 and 5 mg/kg	No	Time to exhaustion unaffected by caffeine dose or intake history. Caffeine-naive subjects showed heightened HR and ventilatory responses.

~5-minute events, caffeine 1 hour pre-exercise					
Perkins and Williams (1975)	Cycling • Incremental test to exhaustion	14 female undergraduate students	0, 4, 7 and 10 mg/kg caffeine consumed 30 minutes prior	No	No effect on performance, HR or RPE either at submaximal or maximal intensities with any caffeine dose
Anderson et al. (2000)	Rowing 2000 m TT	8 well-trained female rowers	0, 6 and 9 mg/kg	Yes	Dose-dependent improvements in time and power, especially in first 500 m of TT. High dose achieved 1.3% improvement and moderate dose achieved 0.7% reduction in time to complete task. Reduction in RER seen with 6 mg/kg only. No effects on RPE.
Bruce et al. (2000)	Rowing • 2000 m TT	8 well-trained female rowers	0, 6 and 9 mg/kg	Yes	6 mg/kg achieved 1.3% improvement, 9 mg/kg achieved 1.0% improvement in TT performance. Changes in RER values during submaximal exercise but similar values during the TT.
Sprint events					
No studies available					

RER = respiratory exchange ratio, RPE = rating of perceived exertion, TT = time trial, HR = heart rate

Cox et al. 2002; Hunter et al. 2002; Conway et al. 2003). Conway and co-workers (2003) investigated the performance of a time trial following 90 minutes of submaximal cycling with supplementation of 6 mg/kg caffeine, either 1 hour pre-trial or 3 mg/kg pre-trial and 3 mg/kg at 45 minutes of exercise (= 3 + 3 mg/kg). There was a large reduction (that is, an improvement) in the mean time to complete the task (28.3, 24.2 and 23.4 minutes for placebo, 6 mg/kg and 3 + 3 mg/kg, respectively); however, differences between trials were not found to be statistically significant (see section 16.4.3.1).

We recently showed that similar performance benefits of a 3% improvement in time-trial performance were achieved when six doses of caffeine of 1 mg/kg were spread throughout a 2-hour submaximal cycling bout prior to the TT, when 6 mg/kg of caffeine was consumed 1 hour prior to the cycling bout, or when small amounts of caffeine (~1.5 mg/kg) were consumed over the last third of the protocol (Cox et al. 2002; see Table 16.4). It may be that subjects become more sensitive to small amounts of caffeine as they become fatigued. Further investigations are required to confirm this and the potential for strategic timing of intake of caffeine in various sporting and exercise activities.

Source of caffeine

A number of studies have investigated the effects of caffeine on exercise, using coffee as the source of caffeine (that is, providing subjects with decaffeinated coffee ± added caffeine) (Costill et al. 1978; Wiles et al. 1992; Trice & Haymes 1995; Graham et al. 1998; Vanakoski et al. 1998; McLellan & Bell 2004). The results of these studies have shown that coffee intake can both enhance performance (Costill et al. 1978; Wiles et al. 1992; Trice & Haymes 1995; McLellan & Bell 2004) and fail to have a detectable effect (Graham et al. 1998; Vanakoski et al. 1998). Only two of these studies (Graham et al. 1998; McLellan & Bell 2004) included trials in which the performance responses to caffeinated coffee were compared to responses to pure caffeine. Graham and co-workers found that runners increased their treadmill running time to exhaustion following the intake of caffeine compared to their endurance following the intake of the same amount of caffeine consumed in coffee. The differences in performance occurred despite similar appearance rates of caffeine and other caffeine metabolites; it has been suggested that other components within coffee might antagonise the responses to the caffeine or counteract its ergogenic effects by directly impairing performances. However, McLellan and Bell (2004) demonstrated that the consumption of one cup of coffee (either decaffeinated or caffeinated) prior to the consumption of pure caffeine failed to dampen the ergogenic effect gained from the larger caffeine doses (see Table 16.4). Further research is needed on this issue, since in the 'real world', athletes often consume coffee before competing or training, either as part of their normal social and dietary patterns, or as an intentional source of caffeine as an ergogenic aid.

Food tables generally provide a range for the typical caffeine content of coffee, to account for the variable quantities of caffeine in the coffee bean and differences in the way that coffee drinks are prepared for consumption by individuals—even among the same 'type' of drink prepared under seemingly standard conditions. For example, we have recently demonstrated larger than anticipated variations in the caffeine content of an individual serve of retail preparations using ground coffee. We found that the caffeine content of a single espresso purchased from a large number of separate outlets varied from 25 to 214 mg/serve (Desbrow, in review). This unexpectedly large, and otherwise unknown, variation in the caffeine content of coffee and the potential interaction between the caffeine and other active ingredients in coffee (for example, derivates of the chlogogenic acids) suggest that coffee should not be the preferred source of caffeine for athletes.

Only one study (Cox et al. 2002) has investigated the effect of the use of cola-containing beverages on the performance of endurance cycling, to mimic the patterns practised in real life where athletes consume a sports (carbohydrate-electrolyte) drink for the first two-thirds of their event before switching to defizzed cola drinks. As summarised in Table 16.4, we found that the consumption of ~750 mL of Coca-cola towards the end of our cycling protocol enhance the performance of a time trial to a similar extent as larger amounts of caffeine. A separate study was then conducted to test whether this effect was achieved by the presence of the caffeine (~1–2 mg/kg BM) or the increase in carbohydrate concentration between the cola and sports drink. The second study confirmed the finding of a 3% enhancement of performance of the time trial with the intake of Coca-cola towards the end of the trial, finding that the majority of this effect (2%, $P < 0.05$) could be explained by the caffeine content (Cox et al. 2002).

Similarly, a single study has been published on the effects of caffeine on exercise when ingested in the form of an 'energy drink' (Alford et al. 2001). This study reported that the consumption of Red Bull Energy Drink (a carbohydrate-containing drink with the additional ingredients of caffeine, taurine and glucuronolactone) enhanced the performance of a battery of tests, including measures of aerobic and anaerobic performance, and psychomotor traits. Unfortunately, this study did not distinguish the contribution of caffeine, and the authors concluded that the results reflected the effects of the combination of ingredients.

Summary of caffeine and exercise

- There is sound evidence that caffeine enhances endurance and provides a small but worthwhile enhancement of performance over a range of exercise protocols. There is still no consensus on the mechanism to explain this performance improvement, but it is unlikely to result from the so-called 'metabolic theory' (increase in fat oxidation and 'sparing' of glycogen utilisation during exercise).

Instead, altered perception of fatigue and effort, or direct effects on the muscle, may underpin performance changes. Most studies of caffeine and performance have been undertaken in laboratories; studies that investigate performance effects in elite athletes under field conditions or during real-life sports events are scarce. Caffeine may enhance competition performance, but is also likely to be a useful training aid, allowing the athlete to undertake better and more consistent training.

- There is evidence, particularly from recent studies, that beneficial effects from caffeine intake occur at very modest levels of intake (1–3 mg/kg BM or ~70–150 mg caffeine), when caffeine is taken before and/or during exercise. Furthermore, there is little evidence of a dose–response relationship to caffeine—that is, performance benefits do *not* appear to increase with increases in the caffeine dose. This information is an advance on the traditional caffeine supplementation protocols, which provided intakes of 6–9 mg/kg BM (for example, 400–600 mg) 1 hour prior to the exercise. Further research is needed to define the range of caffeine intake protocols that provide performance enhancements across various sports or exercise activities.
- The effects of caffeine supplementation differ between individuals. Some people are non-responders and some people experience negative side effects such as tremors, increased heart rate, headaches and impaired sleep. Such side effects are more common at higher doses—for example, exceeding 6–9 mg/kg BM. These side effects may cause a direct impairment of performance. They may also indirectly impair exercise outcomes—for example, disturb the sleep patterns of athletes who compete in a multi-day sport and need to recover between days of competition.
- Coffee is not an ideal vehicle for caffeine supplementation by athletes, because of the variability of caffeine content and the possible presence of chemicals that impair exercise performance. Furthermore, there is a lack of investigations of the effects of available caffeine sources, such as cola drinks, energy drinks and caffeinated sports products, compared to those of pure caffeine. Therefore many athletes may find it difficult to apply the results of caffeine studies to their 'real world' scenarios.

16.5.1.3 Creatine

When the first edition of this book was written in 1994, creatine was the latest 'hot supplement', with testimonials from gold medal winners at the 1992 Barcelona Olympic Games. However, unlike many supplements that draw the attention of athletes, creatine enjoyed some scientific support, with the 1992 publication of a study that showed that muscle creatine stores could be increased by the intake of large doses of an oral source of creatine (Harris et al. 1992). Since then, creatine supplements have become a phenomenon in sports nutrition—an ergogenic aid that records huge annual sales and has been the topic of over 200 investigations, book chapters and reviews. It is not often that scientists and athletes are excited

by the same product. The coincidental rise of the Internet has assisted the rapid spread of scientific and testimonial information.

Although some lay publications and manufacturers have labelled creatine as a 'legal steroid', this is an incorrect and unfair comparison. In fact, creatine is a muscle fuel, and the ability of creatine supplementation to increase muscle creatine stores makes it similar to CHO loading. Creatine (methylguanidine-acetic acid) is a compound derived from amino acids and is stored primarily in skeletal muscle at typical concentrations of 100–150 mmol/kg/dry weight (dw) of muscle. About 60–65% of this creatine is phosphorylated. Creatine phosphate (CrP) provides a rapid but brief source of phosphate for the resynthesis of ATP during maximal exercise, and is therefore an important fuel source in maximal sprints of 5–10 seconds. Other functions of creatine phosphate metabolism are the buffering of hydrogen ions produced during anaerobic glycolysis and the transport of ATP, generated by aerobic metabolism, from the muscle cell mitochondria to the cytoplasm where it can be utilised for muscle contraction. Creatine metabolism is covered in more detail in Chapter 1 and in reviews of creatine metabolism and supplementation (Spriet 1997; Greenhaff 2000, 2001; Hespel et al. 2001).

The daily turnover of creatine, eliminated as creatinine, is approximately 1–2 g/day. This can be partially replaced from dietary creatine intake, found in animal muscle products such as meat and eggs, and typically consumed in amounts of ~1–2 g/day in an omnivorous diet. Additional creatine needs are endogenously synthesised from arginine, glycine and methionine, principally in the liver, and transported to the muscle for uptake. Creatine is transported into the muscle against a high concentration gradient, via saturable transport processes that are stimulated by insulin (Green et al. 1996a, 1996b). High dietary intakes temporarily suppress endogenous creatine production. Vegetarians who do not consume a dietary source of creatine are believed to have a reduced body creatine store, suggesting that they do not totally compensate for the lack of dietary intake (Green et al. 1997). The reason for the variability of muscle creatine concentrations between individuals is uncertain. There are some suggestions that females typically have higher muscle creatine concentrations (Forsberg et al. 1991) and it appears that creatine stores decline with ageing. The effect of training on creatine concentrations also requires further study.

Protocols for creatine supplementation

The watershed study by Harris and colleagues showed that muscle creatine levels were increased as a result of supplementation with repeated doses of creatine, large enough to sustain plasma creatine levels above the threshold for maximal creatine transport into the muscle cell (Harris et al. 1992). The protocol provided four to six doses of 5 g creatine (monohydrate) for 5 days to increase total muscle creatine concentrations by 20%, and reach an apparent muscle threshold of ~150–160 mmol/kg dw. About 20% of the increased muscle creatine content was stored as CrP and saturation occurred after 2–3 days. Increases in muscle

creatine stores were greatest in those who had the lowest pre-supplementation concentrations and when coupled with intensive daily exercise.

Although this discovery appears to be recent, in fact, studies showing that oral creatine doses are largely retained in the body were available 80 years ago (Chanutin 1926). However, it is only now that muscle biopsy procedures and imaging techniques are available to enable scientists to monitor muscle stores of creatine and investigate the success of creatine loading protocols. Over the past decade a number of studies have refined our knowledge of supplementation protocols. Rapid loading is achieved by consuming a daily creatine dose of 20–25 g, in split doses, for 5 days. Alternatively, a daily dose of 3 g/day will achieve a slow loading over 28 days (Hultman et al. 1996). Elevated muscle creatine stores are maintained by continued daily supplementation of 2–3 g (Hultman et al. 1996). Across studies there is evidence that the creatine loading response varies between individuals, with ∼30% of individuals being 'non-responders' or failing to significantly increase muscle creatine stores (Spriet 1997; Greenhaff 2000). Co-ingestion of substantial amounts of CHO (75–100 g) with creatine doses has been shown to enhance creatine accumulation (Green et al. 1996a, 1996b) and to assist individuals to reach the muscle creatine threshold of 160 mmol/kg dw. Creatine appears to be trapped in the muscle; in the absence of continued supplementation, it takes ∼4–5 weeks to return to resting creatine concentrations (Hultman et al. 1996). Many studies have reported an acute gain in body mass (BM) of ∼1 kg during rapid creatine loading. This is likely to be primarily a gain in body water, and is mirrored by a reduction in urine output during the loading days (Hultman et al. 1996).

Effects of creatine supplementation on performance

Many studies have investigated the effect of creatine supplementation on muscle function exercise and performance. Studies vary according to the characteristics of subjects (gender, age, training status), the mode of exercise, and whether supplementation involved an acute loading intervention or a chronic effect on training adaptations. It is beyond the scope of this chapter to summarise the large and growing body of literature on creatine supplementation and performance effects—even those that are carried out in trained individuals with relevance to sports activities. We will provide this information via an updated online resource (www.ais.org.au/nutrition). However, we offer the following summary of this literature, and of recent reviews (Juhn & Tarnopolsky 1998a, 1998b; Kraemer & Volek 1999; Branch 2003; Rawson & Volek 2003; Bemben & Lamont 2005):

16

- The major benefit of creatine supplementation appears to be an increase in the rate of creatine phosphate resynthesis during the recovery between bouts of high-intensity exercise, producing higher creatine phosphate levels at the start of the subsequent exercise bout. Creatine supplementation can enhance the performance of repeated 6–30 s bouts of maximal exercise, interspersed with short recovery intervals (20 s to 5 minutes), where it can attenuate the

normal decrease in force or power production that occurs over the course of the session.

- Oral creatine supplementation cannot be considered ergogenic for single-bout or first-bout sprints because the likely benefit is too small to be consistently detected.
- The exercise situations that have been most consistently demonstrated to benefit from creatine supplementation are laboratory protocols of repeated high-intensity intervals, involving isolated muscular efforts or weight-supported activities such as cycling.
- In theory, acute creatine supplementation might be beneficial for a single competitive event in sports involving repeated high-intensity intervals with brief recovery periods. This description includes team games and racquet sports. Similarly, chronic creatine supplementation may allow the athlete to train harder at exercise programs based on repeated high-intensity exercise, and make greater performance gains. These benefits may apply to the across-season performance of athletes in team and racquet sports, as well as the preparation of athletes who undertake interval training and resistance training (for example, swimmers and sprinters).
- For many specific sports, the benefits of creatine are theoretical since few studies have been undertaken with elite athletes or as 'field studies'. Performance enhancements may not always occur in complex games and sports; even if changes in strength or speed are achieved by creatine-assisted training, these may not translate into improvements in game outcomes (for instance, goals scored).
- Evidence that creatine supplementation is of benefit to endurance exercise is absent or inconsistent although it may enhance muscle glycogen storage.
- Acute creatine loading is associated with an increase in body mass of ~0.6–1.0 kg. Performance enhancements will occur in weight-bearing and weight-sensitive sports (such as light-weight rowing and rock climbing) only if gains in muscular output compensate for increases in body mass.
- There is variability in the performance response to creatine supplementation within and between studies. This may reflect the difficulty of detecting small changes in performance, individual responses to treatment or a combination of both factors.
- Whether the long-term gains in muscle mass reported in studies of resistance training are caused by direct stimulation of increased myofibrillar protein synthesis by creatine, enhanced ability to undertake resistance training or a combination of both factors remains to be determined.

Concerns with creatine use

Whether there are side effects from long-term use of creatine, particularly with the large doses associated with rapid loading, remains to be determined. To date, there are anecdotal reports of nausea, gastrointestinal upset, headaches and muscle

cramping/strains linked to some creatine supplementation protocols. Some of these adverse effects are plausible, particularly in light of increased water retention within skeletal muscle (and perhaps brain) cells. At this time, however, studies have failed to find evidence of an increased prevalence or risk of these problems among creatine users (Greenwood et al. 2003, 2004; Kreider et al. 2003b). Some concern is directed to long-term creatine users, particularly those who self-medicate with doses far in excess of the recommended creatine usage protocols in this chapter. Although it is commonly suggested that creatine supplementation may cause renal impairments, these are limited to case reports in a few patients with pre-existing renal dysfunction. Longitudinal studies have reported that creatine intake had no detrimental effects on renal responses in various athletic populations (Poortmans et al. 1997; Mayhew et al. 2002). Nevertheless, until long-term and large population studies can be undertaken, bodies such as the American College of Sports Medicine have taken a cautious view on the benefits and side effects of creatine supplementation (American College of Sports Medicine 2000). However, a suggestion from a French food safety agency that creatine supplementation is carcinogenic has been discredited (see Hespel et al. 2001). Creatine supplementation should be limited to well-developed athletes. Young athletes are able to make substantial gains in performance through maturation in age and training, without the need to expose themselves to the expense or small potential for long-term consequences of creatine use.

16.5.1.4 Bicarbonate and citrate

Anaerobic glycolysis provides the primary fuel source for exercise of near maximal intensity lasting longer than approximately 20–30 seconds. The total capacity of this system is limited by the progressive increase in the acidity of the intracellular environment, caused by the accumulation of lactate and hydrogen ions (see Chapter 1). When intracellular buffering capacity is exceeded, lactate and hydrogen ions diffuse into the extracellular space, perhaps aided by a positive pH gradient. Since the 1930s it has been recognised that dietary strategies that decrease blood pH (for example, intake of acid salts) impair high-intensity exercise, while alkalotic therapies improve such performance (Dennig et al. 1931; Dill et al. 1932). In theory, an increase in extracellular buffering capacity should delay the onset of muscular fatigue during prolonged anaerobic metabolism by increasing the muscle's ability to dispose of excess hydrogen ions.

Protocols for supplementation with bicarbonate and citrate

The two most popular buffering agents are sodium bicarbonate and sodium citrate. Athletes have practised 'soda loading' or 'bicarbonate loading' for over 70 years, with sodium bicarbonate being ingested in the form of the household product 'bicarb soda' or as pharmaceutical urinary alkalinisers such as Ural. The general protocol for bicarbonate loading is to ingest 0.3 g of sodium bicarbonate/kg BM 1–2 hours prior to exercise; this equates to 4–5 teaspoons of bicarb

powder. Bicarbonate loading is not considered to pose any major health risk, although some individuals suffer gastrointestinal distress such as cramping or diarrhoea. Consuming sodium bicarbonate with plenty of water (for example, a litre or more) may help to prevent hyperosmotic diarrhoea. Sodium citrate is also usually ingested in doses of 0.3–0.5 g/kg BM. Bicarbonate or citrate loading is not considered a banned practice for human performances, although it is not permitted in dog or horse racing. It is difficult to detect the use of bicarbonate- or citrate-loading strategies by athletes, since urinary pH varies according to dietary practices such as vegetarianism and high CHO intake (Heigenhauser & Jones 1991).

Some athletes need to compete in heats, semis and finals to decide the outcome of their event. Swimmers, rowers and track athletes may compete several times over a series of days, and sometimes more than once on the same day. Whether buffering protocols can be repeated on each occasion and how such protocols are best undertaken are questions that require investigation. Issues for study include the determination of the lowest effective dose of bicarbonate or citrate, in order to minimise side effects such as gastrointestinal discomfort or disturbances to post-race recovery. After all, although an acute supplementation protocol may enhance the performance of the immediate race, side effects in the post-race period could jeopardise the outcomes of the following events. It is also important to investigate whether subsequent doses are still effective and without side effects at this level. It is possible that a lower dose may be effective in a repeated supplementation protocol, especially if the first dose has not been completely washed out. It is also possible that a subsequent dose may have a reduced or absent effect. In this case the athlete might need to decide if the priority is to enhance performance to make the final, or to trust that they will make the final without aid and save any supplementation protocols for the most important race.

In the case of bicarbonate, a chronic loading protocol has been investigated as an alternative to the repetition of acute protocols. McNaughton and colleagues studied the effect of 5–6 days of bicarbonate supplementation with a total of 500 mg/kg/day, spread into four doses over the day (McNaughton et al. 1999a; McNaughton & Thompson 2001). This protocol was found to achieve an increase in plasma base excess, which was sustained over the days of bicarbonate intake. Further, it enhanced the performance of a prolonged sprint undertaken on the 1–2 days *after* the bicarbonate supplementation ceased compared to the pre-trial performance (McNaughton & Thompson 2001). The persistence of the ergogenic outcome may be a desirable feature for sports involving a series of competition events. Alternatively, it may allow the athlete to finish their intake of bicarbonate (and the risk of gastrointestinal side effects) on the day prior to their competition, while maintaining the benefit to performance.

Effect of buffering protocols on performance

Bicarbonate or citrate loading may be a useful strategy to enhance the performance of athletic events that are conducted at near maximum intensity for the duration

of 1–7 minutes (for example, 400–1500 m running, 100–400 m swimming, kayaking, rowing and canoeing events). Sports that are dependent on repeated anaerobic bursts, such as team games, might also benefit from bicarbonate loading. It is beyond the scope of this chapter to review individually the 50 or more studies of the effects of bicarbonate or citrate loading on exercise performance in humans (for reviews see Heigenhauser & Jones 1991; Linderman & Fahey 1991; McNaughton 2000). In fact, we will limit our interest to studies involving trained subjects and protocols with relevance to sport or athletic events.

Nevertheless, the findings of a meta-analysis of the general literature on bicarbonate supplementation (Matson & Tran 1993) provide some interesting insights. This analysis included 29 randomised double-blind crossover investigations of bicarbonate loading and physical performance, examining 35 effect sizes from a total pool of 285 subjects (mainly healthy male college students). There was some variation in the protocols of bicarbonate loading, with different doses and times of ingestion being employed. While cycling was the most frequently used mode of exercise, there were a variety of exercise protocols (single efforts of 30 s to 5–7 minutes of near maximal intensity, or repeated intervals of 1 minute with short rest times between) and a variety of performance outcomes (changes in power over a given time period, total work performed in a specified time, or time to exhaustion at a specific exercise intensity).

Overall, this meta-analysis concluded that the ingestion of sodium bicarbonate has a moderate positive effect on exercise performance, with a weighted effect size of 0.44—that is, the mean performance of the bicarbonate trial was, on average, 0.44 standard deviations better than the placebo trial. Overall, there was only a weak relationship reported between the increased blood alkalinity (increase in pH and bicarbonate) attained in the bicarbonate trial and the performance outcome. However, ergogenic effects were related to the level of metabolic acidosis achieved during the exercise, suggesting the importance of attaining a threshold pH gradient across the cell membrane from the combination of the accumulation of intracellular H^+ and the extracellular alkalosis. Significant variability within studies suggests that bicarbonate ingestion has an individual effect on different subjects.

Popular theories about bicarbonate and citrate loading include the likelihood that anaerobically trained athletes should show less response to protocols because their intrinsic buffering capacity is already better, and the risk that performance of *prolonged* high-intensity exercise will be impaired if bicarbonate/citrate supplementation leads to increased rates of glycogen utilisation. However, studies that have examined bicarbonate or citrate loading using sports-specific protocols and well-trained subjects (Table 16.5) fail to support these theories. Some, but not all, studies of well-trained athletes have found performance improvements following bicarbonate/lactate loading prior to brief (1–10 minutes) or prolonged (30–60 minutes) events involving high-intensity exercise (see Table 16.5).

Until further research can clarify the range of exercise activities that might benefit from bicarbonate or citrate enhancement, individual athletes are advised

to experiment in training and minor competitions to judge their own case. It is important that experimentation is conducted in a competition-simulated environment, including the need to undertake multiple loading strategies for heats and finals of an event; the athlete needs to discover not only the potential for performance improvement but also the likelihood of unwanted side effects.

16.5.1.5 Glycerol

Glycerol, a three-carbon alcohol, provides the backbone to the triglyceride molecule. It is released during lipolysis and slowly metabolised via the liver and kidneys. Athletes are interested in glycerol not for its energy potential but, rather, its role as a hyperhydration agent. Oral intake of glycerol, via glycerine or special hyperhydration supplements, achieves a rapid absorption and distribution of glycerol around all body fluid compartments, adding to osmotic pressure. When a substantial volume of fluid is consumed simultaneously with glycerol, there is an expansion of fluid spaces and retention of this fluid. Effective protocols for glycerol hyperhydration are 1–1.5 g/kg glycerol with an intake of 25–35 mL/kg of fluid. Typically, such a protocol achieves a fluid expansion or retention of about 600 mL above a fluid bolus alone via a reduction in urinary volume (see review by Robergs & Griffin 1998).

Glycerol hyperhydration may be useful in the preparation for events that challenge fluid status and thermoregulation, for example for exercise at high intensity and/or in hot and humid environments, where sweat losses are high and opportunities to replace fluid are substantially less than the rates of fluid loss. It may also be useful to enhance the recovery of a moderate-to-large fluid deficit, for example in brief recovery periods between events or important training sessions, or between the weigh-in and competition following 'weight making' strategies in weight-division sports. Scientific investigations have focused on its potential for hyperhydrating prior to an endurance event (see Table 16.6).

Some of the apparent inconsistency in the results of these investigations occurs because of differences in study methodologies. For example, some studies have investigated the effect of glycerol in assisting the body to retain larger amounts of a fluid bolus consumed in the hours before exercise, whereas others have used protocols in which glycerol is consumed with only a modest fluid intake (Inder et al. 1998). At present, the best-supported scenario involves the use of glycerol to maximise the retention of fluid bolus just prior to an event in which a substantial fluid deficit cannot be prevented. In some, but not all, studies of this type, glycerol hyperhydration has been associated with performance benefits, particularly in well-trained athletes (Hitchins et al. 1999; Anderson et al. 2001; Coutts et al. 2002). However, the mechanism for this effect is not clear since the theoretical advantages of increased sweat losses and greater capacity for heat dissipation, and attenuation of cardiac and thermoregulatory challenges, are not consistently seen. Further investigation is needed to replicate and explain performance benefits.

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.5 Placebo-controlled crossover designed studies of bicarbonate or citrate loading with relevance to sports specific performance (for updates see www.ais.org.au/nutrition)

Reference	Subjects	Dose	Exercise protocol	Performance enhancement	Summary
Stephens et al. (2002)	8 endurance-trained male cyclists	300 mg/kg sodium bicarbonate 2 hours pre-exercise	Cycling • 30 min @ 77% $VO_{2\ max}$ + TT (~30 minutes)	No	Increase in blood lactate but no difference in muscle glycogen utilisation or lactate
Schabort et al. (2000)	8 endurance-trained male cyclists	200 mg/kg, 400 mg/kg and 600 mg/kg sodium citrate 1 hour pre-exercise	Cycling • 40 km TT including 500-m, 1-km and 2-km sprints	No	Increasing citrate dose increased blood pH but no effect on sprint performances or overall 40 km TT performance (58:46, 60:24, 61:47 and 60:02 minutes for citrate (200, 400 and 600 mg/kg doses) and placebo)
McNaughton et al. (1999b)	10 well-trained male cyclists	300 mg/kg sodium bicarbonate 90 minutes pre-exercise	Cycling • 60 min TT	Yes	14% more work completed with bicarbonate
Potteiger et al. (1996a)	8 male cyclists	500 mg/kg sodium citrate 90 minutes pre-exercise	Cycling • 30 km TT	Yes	Reduction in TT time (57:36 minutes versus 59:22). Sodium citrate raised pH values from 10 km onwards and improved power output in the initial 25 minutes.

Montfoort et al. (2004)	15 competitive male distance runners	300 mg/kg sodium bicarbonate or 525 mg/kg sodium citrate 90–180 minutes pre-race	Running • Treadmill run to exhaustion at speed designed to last 1–2 minutes	Yes for bicarb Perhaps for citrate		Analysis estimated likelihood of treatments increasing endurance compared to placebo by at least 0.5% (considered to be the smallest worthwhile improvement). Bicarbonate produced 2.7% enhancement of endurance (96% chance of improvement); citrate enhanced endurance by 0.5% (50% chance). Overall, authors concluded that bicarbonate is most effective, and citrate is possibly not as effective. No difference in gastrointestinal symptoms.
Oopik et al. (2003)	17 male collegiate distance runners	500 mg/kg sodium citrate 2 hours pre-exercise	Running • 5000 m treadmill run	Yes		Performance significantly faster ($P < 0.05$) for citrate trial (1153 s) compared with placebo trial (1183 s). High risk of gastrointestinal distress. Blood lactate concentration higher after race with citrate trial.

(*Cont.*)

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.5 (*Continued*)

Reference	Subjects	Dose	Exercise protocol	Performance enhancement	Summary
Shave et al. (2001)	7 elite male + 2 elite female athletes	500 mg/kg sodium citrate 1.5 hour pre-race	Running • 3000 m	Yes	Performance time significantly faster ($P < 0.05$) for citrate trial (610.9 s) compared with placebo trial (621.6 s). High risk of gastrointestinal distress.
Potteiger et al. (1996b)	7 well-trained male runners	300 mg/kg sodium bicarbonate and 500 mg/kg sodium citrate 2 h pre-exercise	Running • 30 minutes @ LT + time to exhaustion @ 100% LT	No	Both citrate and bicarbonate supplementation increased blood pH during steady-state run. No differences in run to exhaustion: 287 s, 172.8 s, 222.3 s for bicarbonate, citrate and placebo.
Tiryaki and Atterbom (1995)	11 collegiate female runners + 4 untrained controls	300 mg/kg sodium citrate or sodium bicarbonate 2.5 hours pre-exercise	Running • 600 m	No	No performance effect despite significant changes to acid–base status.
Bird et al. (1995)	12 trained middle-distance runners	300 mg/kg sodium bicarbonate 90 minutes pre-exercise	Running • 1500 m	Yes	Performance in bicarbonate trial improved compared with placebo trial (253.9 versus 256.8 s, $P < 0.05$)

Goldfinch et al. (1988)	6 trained male runners	400 mg/kg sodium bicarbonate 60 minutes pre-exercise	Running • 400 m	Yes	Improved running time (56.94 s versus 58.63 [placebo] and 58.46 [control]). Elevated post-exercise values for pH and base excess.
Wilkes et al. (1983)	6 varsity track male athletes	300 mg/kg sodium bicarbonate 2.5 hours pre-exercise	Running • 800 m	Yes	Improved running time (2:02.9 minutes versus 2:05.1 [placebo] and 2:05.8 [control]). Elevated post-exercise values for pH, lactate and blood bicarbonate.
Mero et al. (2004)	8 male + 8 female national level swimmers 30-day washout	300 mg/kg bicarbonate or gelatin placebo, 2 hours pre-exercise (6 days @ 20 g/day creatine also taken prior to bicarb trial)	Swimming • 2 × 100 m swims with 10 m passive recovery	Yes (?)	Faster time for second swim with creatine/bicarb trial than with placebo: 1 s reduction in performance from first swim in placebo compared with 0.1 s drop-off in supplement trial ($P < 0.05$). Study unable to indicate individual effect of bicarbonate.
Pierce et al. (1992)	7 male collegiate swimmers	200 mg/kg bicarbonate, sodium chloride placebo or control, 1 hour pre-exercise	Swimming • 100 yards freestyle • 2 × 200 yards swims 20 minutes recovery between each race (simulation of competition program)	No No	No difference in swim times between trials.

(*Cont.*)

Table 16.5 (*Continued*)

Reference	Subjects	Dose	Exercise protocol	Performance enhancement	Summary
Gao et al. (1988)	10 male collegiate swimmers	250 mg/kg sodium bicarbonate 1 hour pre-exercise	Swimming • 5 × 100 yard swim with 2 minute rest (simulation of training program)	Yes	Faster times in 4th and 5th swim ($P < 0.05$). Supplementation also associated with higher post-race blood lactate concentrations.
McNaughton and Cedaro (1991)	5 highly trained male rowers	300 mg/kg sodium bicarbonate 95 minutes pre-exercise	Rowing • 6 minutes maximum effort on ergometer	Yes	Increased work and distance rowed in bicarbonate trial (1861 m versus 1813 m). Increased lactate levels.
Bishop and Claudius (2005)	7 female team sports players	2 × 200 mg/kg bicarbonate @ 90 minutes and 20 minutes pre-exercise	Team sport simulation • Intermittent cycling protocol of 2 × 36-minute 'halves' involving repeated 2 minute blocks (all-out 4 s sprint, 100 s active recovery at 35% $VO_{2\ peak}$, and 20 s of rest)	Yes	Bicarbonate supplementation failed to produce any effect on performance in first half, but caused trend towards improved total work in the second half ($P = 0.08$). In particular, subjects completed significantly more work in 7 of 18 4-s sprints in second half in the bicarbonate trial.

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Price et al. (2003)	8 active male runners	300 mg/kg sodium bicarbonate 1 hour pre-exercise	Team sport simulation: • Intermittent cycling protocol of 30 minutes involving repeated 3-minute blocks (90 s @ 40%, 60 s @ 60% and 14 s @ 90% $VO_{2\,max}$)	Yes	Significant main effect with greater PPO achieved in 14 s sprints across protocol in bicarbonate trial, whereas placebo trial showed gradual decline in PPO across time. Blood lactate levels elevated to 10–12 mmol/L by 10 minutes and remained elevated across rest of protocol. Such values are higher than is generally reported in team sports; thus movement patterns may not reflect the true workloads or physiological limitations of team sports.

TT = time trial, LT = lactate threshold

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.6 Placebo controlled crossover designed studies of glycerol hyperhydration and performance (for updates see www.ais.org.au/nutrition)

Study	Subjects	Glycerol dose	Exercise protocol	Enhanced performance	Comments
Anderson et al. (2001)	6 well-trained male cyclists Crossover design	1 g/kg with 20 mL/kg low joule cordial (compared with low joule cordial overload)	Cycling • 90 minutes @ 98% LT + 15 minutes TT hot environment (35°C)	Yes	Glycerol allowed retention of additional 400 mL of fluid above hyperhydration with cordial alone. 5% improvement in work done in 15 minutes TT. No change in muscle metabolism. Reduced rectal temperature at 90 minutes with glycerol trial.
Hitchins et al. (1999)	8 well-trained male cyclists Crossover design	1 g/kg with 22 mL/kg dilute sports drink, 2.5 hours pre-exercise (compared with sports drink overload)	Cycling • 30 minutes @ fixed power + 30 minutes TT. Hot environment (32°C)	Yes	Glycerol treatment expanded body water by 600 mL and increased (5%) work achieved in TT. This was achieved largely by preventing the drop in power seen at the start of placebo TT. No difference in power profile at end of TTs. No difference in cardiovascular, thermoregulatory, RPE between trials despite differences in power output.

Inder et al. (1998)	8 highly trained male triathletes Crossover design	1 g/kg with 500 mL water, 4 hours pre-exercise (compared with 500 mL water)	Cycling • 60 min @ 70% $VO_{2\ max}$ + incremental ride to exhaustion	No		Glycerol was consumed with a modest fluid load. No increase in pre-exercise hydration status, sweat losses or urine production during exercise. No difference in time to exhaustion or workload reached. Three subjects experienced gastrointestinal problems with glycerol.
Montner et al. (1996)	11 active male and female cyclists 7 active male and female cyclists Crossover design	1.2 g/kg with 26 mL/kg water, 1 hour pre-exercise same pre-treatment + sports drink during exercise	Cycling • Cycling @ 60% W_{max} until exhaustion	Yes		Reduced heart rate and increased time to exhaustion with pre-exercise glycerol treatment by ~20%.
Latzka et al. (1998)	8 heat-acclimatised men Crossover design	1.2 g/kg lean BM + 29 mL/kg water, 1 hour pre-exercise (compared with water hyperhydration or control)	Running • Treadmill running at 55% $Vo_{2\ max}$ until exhaustion or high rectal temperature. Hot environment (35 °C) without further fluid intake	Yes (better than control but equal to water hyper-hydration)		Both hyperhydration trials increased body fluid by ~1400 mL. Time to exhaustion longer in both trials compared with control. Performance changes not explained by differences in sweat losses, cardiac output or temperature control. Some gastrointestinal and headache symptoms with glycerol.

(*Cont.*)

Table 16.6 (*Continued*)

Study	Subjects	Glycerol dose	Exercise protocol	Enhanced performance	Comments
Coutts et al. (2002)	7 male + 3 female well-trained triathletes Crossover design Difference in conditions: • hot day (30°C) • warm day (25°C)	1.2 g/kg BM + 25 mL/kg sports drink, 2 hours pre-exercise (compared with sports drink placebo)	Olympic distance triathlon (field conditions) Hot conditions 25–30°C	Yes	Decrease in triathlon performance (especially run time) between warm and hot conditions was greater in placebo group (11:40 minutes) than glycerol group (1:47 minutes). Greatest difference in times between placebo and glycerol group was found on hot day. Hyperhydration increased fluid retention of drink and reduced diuresis.

TT = time trial, RPE = rating of perceived exertion

P1: FAW/SPH MHBD028-16 P2: FAW/SPH MHBD028-Burke QC: FAW/SPH MHBD028-Burke-v1.cls T1: FAW KEY BOARDED February 1, 2006 4:7

Side effects reported by some subjects following glycerol use include nausea, gastrointestinal distress and headaches resulting from increased intracranial pressure. Fine-tuning of protocols may reduce the risk of these problems, yet some individuals may remain at a greater risk than others. At the present time, although glycerol hyperhydration seems to show some promise for the performance of endurance exercise in hot conditions, it should remain an activity that is supervised and monitored by appropriate sports science/medicine professionals and used in competition situations only after adequate experimentation and fine-tuning have occurred.

16.5.2 *Supplements in Group B of the AIS Sports Supplement Program*

According to the AIS Sports Supplement Program, some supplements enjoy preliminary data that are supportive of performance benefits or hypotheses that strongly suggest such benefits. However, this information is not sufficient to be sure of a positive outcome, nor to define the situations and protocols that would achieve an optimal result. Because these supplements are of interest to athletes and coaches, they should be prioritised for additional research to either confirm their value to athletes or downgrade the interest.

16.5.2.1 Colostrum

Colostrum is a protein-rich substance secreted in breast milk in the first few days after a mother has given birth. It is high in immunoglobulins and insulin-like growth factors (IGFs). Unlike the adult gut, the gut of a baby has 'leaky' junctions that allows it to absorb whole proteins including immunoglobulins, thus developing the immuno-competence needed to survive outside the uterus.

A number of companies have developed supplements rich in bovine colostrum (colostrum derived from cows) for use by humans. In 1997, attention was focused on these products after a study reported that sprinters and jumpers who consumed a colostrum supplement (Bioenervie^{TM}) for 8 days while undertaking resistance and speed training experienced an increase in plasma IGF-1 levels (Mero et al. 1997). Although supplementation failed to improve vertical jump performance in these athletes, the study raised several intriguing issues. First, it appeared to show that humans could absorb intact proteins from a supplement and, second, it appeared to show that colostrum could provide a dietary source of IGF, an anabolic hormone the intentional intake of which is banned by WADA. Subsequent discussion of this paper suggested that the increase in IGF concentrations was spurious, caused by inaccurate techniques for measuring these growth factors. However, a follow-up study by this group (Mero et al. 2002) reported an increase in plasma IGF-1 following supplementation with another colostrum product (Dynamic^{TM}). In this follow-up study, gel electrophoresis

techniques showed that there was little direct absorption of IGF-1 from the oral supplement. This suggests that the intake of colostrum stimulated endogenous production of growth factors. Nevertheless, other studies have failed to demonstrate any change in IGF-1 levels in response to colostrum supplementation (Buckley et al. 2002; Kuipers et al. 2002). There are also inconsistencies in effect of colostrum supplementation on immune parameters, with various studies showing either an increase (Mero et al. 2002) or no change (Mero et al. 1997) in salivary immunoglobulin A (IgA). One study has reported a reduction in the self-reported symptoms of upper respiratory tract infections following colostrum supplementation in a large group of subjects (Brinkworth & Buckley 2003); this finding warrants further investigation.

A number of studies have investigated the chronic effects of supplementation with colostrum products, particularly an Australian product (Intact^{TM}), on the outcome of training programs undertaken by both trained and previously untrained subjects. The results of these studies are summarised in Table 16.7. Buckley and colleagues studied the effects of 8 weeks of running training (3 × 45 minutes/week) in combination with 60g/day of colostrum powder or a whey placebo in two groups of previously untrained men (Buckley et al. 2002). The test set, consisting of two incremental treadmill runs to exhaustion, with a 20-minute recovery interval, was undertaken at 0, 4 and 8 weeks. The study found that after 8 weeks the treatment group completed more work and ran further in the second of two treadmill runs than subjects in the placebo group. However, no differences were seen at 4 weeks, and no measurements were taken to explain the performance improvements seen in the second run at 8 weeks. Another study involving trained cyclists (Coombes et al. 2002) also used a protocol involving two incremental tests to exhaustion separated by 20 minutes. In contrast to the results of the previous study, neither the colostrum nor the placebo groups improved their cycling 'max test' performance in either of the two tests after 4 or 8 weeks of supplementation with colostrum. However, another measure of performance was undertaken by these cyclists on a separate day, in the form of a submaximal ride followed by a time trial. In this protocol, cyclists who had received colostrum recorded a greater improvement in the performance of the time trial at week 8 compared with those who had received a placebo. Again, there were no mechanisms to explain this enhancement of performance.

In several other studies, there have been reports of an enhancement of the performance of the treatment group compared with the group taking a placebo product. However, there is inconsistency in the literature, with one study reporting an improvement in vertical jump in previously untrained subjects who undertook plyometric and resistance training (Buckley et al. 2003) and others finding no enhancement in vertical jump in highly trained team sport players (Hofman et al. 2002) or track and field athletes (Mero et al. 1997). Similarly, colostrum supplementation has been reported to enhance the improvement in sprint performance in one study of previously untrained men (Buckley et al. 2003), while failing to alter this outcome in trained team sport athletes (Hofman

Table 16.7 Placebo-controlled studies of colostrum supplementation and exercise performance (for table updates see www.ais.org.au/nutrition)

Reference	Subjects	Colostrum dose and training	Exercise protocol	Performance enhancement	Comments
Brinkworth et al. (2004)	34 active male subjects Parallel group design	8 weeks @ 60 g/day colostrum or placebo (whey protein) 4/week one-armed resistance training	Tests at baseline and 8 weeks: • 1 RM biceps curl	 No	Increase in biceps curl 1 RM in trained arm, but no difference between placebo and colostrum group. Increase in circumference and MRI determined cross-sectional area of trained arm of colostrum group compared with placebo group ($P < 0.05$), principally due to increase in subcutaneous fat and skin.
Buckley et al. (2003)	51 active males colostrum = 26 placebo = 25 Parallel group design	8 weeks @ 60 g/day Resistance and plyometric training, 3/w	Tests at baseline, 4 weeks and 8 weeks • 3 × vertical jump • 3 × 10 s cycle sprints • 1 RM of a number of resistance movements	 Yes—only @ 8 weeks Yes—only @ 8 weeks No	At week 4, no differences in peak cycling power, anaerobic work capacity or peak vertical jump power between groups. At week 8, peak vertical jump power and peak cycle power higher in colostrum group, but no differences in anaerobic work capacity. No difference in strength over 8 different movements. No changes in IGF-1 in either group

(*Cont.*)

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.7 (*Continued*)

Reference	Subjects	Colostrum dose and training	Exercise protocol	Performance enhancement	Comments
Buckley et al. (2002)	30 active males (colostrum = 17; placebo = 13) Parallel group design	8 weeks @ 60 g/day colostrum or placebo (whey protein) 45 min running @ 3/week	Tests at baseline, 4 weeks and 8 weeks • 2 × ~30 minute incremental running tests to exhaustion separated by 20 minutes	4 weeks—no for either run 8 weeks—no for first run, yes for second run	Training improved peak running speed in both runs in both groups at week 8. No differences between groups in either run at week 4 although trend to lower peak speed in second run with colostrum group. At week 8, no difference in peak speed in first run, but greater speed in second run in colostrum group ($P < 0.05$), suggesting better recovery between runs.
Brinkworth et al. (2002)	13 elite female rowers (colostrum = 6; placebo = 7) Parallel group design	9 weeks @ 60 g/day of colostrum or placebo (whey protein) 18 hours/week rowing + 3/week resistance training	Tests at baseline and 9 weeks: • 2 × incremental rowing tests with 15-minute recovery interval (each = 3 × 4-minute submaximal workloads + 4-minute maximal effort)	No	Rowing performance increased by week 9 in both groups. No difference between groups at week 9 for either maximal rowing performance. Higher value for index of blood buffering capacity at week 9 in colostrum group.
Coombes et al. (2002)	28 trained male cyclists (high dose colostrum = 10; low dose colostrum = 9; placebo = 9) Parallel group design	8 weeks @ 60 g/day colostrum or 20 g/day colostrum or placebo (40 g/day whey protein) 1.5 hours/day cycling	Tests at baseline and 8 weeks on separate days: • 2 × $VO_{2\ max}$ tests separated by 20 minutes • 2 hours @ 65% $VO_{2\ max}$+ ~12 minutes TT	No Yes	No difference between groups or between weeks for performance of either $VO_{2\ max}$ test. Greater improvement at week 8 in TT following 2-hour submaximal ride in both colostrum groups (4%; 19%; 16% $P < 0.05$ for placebo, low dose and high dose).

Hofman et al. (2002)	17 female and 18 male highly trained hockey players Parallel group design	8 weeks @ 60 g/day of colostrum or placebo (whey protein) 3/week training + game 1/week	Tests at baseline and 8 weeks: • 5 × 10 m sprint • vertical jump • shuttle run • 'suicide' agility test	 Yes No No No	No improvements in shuttle run, jump or agility run over 8 weeks in either group. Significant improvement in sprint performance for both groups with larger improvement in colostrum group (0.64 s versus 0.33 s, $P < 0.05$). Similar increases in lean BM in both groups.
Antonio et al. (2001)	Active male + females Parallel group design	8 weeks @ 20 g/day of colostrum or placebo (whey protein) 3/week aerobic and resistance training	Tests at baseline and 8 weeks: • treadmill run to exhaustion • bench press: 1 RM • submaximal repetitions to exhaustion	 No No No	Colostrum group experienced significant increase in lean BM (1.5 kg), while placebo group showed increase in BM (2 kg) as measured by DXA.
Mero et al. (1997)	9 male sprinters and jumpers Crossover design with 13 day wash-out	8 days @ 25 mL/day colostrum or 125 mL/day or placebo (milk whey) 6 sessions speed and resistance training	Tests at day 6 of each program: • counter-movement jump	 No	Serum IGF increased over time with colostrum supplementation (although still within physiological ranges) compared with placebo. No change in serum or saliva immunoglobulins between treatments.

RM = repetition maximum

et al. 2002). Reports of the changes in body composition have also showed inconsistencies. While one study has reported an increase in lean body mass following a period of colostrum supplementation (Antonio et al. 2001), other studies have found no changes in body mass or body composition (Hofman et al. 2002). The finding that a colostrum-supplemented group showed an increase in subcutaneous fat and skin thickness in their arms following resistance training is curious (Brinkworth et al. 2004). The only consistent findings from the present studies of colostrum supplementation are that there are no apparent benefits to the outcomes of resistance training (Antonio et al. 2001; Buckley et al. 2003; Brinkworth et al. 2004), and that when benefits are detected, they are apparent only after more than 4 weeks of treatment (Buckley et al. 2002, 2003).

The results of the current literature have been aggressively marketed by the manufacturers of colostrum supplements. Claims include enhanced recovery, superior muscle buffering capacity and increased growth of muscle contractile proteins. Furthermore, the benefits have been transferred from athletes to other groups including manual workers and sufferers of chronic fatigue. Although the observations of enhanced training or performance outcomes are of real interest to athletes and coaches, there are several explanations for the reluctance of most sports scientists to consider colostrum as a proven ergogenic aid. The inconsistency of the literature is problematic, even when the difficulties of detecting small changes in performance are taken into account. The lack of a plausible hypothesis to explain how colostrum might enhance the response to exercise is also an important absence. Not only is there a lack of support for the current observations, but, without a possible mechanism to explore or exploit, there are difficulties in identifying the type of athletes or situations of exercise that might benefit from colostrum supplementation. Whether all colostrum supplements are of equal quality or efficacy is also a concern.

Finally, colostrum is an expensive supplement. The typical dose provided to subjects in the current studies is 60 g per day, which would cost about A$70 per week to purchase at retail rates. In light of this expense, and the suggestion that it may take up to 8 weeks to provide a detectable outcome, greater levels of support for colostrum are needed before it can pass a cost-benefit analysis.

16.5.2.2 Ribose

Ribose is a pentose (5-carbon) sugar that provides part of the structure of a variety of important chemicals in the body (including DNA and RNA) and the adenine nucleotides ATP, AMP and ADP. Ribose is found naturally in the diet but purified forms have also been released onto the market, finding their way into sports supplements. Oral ribose is quickly absorbed and tolerated even at intakes of 100 g, but, at A$700 per kg, ribose powders represent an expensive form of carbohydrate.

In the body, the pentose phosphate pathway is a rate-limiting pathway for the interconversion of glucose and ribose-5-phosphate. The ribose-5-phosphate can

be converted to phosphoribosyl pyrophosphate (PRPP), which is then involved in the synthesis or salvaging of the adenine nucleotide pool. It has been suggested that suboptimal amounts of PRPP may limit these processes, and ribose infusion has been shown to enhance ATP recovery and exercise function in animal models of myocardial ischaemia (see Op 't Eijnde et al. 2001). High-intensity exercise has been shown to cause a reduction in the muscle ATP content and the total adenine nucleotide pool, possibly because the rate of nucleotide salvaging and synthesis falls behind the massive rates of nucleotide degradation.

It has been suggested that oral intake of ribose might increase the rate of nucleotide salvaging/synthesis and achieve quicker recovery of exercise-mediated reductions in the muscle total adenine nucleotide pool. Sports supplements containing ribose typically provide doses of 3–5 g of this sugar, often in combination with creatine. Marketing claims for such products include 'dramatic reductions in recovery from 72 hours to 12 hours' and 'the most sophisticated energy support systems'. Several early studies that appeared in abstract form from conference presentations reported favourable results following ribose supplementation in heavily training athletes. However, the brief form of these reports does not provide sufficient information to judge the quality of the study and the interpretation of results.

To date, only six studies have been published in full in peer-reviewed journals (see Table 16.8). These studies have investigated daily doses of 2–40 g ribose in conjunction with programs of intermittent high-intensity exercise such as weight training or interval training. Two studies have tracked the muscle content of adenine nucleotides in response to fatiguing protocols of intermittent exercise and ribose supplementation (Op 't Eijnde et al. 2001; Hellsten et al. 2004). In one study, muscle ATP content and power/force characteristics were compared after two intermittent training sessions 24 hours apart on two occasions; the first occasion was a baseline measure on active subjects, whereas the second test set followed a 7-day training program involving two bouts of intermittent exercise each day while taking ribose (four doses of 4 g/day) or placebo. The first exercise bout in each testing occasion caused a decrease in muscle total adenine nucleotide, with muscle ATP content being reduced by 20% at the time of the second bout. However, ribose supplementation did not alter the loss or recovery of ATP resulting from this exercise protocol, nor did it change muscle force or power characteristics during maximal testing (Op 't Eijnde et al. 2001). The authors suggested that plasma ribose concentrations achieved by the supplementation were too low to achieve a significant change in nucleotide synthesis/salvage. However, the doses used in the study were already higher than that recommended by most supplement manufacturers.

In the other study, daily ribose supplementation of 600 mg/kg body mass (~42 g for a 70 kg subject) was provided after a 7-day training program involving twice daily bouts of sprint training (Hellsten et al. 2004). Muscle ATP content was reduced by ~25% immediately after the last training bout, and remained low at 24 hours, in both the supplementation and placebo trials. By 72 hours,

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.8 Placebo-controlled studies of ribose supplementation and exercise performance (for updates see www.ais.org.au/nutrition)

Study	Subjects	Ribose dose and training	Exercise protocol	Performance enhancement	Comments
Hellsten et al. (2004)	8 active males Crossover design 5 day washout	3 days @ 3 × 200 mg/kg ribose following 7 days of 2/day repetition of sprint training (15 × 10 s all-out sprints)	Cycling sprints: • 15 × 10 s all-out sprints, separated by a 50 s rest period, undertaken 72 hours after last training session and following supplementation	No	7-day training program caused reduction in muscle ATP by ∼25% immediately after last bout. ATP remained lower at 5- and 24-hour supplementation. After 72 hours, muscle ATP had returned to pre-training in ribose trial but was still lower in placebo trial. However, mean and peak power outputs during the test performed at 72 hours were similar in both trials.
Kreider et al. (2003a)	19 resistance-trained males Parallel group design	10 g/day D-ribose (2 × 5 g daily) for 5 days	Cycling sprints: • two 30 s Wingate anaerobic sprint tests separated by 3 minutes of rest recovery	No	Test protocol achieved a decrease in power output across 30 s of sprinting, and a lower work output in sprint 2 compared with sprint 1. No difference between pre- and post-supplementation values for peak power, average power, fatigue index or time to peak power for either group. Ribose group showed a higher total work for second sprint during post-supplementation trial than placebo group, due to deterioration in placebo group. No difference in blood lactate and ammonia profiles between groups.

Berardi and Ziegenfuss (2003)	8 recreationally active males Crossover design	32 g powdered ribose spread over 3 days (4 × 8 g doses)	Cycling sprints • 6 × 10 s cycling sprints with 60 s recovery Test protocol undertaken day 1 × 2 (a.m. and p.m.) and day 3 × 1 (p.m.)	No	Ribose supplementation caused a marginal and inconsistent increase in power characteristics of the spring protocol on day 3 compared with placebo trial. It was concluded from this study that ribose supplementation does not have a consistent or substantial effect on anaerobic cycle sprinting.
Falk et al. (2003)	28 resistance-trained males Parallel group design	2 g/day for 8 weeks (as part of an effervescent supplement also containing CHO, creatine and glutamine) Resistance training	Resistance training • 1 RM bench press • repetitions 80% RM bench press to fatigue	No No	Both groups increased LBM, muscle strength and strength endurance over 8 weeks of training, but no differences between groups. Did not utilise a protocol likely to disturb adenine levels, thus may not have allowed the proposed mechanism of ribose supplementation to take effect.
Van Gammeren et al. (2002)	19 recreational male body builders Crossover design	10 g/day for 4 weeks. (2/day, 30–60 minutes pre- and post-training) Resistance training	Resistance training • 1 RM bench press (muscular strength test). • 10 sets @ bench press at 100% body mass to exhaustion with 1 minute recovery (muscular endurance test)	Yes Yes	Both groups increased muscle strength and endurance over 4 weeks of training. However, only in the case of the ribose group did these training effects reach statistical significance, e.g. 20% versus 12% increase in 1 RM for bench press for ribose and placebo groups, respectively. Ribose-supplemented group experienced a significant increase in muscular strength and endurance. This improvement may be related to the role that ribose might play in the phosphagen system. However, ribose-supplemented group seemed to be less trained than placebo group.

(*Cont.*)

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.8 (*Continued*)

Study	Subjects	Ribose dose and training	Exercise protocol	Performance enhancement	Comments
Op 't Eijnde et al. (2001)	Recreationally active males involved in sprint and resistance activities ($n = 19$ M) Parallel group design	16 g/day for 6 day (4×4 g/day) 2/day training: Bout of 15×12 knee extensions with 15 s recovery	Isolated leg extensions • Two exercise bouts separated by 60 minutes. Each bout = 15×12 maximal intermittent knee extensions with the right leg with 15 s rest	No	Oral ribose supplementation at 16 g/day did not enhance the restoration of the fall in ATP concentrations following each exercise bout. The 6-day exercise protocol achieved training effect; mean power output in post-trial testing was 10% higher than pre-trial testing. However, no differences between ribose and placebo group. Authors suggested that the ribose dose was too low to increase plasma levels enough to increase muscle uptake, although dose was higher than recommended by most manufacturers.

RM = repetition maximum

however, ribose supplementation elevated muscle ATP above that seen in the placebo trial and restored it to pre-training levels. This was not accompanied by superior performance of the intermittent sprint protocol. The authors concluded that even though the availability of ribose in the muscle may be a limiting factor for the rate of resynthesis of ATP, the reduction in muscle ATP observed after intense training is not limiting for the performance of intermittent high-intensity exercise.

Overall, the published evidence for benefits from ribose supplementation is not promising. Only one of the published studies has reported an enhancement of performance following ribose use; recreational body builders who consumed 10 g/day over a four week period of resistance training achieved larger gains in strength and muscular endurance than a group receiving a placebo (Van Gammeren et al. 2002). Five other studies failed to detect any performance benefits from the use of ribose. Several of the authors have noted that their ribose treatments were well in excess of the doses recommended by manufacturer and, given the expense of this supplement, there are questions about its cost-effectiveness (Berardi & Ziegenfuss 2003).

16.5.2.3 HMB

β-hydroxy-β-methylbutyrate (HMB), a metabolite of the amino acid leucine, is claimed to increase the gains in strength and lean body mass associated with resistance training and enhance recovery from exercise (see Slater & Jenkins 2000). HMB is claimed to act as an anti-catabolic agent, minimising protein breakdown and the cellular damage that occurs with high-intensity exercise. The hypothesis underpinning these claims is that the anti-catabolic effects that are sometimes associated with leucine feeding during times of stress are mediated by HMB. Interest in HMB supplementation stemmed from animal studies, with some but not all investigations finding that HMB supplementation increased gains in carcass weight or feed efficiency, defined as weight gain per unit feed, during periods of growth (for review see Slater & Jenkins 2000). HMB supplements were first introduced to the sports market in the mid-1990s and by 1998 were achieving annual sales of US$30–50 million in the United States of America alone (Slater & Jenkins 2000).

A number of scientific investigations of HMB supplementation and resistance training have been undertaken with a focus on changes in body composition and strength. The results of investigations that have been published in full in peer-reviewed journals are summarised in Table 16.9. This table shows there is mixed support for the hypothesis that HMB can enhance the response to resistance training as a result of reducing exercise-induced protein breakdown or damage. While some studies have reported a benefit of HMB supplementation (Panton et al. 2000; Jowko et al. 2001; Nissen & Sharp 2003; Thomson 2004), others have failed to detect any enhancement of the training response (Kreider et al. 1999; Slater et al. 2001; O'Connor & Crowe 2003; Ransone et al. 2003; Hoffman et al.

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.9 Placebo-controlled studies of HMB supplementation on training adaptations and performance (for updates see www.ais.org.au/nutrition)

Study	Subjects	HMB dose and training	Exercise protocol	Performance enhancement	Comments
Hoffman et al. (2004)	26 male collegiate football players Parallel group design	3 g/day HMB for 10 days Sports-related training	Tests at baseline and at 10 days: • anaerobic power test	No	No difference in anaerobic power was seen between groups. Plasma concentrations of cortisol decreased and CK increased over the 10-day training in both groups.
Thomson (2004)	34 resistance trained males Parallel group design	3 g/day HMB for 9 weeks Resistance training	Tests at baseline and at 9 weeks: • 1 repetition maximum strength testing	Yes	Significant increase in leg extension strength following HMB supplementation. No effect of HMB supplementation on body composition.
O'Connor and Crowe (2003)	27 elite male rugby league players Parallel group design	3 g/day HMB or 3 g/day HMB-creatine for 6 weeks Sports-related training	Tests at baseline and 6 weeks • multi-stage fitness test • 60 s max cycling test	 No No	No differences in aerobic power from multi-stage fitness test or anaerobic capacity (peak power, total work and peak lactate levels) between groups at end of trial.
Ransone et al. (2003)	35 male collegiate football players Crossover design	3 g/day HMB Sports-specific training (20 hours/week)	Tests pre- and post-each 4 week supplementation • bench press • squats • power cleans	 No No No	No significant changes in muscular strength or in body mass or body fat levels due to supplementation.

Slater et al. (2001)	27 elite male rowers and male water polo players Parallel group design	3 g/day conventional or time-release HMB for 6 weeks Sports-related training including 3/week resistance training Provided with nutritional advice + CHO/protein supplement	Tests at baseline, 3 weeks and 6 weeks: • bench press • leg press • chin-ups	No No No	All groups increased strength and lean BM with no differences in response between groups. No differences in urinary 3-MH or plasma CK—crude markers of muscle breakdown and damage between groups.
Jowko et al. (2001)	40 untrained males Parallel group design	3 g/day HMB, 3 g/day HMB-creatine, or creatine for 3 weeks Resistance training	Tests at baseline and 3 weeks: • strength in various resistance exercises	Yes	Creatine caused greater increase in lean BM and strength than placebo group. Greater strength and trend to greater increase in lean BM with HMB than placebo. Effects were additive. HMB reduced plasma CK levels and urea, suggesting nitrogen sparing.
Vukovich and Dreifort (2001)	8 trained male cyclists Crossover study (2 week washout)	3 g/day leucine or 3 g/day HMB Cycling training	Tests pre- and post-each 2 week supplementation: • $VO_{2\ peak}$	Yes	Significant increase in $VO_{2\ peak}$ following HMB supplementation but not other supplementation periods.
Panton et al. (2000)	39 males and 36 females of varying training status Parallel group design	3 g/day HMB for 4 weeks Resistance training 3/week	Tests at baseline and 4 weeks: • strength in various resistance exercises	Yes	Data pooled across training status and gender. HMB group showed greater increase in upper body strength and a trend to greater gains in lean BM, and loss of body fat than placebo, regardless of gender or training status

(*Cont.*)

Table 16.9 (*Continued*)

Study	Subjects	HMB dose and training	Exercise protocol	Performance enhancement	Comments
Gallagher et al. (2000a)	37 untrained males Parallel group design	3 g/day or 6 g/day HMB for 8 weeks Resistance training 3/week	Tests at baseline and 8 weeks: • muscle strength • peak isokinetic or isometric torque	 No Yes	No differences in strength gains between treatments. 3 g/day HMB supplementation increased gains in some measures of isokinetic or isometric torque and lean BM, and decreased the rise in plasma CK.
Kreider et al. (1999)	40 resistance trained males Parallel group design	3 or 6 g/day HMB for 4 weeks Resistance training 7 hours/week	Tests at baseline and 4 week: • bench press • leg press	 No No	No difference in improvements in strength between groups, or changes in lean BM or body fat levels. No differences between plasma CK level and LDH levels (another marker of catabolism).
Nissen et al. (1996)	41 untrained males Parallel group design	1.5 g/day or 3 g/day for 3 weeks Resistance training 3/week Groups further divided into 117 or 175 g/day protein	Tests at baseline and 3 weeks: • weight lifted in training session	 Yes	HMB associated with decrease in urinary 3-MH and plasma CK. Trend to increased gain in lean BM with HMB. Dose-responsive increase in weight lifted during training session with HMB compared with placebo.
Nissen et al. (1996)	Resistance trained males Parallel group design	3 g/day for 7 weeks Resistance training 2–3 hours/day	Tests at baseline and 7 weeks: • bench press • squat • clean	 Yes No No	Control group was stronger at baseline in upper body strength; gains made by HMB group simply caused groups to be equal in upper and lower body strength at end of study. Greater increase in lean BM during early part of study in HMB group was absent by 7 weeks.? Effects of HMB diminish over time. Diet not controlled.

3-MH = 3-methylhistidine, CK = creatine kinase, LDH = lactate dehydrogenase

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

2004). Other studies that have simply monitored indices of muscle damage following eccentric exercise have found that HMB supplementation either reduced (Knitter et al. 2000) or failed to change the normal responses (Paddon-Jones et al. 2001). A meta-analysis of the studies published up until 2001 reported that HMB supplementation significantly increased net lean mass and strength gains above resistance training alone. However, the effect sizes of these improvements were trivial to small; effect sizes for gain in muscle mass = 0.15 and strength = 0.19 (Nissen & Sharp 2003). In addition, this meta-analysis has received criticism on the basis that the studies emanate from only three different laboratories, and may show experimental bias because of interdependence (Decombaz et al. 2003).

It is difficult to find a common thread to the findings of the present HMB research. One theory is that HMB supplementation might be most valuable in the early phases of a new training program, or when previously untrained subjects undertake resistance training, where it is able to reduce the large catabolic response or damage produced by unaccustomed exercise. However, once adaptation to training occurs, reducing the residual catabolism/damage response, HMB supplementation no longer provides a detectable benefit. If this were the case, it would explain why HMB tends to produce favourable results in novice resistance trainers rather than well-trained subjects, and why positive results are reported in shorter studies (2–4 weeks) but not at the end of longer studies (8 weeks). Further well-controlled studies are required to clarify if, and under what circumstances, HMB is a useful training aid. Short-term supplementation with HMB does not appear to cause any adverse effects on indices of health (Gallagher et al. 2000b; Crowe et al. 2003). Athletes are warned that although HMB itself is not banned by anti-doping codes and does not lead to a positive doping finding (Slater et al. 2000), supplements that are popularly promoted as 'body building' or 'legal alternatives to steroids' are often at risk of contamination with banned substances such as pro-hormones.

16.5.2.4 Glutamine

Glutamine is the most abundant free amino acid in human muscle and plasma. Likely roles of glutamine within the body including transfer of nitrogen between organs, the maintenance of the acid–base balance during acidosis, regulation of protein synthesis and degradation, provision of a nitrogen precursor for synthesis of nucleotides and, finally, a fuel source for gut mucosal cells and cells of the immune system (for review, see Rowbottom et al. 1996). Numerous studies have been conducted to investigate the effects of glutamine supplementation on the immunosuppression that occurs after strenuous exercise; the consensus from this literature will be discussed in the commentary on nutrition for the immune system (see the commentary by Pyne on pp. 581–8). This chapter will focus only on the studies that have directly investigated the effects of acute or long-term glutamine supplementation on exercise performance. These studies are summarised

in Table 16.10. Although the acute intake of glutamine prior to exercise has been hypothesised to enhance blood buffering capacity, the available studies fail to support this theory or any beneficial outcome on the performance of exercise (Haub et al. 1998; Antonio et al. 2002). Similarly, chronic protocols of supplementation with glutamine have not been associated with any enhancement of the adaptations to training (Candow et al. 2001; Falk et al. 2003; Lehmkuhl et al. 2003).

16.5.3 *Supplements in Group C of the AIS Sports Supplement Program*

The claims made for the majority of supplements available to athletes are not supported by sound scientific research. This is because the products have not been studied, or because the available literature has failed to provide evidence of a detectable benefit to training or competition performance.

16.5.3.1 Herbal products

Ginseng

Ginseng, extracted from the roots of ginseng plants, has enjoyed popularity as a health supplement for many centuries. The chemical composition of commercial ginseng supplements is highly variable due to differences in the genetic nature of the plant source, variation in active ingredients according to the season and cultivation methods, and differences in the methods of production into supplements. Several species of ginseng are known to exist: American, Chinese, Korean and Japanese (Bahrke & Morgan 1994). These belong to the *Panax* species and are related. However, Russian or Siberian ginseng is extracted from a different plant (*Eleutherococcus senticoccus*) and often goes by the name of ciwujia.

A number of chemically similar steroid glycosides or saponin chemicals, known as ginsenosides, have been identified as active ingredients in ginsengs. Unfortunately for the process of scientific study, there is a great variability in the active ingredients within and between products. The bioavailability of supplements can also vary according to the method of administration (chewing gum, pill, capsule, tablet or liquid). Some ginseng preparations also provide additional agents such as vitamins, minerals or other herbal compounds.

Ginseng has been used widely in the herbal medicines of oriental cultures to cure fatigue, relieve pain and headaches, and improve mental function and vigour. It is also claimed to increase non-specific resistance to various stressors, described by Russian and Eastern European scientists as an adaptogenic response. An adaptogen is a substance purported to normalise physiology after exposure to a variety of stresses. It exhibits a lack of specificity in its actions and can both reduce and increase a response that has been altered by a stressor. This theory

represents a philosophy of physiology or medicine different from the traditional western understanding.

Despite the history of use in eastern or traditional medicine, ginseng has only recently emerged as a purported ergogenic aid for exercise performance. In athletes, ginseng is claimed to reduce fatigue and improve aerobic conditioning, strength, mental alertness and recovery. However, several reviews of the literature on supplementation with ginsengs on exercise have noted that there is a lack of well-controlled research to support these claims (Bahrke & Morgan 1994; Dowling et al. 1996; Bahrke & Morgan 2000; Goulet 2005). In many cases, the studies that appear to show benefits to athletic performance are either flawed in design (for example, failure to include a control or placebo group) or lacking in detail due to their publication in a foreign language journal. Our review of the literature on ginseng supplement and exercise outcomes (Table 16.10) has not included these studies. Studies that have appeared in abstract form, and have not been published in a peer-reviewed forum, have also been omitted. Finally, we have only included studies that have involved a measurement of exercise capacity or performance.

On the whole, the studies that have been included in Table 16.11 fail to provide clear support for any benefits to performance following ginseng supplementation. Although a few studies have reported enhancement of physical exercise capacity or performance following chronic ginseng use (McNaughton et al. 1989; Liang et al. 2005), the majority have failed to detect an enhanced outcome (Dowling et al. 1996; Morris et al. 1996; Engels et al. 2001, 2003; Hsu et al. 2005). There are claims that ginseng supplementation may be valuable for athletic training in producing an enhancement of immune function, reduction in muscle damage or improved levels of psychomotor performance and wellbeing. Indeed there is some support for some of these claims (Ziemba et al. 1999; Hsu et al. 2005). However, other studies found a failure of supplementation with ginseng to enhance immune system parameters in athletes (Gaffney et al. 2001) or untrained subjects undertaking exercise (Engels et al. 2003), or to improve psychological function or wellbeing (Cardinal & Engels 2001).

A noticeable feature of the summary provided in Table 16.11 is that there are few studies of supplementation with ginsengs in trained subjects. Therefore it is fair to say that the effect of ginseng supplementation on athletic performance has not been adequately researched. However, the range in the types of ginseng and the variability in the content of commercial ginseng supplements create a difficulty in undertaking a thorough investigation in any population. Furthermore, these factors would also create caution in applying the results of a particular study to general education for athletes. For example, Chong and Oberholzer (1998) assayed 50 commercial ginseng preparations and noted that 44 products ranged in ginsenoside concentration from 1.9–9.0%, with the other six preparations failing to produce a detectable level of ginsenosides. Thus, even if well-controlled studies were to report beneficial outcomes from ginseng use, athletes could not be certain of receiving the appropriate dose and type of active ingredients from

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.10 Placebo-controlled studies of glutamine supplementation on training adaptations and performance (for updates see www.ais.org.au/nutrition)

Study	Subjects	Glutamine dose and training	Exercise protocol	Performance enhancement	Comments
Acute supplementation					
Antonio et al. (2002)	6 resistance-trained male subjects Crossover design	0.3 g/kg BM glutamine or 0.3 g/kg BM glycine ingested 60 minutes prior to test protocol	Resistance training: sets of exercise to fatigue: • 2 × leg press @ 200% BM • 2 × bench press @ 100% BM	 No No	No difference in performance of resistance sets between trials. Plasma lactate and pH not measured to test out the hypothesis that acute glutamine supplementation would enhance buffering capacity.
Haub et al. (1998)	10 active male subjects Crossover design	0.03 g/kg BM glutamine, ingested 90 minutes prior to test protocol	Cycling • 4 × 60 s bouts at 100% of maximal power output followed by a time to exhaustion effort	 No	Although researchers speculated that glutamine ingestion would increase buffering capacity, no differences were observed in plasma bicarbonate concentration at any time point.
Chronic supplementation					
Falk et al. (2003)	28 resistance-trained male subjects Parallel group design	3 g/day glutamine for 8 weeks (as part of effervescent supplement with creatine + ribose) Resistance training	Resistance training: • 1 RM bench press • repetitions 80% RM bench press to fatigue	 No No	Both groups increased LBM, muscle strength and strength endurance over 8 weeks of training, but no differences between groups.

Candow et al. (2001)	31 untrained male and female subjects Parallel group design	0.9 g/kg lean tissue mass/day for 6 weeks (consumed after training and prior to bed). Resistance training	• 1 RM bench press • 1 RM squat • Peak knee extensor torque	No No No		Glutamine and placebo groups both increased in strength, knee extensor torque, lean body mass and index of muscle protein degradation (urinary 3-methyl histidine) in response to training. No differences seen between groups.
Lehmkuhl et al. (2003)	19 male and female collegiate track and field athletes Parallel group design	4 g/day glutamine in addition to creatine for 8 weeks (glutamine + creatine versus creatine alone) Supervised event-specific resistance training program	• 5 × 5 s cycling sprints with 50 s recovery • Static jump • Counter-movement jump	No No No		Creatine supplementation in conjunction with training was associated with an increase in cycling power and increase in lean body mass. However, the addition of glutamine did not further enhance these gains.

RM = repetition maximum, LBM = lean body mass

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.11 Placebo-controlled studies of ginseng supplementation and performance (for updates see www.ais.org.au/nutrition)

Study	Subjects	Ginseng dose	Exercise protocol	Performance enhancement	Comments
Liang et al. (2005)	29 active males and females Parallel group design	Chinese ginseng *Panax notoginseng* 1350 mg/day for 30 days	Cycling • Incremental test to exhaustion	Yes	Ginseng group improved endurance by 7 minutes ($P < 0.05$) over treatment while no change seen in placebo group. Ginseng treatment also associated with a reduction in blood pressure and VO_2 during exercise.
Engels et al. (2003)	27 active males and females Parallel group design	G115 Chinese/Korean ginseng (*Panax* CA Meyer) 400 mg/day for 8 weeks	Cycling • 3 consecutive 30-s Wingate tests with 3-minute recovery periods	No	Comparison of post-test to pre-test scores showed no difference between groups in power during cycling or heart rate response. No difference in salivary IgA response to exercise due to ginseng.
Engels et al. (2001)	19 active females Parallel group design	G115 Chinese/Korean ginseng (*Panax* CA Meyer) 400 mg/day for 8 weeks	Cycling • 30 s Wingate test	No	Comparison of post-test to pre-test scores showed no difference between groups in power during cycling or heart rate response.
Ziemba et al. (1999)	15 male soccer players Parallel group design	Unspecified *Panax* ginseng 350 mg/day for 6 weeks	Cycling • Incremental test to exhaustion • Reaction time measured at each stage	No Yes	No change in lactate threshold or $VO_{2\ max}$. However, enhanced reaction time at submaximal workloads.
Allen et al. (1998)	28 active males and females Parallel group design	Chinese/Korean ginseng (*Panax* CA Meyer) 200 mg/day for 3 weeks	Cycling • Incremental test to exhaustion	No	No enhancement of total workload, RPE and lactate at submaximal loads or $VO_{2\ max}$ due to ginseng supplementation

Morris et al. (1996)	8 active males and females Crossover design	Unspecified ginseng 8 mg/kg/day or 16 mg/kg/day for 1 week	Cycling • Time to exhaustion @ 75% $VO_{2\ max}$	 No	No change in time to exhaustion or metabolic parameters. No change in RPE.
Hsu et al. (2005)	13 active males Crossover design	American ginseng 400 mg/day for 4 weeks	Running • 80% $VO_{2\ max}$ to fatigue	 No	No difference in endurance with ginseng supplementation; however, plasma CK levels were lower during exercise and for 2 hours post-exercise in ginseng trial, indicating lower levels of muscle damage.
Dowling et al. (1996)	20 highly trained male and female runners Parallel group design	Siberian ginseng (*Eleutherococcus senticosus*) 60 drops/day (maximum recommended dose) for 6 weeks	Running • 10-minute treadmill test at 10-km race pace • Maximal treadmill test	 No	No change in metabolic characteristics at race pace or performance of treadmill max. and RPE. Low statistical power may prevent small changes from being detected.
Pieralisi et al. (1991)	Active male subjects Crossover design	Ginsana 115 2 capsules/day for 6 weeks (ginseng, vitamins, bitartrate + minerals)	Running • Incremental treadmill test to exhaustion	 Yes	Increased $VO_{2\ max}$ and reduced O_2 consumption at submaximal workloads.
McNaughton et al. (1989)	30 active males and females Crossover design	Chinese ginseng (*Panax* CA Meyer) or Siberian ginseng (*Eleutherococcus senticosus*) 1 g/day for 6 weeks	Physical testing • $VO_{2\ max,}$ grip • pectoral strength • quadriceps strength	 Yes Yes Yes	Significantly greater increase in $VO_{2\ max}$ and pectoral and grip strength with Chinese ginseng. Trends for enhancement with Siberian ginseng.

RPE = ratings of perceived exertion, CK = creatine kinase

all preparations in the commercially available range. Furthermore, one product that was included in this assay contained large amounts of ephedrine (Chong & Oberholzer 1988); this would be a cause of an inadvertent doping outcome. The conclusion that must be made about ginseng at the current time is that there is no substantial evidence to support claims that this supplement is of benefit to performance or recovery.

Cordycepssinensis *and* Rhodiolarosea

Several other herbal compounds with a history of medical use or as tonics in other cultures have recently become available in supplements promoted to athletes. These include *Cordyceps sinensis*, a Chinese herb extracted from a mushroom, and *Rhodiola rosea*, popular in Asian and Eastern European medicine. Whereas *Cordyceps* is claimed to increase vasodilation and facilitate the delivery of oxygen to the working tissue, *Rhodiola* is said to stimulate the nervous system (de Bock et al. 2004; Earnest et al. 2004; Parcell et al. 2004). The small amount of literature on supplementation with these products on exercise capacity or performance is summarised in Table 16.12. To date, there is little evidence to support any of the claims made for these compounds. There has been insufficient research on the effects of these supplements on exercise or athletic performance to allow further discussion.

16.5.3.2 Carnitine

The first reports on carnitine in the early 1900s described it as a vitamin (an essential component of the diet). Following the discovery that carnitine can be manufactured in the liver and kidney from amino acid precursors (lysine and methionine), it is now considered to be a non-essential nutrient. Most animal foods provide a dietary source of carnitine, but due to losses in the cooking and preparation of foods there are few data on the total content of the diet. Carnitine ingested or synthesised by humans is in the L-isoform and is carried via the blood for storage, predominantly in the heart and skeletal muscle. Within these tissues, carnitine plays a number of roles related to fat and carbohydrate metabolism.

Carnitine is a component of the enzymes carnitine palmityltransferase I (CPTI), carnitine palmityltransferase II (CPTII) and carnitine acylcarnitine translocase (CAT). These enzymes are involved in the transportation of long-chain fatty acids (LCFAs) across the mitochondrial membrane to the site of their oxidation (see Chapter 15). Because of this function, it has been suggested that carnitine supplementation might enhance fatty acid transport and oxidation. As a result, carnitine is a popular component of supplements claimed to enhance the loss of body fat, and has been embraced by body builders wanting to 'cut up' and by other populations interested in weight loss. An increase in fatty acid oxidation during exercise could be of advantage to endurance athletes if it resulted in a sparing of glycogen during events in which carbohydrate stores are otherwise limiting.

During exercise, carnitine also plays the role of a 'sink' for acetyl-CoA production. By converting this to acetyl-carnitine and CoA, carnitine helps to maintain CoA availability and to decrease the ratio of acetyl-CoA:CoA. If carnitine supplementation could increase this function it might enhance flux through the citric acid cycle. Furthermore, it could enhance the activity of the enzyme pyruvate dehydrogenase, which is otherwise inhibited by high levels of acetyl-CoA, thus increasing oxidative metabolism of glucose. If this results in lower lactate production, it might enhance exercise performance in situations that might otherwise be limited by excess lactate and hydrogen ion accumulation. Extensive reviews of carnitine function are available (Cerretelli & Marconi 1990; Wagenmakers 1991; Clarkson 1992; Heinonen 1996).

When muscle carnitine activity is inadequate, as in the case of inborn errors of metabolism, individuals demonstrate lipid abnormalities and reduced exercise capacity. Carnitine supplementation is an established medical therapy for these conditions and helps to attenuate such symptoms. However, whether additional carnitine intake in healthy individuals enhances metabolism and exercise performance is a different issue. A positive outcome would require one or more of the following scenarios: heavy training causing suboptimal levels of muscle carnitine; carnitine supplementation increasing muscle carnitine content; carnitine being a limiting factor in fatty acid transport; or carnitine being a limiting factor in pyruvate dehydrogenase activity or citric acid cycle flux. However, thorough reviews cast doubt on the potential for enhanced metabolic function via enhanced carnitine status (Wagenmakers 1991; Heinonen 1996). These reviews summarise that normal muscle carnitine levels appear to be adequate for maximal function of CPTI and CPTII, and that there is no proof that fatty acid transport is the rate-limiting step in fat oxidation. Furthermore, pyruvate dehydrogenase is believed to be fully active within seconds of high-intensity exercise, and additional carnitine is unlikely to stimulate this activity further.

Optimal muscle carnitine content in athletes is probably the most important issue to address. Exercise is known to increase carnitine excretion and it is possible that muscle carnitine content may decrease during intense training. However, a series of reviews conclude that although most human studies find an increase in *plasma* carnitine levels following carnitine supplementation of 1–6 g/day, there is no compelling evidence that *muscle* carnitine levels are enhanced as a result of supplementation (Cerretelli & Marconi 1990; Wagenmakers 1991; Heinonen 1996). While one study has reported an increase in lipid utilisation during exercise following chronic carnitine supplementation in trained men (Gorostiaga et al. 1989), the majority of studies have not reported any changes in substrate utilisation during exercise as a result of carnitine use, even under conditions in which fat availability was increased (Vukovich et al. 1994) or muscle glycogen stores were depleted (Decombaz et al. 1993). Studies that have investigated the effects of carnitine supplementation on exercise performance are summarised in Table 16.13. On balance, there is little credible evidence of increased performance during submaximal or high-intensity exercise resulting from carnitine supplementation.

Table 16.12 Placebo-controlled studies of supplementation with *Cordyceps sinensis* or *Rhodiola rosea* on performance (for updates see www.ais.org.au/nutrition)

Study	Subjects	Supplement dose	Exercise protocol	Performance enhancement	Comments
Acute supplementation					
de Bock et al. (2004)	24 active males Crossover design	200 mg *Rhodiola rosea* 1 hour pre-exercise	Battery of tests: • incremental cycling to fatigue • isokinetic knee torque • speed of limb movement • reaction time • sustained attention	Yes No No No No	Compared with placebo, supplementation with *Rhodiola rosea* produced increased time to exhaustion in cycling protocol. No effect seen on muscle strength, or measures of reaction time and responsiveness to stimuli.
Chronic supplementation					
Parcell et al. (2004)	22 well-trained male cyclists Parallel group design	3.15 g/day *Cordyceps sinensis* (CordyMax Cs-4) for 5 weeks Normal training	Cycling • $VO_{2\ peak}$+ • TT lasting ~1 hour	No No	No change in aerobic capacity ($VO_{2\ peak}$) over time in either group. No change in time to complete cycling time trial over time or between groups.

Earnest et al. (2004)	17 endurance-trained male cyclists Parallel group design	1 g/day *Cordyceps sinensis* + 300 mg *Rhodiola rosea* for 2 weeks (+ chromium, pyruvate, phosphate, ribose, adenosine) Optygen™	Cycling • Incremental cycling time to exhaustion to assess peak power output, $VO_{2\ peak}$	No	No change in cycling endurance or aerobic capacity in either group over time.
de Bock et al. (2004)	23 active males Parallel group design	200 mg *Rhodiola rosea* for 4 weeks	Battery of tests: • incremental cycling to fatigue • isokinetic knee torque • speed of limb movement • reaction time • sustained attention	No No No No No	Neither treatment nor placebo group showed any changes in response to test battery. Previously seen benefits of acute intake of *Rhodiola rosea* on exercise capacity not apparent after chronic supplementation.

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.13 Studies of carnitine supplementation and metabolism on performance

Study	Subjects	Carnitine dose	Exercise protocol	Performance enhancement	Comments
Siliprandi et al. (1990)	10 moderately trained males Crossover design	Acute administration 2 g @ 1 hour before exercise	Cycling • Cycle to exhaustion	Yes	Increased time to exhaustion. Carnitine reduced the increase in plasma lactate and pyruvate after maximal progressive work. However, dose and time frame for uptake into muscle seem unrealistic.
Vecchiet et al. (1990)	10 moderately trained males Crossover design	Acute administration 2 g @ 1 hour before exercise	Cycling • Incremental cycling to exhaustion	Yes	Increase in time (and work) until exhaustion. Decrease in lactate production and oxygen consumption at same workload. However, dose and time frame for uptake into muscle seem unrealistic.
Greig et al. (1987)	9 untrained males and females 10 untrained males and females Crossover design	2 g/day for 2 weeks 2 g for 4 weeks	Cycling • Progressive test to exhaustion	No	No significant physiological changes. Changes in performance were small and inconsistent.

Trappe et al. (1994)	20 highly trained male collegiate swimmers Parallel group design	4 g/day for 7 days	Swimming • 5 × 91.4 m swims	No	No difference in performance times between trials or between groups.
Colombani et al. (1996)	7 endurance-trained male athletes Crossover design	2 g @ 2 hours before run and at 20 km mark	Running • Marathon run + submaximal performance test day after marathon	No	No change in exercise metabolism or marathon running time. No change in recovery and submaximal test performance on following day.
Marconi et al. (1985)	6 national class walkers Crossover design	4 g/day for 2 weeks	Running • supramaximal work (jumps) • treadmill $VO_{2\ max}$	No Yes?	Increase in $VO_{2\ max}$ by 6%. However, no effects on oxygen utilisation and RER at submaximal loads, or change in lactate accumulation with jumps. Results appear inconsistent.

RER = respiratory exchange ratio

Despite the popularity of carnitine in fat-loss supplements and the marketing claims associated with these products, the effect of carnitine supplementation on body-fat levels has not been studied in athletes.

16.5.3.3 Coenzyme Q10

Coenzyme Q10, or ubiquinone, is a non-essential, lipid-soluble nutrient found predominantly in animal foods and in low levels in plant foods. It is located in the body primarily in skeletal and cardiac muscle, inside the mitochondria. Coenzyme Q10 is part of the mitochondrial anti-oxidant defence system, preventing damage to DNA and cell membranes, and provides a link in the electron transport chain producing ATP. Some cardiac and neuromuscular dysfunction is believed to result from coenzyme Q10 deficiency. Indeed, patients with ischaemic heart disease are often seen to have lower plasma coenzyme Q10 concentrations and improve their exercise capacity following coenzyme Q10 supplementation. The marketing campaigns for coenzyme Q10 supplement promote increased vigour and youthfulness as a benefit of their use. For athletes, there are claims of enhanced energy production and reduced oxidative damage from exercise.

Peer-reviewed studies of coenzyme Q10 supplementation on exercise metabolism, oxidative damage caused by exercise and performance are summarised in Table 16.14. There are few data that support an ergogenic benefit of coenzyme Q10 on exercise performance. By contrast, several studies have shown that coenzyme Q10 has an *ergolytic*, or negative, effect on high-intensity performance and training adaptations (Laaksonen et al. 1995; Malm et al. 1996, 1997; Svensson et al. 1999). A series of studies found that coenzyme Q10 supplementation had no effect on indices of lipid oxidation (indicated by plasma malondialdehyde concentrations) or catabolism of adenine nucleotides (indicated by plasma uric acid and hypoxanthine concentrations) when previously untrained men undertook twice daily sessions of repeated sprints (Svensson et al. 1999). In fact, supplementation with coenzyme Q10 may have increased oxidative damage, as indicated by higher plasma creatine kinase levels in response to exercise compared with the placebo trial (Malm et al. 1996). In these circumstances, coenzyme Q10 was believed to act as a pro-oxidant rather than an anti-oxidant. Training adaptations were impaired by coenzyme Q10, with the placebo group outperforming the coenzyme Q10 group either during training or at the end of the supplementation phase (Malm et al. 1996, 1997). Similarly, a crossover study found that trained subjects had greater endurance during a cycling test at the end of the placebo trial compared with the period of coenzyme Q10 supplementation. An increase in plasma Q10 concentrations in response to supplementation is not associated with an increase in Q10 concentrations in skeletal muscle or isolated skeletal muscle mitochondria (Svensson et al. 1999).

Further work is required to investigate the effects of coenzyme Q10 supplementation on exercise performance and training. However, at present there is

no clear evidence to recommend coenzyme Q10 supplementation to athletes undertaking high-intensity training.

16.5.3.4 Inosine

Inosine is a nucleic acid derivative that occurs naturally in brewer's yeast, liver and other glandular organ meats. It is a non-essential nutrient, since our bodies can make all nucleic acids from their amino acid and sugar precursors provided in protein and carbohydrate foods. Specifically, inosine is a purine nucleoside and a precursor of the nucleotide, inosine mono-phosphate (IMP). This is, in turn, an intermediary in the degradation and salvage of the adenine nucleotides ATP, AMP and ADP. Thus, it has been hypothesised that inosine supplementation could increase the muscle content of ATP. Other mechanisms by which inosine supplementation is claimed to enhance exercise performance include an increase in 2,3-diphosphoglycerate in red blood cells, which theoretically shift the oxyhaemoglobin curve to increase the release of oxygen into the muscle. Inosine is also believed to have vasodilatory effects and anti-oxidant properties. However, these are only hypothetical situations that have not been supported by research. Further information on inosine can be found in Williams et al. (1990) and Starling et al. (1996).

The main support for inosine supplementation is testimonial, with reports from athletes, especially from Russian and ex-Eastern-bloc countries, and muscle-building magazines. One popular magazine, *Muscle and Fitness*, published an article describing a 6-week study of inosine supplementation on four trained athletes (Colgan 1988). The report claimed the study was undertaken using a double-blind crossover design and found strength gains as a result of the supplementation. This study has not appeared in a peer-reviewed publication or in adequate detail to judge the validity of these claims. The athletes reported irritability and fatigue while taking the inosine supplements.

Table 16.15 summarises the results of the only three well-controlled studies of inosine supplementation that have been published in the peer-reviewed literature. Inosine was also an ingredient in a multi-compound ergogenic aid (CAPS) that failed to enhance performance of triathletes in a study by Snider and colleagues (1992); this study has been reviewed in section 16.5.3.3. The three studies of isolated inosine supplementation all failed to find either favourable metabolic changes or performance benefits following inosine supplementation in well-trained subjects (Williams et al. 1990; Starling et al. 1996; McNaughton et al. 1999c). There were no data to support any of the theoretical actions of inosine supplementation. Although muscle substrates were not directly measured in these studies, purported changes to ATP concentrations are unlikely to enhance exercise performance since ATP is not depleted by exercise, even at the point of fatigue (see Chapter 1).

Of note, two studies reported that subjects showed better performance of high-intensity tasks while on the placebo treatment than on the inosine trial,

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.14 Studies of coenzyme Q10 supplementation and exercise performance (for updates see www.ais.org.au/nutrition)

Study	Subjects	Coenzyme Q10 dose	Exercise protocol	Performance enhancement	Comments
Bonetti et al. (2000)	28 recreational cyclists Parallel group design	100 mg/day for 8 weeks	Cycling • Incremental test with increase of 50 W/minutes until exhaustion	No	Supplementation did increase plasma Coenzyme Q10 levels, but did not improve aerobic power.
Nielsen et al. (1999)	7 well-trained male triathletes Crossover design	100 mg/day for 6 weeks (+ vitamin E + vitamin C)	Cycling • Incremental $VO_{2\ max}$ test to exhaustion	No	No effect on maximal oxygen uptake or muscle energy metabolism (determined by NMRS).
Malm et al. (1997)	18 males Parallel group design	120 mg/day for 22 days Days 2–9: usual activity Days 11–14: 2/day anaerobic training Days 15–22: recovery	Cycling Anaerobic test (days 1, 11, 15 and 20) • 30 s Wingate cycle + 5 minute recovery + 10 × 10 s sprints Aerobic test (pre-trial and day 18) • Cycling $VO_{2\ max}$ Aerobic test: pre-trial and day 22 • Running $VO_{2\ max}$	 No—in fact, impairment No No	Placebo and Q10 group both improved performance of repeated sprint test after training, however, only placebo group maintained this improvement during recovery to day 20. Placebo group achieved higher average power, and greater improvement in latter intervals during anaerobic training sessions. No change in $VO_{2\ max}$ outcomes in either group over time or in oxygen use during submaximal cycling.
Weston et al. (1997)	18 trained male cyclists and triathletes Parallel group design	1 mg/kg/day for 28 days	Cycling • Incremental test to exhaustion	No	Test undertaken pre- and post 28 d of training; coenzyme Q10 did not enhance performance compared with placebo group

Malm et al. (1996)	15 active males Parallel group design	120 mg/day for 20 days Days 2–10: usual activity Days 11–15: 2/day anaerobic training Days 16–20: recovery	Cycling • Days 1, 11, 15 and 20 • 30 s Wingate cycle + 5 min recovery + 10 × 10 s sprints	No—in fact, impairment	Placebo group improved anaerobic work capacity at day 15 or 20—training effect. However, Q10 group did achieve this training effect. CK levels maintained during placebo trial but were increased at various time points in Q10 group.
Laaksonen et al. (1995)	11 young and 8 older trained males Crossover design	120 mg/day for 6 weeks	Cycling • Prolonged endurance test to exhaustion	No—in fact, performance impairment	No change in muscle coenzyme Q10 concentrations or plasma malondialdehyde as a result of coenzyme Q10 supplementation. Negative effect on time to exhaustion (placebo had greater endurance).
Braun et al. (1991)	10 male cyclists Parallel group design	100 mg/day for 8 weeks	Cycling • Incremental test to exhaustion	No	Performance increased equally in both groups from pre- to post-supplementation. Coenzyme Q10 had no effect on cycling performance or any measured parameters. Malondialdehyde concentrations reduced in both groups after training.
Snider et al. (1992)	11 highly trained triathletes Crossover design	100 mg/day for 4 weeks (+ vitamin E, inosine, cytochrome *c*)	Cycling and running • 90 min on treadmill @ 70% $VO_{2\ max}$ + cycling @ 70% $VO_{2\ max}$ to exhaustion	No	No difference in time to exhaustion between trials. No differences in blood metabolites or RPE.
Ylikoski et al. (1997)	25 national-level cross-country skiers Parallel group design	90 mg/day for 6 weeks	Cross-country skiing • Treadmill pole-walking to exhaustion	Yes	Improved $VO_{2\ max}$ with coenzyme Q10 supplementation. Increase in aerobic and anaerobic thresholds. No control of exercise during supplementation periods.

CK = creatine kinase, RPE = rating of perceived exertion, W = watts

Table 16.15 Studies of inosine supplementation and exercise performance (for updates see www.ais.org.au/nutrition)

Study	Subjects	Inosine 10 000 dose	Exercise protocol	Enhanced performance	Comments
McNaughton et al. (1999c)	7 well-trained males Crossover design	10 000 mg for 5 and 10 days	Cycling • 5 × 6 s sprints • 30 s sprint • 20 minute TT	No	No improvements in sprint times or TT performance. Increase in plasma uric acid concentrations.
Starling et al. (1996)	10 competitive male cyclists Crossover design	5000 mg/day for 5 days	Cycling • Wingate 30 s test • 30-min TT • supramaximal sprint to fatigue	No—in fact, performance impairment	No difference in Wingate performance or 30-minute cycle. Negative effect on time to fatigue. Increase in plasma uric acid concentration.
Williams et al. (1990)	9 highly trained male and female endurance runners Crossover design	6000 mg/day for 2 days (maximum recommended dose)	Running • Submaximal warm-up run • 3-mile treadmill TT • maximal treadmill run	No—in fact, performance impairment	No effect on 3-mile run time, $VO_{2\ peak}$ or other variables. Negative effect on maximal run.

TT = time trial

suggesting that inosine supplementation might actually impair the performance of high-intensity exercise (Williams et al. 1990; Starling et al. 1996). Potential mechanisms for exercise impairment include an increased formation of IMP in the muscle, either at rest or during exercise. High IMP concentrations have been found at the point of fatigue in many exercise studies; furthermore IMP has been shown to inhibit ATPase activity (Sahlin 1992). It is possible that increased resting concentrations of muscle IMP reduced the duration of high-intensity exercise before critically high levels were reached, causing premature fatigue. Such a theory can only be investigated by direct measurements of muscle nucleosides. Another possible mechanism of performance impairment is an increase in levels of uric acid, a product of inosine degradation. In the present studies, two days of inosine supplementation did not change uric acid levels; however, 5 days and 10 days of intake doubled blood concentrations to levels above the normal range (Williams et al. 1990; Starling et al. 1996; McNaughton et al. 1999c). Thus, chronic inosine supplementation may pose a health risk since high uric acid levels are implicated as a cause of gout. In summary, since there is a lack of evidence of performance benefits, and the possibility of performance decrements and side effects, there is little to recommend the use of inosine supplements by athletes.

16.5.3.5 Chromium picolinate

Chromium is an essential trace mineral. Good sources of dietary chromium include liver, eggs, poultry and whole grain cereals; however, absorption of chromium from food is poor. Insufficient data exist to establish a recommended dietary intake for chromium. Adequate intakes, determined from estimates of nutrient intake by healthy people, are within the range of 25–35 μg per day. The lack of reliable food composition data on the chromium content of foods often causes an underestimation of chromium intake.

Chromium plays many roles in maintaining proper metabolism, including roles in glucose, lipid and amino acid metabolism (see Stoecker 1996). Glucose tolerance factor (GTF), found in brewer's yeast, may be the most biologically active and absorbable form of chromium. GTF potentiates insulin activity and is responsible for normal insulin function related to uptake of glucose and amino acids into the cell. Optimal chromium intake appears to decrease the amount of insulin required to maintain normal blood glucose levels. Chromium deficiency is rare, but it is suggested that marginal chromium intakes may contribute to the development of conditions such as insulin resistance and poor growth. People with chromium deficiencies often show improvements in growth or glucose tolerance in response to chromium supplementation (Stoecker 1996). However, research is yet to show convincing proof that chromium supplementation improves glucose metabolism in people with type 2 diabetes. Since exercise has been shown to increase the urinary excretion of chromium, it has been suggested that athletes are at risk of becoming chromium deficient and that supplementation would

be beneficial. Further research is required to determine if the body adapts to increased excretion of chromium by increasing the absorption of chromium. As is the case for many micronutrients, athletes with restricted energy intakes are most at risk of low chromium intakes.

Chromium supplements are available in the form of chromium nicotinate, chloride and picolinate. Chromium picolinate is claimed to be the most biologically active form, and the claims for the efficacy of chromium picolinate have caused an interesting public debate between the patent holders and other trace element/mineral experts (Levafi et al. 1992; Evans 1993; Levafi 1993). A concern with chromium supplementation is that chromium potentially competes with trivalent iron for binding to transferrin, thus predisposing those with chronically high intakes of chromium to iron deficiency (Lukaski et al. 1996). Some (Lukaski et al. 1996), but not all (Campbell et al. 1997), studies have reported a reduction in iron status as a result of chromium picolinate supplementation.

The main claims for chromium supplements are that they will enhance handling of glucose, amino acids and fatty acids, allow dramatic gains in muscle mass and strength, and reduce body fat. Initial studies reported increases in muscle mass and a reduction in body fat following supplementation with chromium picolinate in subjects undertaking aerobic exercise classes (Evans 1993) and weight training (Evans 1989). These studies have been criticised for methodological flaws, such as lack of a control group, inadequate control of diet or training status, and the reliance on unreliable and insensitive methods of assessing body composition (Levafi et al. 1992; Levafi 1993). We have not included such investigations in our summary of the literature (Table 16.16). This summary shows that studies that use 'gold standard' techniques for measuring body composition (underwater weighing, dual X-ray absorptiometry and MRI) have found no change in lean body mass or loss of body fat above the effects achieved by training alone. A study in which chromium picolinate was added to a sports drink consumed during exercise found that there were no additional benefits to exercise performance above that achieved by the carbohydrate in the drink (Davis et al. 2000). Therefore, chromium picolinate supplementation does not appear to provide any acute benefits to carbohydrate metabolism.

In summary, there is certainly no support for the dramatic claims made in some advertisements that position chromium picolinate as a 'legal anabolic' agent. The only situation in which chromium supplementation is likely to be useful is in treating individuals whose dietary intake is inadequate.

16

16.5.3.6 Medium chain triglycerides

Medium-chain triglycerides (MCTs) are fats composed of medium-chain fatty acids (MCFA) with a chain length of six to 10 carbon molecules. They are digested and metabolised differently from the long-chain fatty acids that make up most of our dietary fat intake. Specifically, MCTs can be digested within the intestinal lumen with less need for bile and pancreatic juices than long-chain

triglycerides, with MCFAs being absorbed via the portal circulation. MCFAs can be taken up into the mitochondria without the need for carnitine-assisted transport (see Chapter 15 for more details on fat metabolism). In clinical nutrition, MCT supplements derived from palm kernel and coconut oil are used as energy supplements for patients who have various digestive or lipid metabolism disorders. In the sports world, MCTs have been positioned as easily absorbed and oxidised fuel sources, and have been marketed to body builders as fat sources that are less likely to deposit as body fat. However, the role of MCTs in the general diet of athletes has not been studied.

Another role for MCTs in sport is to provide a fuel source during endurance and ultra-endurance events that could potentially spare glycogen, and prolong the availability of important CHO stores. Jeukendrup and colleagues (1995) reported that the co-ingestion of MCT with CHO during prolonged exercise increased the rate of MCT oxidation, possibly by increasing its rate of absorption; the maximum rate of MCT oxidation was achieved at around 120–180 minutes of exercise, with values of 0.12 g/min. Table 16.17 summarises the findings of studies that have examined the effect of the co-ingestion of MCT and CHO on ultra-endurance performance; the results are inconsistent and appear to depend on the amount of MCT that can be ingested and the prevailing hormonal conditions. Studies in which the intake of large amounts of MCT raised plasma FFA concentrations and allowed glycogen sparing reported a performance benefit at the end of prolonged exercise (van Zyl et al. 1996). However, these metabolic (and performance) benefits may be compromised when exercise is commenced with higher insulin levels, as is the case following a CHO-rich pre-exercise meal (Goedecke et al. 1999; Angus et al. 2000). Critical to the whole issue is the ability of subjects to tolerate the substantial amount of MCT oils required to have a metabolic impact. Jeukendrup et al. found that the gastrointestinal tolerance of MCT is limited to a total intake of about 30 g, which would limit its fuel contribution to 3–7% of the total energy expenditure during typical ultra-endurance events (Jeukendrup et al. 1995). At greater intakes, subjects report gastrointestinal reactions that range in severity from insignificant (van Zyl et al. 1996) to performance-limiting (Jeukendrup et al. 1998; Goedecke et al. 2005). Differences in gastrointestinal tolerance between studies or within studies may reflect differences in the mean chain length of MCTs found in the supplements, or increased tolerance in some athletes due to constant exposure to MCTs. The intensity and mode of exercise may also affect gastrointestinal symptoms.

In summary, although some CHO gels are marketed with the addition of MCTs, there is little evidence to support an ergogenic effect from these special products. In fact, Goedecke and colleagues (2005) reported a performance decrement in an ultra-endurance protocol following the intake of MCTs before and during cycling. This appeared to have causes other than the gastrointestinal disturbances, since all subjects experienced an impairment of time-trial performance, while only half the group reported gastrointestinal problems.

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.16 Studies of chromium picolinate supplementation and body composition and performance (for updates see www.ais.org.au/nutrition)

Study	Subjects	Chromium dose and form	Exercise protocol	Enhanced performance	Comments
Acute supplementation studies					
Davis et al. (2000)	8 active males Crossover design	400 μg/day Cr-Pic (400)	Intermittent high-intensity exercise • shuttle running and fatigue test	 No	Cr added to a CHO-electrolyte sports drink did not enhance performance beyond the benefit of ingesting CHO during exercise.
Chronic supplementation studies					
Hasten et al. (1992)	59 male and female college students Parallel group design	200 Cr-Pic for 12 weeks Resistance training program	Testing at baseline and 12 weeks • strength • body composition	 No No—males Yes—females	Both groups gained BM and reduced body fat. Greater ↑ in BM in females with chromium but no difference with males. No differences in strength changes due to chromium picolinate.
Clancy et al. (1994)	36 male collegiate football (gridiron) players Parallel group design	200 μg/day Cr-Pic for 9 weeks Pre-season resistance and conditioning training	Testing at baseline, mid and 9 weeks: • strength • body composition	 No No	No enhancement of BM, body composition or strength above placebo group.
Lukaski et al. (1996)	36 untrained males Parallel group design	3.4 μmol/day (~200 μg/day) Cr-Pic or Cr-chloride for 8 weeks Resistance training program	Testing at baseline and 8 weeks: • strength • body composition • iron status	 No No No	No beneficial effects on lean BM, body fat or strength above training effect. No difference between chromium preparations. Trend for ↓ iron status (↓ transferrin status) with chromium picolinate.

Hallmark et al. (1996)	16 untrained males Parallel group design	200 µg/day Cr-Pic for 12 weeks Resistance training program	Testing at baseline and 12 weeks: • strength • body composition	 No No	No differences in body composition with training or supplement. Strength increases independent of supplement.
Walker et al. (1998)	20 male collegiate wrestlers Parallel group design	200 µg/day Cr-Pic for 14 weeks Resistance and conditioning training program	Testing at baseline and 14 weeks • strength • peak power • body composition • Wingate test • $VO_{2\ max}$ on run treadmill	 No No No No No	No enhancement of body composition or performance variables beyond improvements seen with training alone.
Livolsi et al. (2001)	15 female collegiate softball players Parallel group design	500 µg/day Cr-Pic for 6 weeks Resistance training program	Testing at baseline and 6 weeks strength • IRM for variety of lifts Body composition • Hydrostatic weighing	 No No	Muscle strength increased with training but no difference between groups. No significant differences in body fat or LBM. Urinary Cr excretion increased in treatment group.

P1: FAW/SPH P2: FAW/SPH QC: FAW/SPH T1: FAW
MHBD028-16 MHBD028-Burke MHBD028-Burke-v1.cls KEY BOARDED February 1, 2006 4:7

Table 16.17 Studies of medium-chain triglycerides + CHO supplementation and ultra-endurance performance (for updates see www.ais.org.au/nutrition)

Study	Subjects	MCT dose	Exercise protocol	Enhanced performance	Comments
Van Zyl et al. (1996)	6 endurance-trained cyclists Crossover design	2 L of 4.3% MCT or 10% CHO or 10% CHO + 4.3% MCT Total intake of MCT = 86 g	Cycling • 2 hours @ 60% $VO_{2\ max}$ + 40 km TT (~70 minutes)	Yes	MCT + CHO enhanced TT performance times (65.1 minutes) compared with CHO (66.8 minutes) and MCT (72.1 minutes). Increase in FFA and glycogen sparing with MCT + CHO.
Jeukendrup et al. (1998)	9 endurance-trained male cyclists/triathletes Crossover design	20 mL/kg of 10% CHO or 10% CHO + 5% MCT or 5% MCT or placebo Total intake of MCT = 86 g	Cycling • 2 hours @ 60% $VO_{2\ max}$ + TT (~15 min)	No	No difference between CHO, CHO + MCT or placebo (~14 minutes) but MCT alone impaired performance (17.3 minutes). MCT + CHO showed slightly higher fat oxidation than CHO alone. No glycogen sparing.
Goedecke et al. (1999)	9 endurance-trained male cyclists Crossover design	1.6 L of 10% CHO or 10% CHO + 1.7% MCT or 10% CHO + 3.4% MCT Total intake of MCT = 26 or 52 g	Cycling • 2 hours @ 63% $VO_{2\ max}$ + 40 km TT (~70 min)	No	No differences in TT performance. 2 subjects experienced gastrointestinal distress with higher MCT intake. Higher FFA with MCT but no change in CHO oxidation.

Angus et al. (2000)	8 endurance-trained male cyclists/ triathletes Crossover design	1 L per hour of 6% CHO + 4% MCT (versus 6% CHO or placebo) Total intake of MCT = 42 g per hour or ~120 g	Cycling • 100 km TT (~3 hours)	No	CHO enhanced performance over placebo, but addition of MCT did not provide further benefits. 4 subjects experienced gastrointestinal problems with MCT. No differences in fat oxidation, plasma FFA between MCT and CHO + MCT. Suppression of fat oxidation may be due to high exercise intensity or pre-trial CHO meal causing high insulin concentrations.
Vistisen et al. (2003)	Well-trained cyclists (7 M) Crossover design	2.4 g/kg CHO or 2.4 g/kg CHO + 1.5 g/kg MCT/LCFA mixture over 4 hours Total intake of MCT mixture = 93–128 g over 4 hours	Cycling • 3 h @ 55% $VO_{2\,max}$ + 800 kJ TT (~50 min)	No	No difference in TT performance between CHO and CHO + MCT mixture (50.8 ± 3.6 versus 50.0 ± 1.8 minutes, NS). Significantly lower RER (greater fat use) during first hour of ride, but not significantly different thereafter, indicating only minor differences in substrate utilisation as a result of the treatment. No major GI side effects during trial, but problems experienced next day with CHO + MCT mixture trial.
Goedecke et al. (2005)	8 male endurance-trained cyclists Crossover design	1 hour pre-exercise 75 g CHO or 32 g MCT During exercise 600 mL per h of 10% CHO or 10% CHO + 4.2% MCT Total intake of MCT = 148 g over 6 hours	Cycling • 4.5 hours @ 50% PPO + 200 kJ TT (~15 minutes)	No—in fact impaired	No difference in substrate utilisation (RER) during submaximal exercise. Half the subjects experienced GI side effects with MCT. Overall, TT performance compromised in MCT trial (12.36 versus 14.30 minutes)

16.6 Summary

Sports dietitians frequently observe a chaotic pattern of use of supplements and sports foods by athletes and coaches, and an almost never-ending range of products that are claimed to achieve benefits needed to enhance sports performance. The poor regulation of supplements and sports foods in many countries allows athletes and coaches to be the target of marketing campaigns based on exaggerated claims and hype rather than documented benefits. However, scientific study has identified a number of products that offer true benefits to performance or the achievement of nutritional goals. A systematic approach to educating athletes and coaches about supplements and sports foods, and managing their provision to athletes and teams, can allow sports people to include the successful use of these products with the activities that underpin optimal performance.

References

Alford C, Cox H, Wescott R. The effects of Red Bull Energy Drink on human performance and mood. Amino Acids 2001;21:139–50.

Allen JD, McLung J, Nelson AG, Welsch M. Ginseng supplementation does not enhance healthy young adults' peak aerobic exercise performance. J Am Coll Nutr 1998;17:462–6.

American Academy of Pediatrics Committee on Sports Medicine and Fitness. Position on use of performance-enhancing substances. Pediatrics 2005;115:1103–6.

American College of Sports Medicine. Roundtable: The physiological and health effects of oral creatine supplementation. Med Sci Sports Exerc 2000;32:706–17.

Anderson ME, Bruce CR, Fraser SF, Stepto NK, Klein R, Hopkins WG, Hawley JA. Improved 2000-metre rowing performance in competitive oarswomen after caffeine ingestion. Int J Sport Nutr Exerc Metab 2000;10:436–47.

Anderson MJ, Cotter JD, Garnham AP, Casley DJ, Febbraio MA. Effect of glycerol-induced hyperhydration on thermoregulation and metabolism in the heat. Int J Sport Nutr Exerc Metab 2001;11:315–33.

Angus DJ, Hargreaves M, Dancey J, Febbraio MA. Effect of carbohydrate or carbohydrate plus medium-chain triglyceride ingestion on cycling time trial performance. J Appl Physiol 2000;88:113–19.

Antonio J, Sanders MS, Van Gammeren D. The effects of bovine colostrum supplementation on body composition and exercise performance in active men and women. Nutrition 2001;17:243–7.

Antonio J, Sanders MS, Kalman D, Woodgate D, Street C. The effects of high-dose glutamine ingestion on weightlifting performance. J Strength Cond Res 2002;16:157–60.

Ariel G, Saville W. Anabolic steroids: the physiological effects of placebos. Med Sci Sports Exerc 1972;4:124–6.

Bahrke MS, Morgan WP. Evaluation of the ergogenic properties of ginseng. Sports Med 1994;18:229–48.

Bahrke MS, Morgan WR. Evaluation of the ergogenic properties of ginseng: an update. Sports Med 2000;29:113–33.

Baylis A, Cameron-Smith D, Burke LM. Inadvertent doping though supplement use by athletes: assessment and management of the risk in Australia. Int J Sport Nutr Exerc Metab 2001;11:365–83.

Bell DG, McLellan TM. Exercise endurance 1, 3, and 6 h after caffeine ingestion in caffeine users and nonusers. J Appl Physiol 2002;93:1227–34.

Bell DG, McLellan TM. Effect of repeated caffeine ingestion on repeated exhaustive exercise endurance. Med Sci Sports Exerc 2003;35:1348–54.

Bemben MG, Lamont HS. Creatine supplementation and exercise performance. Recent findings. Sports Med 2005;35:107–25.

Berardi JM, Ziegenfuss TN. Effects of ribose supplementation on repeated sprint performance in men. Int J Sport Nutr Exerc Metab 2003;17:47–52.

Bird SR, Wiles J, Robbins J. The effect of sodium bicarbonate ingestion on 1500-m racing time. J Sports Sci 1995;13:399–403.

Bishop D, Claudius B. Effects of induced metabolic alkalosis on prolonged intermittent-sprint performance. Med Sci Sports Exerc 2005;37:759–67.

Blue JG, Lombardo JA. Steroids and steroid-like compounds. Clin Sports Med 1999;18:667–89.

Bonetti A, Solito F, Carmosino G, Bargossi AM, Fiorella PL. Effect of ubidecarenone oral treatment on aerobic power in middle-aged trained subjects. J Sports Med Phys Fitness 2000;40:51–7.

Branch JD. Effect of creatine supplementation on body composition and performance: a meta-analysis. Int J Sport Nutr Exerc Metab 2003;13:198–226.

Braun B, Clarkson PM, Freedson PS, Kohl RL. Effects of coenzyme Q10 supplementation and exercise performance, $VO_{2\ max}$, and lipid perodixation in trained subjects. Int J Sport Nutr 1991;1:353–65.

Brinkworth GD, Buckley JD, Bourdon PC, Gulbin JP, David AZ. Oral bovine colostrum supplementation enhances buffer capacity but not rowing performance in elite female rowers. Int J Sport Nutr Exerc Metab 2002;12:349–63.

Brinkworth GD, Buckley JD. Concentrated bovine colostrum protein supplementation reduces the incidence of self-reported symptoms of upper respiratory tract infection in adult males. Eur J Nutr 2003;42:228–32.

Brinkworth GD, Buckley JD, Slavotinek JP, Kurmis AP. Effect of bovine colostrum supplementation on the composition of resistance trained and untrained limbs in healthy young men. Eur J Appl Physiol 2004;91:53–60.

Bruce CR, Anderson ME, Fraser SF, Stepto NK, Klein R, Hopkins WG, Hawley JA. Enhancement of 2000-m rowing performance after caffeine ingestion. Med Sci Sports Exerc 2000;32:1958–63.

Buckley JD, Abbott MJ, Brinkworth GD, Whyte PBD. Bovine colostrum supplementation during endurance running training improves recovery, but not performance. J Sci Med Sport 2002;5:65–79.

Buckley JD, Brinkworth GD, Abbott MJ. Effect of bovine colostrum on anaerobic exercise performance and plasma insulin-like growth factor. J Sports Sci 2003;21:577–88.

Burke LM. An interview with Dr Gary Green about supplements and doping problems from an NCAA perspective. Int J Sport Nutr Exerc Metab 2001;11:397–400.

Burke LM. An overview of sports foods and supplements. In: Burke LM. Applied sports nutrition. Champaign, Illinois: Human Kinetics, 2006.

Campbell WW, Beard JL, Joseph LJ, Davey SL, Evans WJ. Chromium picolinate supplementation and resistive training by older men: effects on iron-status and hematologic indexes. Am J Clin Nutr 1997;66:944–9.

Candow DG, Chilibeck PD, Burke DG, Davison KS, Smith-Palmer T. Effect of glutamine supplementation combined with resistance training in young adults. Eur J Appl Physiol 2001;86:142–9.

Cardinal BJ, Engels HJ. Ginseng does not enhance psychological well-being in healthy, young adults: results of a double-blind, placebo-controlled, randomized clinical trial. J Am Diet Assoc 2001;101:655–60.

Cerretelli P, Marconi C. L-carnitine supplementation in humans. The effects on physical performance. Int J Sports Med 1990;11:1–14.

Chanutin A. The fate of creatine when administered to man. J Biol Chem 1926;67:29–37.

Chong SKF, Oberholzer VGP. Ginseng—is there a clinical use in medicine? Postgrad Med 1988;65:841–6.

Clancy SP, Clarkson PM, DeCheke ME, Nosaka K, Freedson PS, Cunningham JJ, Valentine B. Effects of chromium picolinate supplementation on body composition, strength, and urinary chromium loss in football players. Int J Sport Nutr 1994;4:142–53.

Clark VR, Hopkins WG, Hawley JA, Burke LM. Placebo effect of carbohydrate feedings during a 40-km cycling time trial. Med Sci Sports Exerc 2000;32:1642–7.

Clarkson PM. Nutritional ergogenic aids: carnitine. Int J Sport Nutr 1992;2:185–90.

Cohen BS, Nelson AG, Prevost MC, Thompson GD, Marx BD, Morris GS. Effects of caffeine ingestion on endurance racing in heat and humidity. Eur J Appl Physiol 1996;73:358–63.

Colgan M. Inosine. Muscle and Fitness 1988;49:94–6, 204, 206, 210.

Colombani P, Wenk C, Kunz I, Krahenbuhl S, Kuhnt M, Arnold M, Frey-Rindova P, Frey W, Langhans W. Effects of L-carnitine supplementation on physical performance and energy metabolism of endurance-trained athletes: a double-blind crossover field study. Eur J App Phys 1996;73:434–9.

Conway KJ, Orr R, Stannard SR. Effect of a divided dose of endurance cycling performance, postexercise urinary caffeine concentration and plasma paraxanthine. J Appl Physiol 2003;94:1557–62.

Coombes JS, Hamilton KL. The effectiveness of commercially available sports drinks. Sports Med 2000;29:181–209.

Coombes JS, Conacher M, Austen SK, Marshall PA. Dose effects of oral bovine colostrum on physical work capacity in cyclists. Med Sci Sports Exerc 2002;34:1184–8.

Costill DL, Dalsky GP, Fink WJ. Effects of caffeine ingestion on metabolism and exercise performance. Med Sci Sports Exerc 1978;10:155–8.

Coutts A, Reaburn P, Mummery K, Holmes M. The effect of glycerol hyperhydration on Olympic distance triathlon performance in high ambient temperatures. Int J Sport Nutr Exerc Metab 2002;12:105–19.

Cox GR, Desbrow B, Montgomery PG, Anderson ME, Bruce CR, Macrides TA, Martin DT, Moquin A, Roberts A, Hawley JA, Burke LM. Effect of different protocols of caffeine intake on metabolism and endurance performance. J Appl Physiol 2002a;93:990–9.

Crowe MJ, O'Connor DM, Lukins JE. The effects of B-hydroxy-B-methylbutyrate (HMB) and HMB/creatine supplementation on indices of health in highly trained athletes. Int J Sport Nutr Exerc Metab 2003;13:184–97.

Davis JM, Welsh RS, Alderson NA. Effects of carbohydrate and chromium ingestion during intermittent high-intensity exercise to fatigue. Int J Sport Nutr Exerc Metab 2000;10: 476–85.

de Bock K, Eijnde BO, Ramaekers M, Hespel P. Acute *Rhodiola rosea* intake can improve endurance exercise performance. Int J Sport Nutr Exerc Metab 2004;14:298–307.

Decombaz J, Deriaz O, Acheson K, Gmuender B, Jequier E. Effect of L-carnitine on submaximal exercise metabolism after depletion of muscle glycogen. Med Sci Sports Exerc 1993;25:733–40.

Decombaz J, Bury A, Hager C. HMB meta-analysis and the clustering of data sources (letter to editor). J Appl Physiol 2003;95:2180–2.

Dennig H, Talbot JH, Edwards HT, Dill B. Effects of acidosis and alkalosis upon the capacity for work. J Clin Invest 1931;9:601–13.

Desbrow B, Leveritt M, Hughes R, Jones L and Scheelings P (in review). An independent analysis of consumer exposure to caffeine from retail coffees. Aust N Zeal J Pub Health.

Dill DB, Edwards HT, Talbot JH. Alkalosis and the capacity for work. J Biol Chem 1932;97:58–9.

Dodd SL, Brooks E, Powers SK, Tulley R. The effects of caffeine on graded exercise performance in caffeine naive versus habituated subjects. Eur J Appl Physiol 1991;62:424–9.

Doherty M, Smith PM. Effects of caffeine ingestion on exercise testing. Int J Sport Nutr Exerc Metab 2004;14:626–46.

Doherty M, Smith PM. Effects of caffeine ingestion on rating of perceived exertion during and after exercise: a meta-analysis. Scand J Med Sci Sports 2005;15:69–78.

Dowling EA, Redondo DR, Branch JD, Jones SGM, Williams MH. Effect of *Eleutherococcus senticosus* on submaximal and maximal exercise performance. Med Sci Sports Exerc 1996;28:482–9.

Earnest CP, Morss GM, Wyatt F, Jordan AN, Colson S, Church TS, Fitzgerald Y, Autrey L, Jurca R, Lucia A. Effects of a commercial herbal-based formula on exercise performance in cyclists. Med Sci Sports Exerc 2004;36:504–9.

Engels HJ, Kolokouri I, Cieslak TJ, Wirth JC. Effects of ginseng supplementation on supramaximal exercise performance and short-term recovery. J Strength Cond Res 2001;15:290–5.

Engels HJ, Fahlman MM, Wirth JC. Effects of ginseng on secretory IgA, performance, and recovery from interval exercise. Med Sci Sports Exerc 2003;35:690–6.

Evans GW. The effect of chromium picolinate on insulin controlled parameters in humans. Int J Bio Med Res 1989;11:163–80.

Evans GW. Chromium picolinate is an efficacious and safe supplement (letter). Int J Sport Nutr 1993;3:117–22.

Falk DJ, Heelan KA, Thyfault JP, Koch AJ. Effects of effervescent creatine, ribose, and glutamine supplementation on muscular strength, muscular endurance, and body composition. J Strength Cond Res 2003;17:810–16.

Forsberg AM, Nilsson E, Werneman J, Bergstrom J, Hultman E. Muscle composition in relation to age and sex. Clin Sci 1991;81:249–56.

Fredholm B, Battig K, Holmen J, Nehlig A, Zvartau E. Actions of caffeine in the brain with special reference to factors that contribute to its widespread use. Pharmacol Rev 1999;51:83–133.

Froiland K, Koszewski W, Hingst J, Kopecky L. Nutritional supplement use among college athletes and their sources of information. Int J Sport Nutr Exerc Metab 2004;14:104–20.

Gaffney BT, Hugel HM, Rich PA. The effects of *Eleutherococcus senticosus* and *Panax* ginseng on steroidal hormone indices of stress and lymphocyte subset numbers in endurance athletes. Life Sci 2001;70:431–42.

Gallagher PM, Carrithers JA, Godard MP, Schulze KE, Trappe SW. Beta-hydroxy-beta-methyl-butyrate ingestion, Part II: effects on hematology, hepatic and renal function. Med Sci Sports Exerc 2000a;32:2116–19.

Gallagher PM, Carrithers JA, Godard MP, Schulze KE, Trappe SW. Beta-hydroxy-beta-methyl-butyrate ingestion, Part I: effects on strength and fat free mass. Med Sci Sports Exerc 2000b;32:2109–15.

Gao J, Costill DL, Horswill CA, Park SH. Sodium bicarbonate ingestion improves performance in interval swimming. Eur J App Phys 1988;58:171–4.

Geyer H, Parr MK, Mareck U, Reinhart U, Schrader Y, Schanzer W. Analysis of non-hormonal nutritional supplements for anabolic-androgenic steroids—results of an international study. Int J Sports Med 2004;25:124–9.

Goedecke JH, Elmer-English R, Dennis SC, Schloss I, Noakes TD, Lambert EV. Effects of medium-chain triacylglycerol ingested with carbohydrate on metabolism and exercise performance. Int J Sport Nutr 1999;9:35–47.

Goedecke JH, Clark VR, Noakes TD, Lambert EV. The effects of medium-chain triacylglycerol and carbohydrate ingestion on ultra-endurance exercise performance. Int J Sport Nutr Exerc Metab 2005;15:15–28.

Goldfinch J, McNaughton L, Davies P. Induced metabolic alkalosis and its effects on 400-m racing time. Eur J App Phys 1988;57:45–8.

Gorostiaga EM, Maurer CA, Eclache JP. Decrease in respiratory quotient during exercise following L-carnitine supplementation. Int J Sports Med 1989;10:169–74.

Goulet EDB. Assessment of the effects of *Eleutherococcus senticosus* on endurance performance. Int J Sport Nutr Exerc Metab 2005;15:75–83.

Graham TE, Spriet LL. Performance and metabolic responses to a high caffeine dose during prolonged exercise. J Appl Physiol 1991;71:2292–8.

Graham TE, Spriet LL. Metabolic, catecholamine, and exercise performance responses to various doses of caffeine. J Appl Physiol 1995;78:867–74.

Graham TE, Hibbert E, Sathasivam P. Metabolic and exercise endurance effects of coffee and caffeine ingestion. J Appl Physiol 1998;85:883–9.

Graham TE. Caffeine and exercise: metabolism, endurance and performance. Sports Med 2001a;31:765–807.

Graham TE. Caffeine, coffee and ephedrine: impact on exercise performance and metabolism. Can J Appl Physiol 2001b;26:S103–9.

Green AL, Hultman E, Macdonald IA, Sewell DA, Greenhaff PL. Carbohydrate ingestion augments skeletal muscle creatine accumulation during supplementation in man. Am J Physiol Endocrinol Metab 1996a;271:E812–26.

Green AL, Simpson EJ, Littlewood JJ, MacDonald IA, Greenhaff PL. Carbohydrate ingestion augments creatine retention during creatine feeding in humans. Acta Physiol Scand 1996b;158:195–202.

Green AL, MacDonald IA, Greenhaff PL. The effects of creatine and carbohydrate on whole body creatine retention in vegetarians. Proc Nutr Soc 1997;56:81A.

Greenhaff PL, Bodin K, Soderlund K, Hultman E. Effect of oral creatine supplementation on skeletal phosphocreatine resynthesis. Am J Phys Endocrin Metab 1994;266:E725–30.

Greenhaff PL. Creatine. In: Maughan RJ, ed. Nutrition in sport. Oxford: Blackwell Science, 2000:367–78.

Greenhaff PL. The creatine-phosphocreatine system: there's more than one song in its repertoire. J Physiol (Lond) 2001;537:657.

Greenwood M, Kreider RB, Melton C, Rasmussen C, Lancaster S, Cantler E, Milnor P, Almada A. Creatine supplementation during college football training does not increase the incidence of cramping or injury. Mol and Cell Biochem 2003;244:83–8.

Greenwood M, Kreider RB, Greenwood L, Byars A. Cramping and injury incidence in collegiate football players are reduced by creatine supplementation. J Ath Train 2004;38:216–19.

Greig C, Finch KM, Jones DA, Cooper M, Sargeant AJ, Forte CA. The effect of oral supplementation with L-carnitine on maximum and submaximum exercise capacity. Eur J App Phys 1987;56:457–60.

Grunewald KK, Bailey RS. Commercially marketed supplements for bodybuilding athletes. Sports Med 1993;15:90–103.

Gurley BJ, Wang P, Gardner SF. Ephedrine-type alkaloid content of nutritional supplements containing *Ephedra sinica* (Ma Huang) as determined by high performance liquid chromatography. J Pharm Sc 1998;87:1547–53.

Hahm H, Kujawa J, Ausberger L. Comparison of melatonin products against USP's nutritional supplements standards and other criteria. J Am Pharm Assoc (Wash) 1999;39:27–31.

Hallmark MA, Reynolds TH, deSouza CA, Dotson CO, Anderson RA, Rogers MA. Effects of chromium and resistive training on muscle strength and body composition. Med Sci Sports Exerc 1996;28:139–44.

Harris RC, Soderlund K, Hultman E. Elevation of creatine in resting and exercised muscle of normal subjects by creatine supplementation. Clin Sci 1992;83:367–74.

Hasten DL, Rome EP, Franks BD, Hegsted M. Effects of chromium picolinate on beginning weight training students. Int J Sport Nutr 1992;2:343–50.

Haub MD, Potteiger JA, Nau KL, Webster MJ, Zebas CJ. Acute L-glutamine ingestion does not improve maximal effort exercise. J Sports Med Phys Fitness 1998;38:240–4.

Heigenhauser GJF, Jones NL. Bicarbonate loading. In: Lamb DR and Williams MH, eds. Perspectives in exercise science and sports medicine. Dubuque, IN: Brown & Benchmark, 1991:183–212.

Heinonen OJ. Carnitine and physical exercise. Sports Med 1996;22:109–32.

Hellsten Y, Skadhauge L, Bangsbo J. Effect of ribose supplementation on resynthesis of adenine nucleotides after intense training in humans. Am J Physiol Reg 2004;286:R182–8.

Hespel P, Op 't Eijnde B, Derave W, Richter EA. Creatine supplementation: exploring the role of the creatine kinase/phosphocreatine system in the human muscle. Can J Appl Physiol 2001; 26:S79–102.

Hitchins S, Martin DT, Burke L, Yates K, Fallon K, Hahn A, Dobson GP. Glycerol hyperhydration improves cycle time trial performance in hot humid conditions. Eur J App Phys 1999;80: 494–501.

Hoffman JR, Cooper J, Wendell M, Im J, Kang J. Effects of beta-hydroxy-beta-methylbutyrate on power performance and indices of muscle damage and stress during high-intensity training. J Strength Cond Res 2004;18:747–52.

Hofman Z, Smeets R, Verlaan G, van der Lugt R, Verstappen PA. The effect of bovine colostrum supplementation on exercise performance in elite field hockey players. Int J Sport Nutr Exerc Metab 2002;12:461–9.

Hopkins WG, Hawley JA, Burke LM. Design and analysis of research on sport performance enhancement. Med Sci Sports Exerc 1999;31:472–85.

Hsu CC, Ho MC, Lin LC, Su B, Hsu MC. American ginseng supplementation attenuates creatine kinase level induced by submaximal exercise in human beings. World J Gastroenterol 2005;11:5327–31.

Hultman E, Soderlund K, Timmons JA, Cederblad G, Greenhaff PL. Muscle creatine loading in men. J Appl Physiol 1996;81:232–7.

Hunter AM, St Clair Gibson A, Collins M, Lambert M, Noakes TD. Caffeine ingestion does not alter performance during a 100-km cycling time-trial performance. Int J Sport Nutr Exerc Metab 2002;12:438–52.

Inder WJ, Swanney MP, Donald RA, Prickett TCR, Hellemans J. The effect of glycerol and desmopressin on exercise performance and hydration in triathletes. Med Sci Sports Exerc 1998;30:1263–9.

Ivy JL, Costill DL, Fink WJ, Lower RW. Influence of caffeine and carbohydrate feedings on endurance performance. Med Sci Sports Exerc 1979;11:6–11.

Jeukendrup AE, Saris WHM, Schrauwen P, Brouns F, Wagenmakers AJM. Metabolic availability of medium-chain triglycerides coingested with carbohydrates during prolonged exercise. J Appl Physiol 1995;79:756–62.

Jeukendrup AE, Thielen JJHC, Wagenmakers AJM, Brouns F, Saris WHM. Effect of medium-chain triacylglycerol and carbohydrate ingestion during exercise on substrate utilization and subsequent cycling performance. Am J Clin Nutr 1998;67:397–404.

Jowko E, Ostaszewski P, Jank M, Sacharuk J, Zieniewicz A, Wilczak J, Nissen S. Creatine and beta-hydroxy-beta-methylbutyrate (HMB) additively increase lean body mass and muscle strength during a weight-training program. Nutrition 2001;17:558–66.

Juhn MS, Tarnopolsky M. Potential side-effects of oral creatine supplementation: a critical review. Clin J Sport Med 1998a;8:298–304.

Juhn MS, Tarnopolsky M. Oral creatine supplementation and athletic performance: a critical review. Clin J Sport Med 1998b;8:286–97.

Knitter AE, Panton L, Rathmacher JA, Petersen A, Sharp R. Effects of beta-hydroxy-beta-methylbutyrate on muscle damage after a prolonged run. J Appl Physiol 2000;89:1340–4.

Kovacs EMR, Stegen JHCH, Brouns F. Effect of caffeinated drinks on substrate metabolism, caffeine excretion, and performance. J Appl Physiol 1998;85:709–15.

Kozyrskyj A. Herbal products in Canada. How safe are they? Can Fam Physician 1997;43:697–702.

Kraemer WJ, Volek JS. Creatine supplementation: its role in human performance. Clin Sports Med 1999;18:651–66.

Kreider RB, Ferreira M, Wilson M, Almada AL. Effects of calcium β-hydroxy-β-methylbutyrate (HMB) supplementation during resistance-training on markers of catabolism, body composition and strength. Int J Sports Med 1999;20:503–9.

Kreider RB, Melton C, Greenwood M, Rasmussen CJ, Lundberg J, Earnest C, Almada AL. Effects of oral D-ribose supplementation on anaerobic capacity and selected metabolic markers in healthy males. Int J Sport Nutr Exerc Metab 2003a;13:76–86.

Kreider RB, Melton C, Rasmussen CJ, Greenwood M, Lancaster S, Cantler EC, Milnor P, Almada AL. Long-term creatine supplementation does not significantly affect clinical markers of health in athletes. Mol and Cell Biochem 2003b;244:95–104.

Krumbach CJ, Ellis DR, Driskell JA. A report of vitamin and mineral supplement use among university athletes in a Division I institution. Int J Sport Nutr 1999;9:416–25.

Kuipers H, Van Breda E, Verlaan G, Smeets R. Effects of oral bovine colostrum supplementation on serum insulin-like growth factor 1 levels. Nutrition 2002;18:566–7.

Laaksonen R, Fogelholm M, Himberg JJ, Laakso J, Salorinne Y. Ubiquinone supplementation and exercise capacity in trained young and older men. Eur J App Phys 1995;72:95–100.

Latzka WA, Sawka MN, Montain SJ, Skrinar GS, Fielding RA, Matott RP, Pandolf KB. Hyperhydration: tolerance and cardiovascular effects during uncompensable exercise-heat stress. J Appl Physiol 1998;84:1858–64.

Lehmkuhl MJ, Malone M, Justice B, Trone G, Pistilli EE, Vinci D, Haff EE, Kilgore JL, Haff GG. The effects of 8 weeks of creatine monohydrate and glutamine supplementation on body composition and performance measures. J Strength Cond Res 2003;17:425–38.

Levafi RG, Anderson RA, Keith RE, Wilson GD, McMillan JL, Stone MH. Efficacy of chromium supplementation in athletes: emphasis on anabolism. Int J Sport Nutr 1992;2:111–22.
Levafi RG. Response to GW Evans. Int J Sport Nutr 1993;3:120–1.
Liang MT, Podolka TD, Chuang WJ. *Panax notoginseng* supplementation enhances physical performance during endurance exercise. J Strength Cond Res 2005;19:108–14.
Linderman J, Fahey TD. Sodium bicarbonate ingestion and exercise performance. Sports Med 1991;11:71–7.
Livolsi JM, Adams GM, Laguna PL. The effect of chromium picolinate on muscular strength and body composition in women athletes. J Strength Cond Res 2001;15:161–6.
Lukaski HC, Bolonchuk WW, Siders WA, Milne DB. Chromium supplementation and resistance training: effects on body composition, strength, and trace element status of men. Am J Clin Nutr 1996;63:954–63.
Malm C, Svensson M, Sjoberg B, Ekblom B, Sjodin B. Supplementation with ubiquinone-10 causes cellular damage during intense exercise. Acta Physiol Scand 1996;157:511–12.
Malm C, Svensson M, Ekblom B, Sjodin B. Effects of ubiquinone-10 supplementation and high intensity training on physical performance in humans. Acta Physiol Scand 1997;161:379–84.
Marconi C, Sassi G, Carpinelli A, Cerretelli P. Effects of L-carnitine loading on the aerobic and anaerobic performance of endurance athletes. Eur J App Phys 1985;54:131–5.
Massad SJ, Shier NW, Koceja DM, Ellis NT. High school athletes and nutritional supplements: a study of knowledge and use. Int J Sport Nutr 1995;5:232–45.
Matson LG, Tran ZT. Effects of sodium bicarbonate ingestion on anaerobic performance: a meta-analytic review. Int J Sport Nutr 1993;3:2–28.
Maughan RJ. Contamination of dietary supplements and positive drug tests in sport. J Sports Sci 2005:23;883–9.
Mayhew DL, Mayhew JL, Ware JS. Effects of long-term creatine supplementation on liver and kidney functions in American college football players. Int J Sport Nutr Exerc Metab 2002;12:453–60.
McLellan TM, Bell DG. The impact of prior coffee consumption on the subsequent ergogenic effect of anhydrous caffeine. Int J Sport Nutr Exerc Metab 2004;14:698–708.
McNaughton L, Egan G, Caelli G. A comparison of Chinese and Russian ginseng as ergogenic aids to improve various facets of physical fitness. Int Clin Nutr Rev 1989;9:32–5.
McNaughton LR, Cedaro R. The effect of sodium bicarbonate on rowing ergometer performance in elite rowers. Aust J Sci Med Sport 1991;23:66–9.
McNaughton L, Backx K, Palmer G, Strange N. Effects of chronic bicarbonate ingestion on the performance of high-intensity work. Eur J App Phys 1999a;80:333–6.
McNaughton L, Dalton B, Palmer G. Sodium bicarbonate can be used as an ergogenic aid in high-intensity, competitive cycle ergometry of 1 h duration. Eur J App Phys 1999b;80:64–9.
McNaughton L, Dalton B, Tarr J. Inosine supplementation has no effect on aerobic or anaerobic cycling performance. Int J Sport Nutr 1999c;9:333–44.
McNaughton LR. Bicarbonate and citrate. In: Maughan RJ, ed. Nutrition in sport. Oxford: Blackwell Science, 2000:393–404.
McNaughton L, Thompson D. Acute versus chronic sodium bicarbonate ingestion and anaerobic work and power output. J Sports Med Phys Fitness 2001;41:456–62.
Mero A, Mikkulainen H, Riski J, Pakkanen R, Aalto J, Takala T. Effects of bovine colostrum supplement on serum IGF-1, IgG, hormone and saliva IgA during training. J Appl Physiol 1997;83:1144–51.

Mero A, Kahkonen J, Nykanen T, Parviainen T, Jokinen I, Takala T, Nikula T, Rasi S, Leppaluoto J. IGF-I, IgA, and IgG responses to bovine colostrum supplementation during training. J Appl Physiol 2002;93:732–9.

Mero AA, Keskinen KL, Malvela MT, Sallinen JM. Combined creatine and sodium bicarbonate supplementation enhances interval swimming. J Strength Cond Res 2004;18:306–10.

Montfoort MCE, Van Dieren L, Hopkins WG, Shearman JP. Effects of ingestion of bicarbonate, citrate, lactate, and chloride on sprint running. Med Sci Sports Exerc 2004;36:1239–43.

Montner P, Stark DM, Riedesel ML, Murata G, Robergs R, Timms M, Chick TW. Pre-exercise glycerol hydration improves cycling endurance time. Int J Sports Med 1996;17:27–33.

Morris AC, Jacobs I, McLellan TM, Klugerman A, Wang LCH, Zamecnik J. No ergogenic effects of ginseng ingestion. Int J Sport Nutr 1996;6:263–71.

Nielsen AN, Mizuno M, Ratkevicius A, Mohr T, Rohde M, Mortensen SA, Quistorff B. No effect of antioxidant supplementation in triathletes on maximal oxygen uptake, 31P-NMRS detected muscle energy metabolism and muscle fatigue. Int J Sports Med 1999;20:154–8.

Nissen S, Sharp R, Ray M, Rathmacher JA, Rice D, Fuller JC, Connelly AS, Abumrad N. Effect of leucine metabolite β-hydroxy-β-methylbutyrate on muscle metabolism during resistance-exercise training. J Appl Physiol 1996;81:2095–104.

Nissen SL, Sharp RL. Effect of dietary supplements on lean mass and strength gains with resistance exercise: a meta-analysis. J Appl Physiol 2003;94:651–9.

O'Connor DM, Crowe MJ. Effects of beta-hydroxy-beta-methylbutyrate and creatine monohydrate on aerobic and anaerobic capacity of highly trained athletes. J Sports Med Phys Fitness 2003;41:64–8.

Oopik V, Saaremets I, Medijainen L, Karelson K, Janson T, Timpmann S. Effects of sodium citrate ingestion before exercise on endurance performance in well-trained runners. Br J Sports Med 2003;37:485–9.

Op 't Eijnde B, van Leemputte M, Brouns F, Van Der Vusse GJ, Larbarque V, Ramaekers M, van Schuylenberg R, Verbessem P, Wijnen H, Hespel P. No effects of oral ribose supplementation on repeated maximal exercise and ATP resynthesis. J Appl Physiol 2001;91:2274–81.

Paddon-Jones D, Keech A, Jenkins D. Short-term B-hydroxy-B-methylbutyrate supplementation does not reduce symptoms of eccentric muscle damage. Int J Sport Nutr Exerc Metab 2001;11:442–50.

Panton LB, Rathmacher JA, Baier S, Nissen S. Nutritional supplementation of the leucine metabolite beta-hydroxy-beta-methylbutyrate (HMB) during resistance training. Nutrition 2000;16:734–9.

Parasrampuria J, Schwartz K, Petesch R. Quality control of dehydroepiandrosterone dietary supplement products. J Am Med Assoc 1998;280:1565.

Parcell AC, Smith JM, Schulthies SS, Myrer JW, Fellingham G. *Cordyceps sinensis* (CordyMax Cs-4) supplementation does not improve endurance exercise performance. Int J Sport Nutr Exerc Metab 2004;14:236–42.

Pasman WJ, van Baak MA, Jeukendrup AE, de Haan A. The effect of different dosages of caffeine on endurance performance time. Int J Sports Med 1995;16:225–30.

Perharic L, Shaw D, Collbridge M, House I, Leon C, Murray V. Toxicological problems resulting from exposure to traditional remedies and food supplements. Drug Saf 1994;11:284–94.

Perkins R, Williams MH. Effect of caffeine upon maximal muscular endurance of females. Med Sci Sports Exerc 1975;7:221–4.

Pieralisi G, Ripari P, Vecchiet L. Effects of standardised ginseng extract combined with dimethylaminoethanol bitartrate, vitamins, minerals and trace elements on physical performance during exercise. Clin Therapeut 1991;12:373–82.

Pierce EF, Eastman NW, Hammer WH, Lynn TD. Effect of induced alkalosis on swimming time trials. J Sports Sci 1992:255–9.

Poortmans JR, Auquier H, Renaut V, Durussel A, Saugy M, Brisson GR. Effect of short-term creatine supplementation on renal responses in men. Eur J App Phys 1997;76:566–7.

Potteiger JA, Nickel GL, Webster MJ, Haub MD, Palmer RJ. Sodium citrate ingestion enhances 30 km cycling performance. Int J Sports Med 1996a;17:7–11.

Potteiger JA, Webster MJ, Nickel GK, Haub MD, Palmer RJ. The effects of buffer ingestion on metabolic factors related to distance running performance. Eur J App Phys 1996b;72:365–71.

Price M, Moss P, Rance S. Effects of sodium bicarbonate ingestion on prolonged intermittent exercise. Med Sci Sports Exerc 2003;38:1303–8.

Ransone J, Neighbours K, Lefavi R, Chromiak J. The effect of B-hydroxy-B-methylbutyrate on muscular strength and body composition in collegiate football players. J Strength Cond Res 2003;17:34–9.

Rawson ES, Volek JS. Effects of creatine supplementation and resistance training on muscle strength and weightlifting performance. J Strength Cond Res 2003;17:822–31.

Rivers W, Webber H. The action of caffeine on the capacity for muscular work. J Physiol 1907;36:33–47.

Robergs RA, Griffin SE. Glycerol: biochemistry, pharmacokinetics and clinical and practical applications. Sports Med 1998;26:145–67.

Roufs JB. Review of L-tryptophan and eosinophilia-myalgia syndrome. J Am Diet Assoc 1992;92:844–50.

Rowbottom DG, Keast D, Morton AR. The emerging role of glutamine as an indicator of exercise stress and overtraining. Sports Med 1996;21:80–97.

Sahlin K. Metabolic factors in fatigue. Sports Med 1992;13:99–107.

Schabort EJ, Wilson G, Noakes TD. Dose-related elevations in venous pH with citrate ingestion do not alter 40-km cycling time-trial performance. Eur J App Phys 2000;83:320–7.

Shave R, Whyte G, Siemann A, Doggart L. The effects of sodium citrate ingestion on 3,000-metre time-trial performance. J Strength Cond Res 2001;15:230–4.

Shaw D, Leon C, Kolev S, Murray V. Traditional remedies and food supplements. A 5-year toxicological study (1991–1995). Drug Saf 1997;17:342–56.

Siliprandi N, Di Lisa F, Pieralisi G, Ripari P, Maccari F, Menabo R, Giamberardino MA, Vecchiet L. Metabolic changes induced by maximal exercise in human subjects following L-carnitine administration. Biochim Biophys Acta 1990;1034:17–21.

Slater GJ, Jenkins D. B-hydroxy-B-methylbutyrate (HMB) supplementation and the promotion of muscle growth and strength. Sports Med 2000;30:105–16.

Slater G, Jenkins D, Logan P, Lee H, Vukovich M, Rathmacher JA, Hahn AG. B-hydroxy-B-methylbutyrate (HMB) supplementation does not affect changes in strength or body composition during resistance training in trained men. Int J Sport Nutr Exerc Metab 2001;11:384–96.

Snider IP, Bazzarre TL, Murdoch SD, Goldfarb A. Effects of coenzyme athletic performance system as an ergogenic aid on endurance performance to exhaustion. Int J Sport Nutr 1992;2: 272–86.

Spriet LL. Ergogenic aids: recent advances and retreats. IN: Lamb DR, Murray R, eds. Perspectives in exercise science and sports medicine. Carmel, IN: Cooper, 1997:185–238.

Starling RD, Trappe TA, Short KR, Sheffield-Moore M, Joszi AC, Fink WJ, Costill DL. Effect of inosine supplementation on aerobic and anaerobic cycling performance. Med Sci Sports Exerc 1996;28:1193–8.

Stephens TJ, McKenna MJ, Canny BJ, Snow RJ, McConell GK. Effect of sodium bicarbonate on muscle metabolism during intense endurance cycling. Med Sci Sports Exerc 2002;34:614–21.

Stoecker BJ. Chromium. In: Ziegler EE, Filer LJ, eds. Present knowledge in nutrition, 7th edn. Washington: ILSI Press, 1996:344–52.

Svensson M, Malm C, Tonkonogi M, Ekblom B, Sjodin B, Sahlin K. Effect of Q10 supplementation on tissue Q10 levels and adenine nucleotide catabolism during high-intensity exercise. Int J Sport Nutr 1999;9:166–80.

Tarnopolsky MA. Caffeine and endurance performance. Sports Med 1994;18:109–25.

Thomson JS. Beta-hydroxy-Beta-methylbutyrate (HMB) supplementation of resistance trained men. Asia Pac J Clin Nutr 2004;13:S59.

Tiryaki GR, Atterbom HA. The effects of sodium bicarbonate and sodium citrate on 600 m running time of trained females. J Sports Med Phys Fitness 1995;35:194–8.

Trappe SW, Costill DL, Goodpaster B, Vukovich MD, Fink WJ. The effects of L-carnitine supplementation on performance during interval swimming. Int J Sports Med 1994;15:181–5.

Trice I, Haymes EM. Effects of caffeine ingestion on exercise-induced changes during high-intensity intermittent exercise. Int J Sport Nutr 1995;5:37–44.

Van Gammeren D, Falk D, Antonio J. The effects of four weeks of ribose supplementation on body composition and exercise performance in healthy, young, male recreational body builders: a double-blind, placebo-controlled trial. Cur Therapeut Res 2002;63:486–95.

Van Zyl CG, Lambert EV, Hawley JA, Noakes TD, Dennis SC. The effect of medium-chain triglyceride ingestion on fuel metabolism and cycling performance. J Appl Physiol 1996; 80:2217–25.

Vanakoski J, Kosunen V, Merirrine E, Seppala T. Creatine and caffeine in anaerobic and aerobic exercise: effects of physical performance and pharmacokinetic considerations. Int J Clin Pharmac Therapeut 1998;36:258–63.

Vecchiet L, Di Lisa F, Pieralisi G, Ripari P, Menabo R, Giamberardino MA, Siliprandi N. Influence of L-carnitine administration on maximal physical exercise. Eur J App Phys 1990;61:486–90.

Vistisen B, Nybo L, Xuebing X, Hoy CE, Kiens B. Minor amounts of plasma medium-chain fatty acids and no improved time trial performance after consuming lipids. J Appl Physiol 2003; 95:2434–43.

Vukovich MD, Costill DL, Fink WJ. Carnitine supplementation: effect on muscle carnitine and glycogen content during exercise. Med Sci Sports Exerc 1994;26:1122–9.

Vukovich MD, Dreifort GD. Effect of B-hydroxy-B-methylbutyrate on the onset of blood lactate accumulation and $VO_{2\ peak}$ in endurance-trained cyclists. J Strength Cond Res 2001;15:491–7.

Wagenmakers AJM. L-carnitine supplementation and performance in man. In: Brouns F, ed. Advances in nutrition and top sport. Basel: Karger, 1991:110–27.

Walker LS, Bemben MG, Bemben DA, Knehans AW. Chromium picolinate effects on body composition and muscular performance in wrestlers. Med Sci Sports Exerc 1998;30:1730–7.

Weston SB, Zhou S, Weatherby RP, Robson SJ. Does exogenous coenzyme Q10 affect aerobic capacity in endurance athletes? Int J Sport Nutr 1997;7:197–206.

Wiles JD, Bird SR, Hopkins J, Riley M. Effect of caffeinated coffee on running speed, respiratory factors, blood lactate and perceived exertion during 1500-m treadmill running. Br J Sports Med 1992;26:116–20.

Wilkes D, Geldhill N, Smyth R. Effect of acute induced metabolic alkalosis on 800-m racing time. Med Sci Sports Exerc 1983;15:277–80.

Williams MH, Kreider RB, Hunter DW, Somma CT, Shall LM, Woodhouse ML, Rokitzki L. Effect of inosine supplementation on 3-mile treadmill run performance and $VO_{2\ peak}$. Med Sci Sports Exerc 1990;22:517–22.

Ylikoski T, Piirainen J, Hanninen O, Penttinen J. The effect of coenzyme Q10 on the exercise performance of cross-country skiers. Mol Aspects Med 1997;18 (Supp):S283–90.

Ziemba AW, Chmura J, Kaciuba-Uscilko H, Nazar K, Wisnik P, Gawronski W. Ginseng treatment improves psychomotor performance at rest and during graded exercise in young athletes. Int J Sport Nutr 1999;9:371–7.