Dietary supplements and sport performance – A comprehensive review

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Abstract

Aim: Comprehensive articles on dietary supplements and their impact on sport performance, which would provide professional and recreational athletes with evidence-based information, are sparse.

Methods: Investigation involved eight different dietary supplements, commonly used among recreational and endurance athletes according to available literature obtained by searching the PubMed database, namely: *Antioxidants, beta-alanine (B-alanine), branched-chain amino acids (BCAAs), caffeine, carbohydrates, creatine, nitric oxide/nitrates, and proteins*. Their mechanisms of action have been briefly presented, along with their potential beneficial and harmful side effects and safety.

Results: i.) *Antioxidants*: A sufficient amount of antioxidants is available in a balanced diet ii.) *B-alanine*: Supplementation is likely to be beneficial in high-intensity exercises. iii.) *BCAAs*: No review articles in English were available iv.) *Caffeine*: Caffeine supplementation is beneficial in endurance exercises v.) *Carbohydrates*: Carbohydrate supplementation is probably beneficial in exercises lasting longer than one hour vi.) *Creatine*: Creatine supplementation is effective in high intensity, short-lasting exercise, while it does not seem to have any ergogenic effect in aerobic exercise. vii.) *Nitric oxide/nitrates*: Nitrate supplementation has a small but significant performance-enhancing effect, most apparently in situations of insufficient perfusion. viii.) *Proteins*: Protein supplementation, in combination with resistance exercise, most likely has beneficial effects on lean body mass and muscle strength.

Conclusion: Most of the analyzed dietary supplements, if used for intended exercise regime, provide a kind of sport performance enhancement. On the other hand, long-term studies about their safety are mostly lacking.

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Abbreviations

BCAAs – branched-chain amino acids

ROS - reactive oxygen species

cAMP - cyclic adenosine monophosphate

C-P - creatine phosphate

NO – nitric oxide

B-alanine – beta-alanine

B-carotene – beta-carotene

Introduction

Professional athletes and amateurs alike are in constant search for new means which would enable them to improve their sport results in shorter time. Among those means, a prominent place belongs to dietary supplements (1). The use of dietary supplements among athletes varies quite substantially (2–5), and can reach numbers as high as 98% (4), with one of the main reasons for their utilization being the improvement in sport performance (2–5).

There are a lot of studies, assessing different dietary supplements and their influence on athletic performance, as well as numerous review articles and meta-analyses evaluating individual supplements or family of supplements (whey proteins, branched-chain amino acids (BCAAs), antioxidants…) with respect to sport performance. Yet, a systematic review of literature that could give an athlete a more comprehensive overview of the vast and diverse field of dietary supplements is lacking.

Review articles and meta-analyses are tools used in science to evaluate evidence and also to make scientific conclusions, since they sum up and critically assess the knowledge about a particular topic that is usually dispersed in the form of original articles. The goal of this paper was to gather currently available and evidence-based information in the form of review articles and/or meta-analyses on most currently used sport performance-enhancing dietary supplements and present them to a reader in an understandable manner, as it has been shown that the acquisition of information about dietary supplements usually does not come from evidence-based source of information, but rather from family members, friends and coaches (6). Accordingly, we have identified the most commonly used performance-enhancing dietary supplements and studied recently published review articles/meta-analyses about those products, with an aim to write a comprehensive overview of dietary supplements that are used for sport performance enhancement.

Methods

PubMed was searched using the search string "(spor*[Title] OR athl*[Title] OR train*[Title]) AND performan*[Title]", to recognize papers that presented any facts connected to enhancing sport performance (different types of dietary supplements, different exercise procedures …) published in the last five years. Analyzing the titles and abstracts of those articles, we identified the most commonly used dietary supplements or groups of dietary supplements associated with enhancing sport performance, and then searched the PubMed library to find review articles/meta-analyses that evaluated each individual dietary supplement or a group of dietary supplements (i.e. string "(carbohy*[Title]) AND (sport*[Title] OR athl*[Title] OR exercis*[Title]) AND (revie*[Title] OR analys*[Title])" was used to find review articles/meta-analyses focusing on carbohydrate supplements used in sports). If a search string returned many review articles/meta-analyses, just the most recent ones were included in the analysis (and reported in the results section). The reference lists of included articles (articles writing about supplements used to enhance sport performance in general, not inside a specific context [i.e. just endurance sports]) were examined to find additional papers.

Results

Eight different dietary supplements or groups of dietary supplements were recognized: i.) antioxidants, ii.) beta-alanine (B-alanine), iii.)

branched-chain amino acids (BCAAs), iv.) caffeine, v.) carbohydrates, vi.) creatine, vii.) nitric oxide (NO)/nitrates and viii.) proteins (whey and other proteins).

3.1. Antioxidants: The review articles/meta-analyses for the effects of antioxidants were found using the search string "antiox*[Title] AND (sport*[Title] OR athl*[Title] OR exercis*[Title]) AND (revie*[Title] OR analys*[Title])" on PubMed. The search returned four articles, one of which was about exercise and pregnancy and was therefore excluded from the analysis. Out of the three that remained, the most recent one (7) was included in the analysis (it was published in 2015; the other two were written in 1999 and 1993, respectively). Another review article, describing vitamin C and its effect on performance, was found while searching through the reference list of the first article and was also included in the analysis.

3.1.1. Mechanism(s) of action: During exercise, the production of reactive oxygen species (ROS) in the skeletal muscle cells increases (8), and this can have damaging effects as ROS can alter cell structure and function, and cause fatigue (9). On the other hand, ROS are speculated to be involved in glycogen resynthesis (10) and also in adaptive responses induced by training (11–14). The use of the adequate amounts of antioxidants can therefore, in theory, optimize the balance between pro and anti-ergogenic effects of ROS and consequently improve performance.

3.1.2. Meta-analysis/revision conclusions: Braakhuis and Hopkins (2015), who analyzed 71 studies examining the impact of various antioxidants (vitamin E, quercetin, resveratrol, beetroot juice, other food derived polyphenols, spirulina and N-acetylcysteine) on performance, concluded that the only antioxidant exerting beneficial acute effects on performance was N-acetylcysteine when injected intravenously, but this route of administration was not recommended (7).

The review of Braakhuis (2012), which considered 11 articles that examined potential effects of vitamin C on sport performance, found that large doses (more than 1 g/day) of vitamin C appeared to reduce the training-induced adaptations by reducing mitochondrial biogenesis or possibly by altering vascular function (15). They also concluded that small doses of vitamin C (approximately 0.2 g/day), provided by five servings of fruit and vegetables per day, may be sufficient to reduce oxidative stress without reaching the threshold that would impair optimal training adaptations. Moreover, a short-term intake (during a period of one to two weeks) of doses greater than 2 g/day seems to be beneficial for athletes during times of increased stress (15).

3.2. B-alanine: The review articles/meta-analyses for the effects of B-alanine were found using the search string "*alanin*[Title] AND (sport*[Title] OR athl*[Title] OR exercis*[Title]) AND (revie*[Title] OR analys*[Title])" on PubMed. The search retrieved two papers. Of the two, the first was a review article written in 2010 (16), and the other one was a meta-analysis conducted in 2012 (17).

3.2.1. Mechanism(s) of action: The effects of B-alanine supplementation can mostly be attributable to an increase in concentration of carnosine (a dipeptide of the amino acids B-alanine and histidine concentrated in muscle and brain tissue) in the skeletal muscle cells, as concentration of B-alanine is thought to be the rate-limiting step in carnosine synthesis (B-alanine and L-histidine [carnosine synthase]) (18–20). Carnosine is speculated to exert buffering (20), antioxidant (21,22) and calcium (Ca^{2+}) regulatory (23,24) effects, that could potentially enhance performance.

3.2.2. Meta-analysis/revision conclusions: The meta-analysis was conducted on 15 papers. Authors concluded that B-alanine supplementation elicited a significant performance-enhancing effect on high-intensity exercise, particularly when exercise lasted between one and four minutes (17). As B-alanine improved predominantly short-lasting anaerobic exercise performance, the authors argue that those data provide further evidence that supplementation of B-alanine increases intramuscular carnosine, which has pH buffering capacity (17).

3.3. *BCAAs*: The review articles/meta-analyses for the effects of BCAAs were found using the search string "(BCAA*[Title] OR branch*[Title]) AND (sport*[Title] OR athl*[Title] OR exercis*[Title]) AND (revie*[Title] OR analys*[Title])" on PubMed. The search retrieved only one review writing about BCAAs and sport performance enhancement (of the nine retrieved by the search, seven were focused on exercise and heart bundle branch blocks, and one was focused on exercise and dissection of the celiac trunk and its branches), As it was written in Spanish, we only assume the proposed mechanisms of *BCAAs* actions.

3.3.1. Mechanism(s) of action: BCAAs are thought to improve performance by diminishing the exercise-induced increase in serotonin, which is thought to be at least partly responsible for the central feeling of fatigue during exercise (25). The exercise-induced increase in serotonin is thought to be induced by an increase of plasma free tryptophan. The concentration of free tryptophan rises during exercise because of increased levels of non-esterified fatty acids, the levels of which are also higher during exercise, and which compete with tryptophan for the same binding sites on albumin (26). The transport of tryptophan across the blood-brain barrier is considered to be the rate-limiting step in the synthesis of serotonin. BCAAs compete with tryptophan in that transport (27).

3.3.2. Meta-analysis/revision conclusions: The search string on PubMed returned only one article, which was in Spanish, so we have no results to report in this section.

3.4. Caffeine: The review articles/meta analyses for the effects of caffeine were found using a search string: "(caffei*[Title]) AND (sport*[Title] OR athl*[Title] OR exercis*[Title]) AND (revie*[Title] OR analysi*[Title])" on pubMed. The search returned seven articles. According to the titles and abstracts of those articles, none was appropriate (some of them were dealing with caffeine and sport performance in a specific setting [endurance performance, high intensity performance, …] others were about pharmacological aspects of caffeine, while another one dated as far back as to the year 1994), so we included a review (28) article in the "similar articles" section in the PubMed.

3.4.1. Mechanism(s) of action: Caffeine exerts various effects on many organ systems. It is an inhibitor of phosphodiesterase (increasing the intracellular cyclic adenosine monophosphate [cAMP]) and also an antagonist of adenosine receptors (its psychoactive effect) (29). Its actions on sport performance are thought to be mediated through its effects on the cardiovascular system (an increase in heart rate and blood pressure), the pulmonary system, the endocrine system and the central nervous system (28).

3.4.2. Meta-analysis/revision conclusions: Authors of the review (28) concluded that caffeine is beneficial in endurance exercise, as it has been shown to increase work output and the time to exhaustion. They also stated that it should be ingested one hour before prolonged endurance events and that, if an athlete decides to stop consuming caffeine before competition with an aim to increase its ergogenic effects during competition (since a person can get habituated), one should reduce caffeine consumption at least one week before the competition, to be completely free from its withdrawal effects. Furthermore, to avoid potential negative symptoms, the dose should gradually be reduced over three to four days, instead of quitting abruptly. Resuming caffeine on the day of competition can again provide the desired ergogenic effects, similarly as it would for a nonuser (28).

They have also concluded that because caffeine increases the plasma concentration of lactate and hence decreases pH, it may be contraindicated in athletes engaging in sprint events which last between 30 seconds and three minutes (28).

3.5. Carbohydrates: The review articles/meta analyses for the effects of carbohydrates were found using a search string "(carbohy*[Title]) AND (sport*[Title] OR athl*[Title] OR exercis*[Title]) AND (revie*[Title] OR analysi*[Title])" on PubMed. The search returned nine articles; yet, only one was appropriate for inclusion in the analysis (30), since others were either about carbohydrates taken in combination with proteins, or about the effects of carbohydrates on lipid metabolism and about different ways of use of carbohydrates (mouth rinse).

3.5.1. Mechanism(s) of action: There are two proposed mechanisms when trying to explain how carbohydrate supplementation during exercise improves performance (30): i.) mental cognitive stimulation of the central nervous system by carbohydrate exposure during exercises of shorter duration (less than one hour - the glycogen stores are not a limiting factor) (31–33) and ii.) a direct exogenous carbohydrate contribution to carbohydrate oxidation during muscle glycogen limiting exercises (duration longer than two hours) (34–36).

3.5.2. *Meta-analysis/revision conclusions:* The revision included 61 different performance studies performed on 679 subjects. Eighty-two percent of the studies showed performance benefit, while 18 % showed no performance improvement compared to placebo (30). Based on the revision of the studies, authors recommend that for exercises of shorter duration (less than one hour) and high intensity, small amounts of liquid carbohydrate solutions provide performance benefit through stimulation of the pleasure and reward center in the brain (30). By increasing the duration of exercise (duration of one to two hours), moderate amounts of carbohydrate supplementation (30-60 g/h) consumed frequently throughout the exercise appear to maximize the performance advantage of carbohydrate supplementation (liquid carbohydrate sources are recommended (30)). With the duration of exercise extending beyond two hours (with concurrently reduced intensity), a greater variety of carbohydrate foods and fluids can be included to meet the high hourly carbohydrate intake recommendations of 40-110 g/h (30).

3.6. Creatine: The review articles/meta analyses for the effects of creatine were found by using a search string: "(creati*[Title]) AND (sport*[Title] OR athl*[Title] OR exercis*[Title]) AND (revie*[Title] OR analysi*[Title])" on PubMed. The search string retrieved seven articles, four of which were appropriate (they were about sport performance in general with regard to creatine use), with the most recent one dating to 2003 (37).

3.6.1. Mechanism of action: Creatine supplementation is thought to increase intramuscular storage of creatine phosphate (C-P), which is responsible for anaerobic ATP resynthesis during high-intensity, short-duration exercises (38,39). Based on the available data, positive correlations between muscle creatine uptake and exercise performance (40) were shown.

3.6.2. *Meta-analysis/revision conclusions:* Based on the available research data, authors concluded that creatine supplementation could increase the skeletal muscle C-P content, which may improve performance involving short periods of extreme exertion , especially during repeated bouts of exercise (37). On the other hand, creatine supplementation did not appear to increase the maximal isometric strength, the rate of maximal force production, or the aerobic exercise performance (37).

3.7. Nitrates: The review articles/meta-analyses for the effects of nitrates were found using a search string: "(nitr*[Title]) AND (sport*[Title] OR athl*[Title] OR exercis*[Title]) AND (revie*[Title] OR analysi*[Title])". The search retrieved five articles: only two (41,42) of them were appropriate (dealing with nitrate supplementation and exercise performance), while others were mainly focused on other issues, such as the effects of exercise and nitrates on vascular endothelial function, the effects of nitrates on exercise-induced bronchospasm, etc.), so the most recent one (42) was analyzed.

3.7.1. Mechanism of action: It is believed that inorganic nitrate can be converted to its antecedents (nitrite and NO), especially in the presence of hypoxia and acidosis (41). NO is thought to exert multiple effects in the body, including its effects on neurotransmission (43), on vascular tone control (44), mitochondrial respiration (45) and skeletal muscle contraction (46), thus its influence on exercise is complex.

3.7.2. *Meta-analysis/revision conclusions:* The authors state that nitrate supplementation has no or little effect on maximal oxygen consumption (V_{O2max}) but it can lower the oxygen deficit of submaximal exercise (that is, improve skeletal muscle efficiency or economy), at least in subjects who are not highly trained (42). This may lead to a small increase in the sustainable power output for a given metabolic rate. They also conclude that at least in situations where some fraction of the working muscle mass may be relatively under-perfused (in hypoxia, during high-intensity exercise in subjects with low aerobic fitness - when their muscles are relatively under-perfused with respect to the heart) (42), nitrate supplementation can speed up the oxygen kinetics and thus have an ergogenic effect. The optimally efficient nitrate dose is likely to vary between subjects but is hypothesized to be generally more pronounced in highly trained individuals (42).

3.8. Proteins (whey): The review articles/meta analyses for the effects of proteins were retrieved using the search string: "(protei*[Title]) AND (sport*[Title] OR athl*[Title] OR exercis*[Title]) AND (revie*[Title] OR analysi*[Title])" on PubMed. The search returned 27 articles, three of which were appropriate for analysis (dealing with protein supplementation and sport performance), and since the most recent one (47) was funded by a commercially orientated consortium, the second most recent one was chosen for analysis (48).

3.8.1. Mechanism(s) of action: Protein balance in the human body depends on protein synthesis and protein degradation. When the synthesis is higher than the breakdown, one will have a positive protein balance, otherwise the protein balance will be negative (49). Amino acid intake (50,51) and resistance exercise training (52–56) have separately been shown to have a positive effect on protein synthesis. Moreover, their combined effect (i.e. ingesting proteins after resistance training) was shown to be greater than just adding two separate effects together (57–59).

3.8.2. Meta-analysis/revision conclusions: The meta-analysis consisted of 22 randomized controlled trials that, in the aggregate, included 680 subjects (48). Authors concluded that dietary protein supplementation represented an effective dietary strategy to augment the adaptive response of skeletal muscle to prolonged resistance-type exercise training in healthy younger (younger than 50) and older (older than 50) adults. Furthermore, in younger adults, protein supplementation during prolonged (more than six weeks) resistance-type exercise training significantly augmented the gains in fat-free mass, type I and II muscle fiber cross-sectional area, and one-repetition maximum leg press strength compared to resistance-type exercise training without a dietary protein-based cointervention (48). The findings in the group of younger adults were evident, despite the fact that, before the intervention, all groups were already consuming a more than adequate dietary protein intake of 1.2 g/kg body weight/day (48). From a practical point of view, it is worth noting that subjects were supplemented with an average of 50 ± 32 g proteins / day (in excess of their normal diet) and, in most cases, the protein supplements were ingested before or immediately after each exercise session.

Discussion

In the era of highly competitive sports, more and more individuals are using performance-enhancing nutritional supplements to enhance not only their sport performance but also their visual appearance and self-confidence. Consumers of those supplements are overwhelmed by the manufacturers' claims of increased strength, weight loss, and improved body definition, but information about the efficacy is rarely acquired or presented in an evidence-based manner (6).

There is a large body of information in the form of original articles and/or review articles and meta-analyses about a particular nutritional supplement, but a more comprehensive overview of the vast and diverse field of dietary supplements is lacking. Keeping that in mind, a review article was written, identifying the common sport performance-enhancing dietary supplements, finding the relevant and recent review articles/meta-analyses about those supplements, and summarizing their findings and conclusions.

Eight dietary supplements/groups of dietary supplements were identified and focused on: antioxidants, Β-alanine, BCAAs, caffeine, carbohydrates, creatine, NO/nitrates and proteins (whey and other proteins).

Regarding antioxidants, of all the tested antioxidants (vitamin E, quercetin, resveratrol, beetroot juice, other food-derived polyphenols, spirulina and N-acetylcysteine), the authors found strong evidence for performance-enhancing effect only for N-acetylcysteine (but with the very impractical administration route, namely i.v.) (7). The authors also speculated that antioxidants could reduce the impairment of performance during tournaments or repeated efforts, presumably by reducing the severity of inflammation (7). Similar speculations were hypothesized in a review about the influence of vitamin C on performance (15), where the authors concluded that the amount obtained in five servings of fruit and vegetables would be sufficient to reduce oxidative stress, and that higher doses might be beneficial only during periods of intensified stress (15). Accordingly, based on the conclusions of those two reviews, the amount of antioxidants we get in a balanced diet is probably sufficient, even for athletes, and thus, the supplementation of antioxidants should be considered only in periods of increased stress (tournaments, world series). The safety of long term antioxidant use should also be taken into account, when considering antioxidant supplementation for enhancing sport performance, since a double-blinded, placebo-controlled study about the use of vitamin A and beta-carotene (Β-carotene) and their effect on lung cancer, the Beta-Carotene and Retinol Efficacy Trial, showed, on 18314 participants, that there was a significantly higher relative risk for lung cancer and lung cancer associated mortality among the patients who were receiving a combination of Β-carotene and vitamin A, compared to placebo (60). The results of this study were concordant with the results of the randomized, double-blinded, placebo-controlled trial conducted on 29133 Finnish smokers, which examined the effects of alpha-tocopherol and/or Β-carotene, and found an eight percent higher overall mortality among patients receiving Β-carotene (compared to the ones who did not receive it) (61). The results of a recently published Cochrane meta-analysis (approximately 300,000 participants) which compared the effects of antioxidant supplements (beta-carotene, vitamin A, vitamin C, vitamin E, and selenium) versus placebo or no intervention, were also worrying as they found that Β-carotene and vitamin E seemed to increase mortality; a similar possibility was suggested for larger doses of vitamin A (62).

As for Β-alanine supplementation, the authors of a meta-analysis conducted in 2012 (17) concluded that Β-alanine supplementation had an ergogenic effect on high intensity exercises lasting between one and four minutes, possibly contributable to pH buffering capacity of intramuscular carnosine, the concentration of which rises with supplementation. The authors of a 2010 review (16) also noted similar observations, concluding that Β-alanine carries potentially beneficial effects in high-intensity exercise including anaerobic sprints and resistance training. Β-alanine supplementation is thus likely to be beneficial in high-intensity exercises. A systematic review from 2014 (63) found similar results regarding performance, indicating that Β-alanine may increase power output and working capacity, decrease the feeling of fatigue and exhaustion, and have positive effects on body composition and carnosine content. In addition, this study concentrated on side effects of Β-alanine supplementation, and found that they were mostly mild, consisting of paraesthesia and/or infrequent mild transient symptoms such as tingling in hands and fingers. The study also stressed the need for more studies dealing with long term effects of Β-alanine supplementation.

The ergogenic effect of caffeine on endurance performance was demonstrated by multiple meta-analyses/review articles which also concluded that in habituated caffeine consumers, the abstinence from caffeine at least seven days before competition would give the greatest chance of optimizing its ergogenic effect (28,64). However, the effect of caffeine on high-intensity performance is not well established, since caffeine increases plasma lactate concentration and hence decreases pH (28). On the other hand, a systematic review (65) of the effect of acute caffeine ingestion on short-term high-intensity exercise performance showed that 11 (of 17) studies revealed significant improvements in team sports exercise and power-based sports after caffeine ingestion, while further six (of 11) studies showed significant benefits for resistance training. Based on the results of the above studies, caffeine supplementation for endurance exercises seems to be beneficial, but when it comes to the effects of caffeine on high-intensity exercise, further investigation is required. Long-term ingestion of moderate doses of coffee (three to four coups [less than 400 mg/day]), is suggested to have mostly beneficial effects and has been shown to be inversely associated with the risk for various diseases (66). Epidemiological data support the view that habitual coffee consumption lowers the risks of Parkinson's and Alzheimer's disease, has a favorable effect on liver function, a possible role in weight loss (66), and also decreases the risk for developing certain types of cancer (endometrial, prostatic, colorectal, liver) (67,68). On the other hand, coffee intake has been associated with bone loss and adverse effects in pregnancy (66). Nevertheless, the growing body of evidence from epidemiological studies supports the notion that moderate coffee consumption exerts mostly beneficial effects on health and reduces mortality (67). Unfortunately, the association does not show causality, so large double-blinded, placebo-controlled studies are needed to clarify the effects of coffee consumption on health per se. Moreover, the effects of coffee consumption are not attributable solely to caffeine (since coffee has more than 1,000 different compounds (66)), while the supplements that are used to increase sport performance use mostly caffeine as an active compound, and lack other compounds found in a cup of coffee. Consequently, to determine the safety of caffeine-containing sport performance-enhancing supplements, additional studies on those supplements should be more thoroughly evaluated before giving adequate evidence-based statements about the safety of those supplements.

Several systematic reviews (30,31) confirmed the efficacy of carbohydrate mouth rinse on exercise performance with activities lasting less than one hour, potentially attributable to activation of pleasure and reward center in the brain (30).

As for ingestion of carbohydrates, a systematic review (69), which included only studies mimicking real life situations (subjects exercising in the postprandial state) and excluding studies that followed rigorous criteria like keeping athletes in a fasted state, concluded that carbohydrate supplementation during exercise bouts of less than 70 minutes is unlikely to be beneficial (69). On the other hand, a beneficial effect of carbohydrate supplementation during exercise lasting more than 70 minutes was confirmed in a systematic review that included all types of studies (those mimicking real life situations and also studies following rigorous inclusion criteria) (30) and also in the review (69) that included just studies mimicking real life situations. The most probable beneficial effect was attributed to the replacement of exhausted glycogen storage (30, 69). Taken together, carbohydrate supplementation is probably beneficial in exercises of longer duration (more than one hour), while in short-lasting exercise (less than one hour), more research is required to determine the efficacy in 'real-life situations mimicking' scenarios.

As for creatine, several review articles/meta-analyses (37,70) showed that it was effective in increasing performance in high-intensity, short-lasting (less than 30 seconds) exercises, and also that the effect of creatine diminished with increasing duration of exercise (70). It seems that creatine does not have any ergogenic effect on aerobic exercise (37). Short-term administration of creatine supplementation seems to be safe, since studies have not found clinically significant deviations from normal values in the renal, hepatic, cardiac, gastrointestinal or muscle function (71,72). In fact, most reports on its potential side effects, such as muscle cramping, gastrointestinal symptoms, changes in renal and hepatic laboratory values, remain anecdotal (72). Studies which would evaluate the safety of long-term creatine supplementation are lacking. A few studies that examined the long-term effect of creatine supplementation on kidney function (73), or on various blood and urinary markers of health (metabolic markers, skeletal muscle and liver enzymes, electrolytes, lipid profile, hematological markers, and lymphocytes) (74), showed no differences between the measured outcomes in the creatine-taking group compared to the control group. Additional studies on larger number of participants are needed to give firm evidence-based conclusions regarding long-term safety of creatine supplements.

Regarding nitrate supplementation, the analyzed review articles/meta-analyses (41,42) have concluded that nitrate supplementation had a small but significant (41) performance-enhancing effect. The effect was most apparent in situations where skeletal muscles were insufficiently perfused, such as during hypoxia, or high-intensity exercise in subjects exhibiting low VO2max, when the contracting muscle is in a disadvantageous position relative to the heart and is relatively under-perfused (42).

A recent study has shown that short-term nitrate supplementation (up to 28 days) was safe, and all hematological safety markers remained in a normal range (75), but long-term studies regarding safety are needed.

The effects of protein supplementation (50 ± 32 g/day [above the usual diet]) were shown to be beneficial in augmenting the gains of fat-free muscle mass, type I and II muscle fiber cross-sectional area, and muscle strength, especially in combination with resistance training of longer duration (more than six weeks) (48). On the other hand, another review (76) showed that for untrained individuals, consuming supplemental proteins most likely had no impact on lean mass and muscle strength during the initial weeks of resistance training. However, as the duration, frequency, and volume of resistance training increase, protein supplementation may promote muscle hypertrophy and enhance gains in muscle strength in both untrained and trained individuals (76). Additionally, a third meta-analysis (47) showed similar beneficial effects of whey protein consumption on body composition parameters, which were most pronounced with resistance training exercise. We may conclude that protein supplementation, in combination with resistance exercise of longer duration (more than six weeks), most likely has beneficial effects on body composition (lean body mass) and possibly also on muscle strength.

Mounting evidence suggests that protein intake in excess of two to three times the recommended daily allowance may have harmful effects on the homeostasis of calcium and, possibly, bone mass, particularly for proteins from primarily animal sources and in situations where potential loss of bone calcium has not been minimized by additionally supplementing other dietary elements such as potassium or bicarbonate. Additional potential harmful effects of high-protein intake on kidneys, the cardiovascular system, and carcinogenesis have been suggested but available data remain inconclusive, and further research is necessary (77).

Conclusion

Most of the revised dietary supplements, if used for the intended exercise regime, provide some sort of sport performance enhancement. Sport performance enhancement can be a clear-cut one, or it can be observed only in strict laboratory conditions, it may involve unusual routes of administration or may only be successful in a subset of people. Nevertheless, at least in professional sport, where milliseconds decide between success and failure, the competitive edge that dietary supplements can bring, can give an athlete an advantage to succeed. On the other hand, the safety of long-term supplementation, being another and even more important aspect, should also be taken into account when considering whether or not performance-enhancing supplements should be encouraged and consumed. Unfortunately, these kinds of studies, dealing with long-term safety of the supplements, are mostly lacking.

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