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INVITED REVIEW

Creatine supplementation in exercise, sport, and medicine

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ABSTRACT

Creatine has become one of the most popular nutritional ergogenic aids for athletes. Studies have consistently indicated that creatine supplementation increases muscle creatine and phosphocreatine concentrations by approximately 15-40%, enhances anaerobic exercise capacity, and increases training volume leading to greater gains in strength, power, and muscle mass. In addition, a number of potential therapeutic benefits have been reported in clinical populations. Consequently, creatine supplementation is not only a popular dietary strategy used to optimize training and performance of athletes but also has increasing become a nutritional strategy to promote general health and/or provide therapeutic benefits to clinical populations. The purpose of this review is to provide an update to the current literature regarding the potential role that creatine supplementation may play in exercise, sport, and medicine.

Keywords: ergogenic aids, performance enhancement, sport nutrition, athletes, muscular strength, muscle power, phosphagen

BACKGROUND

Creatine is a naturally occurring compound that is a member of the guanidine phosphagen family [1]. Creatine is primarily found in the skeletal muscle (~95%) with small amounts found in the brain and testes (~5%). About two thirds of creatine in the muscle is stored as phosphocreatine (PCr) while the remaining amount of creatine is stored as free creatine. The total creatine pool (PCr + free creatine) in the muscle averages about 120 grams for a 70 kg individual [2]. However, the upper limit of creatine storage appears to be about 160 grams of creatine in most individuals [2-4]. About 1-2% of the creatine in the muscle is degraded into creatinine and excreted in the urine per day. Therefore, the body needs to replenish about 1-3 grams of creatine per day to maintain creatine stores. About half of the daily need for creatine is obtained from the diet. For example, there is about 1-2 grams of creatine in a pound of uncooked beef and salmon [5]. The remaining amount of creatine is synthesized from arginine, glycine, and methionine (see Fig. 1) [6]. Vegetarians have been reported to have muscle creatine stores in the 90-110 gram range [7]. Additionally, some people have been found to have creatine synthesis deficiencies and therefore must depend on dietary creatine intake in order to maintain normal muscle and brain concentrations of creatine and phosphocreatine [8].

The primary metabolic role of creatine (Cr) is to combine with a phosphoryl group (Pi) to form PCr through the enzymatic reaction of creatine kinase (CK). Wallimann and colleagues [9-12] suggested that the pleiotropic effects of Cr are mostly related to the functions of CK and PCr (i.e., CK/PCr system). As adenosine triphosphate (ATP) is degraded into adenosine diphosphate (ADP) and Pi to provide

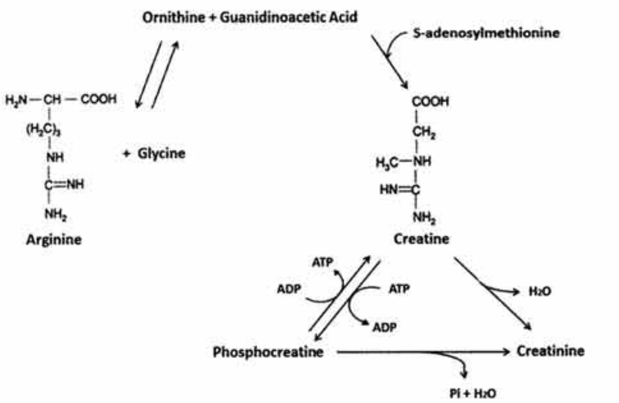

Fig. 1. Chemical structure and biochemical pathway for creatine synthesis. Adapted from Padden-Jones *et al.* [6]

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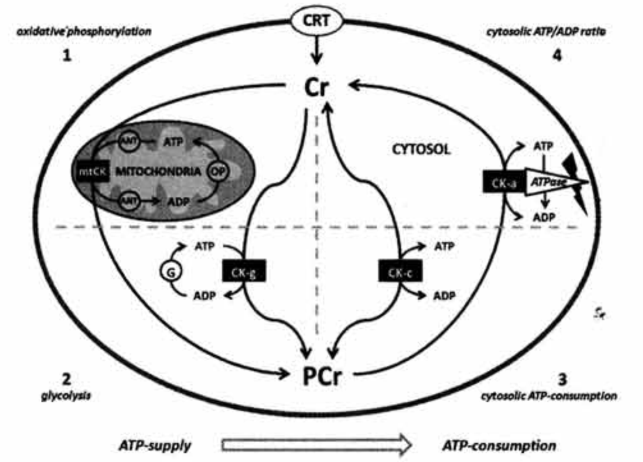

Fig. 2. Proposed creatine kinase / phosphocreatine (CK/PCr) energy shuttle. CRT = creatine transporter; ANT = adenine nucleotide translocator; ATP = adenine triphosphate; ADP = adenine diphosphate; OP = oxidative phosphorylation; mtCK = mitochondrial creatine kinase; G = glycolysis; CK-g = creatine kinase associated with glycolytic enzymes; CK-c = cytosolic creatine kinase; CK-a = creatine kinase associated with subcellular sites of ATP utilization; 1-4 sites of CK/ATP interaction. Adapted from Wallimann *et al* [10].

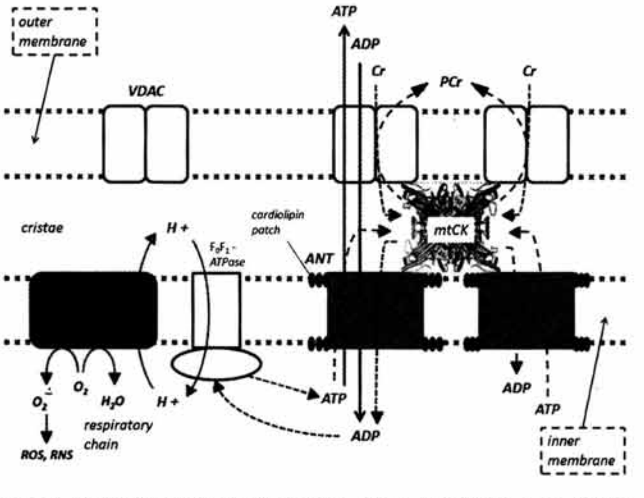

Fig. 3. Role of mitochondrial creatine kinase (mtCK) in high energy metabolite transport and cellular respiration. VDAC = voltage-dependent anion channel; ROS = reactive oxygen species; RNS = reactive nitrogen species; ANT = adenine nucleotide translocator; ATP = adenine triphosphate; ADP = adenine diphosphate; Cr = creatine; and, PCr = phosphocreatine. Adapted from Wallimann *et al* [10].

free energy for metabolic activity, the free energy released from the hydrolysis of PCr into Cr + Pi can be used as a buffer to resynthesize ATP. This helps maintain ATP availability particularly during maximal effort anaerobic sprint-type exercise. The CK/PCr system also plays an important role in shuttling intracellular energy from the mitochondria into the cytosol (see Fig. 2). The CK/PCr energy shuttle connects sites of ATP production (glycolysis and mitochondrial oxidative phosphorylation) with subcellular sites of ATP utilization (ATPases) [10]. In this regard, creatine enters the cytosol through a creatine transporter (CRT). In the cytosol, creatine and associated cytosolic and glycolytic CK isoforms help maintain glycolytic ATP levels, the cytosolic ATP/ADP ratio, and cytosolic ATP-consumption [10]. Additionally, creatine diffuses into the mitochondria and couples with ATP produced from oxidative phosphorylation and the adenine nucleotide translocator (ANT) via mitochondrial CK (see Fig. 3). ATP and PCr can then diffuse back into the cytosol and help buffer energy needs. This coupling also reduces formation of reactive oxygen species (ROS) and can therefore act as a direct and/or indirect anti-oxidant. The CK/PCr energy shuttle thereby connects sites of ATP production (glycolysis and mitochondrial oxidative phosphorylation) with subcellular sites of ATP utilization (ATPases) in order to fuel energy metabolism [10]. In this way, the CK/PCr system thereby serves as an important regulator of metabolism which may help explain the ergogenic and potential health benefits of creatine supplementation [1,10,13].

Supplementation protocols

Dietary supplementation of creatine serves to increase muscle creatine and PCr by 10-40% [2,14]. The most common way to increase muscle creatine stores is to "load" creatine by taking 5 grams of creatine monohydrate four times daily for 5-7 days. This equates to a relative intake of about 0.3 grams/kg/day. Once muscle creatine stores are saturated, studies indicate that creatine stores can be maintained by ingesting 3-5 grams of creatine monohydrate per day (i.e., 0.03-0.05 grams/kg/day). More recent studies indicate that in may only take 2-3 days to maximize creatine stores particularly if creatine is ingested with carbohydrate and/or protein [3,4, 15-17]. An alternative supplementation protocol is to ingest 3 grams/day of creatine monohydrate for 28 days [2]. Studies show that this method can increase muscle concentrations of creatine as effectively as creatine loading techniques. However, this method would only result in a gradual increase in muscle creatine content compared to the more rapid loading method. Willoughby and colleagues [18,19] reported that 6 grams/day of creatine during 12-weeks of training was sufficient to promote positive changes in strength and muscle mass. Some athletes also cycle on and off creatine by taking loading doses of creatine monohydrate for 3-5 days every 3-4 weeks during training. Theoretically, since it takes 4-6 weeks for elevated creatine stores to return to baseline [2,20], this protocol would be effective in increasing and maintaining elevated creatine stores over time [21].

BIOAVAILABILITY

The uptake of creatine involves the absorption of creatine into the blood and then uptake by the target tissue [22]. Plasma levels of creatine typically peak at about 60 minutes after oral ingestion of creatine monohydrate [2]. An initial rise in plasma creatine levels, followed by a reduction in plasma levels can be used to indirectly indicate suggest increased uptake into the target tissue [22]. However, conclusive evidence of an increase in bioavailability can only be gained from assessing the amount of creatine reaching the target tissue measured by magnetic resonance spectroscopy (MRS), muscle biopsy, and/or whole body creatine retention assessed by measuring the difference between creatine intake and urinary excretion of creatine [22].

In contrast to its stability in a solid state form, creatine is not stable in aqueous solution due to an intramolecular cyclization [23]. Generally, creatine is converted to creatinine the lower the pH and the higher the temperature. For example, research has shown that creatine is relatively stable in solution at neutral pH (7.5 or 6.5). However, after 3 days of storage at 25℃, creatine degrades to creatinine (e.g., 4% at pH 5.5; 12% at pH 4.5; and 21% at pH 3.5) [22,24,25]. The degradation of creatine into creatinine over time is the main reason that creatine is sold in solid form. However, this does not mean that creatine is degraded into creatinine *in vivo* through the digestive process. In this regard, the degradation of creatine can be reduced or halted be either lowering the pH under 2.5 or increasing the pH [22]. A very low pH results in the protonation of the amide function of the creatine molecule, thereby preventing the intra-molecular cyclization [22]. Therefore, the conversion of creatine to creatinine in the gastrointestinal tract is minimal regardless of transit time and absorption into the blood is nearly 100% [22,26-28]. The vast majority of studies assessing the efficacy of creatine supplementation on muscle phosphagen levels, whole body creatine retention, and/or performance have evaluated creatine monohydrate. Claims that different forms of creatine are degraded to a lesser degree than creatine monohydrate *in vivo* or result in a greater uptake to muscle are currently unfounded [22].

Effects of creatine supplementation on muscle creatine stores

Fig. 4 shows the approximate total muscle creatine content for vegetarians, individuals consuming a normal diet, and levels typically reported in the literature following creatine loading with or without carbohydrate and/or carbohydrate and protein. It has been well documented that dietary supplementation of creatine monohydrate increases muscle creatine and phosphocreatine content by 10 to 40% [2,20,29,30]. The upper limit of muscle creatine stores is typically about 160 mmol/kg dry muscle weight (DW) although some individuals have been found to exceed this level in some studies [3,4]. The amount of creatine retained in the muscle following creatine supplementation depends on the amount of creatine in the muscle before supplementation [2,20,31-33]. Individuals with lower creatine content in muscle prior to supplementation may increase creatine stores by 20-40% while individuals with relatively high creatine levels before supplementation may only experience a 10-20% increase in muscle creatine content. Performance changes in response to creatine supplementation have been correlated with the magnitude of increase in muscle creatine levels [2,20,30]. However, co-ingesting creatine with carbohydrate [3,4,16], carbohydrate and protein [34], and/or nutrients that may improve insulin sensitivity [35,36] have been reported to optimize muscle creatine uptake even in individuals with relatively high initial creatine levels. Once creatine levels are elevated and an individual stops taking creatine, studies indicate it may take 4-6 weeks before creatine levels return to baseline [37]. There is no evidence that muscle creatine levels fall below baseline after cessation of creatine supplementation which might suggest a long-term suppression of endogenous creatine synthesis [38,39]. Additionally, there is no evidence that different forms of creatine such as creatine citrate [16], creatine serum [38,40], or creatine ethyl ester [41] promote greater creatine retention than creatine monohydrate [22].

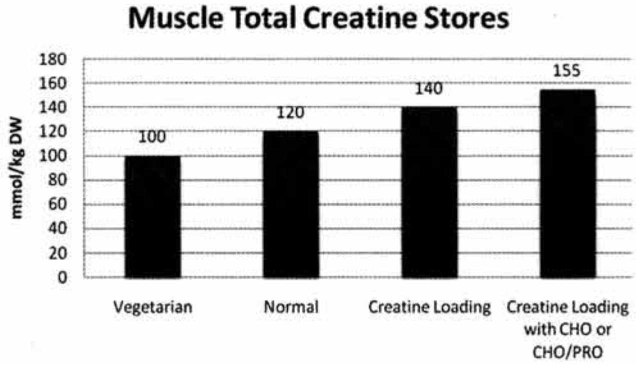

Fig. 4. Approximate muscle total creatine levels in mmol/kg dry weight muscle reported in the literature for vegetarians, individuals following a normal diet, and in response to creatine loading with or without carbohydrate (CHO) or CHO and protein (PRO).

Potential benefits of creatine supplementation

Table 1 presents the potential ergogenic benefits of creatine supplementation. Increasing muscle availability of creatine

Table 1. Potential ergogenic benefits of creatine supplementation.

• Increased single and repetitive sprint performance
• Increased muscle mass & strength adaptations during training
• Enhanced glycogen synthesis
• Increased anaerobic threshold
• Possible enhancement of aerobic capacity via greater shuttling of ATP from mitochondria
• Increased work capacity
• Enhanced recovery
• Greater training tolerance

Adapted from Kreider, Leutholtz, Katch & Katch [64].

and PCr can affect exercise, training, or health in several ways. In terms of exercise, increasing the availability of PCr in the muscle would help buffer ATP levels during high intensity exercise like sprinting and intense weightlifting as well as help individuals recover from intense exercise. These adaptations would allow an athlete to do more work over a series of sprints and/or sets of exercise theoretically leading to greater gains in strength, muscle mass, and/or performance over time. For this reason, creatine supplementation has primarily been recommended as an ergogenic aid for power/strength athletes to help them optimize training adaptations or athletes who need to sprint intermittently and recover during competition (e.g., soccer, basketball, football, tennis, etc.).

However, there is also evidence that endurance athletes may also benefit from creatine supplementation. For example, creatine loading prior to carbohydrate loading has been reported to promote greater glycogen retention [42]. Additionally, studies indicate that ingesting creatine with carbohydrate during carbohydrate loading promotes greater creatine and glycogen retention [43-46]. Theoretically, this may improve glycogen availability for endurance athletes and allow an athlete to sustain high intensity endurance exercise for a longer period of time. Creatine has also been shown to improve anaerobic threshold in some studies which could help endurance athletes maintain a faster race pace during competition [47,48]. Moreover, since endurance athletes incorporate interval training techniques in an attempt to improve speed and anaerobic threshold, creatine supplementation during training may improve interval training adaptations leading to improved performance. Finally, studies also indicate that creatine supplementation can help maintain body weight and muscle mass during training. Since many endurance athletes have difficulty maintaining body mass during training, creatine supplementation may help maintain optimal body composition.

Effects of creatine on exercise performance and training adaptations

As of this writing, there are over 600 references cited in the National Library of Medicine's PubMed related to creatine supplementation. Over 350 of these articles examine the role of creatine supplementation on exercise performance and/or training adaptations. Initial research on creatine supplementation focused on assessing the impact of creatine supplementation on muscle phosphagen levels and the impact of increasing muscle phosphagen levels on muscular performance and recovery. Although research on creatine had been conducted for decades, research by Harris [28], Hultman [2,28,49], and Greenhaff [20,30,32,33] spurred contemporary interest in creatine supplementation for sport. This was followed by several classic training related studies by Earnest [50], Kreider [51-54], Vandenberghe [37,55], Volek [56,57] and others that showed that creatine supplementation during resistance training augmented gains in performance, strength and/or muscle mass. The majority of these studies indicated that creatine supplementation promotes a statistically significant improvement in exercise capacity [14]. The average gain in performance from these studies typically ranges between 10 to 15% [14]. For example, short-term creatine supplementation has been reported to improve maximal power/strength (5-15%), work performed during sets of maximal effort muscle contractions (5-15%), single-effort sprint performance (1-5%), and work performed during repetitive sprint performance (5-15%) [14]. Long-term creatine supplementation appears to enhance the quality of training generally leading to 5 to 15% greater gains in strength and performance [14]. Additionally, most studies indicate that creatine supplementation increases body mass by about 1 to 2 kg in the first week of loading [14]. Although the initial weight gain has been suggested to be related to fluid retention, subjects taking creatine typically gain about twice as much body mass and/or fat free mass during training than subjects taking a placebo (e.g., an extra 1-2 kg of muscle mass during 4 to 12 weeks of training). No study has reported that creatine supplementation significantly impairs exercise capacity.

More contemporary studies on creatine supplementation have examined additional mechanisms of action as well as application for various sport-activities. For example, a number of studies examined whether observed increases in fat free mass were a result of an influence of creatine supplementation on fluid retention and/or muscle hypertrophy. These studies indicated that creatine supplementation during training increases muscle fiber diameter due to increases in myofibrillar protein content [19,57], satellite cell number and myonuclei concentration [58,59], and influences myogenic regulating factors in muscle [18,60]. Additionally, although studies suggest that creatine supplementation does not directly influence protein synthesis

Table 2. Examples of sports events that may be theoretically enhanced by creatine supplementation.

Increased PCr
• Track sprints: 100, 200 meters
• Swim sprints: 50 meters
• Pursuit cycling
Increased PCr Resynthesis
• Basketball
• Field hockey
• Football (American)
• Ice hockey
• Lacrosse
• Volleyball
Reduced Muscle Acidosis
• Downhill skiing
• Rowing
• Swim events: 100, 200 meters
• Track events: 400, 800 meters
Oxidative Metabolism
• Basketball
• Soccer
• Team handball
• Tennis
• Volleyball
• Interval Training in Endurance Athletes
Increased Body Mass/Muscle Mass
• Football
• Bodybuilding
• Wrestling
• Power lifting
• Rugby
• Track/Field events (Shot put; javelin; discus)
• Olympic Weightlifting

Adapted from Williams, Kreider, and Branch [63].

rates, there is some evidence that creatine supplementation may serve as an anti-catabolic nutrient in response to intense exercise [6,18,19,58,59,61,62].

Table 2 lists the types of sport events that creatine may provide ergogenic benefit based on the metabolic demands and types of training involved [63,64]. Creatine supplementation has been reported to provide ergogenic value to sport-related activities such as resistance-training [18,37, 65-91], sprint performance [54,55,92-106], American football [38,54,82,107,108], track and field [109,110], swimming [53,92,111-116], soccer [96,117-119], and military-type field events [120-122]. More recently, researchers have been investigating the effects of combining creatine with other potentially ergogenic nutrients like carbohydrate [3,4,15,54,123, 124], protein [75,89,108,125-127], ß-hydroxy-ß-methylbutyrate (HMB) [128-130], conjugated linoleic acids [131,132], alpha lipoic acid [133,134], fenugreek extract [135], and ß-alanine [136-138] on exercise performance and/or training adaptations. These studies generally indicate that creatine supplementation with other nutrients provides additive benefits. Thus, the preponderance of scientific evidence indicates that creatine supplementation is an effective nutritional ergogenic aid for a variety of exercise tasks in a number of athletic populations [14,63].

After extensively reviewing the scientific literature, the International Society of Sports Nutrition (ISSN) published a position stand related to creatine supplementation [21] that concluded the following:

1. Creatine monohydrate is the most effective ergogenic nutritional supplement currently available to athletes in terms of increasing high-intensity exercise capacity and lean body mass during training.
2. Creatine monohydrate supplementation is not only safe, but possibly beneficial in regard to preventing injury and/or management of select medical conditions when taken within recommended guidelines.
3. There is no compelling scientific evidence that the short- or long-term use of creatine monohydrate has any detrimental effects on otherwise healthy individuals.
4. If proper precautions and supervision are provided, supplementation in young athletes is acceptable and may provide a nutritional alternative to potentially dangerous anabolic drugs.
5. At present, creatine monohydrate is the most extensively studied and clinically effective form of creatine for use in nutritional supplements in terms of muscle uptake and ability to increase high-intensity exercise capacity.
6. The addition of carbohydrate or carbohydrate and protein to a creatine supplement appears to increase muscular retention of creatine, although the effect on performance measures may not be greater than using creatine monohydrate alone.
7. The quickest method of increasing muscle creatine stores appears to be to consume ~0.3 grams/kg/day of creatine monohydrate for at least 3 days followed by 3-5 g/d thereafter to maintain elevated stores. Ingesting smaller amounts of creatine monohydrate (e.g., 2-3 g/d) will increase muscle creatine stores over a 3-4 week period, however, the performance effects of this method of supplementation are less supported.
8. Creatine monohydrate has been reported to have a number of potentially beneficial uses in several clinical populations, and further research is warranted in these areas.

Potential medical uses of creatine

Given the evidence that creatine supplementation influences muscle phosphagen stores, plays an important role in energy metabolism, improves exercise performance and training adaptations, and increases muscle mass; there has also been interest in the potential therapeutic benefits of creatine supplementation. In fact, a seminal conference was held during the summer of 2010 at Cambridge University in the United Kingdom to provide an update regarding our current understanding of the role of creatine in health, medicine, and sport [1]. Papers from this conference were published in a special issue of *Amino Acids* in the spring of 2011 [1,8, 10,13,22,39,139-142]. For those interested in the potential medical applications of creatine, we highly recommend that readers review these papers.

In terms of potential medical uses of creatine, it is well known that creatine synthesis deficiencies and/or abnormal availability of creatine and PCr have been reported to cause a number of medical problems [8]. For this reason, the potential medical uses of creatine have been investigated since the mid-1970s. Initially, research focused on the role of creatine and/or creatine phosphate in reducing heart arrhythmias and/or improving heart function during ischemia events [63,143-146] and treating various medical populations who had creatine deficiencies such as gyrate atrophy [147-150] and children with low levels of PCr in the brain [8,151-153]. Interest in the potential medical uses of creatine has markedly increased over the last decade. Researchers have been particularly interested in determining whether creatine supplementation may reduce rates of muscle atrophy and/or wasting; enhance recovery from musculoskeletal and/or spinal cord injuries; improve strength and muscle endurance in patients with various neuromuscular disease; and, promote general health benefits [1,8,10,13,22,39,63,139-142,154,155].

For example, researchers have been evaluating whether creatine supplementation may improve clinical outcomes in patients with neuromuscular diseases and/or spinal cord injuries [156-168], muscular dystrophy [13,158,161,169-180], myophathies [13,171,172,181-185], Huntington's disease [139, 156,163,165,186-196], amyotrophic lateral sclerosis or Lou Gerhig's Disease [139,160,163,165,187,193,195,197-205], arthritis [206-208], and diabetes [39,44,140,156,188,209-212]. In addition, there is some evidence that creatine supplementation may help lower cholesterol and triglyceride levels [54,213], elevate homocysteine levels [34,214-220], serve as an antioxidant [221-223], and help maintain muscle mass and improve cognitive function in the elderly [65,101, 131,141,197,224-227]. Other studies have reported that creatine supplementation during training reduces injury rates in athletes [118,228-233] and/or allows athletes to tolerate intensified training to a greater degree [87]. Available short and long-term studies indicate that dietary creatine supplementation poses no adverse health risks [22,38,39,141, 195,234-238]. Therefore, a conclusion of the Cambridge meeting was that creatine supplementation is not only safe and effective for athletic and clinical populations that may benefit but that given the general health benefits known to date it may be advisable for the general population to take 2-3 grams of creatine monohydrate per day particularly as they get older [1,10,13,22,39,139-142,156].

SUMMARY

Creatine remains one of the most extensively studied nutritional ergogenic aids available for athletes. Hundreds of studies have reported that increasing muscle creatine stores through creatine supplementation can augment muscle creatine content, improve exercise and training adaptations, and/or provide some therapeutic benefit to some clinical populations. Additionally, a number of health benefits have been reported.

REFERENCES

[1] Harris R. Creatine in health, medicine and sport: an introduction to a meeting held at Downing College, University of Cambridge, July 2010. Amino Acids. 2011; 40(5):1267-70.

[2] Hultman E, Soderlund K, Timmons JA, Cederblad G, Greenhaff PL. Muscle creatine loading in men. J Appl Physiol. 1996;81(1):232-7.

[3] Green AL, Hultman E, Macdonald IA, Sewell DA, Greenhaff PL. Carbohydrate ingestion augments skeletal muscle creatine accumulation during creatine supplementation in humans. Am J Physiol. 1996;271(5 Pt 1):E821-6.

[4] Green AL, Simpson EJ, Littlewood JJ, Macdonald IA, Greenhaff PL. Carbohydrate ingestion augments creatine retention during creatine feeding in humans. Acta Physiol Scand. 1996;158(2):195-202.

[5] Balsom PD, Soderlund K, Ekblom B. Creatine in humans with special reference to creatine supplementation. Sports Med. 1994;18(4):268-80.

[6] Paddon-Jones D, Borsheim E, Wolfe RR. Potential ergogenic effects of arginine and creatine supplementation. J Nutr. 2004;134(10 Suppl):2888S-94S; discussion 95S.

[7] Benton D, Donohoe R. The influence of creatine supplementation on the cognitive functioning of vegetarians and omnivores. Br J Nutr. 2011;105(7):1100-5.

[8] Braissant O, Henry H, Beard E, Uldry J. Creatine deficiency

syndromes and the importance of creatine synthesis in the brain. Amino Acids. 2011;40(5):1315-24.
[9] Wallimann T, Schlosser T, Eppenberger HM. Function of M-line-bound creatine kinase as intramyofibrillar ATP regenerator at the receiving end of the phosphorylcreatine shuttle in muscle. J Biol Chem. 1984;259(8):5238-46.
[10] Wallimann T, Tokarska-Schlattner M, Schlattner U. The creatine kinase system and pleiotropic effects of creatine. Amino Acids. 2011;40(5):1271-96.
[11] Wallimann T, Dolder M, Schlattner U, Eder M, Hornemann T, Kraft T, Stolz M. Creatine kinase: an enzyme with a central role in cellular energy metabolism. MAGMA. 1998;6(2-3):116-9.
[12] Wallimann T, Dolder M, Schlattner U, Eder M, Hornemann T, O'Gorman E, Ruck A, Brdiczka D. Some new aspects of creatine kinase (CK): compartmentation, structure, function and regulation for cellular and mitochondrial bioenergetics and physiology. Biofactors. 1998;8(3-4): 229-34.
[13] Tarnopolsky MA. Creatine as a therapeutic strategy for myopathies. Amino Acids. 2011;40(5):1397-407.
[14] Kreider RB. Effects of creatine supplementation on performance and training adaptations. Mol Cell Biochem. 2003;244(1-2):89-94.
[15] Steenge GR, Simpson EJ, Greenhaff PL. Protein- and carbohydrate-induced augmentation of whole body creatine retention in humans. J Appl Physiol. 2000;89(3): 1165-71.
[16] Greenwood M, Kreider R, Earnest C, Rasmussen C, Almada A. Differences in creatine retention among three nutritional formulations of oral creatine supplements.. Journal of Exercise Physiology: Online. 2003;6(2):37-43.
[17] Kreider R, Willoughby DS, Greenwood M, Parise G, Payne D, Tarnopolsky M. Effects of serum creatine supplementation on muscle creatine content. Journal of Exercise Physiology: online. 2003;6(4):24-33.
[18] Willoughby DS, Rosene JM. Effects of oral creatine and resistance training on myogenic regulatory factor expression. Med Sci Sports Exerc. 2003;35(6):923-9.
[19] Willoughby DS, Rosene J. Effects of oral creatine and resistance training on myosin heavy chain expression. Med Sci Sports Exerc. 2001;33(10):1674-81.
[20] Greenhaff PL, Casey A, Short AH, Harris R, Soderlund K, Hultman E. Influence of oral creatine supplementation of muscle torque during repeated bouts of maximal voluntary exercise in man. Clin Sci (Lond). 1993;84(5):565-71.
[21] Buford TW, Kreider RB, Stout JR, Greenwood M, Campbell B, Spano M, Ziegenfuss T, Lopez H, Landis J, Antonio J. International Society of Sports Nutrition position stand: creatine supplementation and exercise. J Int Soc Sports Nutr. 2007;4:6.
[22] Jager R, Purpura M, Shao A, Inoue T, Kreider RB. Analysis of the efficacy, safety, and regulatory status of novel forms of creatine. Amino Acids. 2011;40(5):1369-83.
[23] Howard AN, Harris RC, inventors; Compositions containing creatine. US1999.
[24] Edgar G, Shiver HE. The equilibrium between creatine and creatinine, in aqueous solution: the effect of hydrogen ion. J Am Chem Soc. 1925;47:1179-88.
[25] Cannon JG, Orencole SF, Fielding RA, Meydani M, Meydani SN, Fiatarone MA, Blumberg JB, Evans WJ. Acute phase response in exercise: interaction of age and vitamin E on neutrophils and muscle enzyme release. Am J Physiol. 1990;259(6 Pt 2):R1214-9.
[26] Deldicque L, Decombaz J, Zbinden Foncea H, Vuichoud J, Poortmans JR, Francaux M. Kinetics of creatine ingested as a food ingredient. Eur J Appl Physiol. 2008;102(2): 133-43.
[27] Persky AM, Brazeau GA, Hochhaus G. Pharmacokinetics of the dietary supplement creatine. Clin Pharmacokinet. 2003;42(6):557-74.
[28] Harris RC, Soderlund K, Hultman E. Elevation of creatine in resting and exercised muscle of normal subjects by creatine supplementation. Clin Sci (Colch). 1992;83(3): 367-74.
[29] Green AL, Simpson EJ, Littlewood JJ, Macdonald IA, Greenhaff P. Carbohydrate ingestion augments creatine retention during creatine feeding in humans. Acta Physiol Scand. 1996;158:195-202.
[30] Greenhaff PL, Bodin K, Soderlund K, Hultman E. Effect of oral creatine supplementation on skeletal muscle phosphocreatine resynthesis. Am J Physiol. 1994;266(5 Pt 1):E725-30.
[31] Greenhaff PL. Creatine and its application as an ergogenic aid. Int J Sport Nutr. 1995;5 Suppl:S100-10.
[32] Greenhaff P. The nutritional biochemistry of creatine. Journal of Nutritional Biochemistry. 1997;11:610-8.
[33] Greenhaff P, Constantin-Teodosiu D, Casey A, Hultman E. The effectof oral creatine supplementation on skeletal muscle ATP degradation during repeated bouts of maximal voluntary exercise in man. J Physiol. 1994;476: 84P.
[34] Steenge GR, Verhoef P, Greenhaff PL. The effect of creatine and resistance training on plasma homocysteine concentration in healthy volunteers. Arch Intern Med. 2001;161(11):1455-6.
[35] Greenwood M, Kreider RB, Rasmussen C, Almada AL, Earnest CP. D-Pinitol augments whole body creatine

retention in man. J Exerc Physiol Online. 2001;4(4):41-7.
[36] Kerksick CM, Wilborn CD, Campbell WI, Harvey TM, Marcello BM, Roberts MD, Parker AG, Byars AG, Greenwood LD, Almada AL, Kreider RB, Greenwood M. The effects of creatine monohydrate supplementation with and without D-pinitol on resistance training adaptations. J Strength Cond Res. 2009;23(9):2673-82.
[37] Vandenberghe K, Goris M, Van Hecke P, Van Leemputte M, Vangerven L, Hespel P. Long-term creatine intake is beneficial to muscle performance during resistance training. J Appl Physiol. 1997;83(6):2055-63.
[38] 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 Cell Biochem. 2003;244(1-2):95-104.
[39] Kim HJ, Kim CK, Carpentier A, Poortmans JR. Studies on the safety of creatine supplementation. Amino Acids. 2011;40(5):1409-18.
[40] Almada A, Harris RC, Harris DB. Ingestion of creatine serum has no effect on plasma creatine. FASEB J. 2001; 15:LB61.
[41] Spillane M, Schoch R, Cooke M, Harvey T, Greenwood M, Kreider R, Willoughby DS. The effects of creatine ethyl ester supplementation combined with heavy resistance training on body composition, muscle performance, and serum and muscle creatine levels. J Int Soc Sports Nutr. 2009;6:6.
[42] Nelson AG, Arnall DA, Kokkonen J, Day, Evans J. Muscle glycogen supercompensation is enhanced by prior creatine supplementation. Med Sci Sports Exerc. 2001;33(7):1096-100.
[43] van Loon LJ, Murphy R, Oosterlaar AM, Cameron-Smith D, Hargreaves M, Wagenmakers AJ, Snow R. Creatine supplementation increases glycogen storage but not GLUT-4 expression in human skeletal muscle. Clin Sci (Lond). 2004;106(1):99-106.
[44] Op 't Eijnde B, Urso B, Richter EA, Greenhaff PL, Hespel P. Effect of oral creatine supplementation on human muscle GLUT4 protein content after immobilization. Diabetes. 2001;50(1):18-23.
[45] Kehnder M, Rico-Sanz J, Kuhne G, Dambach M, Buchli R, Boutellier U. Muscle phosphocreatine and glycogen concentrations in humans after creatine and glucose polymer supplementation measured noninvasively by 31P and 13C-MRS. Medicine & Science in Sports & Exercise. 1998;30:S264.
[46] Casey A, Constantin-Teodosiu D, Howell S, Hultman E, Greenhaff PL. Metabolic response of type I and II muscle fibers during repeated bouts of maximal exercise in humans. Am J Physiol. 1996;271(1 Pt 1):E38-43.
[47] Chwalbinska-Moneta J. Effect of creatine supplementation on aerobic performance and anaerobic capacity in elite rowers in the course of endurance training. Int J Sport Nutr Exerc Metab. 2003;13(2):173-83.
[48] Nelson AG, Day R, Glickman-Weiss EL, Hegsted M, Kokkonen J, Sampson B. Creatine supplementation alters the response to a graded cycle ergometer test. Eur J Appl Physiol. 2000;83(1):89-94.
[49] Balsom PD, Ekblom B, Soderlund K, Sjodin B, Hultman E. Creatine supplementation and dynamic high-intensity intermittent exercise. Scand J Med Sci Sports. 1993;3:143-9.
[50] Earnest CP, Snell P, Rodriguez R, Almada A, Mitchell TL. The effect of creatine monohyerate ingestion on anaerobic power indices, muscular strength and body composition. Acta Physiol Scand. 1995;153:207-9.
[51] Kreider RB, Klesges R, Harmon K, Grindstaff P, Ramsey L, Bullen D, Wood L, Li Y, Almada A. Effects of ingesting supplements designed to promote lean tissue accretion on body composition during resistance training. Int J Sport Nutr. 1996;6(3):234-46.
[52] Kreider RB, Klesges RC, Lotz D, Davis M, Cantler E, Harmon-Clayton K, Dudley R, Grindstaff P, Ramsey L, Bullen D, Wood L, Almada A. Effects of nutritional supplementation during off-season college football training on body composition and strength Journal of Exercise Physiology online. 1999.;2(2):24-39.
[53] Grindstaff PD, Kreider R, Bishop R, Wilson M, Wood L, Alexander C, Almada A. Effects of creatine supplementation on repetitive sprint performance and body composition in competitive swimmers. Int J Sport Nutr. 1997;7(4): 330-46.
[54] Kreider RB, Ferreira M, Wilson M, Grindstaff P, Plisk S, Reinardy J, Cantler E, Almada AL. Effects of creatine supplementation on body composition, strength, and sprint performance. Med Sci Sports Exerc. 1998;30(1): 73-82.
[55] Vandebuerie F, Vanden Eynde B, Vandenberghe K, Hespel P. Effect of creatine loading on endurance capacity and sprint power in cyclists. Int J Sports Med. 1998;19(7): 490-5.
[56] Volek JS, Kraemer WJ, Bush JA, Boetes M, Incledon T, Clark KL, Lynch JM. Creatine supplementation enhances muscular performance during high- intensity resistance exercise. J Am Diet Assoc. 1997;97(7):765-70.
[57] Volek JS, Duncan ND, Mazzetti SA, Staron RS, Putukian M, Gomez AL, Pearson DR, Fink WJ, Kraemer WJ. Performance and muscle fiber adaptations to creatine

supplementation and heavy resistance training. Med Sci Sports Exerc. 1999;31(8):1147-56.
[58] Dangott B, Schultz E, Mozdziak PE. Dietary creatine monohydrate supplementation increases satellite cell mitotic activity during compensatory hypertrophy. Int J Sports Med. 2000;21(1):13-6.
[59] Olsen S, Aagaard P, Kadi F, Tufekovic G, Verney J, Olesen JL, Suetta C, Kjaer M. Creatine supplementation augments the increase in satellite cell and myonuclei number in human skeletal muscle induced by strength training. J Physiol. 2006;573(Pt 2):525-34.
[60] Hespel P, Op't Eijnde B, Van Leemputte M, Urso B, Greenhaff PL, Labarque V, Dymarkowski S, Van Hecke P, Richter EA. Oral creatine supplementation facilitates the rehabilitation of disuse atrophy and alters the expression of muscle myogenic factors in humans. J Physiol. 2001;536(Pt 2):625-33.
[61] Parise G, Mihic S, MacLennan D, Yarasheski KE, Tarnopolsky MA. Effects of acute creatine monohydrate supplementation on leucine kinetics and mixed-muscle protein synthesis. J Appl Physiol. 2001;91(3):1041-7.
[62] Louis M, Poortmans JR, Francaux M, Hultman E, Berre J, Boisseau N, Young VR, Smith K, Meier-Augenstein W, Babraj JA, Waddell T, Rennie MJ. Creatine supplementation has no effect on human muscle protein turnover at rest in the post-absorptive or fed states. Am J Physiol Endocrinol Metab. 2002.
[63] Williams MH, Kreider R, Branch JD. Creatine: The power supplement. Champaign, IL: Human Kinetics Publishers; 1999
[64] Kreider R, Leutholtz B, Katch F, Katch V. Exercise & Sport Nutrition. Santa Barbara: Fitness Technologies Press. Available at www.ExerciseAndSportNutrition.com; 2009
[65] Brown LE, Whetehurst M, Grant KE, Roberts JE. The effect of creatine supplementation and periodized resistance training on strength in the elderly. Journal of Strength and Conditioning Research. 1998;12(4).
[66] Syrotuik DG, Bell GJ, Burnham R, Sim LL, Calvert RA, Maclean IM. Absolute and relative strength performance following creatine monohydrate supplementation combined with periodized resistance training. Journal of Strength and Conditioning Research. 1998;12(4):278.
[67] Volek JS, Duncan ND, Mazzetti SA, Putukian M, Gomez AL, Staron RS, Kraemer WJ. Performance and muscle fiber adaptations to 12 weeks of creatine supplementation and heavy resistance training. Medicine & Science in Sports & Exercise. 1999;31(5).
[68] Becque MD, Lochmann JD, Melrose DR. Effects of oral creatine supplementation on muscular strength and body composition. Med Sci Sports Exerc. 2000;32(3):654-8.
[69] Brenner M, Walberg Rankin J, Sebolt D. The effect of creatine supplementation during resistance training in women. J Strength Cond Res. 2000;14(2):207-13.
[70] Burke DG, Silver S, Holt LE, Smith Palmer T, Culligan CJ, Chilibeck PD. The effect of continuous low dose creatine supplementation on force, power, and total work. Int J Sport Nutr Exerc Metab. 2000;10(3):235-44.
[71] Candow DG, Chrusch MJ, Chilibeck PD, Chad KE, Davison KS, Burke DG. Effect of creatine supplementation cessation with maintenance of resistance training in older men. Medicine & Science in Sports & Exercise. 2000;32(5).
[72] Chrusch MJ, Chilibeck PD, Davison KS, Yu PH, Burke DG, Chad KE. Creatine supplementation combined with resistance training in older men. Medicine & Science in Sports & Exercise. 2000;32(5).
[73] Ratamess NA, Volek JS, Rubin MR, Gomez AL, Wickham RB, Mazzetti SA, Doan BK, Newton RU, Kraemer WJ. Muscular strength and power enhancement with creatine supplementation during short-term resistance training overreaching. Journal of Strength and Conditioning Research. 2000;14(3).
[74] Syrotuik DG, Bell DG, Burnham R, Sim LL, Calvert RA, Maclean IM. Absolute and relative strength performance following creatine monohydrate supplementation combined with periodized resistance training. Journal of Strength and Conditioning Research. 2000;14(2):182-90.
[75] Tarnopolsky MA, Parise G, Yarkley NJ, Ballantyne CN, Olatunji S, Phillips SM. Post-exercise glucose-protein and glucose-creatine result in similar increases in strength, power and fat-free-mass during resistance training. Medicine & Science in Sports & Exercise. 2000;32(5).
[76] Bemben MG, Bemben DA, Loftiss DD, Knehans AW. Creatine supplementation during resistance training in college football athletes. Med Sci Sports Exerc. 2001; 33(10):1667-73.
[77] Chrusch MJ, Chilibeck PD, Chad KE, Davison KS, Burke DG. Effect of creatine supplementation combined with resistance training on whole body bone mineral in older men. Medicine & Science in Sports & Exercise. 2001;33(5).
[78] Chrusch MJ, Chilibeck PD, Chad KE, Davison KS, Burke DG. Creatine supplementation combined with resistance training in older men. Med Sci Sports Exerc. 2001;33(12):2111-7.
[79] Stevenson SW, Dudley GA. Dietary creatine supplementation and muscular adaptation to resistive overload. Med Sci Sports Exerc. 2001;33(8):1304-10.

[80] Syrotuik DG, Game AB, Gillies EM, Bell GJ. Effects of creatine monohydrate supplementation during combined strength and high intensity rowing training on performance. Can J Appl Physiol. 2001;26(6):527-42.

[81] McBride TA, Gregory MA. Effect of Creatine Supplementation During High Resistance Training on Mass, Strength, and Fatigue Resistance in Rat Skeletal Muscle. J Strength Cond Res. 2002;16(3):335-42.

[82] Wilder N, Gilders R, Hagerman F, Deivert RG. The Effects of a 10-Week, Periodized, Off-Season Resistance-Training Program and Creatine Supplementation Among Collegiate Football Players. J Strength Cond Res. 2002; 16(3):343-52.

[83] Burke DG, Chilibeck PD, Parise G, Candow DG, Mahoney D, Tarnopolsky M. Effect of creatine and weight training on muscle creatine and performance in vegetarians. Med Sci Sports Exerc. 2003;35(11):1946-55.

[84] Kilduff LP, Pitsiladis YP, Tasker L, Attwood J, Hyslop P, Dailly A, Dickson I, Grant S. Effects of creatine on body composition and strength gains after 4 weeks of resistance training in previously nonresistance-trained humans. Int J Sport Nutr Exerc Metab. 2003;13(4): 504-20.

[85] Rawson ES, Volek JS. Effects of creatine supplementation and resistance training on muscle strength and weightlifting performance. J Strength Cond Res. 2003; 17(4):822-31.

[86] Candow DG, Chilibeck PD, Chad KE, Chrusch MJ, Davison KS, Burke DG. Effect of ceasing creatine supplementation while maintaining resistance training in older men. J Aging Phys Act. 2004;12(3):219-31.

[87] Volek JS, Ratamess NA, Rubin MR, Gomez AL, French DN, McGuigan MM, Scheett TP, Sharman MJ, Hakkinen K, Kraemer WJ. The effects of creatine supplementation on muscular performance and body composition responses to short-term resistance training overreaching. Eur J Appl Physiol. 2004;91(5-6):628-37.

[88] Aguiar AF, Aguiar DH, Felisberto AD, Carani FR, Milanezi RC, Padovani CR, Dal-Pai-Silva M. Effects of creatine supplementation during resistance training on myosin heavy chain (MHC) expression in rat skeletal muscle fibers. J Strength Cond Res. 2010;24(1):88-96.

[89] Bemben MG, Witten MS, Carter JM, Eliot KA, Knehans AW, Bemben DA. The effects of supplementation with creatine and protein on muscle strength following a traditional resistance training program in middle-aged and older men. J Nutr Health Aging. 2010;14(2):155-9.

[90] Saremi A, Gharakhanloo R, Sharghi S, Gharaati MR, Larijani B, Omidfar K. Effects of oral creatine and resistance training on serum myostatin and GASP-1. Mol Cell Endocrinol. 2010;317(1-2):25-30.

[91] Candow DG, Chilibeck PD, Burke DG, Mueller KD, Lewis JD. Effect of Different Frequencies of Creatine Supplementation on Muscle Size and Strength in Young Adults. J Strength Cond Res. 2011.

[92] Peyrebrune MC, Nevill ME, Donaldson FJ, Cosford DJ. The effects of oral creatine supplementation on performance in single and repeated sprint swimming. J Sports Sci. 1998;16(3):271-9.

[93] Snow RJ, McKenna MJ, Selig SE, Kemp J, Stathis CG, Zhao S. Effect of creatine supplementation on sprint exercise performance and muscle metabolism. J Appl Physiol. 1998;84(5):1667-73.

[94] Thorensen E, McMillan J, Guion K, Joyner B. The effect of creatine supplementation on repeated sprint performance. Journal of Strength and Conditioning Research. 1998; 12(4):278.

[95] Jones AM, Atter T, Georg KP. Oral creatine supplementation improves multiple sprint performance in elite ice-hockey players. J Sports Med Phys Fitness. 1999; 39(3):189-96.

[96] Mujika I, Padilla S, Ibanez J, Izquierdo M, Gorostiaga E. Creatine supplementation and sprint performance in soccer players. Med Sci Sports Exerc. 2000;32(2): 518-25.

[97] McFarlane WJ, Heigenhauser GJ, McDonald DG. Creatine supplementation affects sprint endurance in juvenile rainbow trout. Comp Biochem Physiol A Mol Integr Physiol. 2001;130(4):857-66.

[98] Rockwell JA, Rankin JW, Toderico B. Creatine supplementation affects muscle creatine during energy restriction. Med Sci Sports Exerc. 2001;33(1):61-8.

[99] Romer LM, Barrington JP, Jeukendrup AE. Effects of oral creatine supplementation on high intensity, intermittent exercise performance in competitive squash players. Int J Sports Med. 2001;22(8):546-52.

[100] Skare OC, Skadberg, Wisnes AR. Creatine supplementation improves sprint performance in male sprinters. Scand J Med Sci Sports. 2001;11(2):96-102.

[101] Wiroth JB, Bermon S, Andrei S, Dalloz E, Hebuterne X, Dolisi C. Effects of oral creatine supplementation on maximal pedalling performance in older adults. Eur J Appl Physiol. 2001;84(6):533-9.

[102] Cottrell GT, Coast JR, Herb RA. Effect of recovery interval on multiple-bout sprint cycling performance after acute creatine supplementation. J Strength Cond Res. 2002;16(1):109-16.

[103] Cox G, Mujika I, Tumilty D, Burke L. Acute creatine

supplementation and performance during a field test simulating match play in elite female soccer players. Int J Sport Nutr Exerc Metab. 2002;12(1):33-46.
[104] Izquierdo M, Ibanez J, Gonzalez-Badillo JJ, Gorostiaga EM. Effects of creatine supplementation on muscle power, endurance, and sprint performance. Med Sci Sports Exerc. 2002;34(2):332-43.
[105] Delecluse C, Diels R, Goris M. Effect of creatine supplementation on intermittent sprint running performance in highly trained athletes. J Strength Cond Res. 2003; 17(3):446-54.
[106] Van Schuylenbergh R, Van Leemputte M, Hespel P. Effects of oral creatine-pyruvate supplementation in cycling performance. Int J Sports Med. 2003;24(2):144-50.
[107] 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(4):453-60.
[108] Kreider RB, Klesges RC, Lotz D, Davis M, Cantler E, Harmon K, Clayton R, Dudley R, Grindstaff P, Ramsey L, Bullen D, Wood L, Almada A. Effects of nutritional supplementation during off season college football training on body composition and strength. Journal of Exercise Physiology Online. 1999;2(2):24-39.
[109] Kirksey KB, Stone MH, Warren BJ, Johnson RL, Stone M, Haff G, Williams FE, Proulx C. The effects of 6 weeks of creatine monohydrate supplementation on performance measures and body composition in collegiate track and field athletes. J Strength Cond Res. 1999;13(2):148-56.
[110] Lehmkuhl M, Malone M, Justice B, Trone G, Pistilli E, 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(3):425-38.
[111] Burke LM, Pyne DB, Telford RD. Effect of oral creatine supplementation on single-effort sprint performance in elite swimmers. Int J Sport Nutr. 1996;6(3):222-33.
[112] Leenders NM, Lesniewski L, Sherman WM, Sand G, Sand S, Mulroy M, Lamb DR, editors. Dietary creatine supplementation and swimming performance. Overtraining and Overreaching in Sports Conference Abstracts; 1996 July, 1996.
[113] Leenders NM, Lamb DR, Nelson TE. Creatine supplementation and swimming performance. Int J Sport Nutr. 1999;9(3):251-62.
[114] Theodorou AS, Cooke CB, King RF, Hood C, Denison T, Wainwright BG, Havenetidis K. The effect of longer-term creatine supplementation on elite swimming performance after an acute creatine loading. J Sports Sci. 1999; 17(11):853-9.
[115] Dawson B, Vladich T, Blanksby BA. Effects of 4 weeks of creatine supplementation in junior swimmers on freestyle sprint and swim bench performance. J Strength Cond Res. 2002;16(4):485-90.
[116] Selsby JT, Beckett KD, Kern M, Devor ST. Swim performance following creatine supplementation in Division III athletes. J Strength Cond Res. 2003;17(3): 421-4.
[117] Larson-Meyer DE, Hunter GR, Trowbridge CA, Turk JC, Ernest JM, Torman SL, Harbin PA. The effect of creatine supplementation on muscle strength and body composition during off-season training in female soccer players. J Strength Cond Res. 2000;14(4):434-42.
[118] Ortega Gallo PA, Dimeo F, Batista J, Bazan F, Betchakian L, Garcia Cambon C, Griffa J. Creatine supplementation in soccer players, effects in body composition and incidence of sport-related injuries. Med Sci Sports Exerc. 2000;32(5):S134.
[119] Ostojic SM. Creatine supplementation in young soccer players. Int J Sport Nutr Exerc Metab. 2004;14(1):95-103.
[120] Bennett T, Bathalon G, Armstrong D, 3rd, Martin B, Coll R, Beck R, Barkdull T, O'Brien K, Deuster PA. Effect of creatine on performance of militarily relevant tasks and soldier health. Mil Med. 2001;166(11):996-1002.
[121] Warber JP, Tharion WJ, Patton JF, Champagne CM, Mitotti P, Lieberman HR. The effect of creatine monohydrate supplementation on obstacle course and multiple bench press performance. J Strength Cond Res. 2002;16(4):500-8.
[122] Ensigh WY, Jacobs I, Prusaczyk WK, Goforth Jr. HW, Law PG, Schneider KE. Effects of creatine supplementation on short-term anaerobic exercise performance of U.S. Navy Seals. Medicine & Science in Sports & Exercise. 1998;30(5):S265.
[123] Robinson TM, Sewell DA, Hultman E, Greenhaff PL. Role of submaximal exercise in promoting creatine and glycogen accumulation in human skeletal muscle. J Appl Physiol. 1999;87(2):598-604.
[124] Tarnopolsky MA, Parise G, Yardley NJ, Ballantyne CS, Olatinji S, Phillips SM. Creatine-dextrose and protein-dextrose induce similar strength gains during training. Med Sci Sports Exerc. 2001;33(12):2044-52.
[125] Kerksick CM, Rasmussen C, Lancaster S, Starks M, Smith P, Melton C, Greenwood M, Almada A, Kreider R. Impact of differing protein sources and a creatine containing nutritional formula after 12 weeks of resistance training. Nutrition. 2007;23(9):647-56.
[126] Burke DG, Chilibeck PD, Davidson KS, Candow DG,

Farthing J, Smith-Palmer T. The effect of whey protein supplementation with and without creatine monohydrate combined with resistance training on lean tissue mass and muscle strength. Int J Sport Nutr Exerc Metab. 2001;11(3):349-64.

[127] Derave W, Op'T Eijinde B, Richter EA, Hespel P. Combined creatine and protein supplementation improves glucose tolerance and muscle glycogen accumulation in humans. Abstracts of 6th Internationl Conference on Guanidino Compounds in Biology and Medicine. 2001.

[128] Crowe MJ, O'Connor DM, Lukins JE. The effects of beta-hydroxy-beta-methylbutyrate (HMB) and HMB/creatine supplementation on indices of health in highly trained athletes. Int J Sport Nutr Exerc Metab. 2003;13(2): 184-97.

[129] O'Connor DM, Crowe MJ. Effects of beta-hydroxy-beta-methylbutyrate and creatine monohydrate supplementation on the aerobic and anaerobic capacity of highly trained athletes. J Sports Med Phys Fitness. 2003; 43(1):64-8.

[130] 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(7-8):558-66.

[131] Tarnopolsky MA, Safdar A. The potential benefits of creatine and conjugated linoleic acid as adjuncts to resistance training in older adults. Appl Physiol Nutr Metab. 2008;33(1):213-27.

[132] Cornish SM, Candow DG, Jantz NT, Chilibeck PD, Little JP, Forbes S, Abeysekara S, Zello GA. Conjugated linoleic acid combined with creatine monohydrate and whey protein supplementation during strength training. Int J Sport Nutr Exerc Metab. 2009;19(1):79-96.

[133] Berg EP, Maddock KR, Linville ML. Creatine monohydrate supplemented in swine finishing diets and fresh pork quality: III. Evaluating the cumulative effect of creatine monohydrate and alpha-lipoic acid. J Anim Sci. 2003;81(10):2469-74.

[134] Burke DG, Chilibeck PD, Parise G, Tarnopolsky MA, Candow DG. Effect of alpha-lipoic acid combined with creatine monohydrate on human skeletal muscle creatine and phosphagen concentration. Int J Sport Nutr Exerc Metab. 2003;13(3):294-302.

[135] Taylor L, Poole C, Pena E, Lewing M, Kreider R, Foster C, Wilborn C. Effects of combined creatine plus fenugreek extract vs. creatine plus carbohdrate supplementation on resistance training adaptations. Journal of Sport Sciences & Medicine. 2011;10:254-60.

[136] Stout JR, Cramer JT, Mielke M, O'Kroy J, Torok DJ, Zoeller RF. Effects of twenty-eight days of beta-alanine and creatine monohydrate supplementation on the physical working capacity at neuromuscular fatigue threshold. J Strength Cond Res. 2006;20(4):928-31.

[137] Hoffman J, Ratamess N, Kang J, Mangine G, Faigenbaum A, Stout J. Effect of creatine and beta-alanine supplementation on performance and endocrine responses in strength/power athletes. Int J Sport Nutr Exerc Metab. 2006;16(4):430-46.

[138] Zoeller RF, Stout JR, O'Kroy J A, Torok DJ, Mielke M. Effects of 28 days of beta-alanine and creatine monohydrate supplementation on aerobic power, ventilatory and lactate thresholds, and time to exhaustion. Amino Acids. 2007;33(3):505-10.

[139] Klopstock T, Elstner M, Bender A. Creatine in mouse models of neurodegeneration and aging. Amino Acids. 2011;40(5):1297-303.

[140] Nicastro H, Gualano B, de Moraes WM, de Salles Painelli V, da Luz CR, Dos Santos Costa A, de Salvi Guimaraes F, Medeiros A, Brum PC, Lancha AH, Jr. Effects of creatine supplementation on muscle wasting and glucose homeostasis in rats treated with dexamethasone. Amino Acids. 2011.

[141] Rawson ES, Venezia AC. Use of creatine in the elderly and evidence for effects on cognitive function in young and old. Amino Acids. 2011;40(5):1349-62.

[142] Sahlin K, Harris RC. The creatine kinase reaction: a simple reaction with functional complexity. Amino Acids. 2011;40(5):1363-7.

[143] Hultman J, Ronquist G, Forsberg JO, Hansson HE. Myocardial energy restoration of ischemic damage by administration of phosphoenolpyruvate during reperfusion. A study in a paracorporeal rat heart model. Eur Surg Res. 1983;15(4):200-7.

[144] Thelin S, Hultman J, Ronquist G, Hansson HE. Metabolic and functional effects of creatine phosphate in cardioplegic solution. Studies on rat hearts during and after normothermic ischemia. Scand J Thorac Cardiovasc Surg. 1987;21(1):39-45.

[145] Osbakken M, Ito K, Zhang D, Ponomarenko I, Ivanics T, Jahngen EG, Cohn M. Creatine and cyclocreatine effects on ischemic myocardium: 31P nuclear magnetic resonance evaluation of intact heart. Cardiology. 1992; 80(3-4):184-95.

[146] Thorelius J, Thelin S, Ronquist G, Halden E, Hansson HE. Biochemical and functional effects of creatine phosphate in cardioplegic solution during aortic valve surgery--a clinical study. Thorac Cardiovasc Surg. 1992;

40(1):10-3.

[147] Sipila I, Rapola J, Simell O, Vannas A. Supplementary creatine as a treatment fo gyrate atrophy of the choroid and retina. New Engl J Med. 1981;304:867-70.

[148] Vannas-Sulonen K, Sipila I, Vannas A, Simell O, Rapola J. Gyrate atrophy of the choroid and retina. A five-year follow-up of creatine supplementation. Ophthalmology. 1985;92(12):1719-27.

[149] Heinanen K, Nanto-Salonen K, Komu M, Erkintalo M, Alanen A, Heinonen OJ, Pulkki K, Nikoskelainen E, Sipila I, Simell O. Creatine corrects muscle 31P spectrum in gyrate atrophy with hyperornithinaemia. Eur J Clin Invest. 1999;29(12):1060-5.

[150] Nanto-Salonen K, Komu M, Lundbom N, Heinanen K, Alanen A, Sipila I, Simell O. Reduced brain creatine in gyrate atrophy of the choroid and retina with hyperornithinemia. Neurology. 1999;53(2):303-7.

[151] Ensenauer R, Thiel T, Schwab KO, Tacke U, Stockler-Ipsiroglu S, Schulze A, Hennig J, Lehnert W. Guanidinoacetate methyltransferase deficiency: differences of creatine uptake in human brain and muscle. Mol Genet Metab. 2004;82(3):208-13.

[152] Schulze A. Creatine-deficiency syndromes. Abstracts of 6th Internationl Conference on Guanidino Compounds in Biology and Medicine. 2001.

[153] Ganesan V, Johnson A, Connelly A, Eckhardt S, Surtees RA. Guanidinoacetate methyltransferase deficiency: new clinical features. Pediatr Neurol. 1997;17(2):155-7.

[154] Williams MH. Facts and fallacies of purported ergogenic amino acid supplements. Clin Sports Med. 1999;18(3): 633-49.

[155] Kreider RB, Wilborn CD, Taylor L, Campbell B, Almada AL, Collins R, Cooke M, Earnest CP, Greenwood M, Kalman DS, Kerksick CM, Kleiner SM, Leutholtz B, Lopez H, Lowery LM, Mendel R, Smith A, Spano M, Wildman R, Willoughby DS, Ziegenfuss TN, Antonio J. ISSN exercise & sport nutrition review: research & recommendations. J Int Soc Sports Nutr. 2010;7:7.

[156] Gualano B, Artioli GG, Poortmans JR, Lancha Junior AH. Exploring the therapeutic role of creatine supplementation. Amino Acids. 2010;38(1):31-44.

[157] Guerrero-Ontiveros ML, Wallimann T. Creatine supplementation in health and disease. Effects of chronic creatine ingestion in vivo: down-regulation of the expression of creatine transporter isoforms in skeletal muscle. Mol Cell Biochem. 1998;184(1-2):427-37.

[158] Tarnopolsky MA, Parise G. Direct measurement of high-energy phosphate compounds in patients with neuromuscular disease. Muscle Nerve. 1999;22(9): 1228-33.

[159] Braegger CP, Schlattner U, Wallimann T, Utiger A, Frank F, Schaefer B, Heizmann CW, Sennhauser FH. Effects of creatine supplementation in cystic fibrosis: results of a pilot study. J Cyst Fibros. 2003;2(4):177-82.

[160] Ellis AC, Rosenfeld J. The role of creatine in the management of amyotrophic lateral sclerosis and other neurodegenerative disorders. CNS Drugs. 2004;18(14): 967-80.

[161] Tarnopolsky MA. Clinical use of creatine in neuromuscular and neurometabolic disorders. Subcell Biochem. 2007;46:183-204.

[162] Matthews RT, Ferrante RJ, Klivenyi P, Yang L, Klein AM, Mueller G, Kaddurah-Daouk R, Beal MF. Creatine and cyclocreatine attenuate MPTP neurotoxicity. Exp Neurol. 1999;157(1):142-9.

[163] Zhu S, Li M, Figueroa BE, Liu A, Stavrovskaya IG, Pasinelli P, Beal MF, Brown RH, Jr., Kristal BS, Ferrante RJ, Friedlander RM. Prophylactic creatine administration mediates neuroprotection in cerebral ischemia in mice. J Neurosci. 2004;24(26):5909-12.

[164] Hausmann ON, Fouad K, Wallimann T, Schwab ME. Protective effects of oral creatine supplementation on spinal cord injury in rats. Spinal Cord. 2002;40(9): 449-56.

[165] Klein AM, Ferrante RJ. The neuroprotective role of creatine. Subcell Biochem. 2007;46:205-43.

[166] Brustovetsky N, Brustovetsky T, Dubinsky JM. On the mechanisms of neuroprotection by creatine and phosphocreatine. J Neurochem. 2001;76(2):425-34.

[167] Sullivan PG, Geiger JD, Mattson MP, Scheff SW. Dietary supplement creatine protects against traumatic brain injury. Ann Neurol. 2000;48(5):723-9.

[168] Jacobs PL, Mahoney ET, Cohn KA, Sheradsky LF, Green BA. Oral creatine supplementation enhances upper extremity work capacity in persons with cervical-level spinal cord injury. Arch Phys Med Rehabil. 2002;83(1): 19-23.

[169] Pulido SM, Passaquin AC, Leijendekker WJ, Challet C, Wallimann T, Ruegg UT. Creatine supplementation improves intracellular Ca2+ handling and survival in mdx skeletal muscle cells. FEBS Lett. 1998;439(3): 357-62.

[170] Felber S, Skladal D, Wyss M, Kremser C, Koller A, Sperl W. Oral creatine supplementation in Duchenne muscular dystrophy: a clinical and 31P magnetic resonance spectroscopy study. Neurol Res. 2000;22(2): 145-50.

[171] Tarnopolsky MA. Potential use of creatine monohydrate in muscular dystrophy and nuerometabolic disorders. Abstracts of 6th Internationl Conference on Guanidino Compounds in Biology and Medicine. 2001.

[172] Tarnopolsky MA, Parshad A, Walzel B, Schlattner U, Wallimann T. Creatine transporter and mitochondrial creatine kinase protein content in myopathies. Muscle Nerve. 2001;24(5):682-8.

[173] Passaquin AC, Renard M, Kay L, Challet C, Mokhtarian A, Wallimann T, Ruegg UT. Creatine supplementation reduces skeletal muscle degeneration and enhances mitochondrial function in mdx mice. Neuromuscul Disord. 2002;12(2):174-82.

[174] Louis M, Lebacq J, Poortmans JR, Belpaire-Dethiou MC, Devogelaer JP, Van Hecke P, Goubel F, Francaux M. Beneficial effects of creatine supplementation in dystrophic patients. Muscle Nerve. 2003;27(5):604-10.

[175] Louis M, Raymackers JM, Debaix H, Lebacq J, Francaux M. Effect of creatine supplementation on skeletal muscle of mdx mice. Muscle Nerve. 2004;29(5):687-92.

[176] Tarnopolsky M, Mahoney D, Thompson T, Naylor H, Doherty TJ. Creatine monohydrate supplementation does not increase muscle strength, lean body mass, or muscle phosphocreatine in patients with myotonic dystrophy type 1. Muscle Nerve. 2004;29(1):51-8.

[177] Tarnopolsky MA, Mahoney DJ, Vajsar J, Rodriguez C, Doherty TJ, Roy BD, Biggar D. Creatine monohydrate enhances strength and body composition in Duchenne muscular dystrophy. Neurology. 2004;62(10):1771-7.

[178] Pearlman JP, Fielding RA. Creatine monohydrate as a therapeutic aid in muscular dystrophy. Nutr Rev. 2006; 64(2 Pt 1):80-8.

[179] Davidson ZE, Truby H. A review of nutrition in Duchenne muscular dystrophy. J Hum Nutr Diet. 2009; 22(5):383-93.

[180] Banerjee B, Sharma U, Balasubramanian K, Kalaivani M, Kalra V, Jagannathan NR. Effect of creatine monohydrate in improving cellular energetics and muscle strength in ambulatory Duchenne muscular dystrophy patients: a randomized, placebo-controlled 31P MRS study. Magn Reson Imaging. 2010;28(5):698-707.

[181] Zange J, Kornblum C, Muller K, Kurtscheid S, Heck H, Schroder R, Grehl T, Vorgerd M. Creatine supplementation results in elevated phosphocreatine/adenosine triphosphate (ATP) ratios in the calf muscle of athletes but not in patients with myopathies. Ann Neurol. 2002;52(1):126; discussion -7.

[182] Koumis T, Nathan JP, Rosenberg JM, Cicero LA. Strategies for the prevention and treatment of statin-induced myopathy: is there a role for ubiquinone supplementation? Am J Health Syst Pharm. 2004;61(5):515-9.

[183] Borchert A, Wilichowski E, Hanefeld F. Supplementation with creatine monohydrate in children with mitochondrial encephalomyopathies. Muscle Nerve. 1999;22(9):1299-300.

[184] Tarnopolsky MA, Roy BD, MacDonald JR. A randomized, controlled trial of creatine monohydrate in patients with mitochondrial cytopathies. Muscle Nerve. 1997;20(12):1502-9.

[185] Komura K, Hobbiebrunken E, Wilichowski EK, Hanefeld FA. Effectiveness of creatine monohydrate in mitochondrial encephalomyopathies. Pediatr Neurol. 2003;28(1):53-8.

[186] Matthews RT, Yang L, Jenkins BG, Ferrante RJ, Rosen BR, Kaddurah-Daouk R, Beal MF. Neuroprotective effects of creatine and cyclocreatine in animal models of Huntington's disease. J Neurosci. 1998;18(1):156-63.

[187] Andreassen OA, Dedeoglu A, Ferrante RJ, Jenkins BG, Ferrante KL, Thomas M, Friedlich A, Browne SE, Schilling G, Borchelt DR, Hersch SM, Ross CA, Beal MF. Creatine increase survival and delays motor symptoms in a transgenic animal model of Huntington's disease. Neurobiol Dis. 2001;8(3):479-91.

[188] Ferrante RJ, Andreassen OA, Jenkins BG, Dedeoglu A, Kuemmerle S, Kubilus JK, Kaddurah-Daouk R, Hersch SM, Beal MF. Neuroprotective effects of creatine in a transgenic mouse model of Huntington's disease. J Neurosci. 2000;20(12):4389-97.

[189] Verbessem P, Lemiere J, Eijnde BO, Swinnen S, Vanhees L, Van Leemputte M, Hespel P, Dom R. Creatine supplementation in Huntington's disease: a placebo-controlled pilot trial. Neurology. 2003;61(7):925-30.

[190] Evangeliou A, Vasilaki K, Karagianni P, Nikolaidis N. Clinical applications of creatine supplementation on paediatrics. Curr Pharm Biotechnol. 2009;10(7):683-90.

[191] Dedeoglu A, Kubilus JK, Yang L, Ferrante KL, Hersch SM, Beal MF, Ferrante RJ. Creatine therapy provides neuroprotection after onset of clinical symptoms in Huntington's disease transgenic mice. J Neurochem. 2003;85(6):1359-67.

[192] Bender A, Auer DP, Merl T, Reilmann R, Saemann P, Yassouridis A, Bender J, Weindl A, Dose M, Gasser T, Klopstock T. Creatine supplementation lowers brain glutamate levels in Huntington's disease. J Neurol. 2005;252(1):36-41.

[193] Adhihetty PJ, Beal MF. Creatine and its potential therapeutic value for targeting cellular energy impairment in neurodegenerative diseases. Neuromolecular Med.

2008;10(4):275-90.

[194] Kaemmerer WF, Rodrigues CM, Steer CJ, Low WC. Creatine-supplemented diet extends Purkinje cell survival in spinocerebellar ataxia type 1 transgenic mice but does not prevent the ataxic phenotype. Neuroscience. 2001; 103(3):713-24.

[195] Wyss M, Schulze A. Health implications of creatine: can oral creatine supplementation protect against neurological and atherosclerotic disease? Neuroscience. 2002;112(2): 243-60.

[196] Persky AM, Brazeau GA. Clinical pharmacology of the dietary supplement creatine monohydrate. Pharmacol Rev. 2001;53(2):161-76.

[197] Tarnopolsky MA. Potential benefits of creatine monohydrate supplementation in the elderly. Curr Opin Clin Nutr Metab Care. 2000;3(6):497-502.

[198] Drory VE, Gross D. No effect of creatine on respiratory distress in amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord. 2002;3(1): 43-6.

[199] Mazzini L, Balzarini C, Colombo R, Mora G, Pastore I, De Ambrogio R, Caligari M. Effects of creatine supplementation on exercise performance and muscular strength in amyotrophic lateral sclerosis: preliminary results. J Neurol Sci. 2001;191(1-2):139-44.

[200] Pena-Altamira E, Crochemore C, Virgili M, Contestabile A. Neurochemical correlates of differential neuroprotection by long-term dietary creatine supplementation. Brain Res. 2005;1058(1-2):183-8.

[201] Vielhaber S, Kaufmann J, Kanowski M, Sailer M, Feistner H, Tempelmann C, Elger CE, Heinze HJ, Kunz WS. Effect of creatine supplementation on metabolite levels in ALS motor cortices. Exp Neurol. 2001;172(2): 377-82.

[202] Andreassen OA, Jenkins BG, Dedeoglu A, Ferrante KL, Bogdanov MB, Kaddurah-Daouk R, Beal MF. Increases in cortical glutamate concentrations in transgenic amyotrophic lateral sclerosis mice are attenuated by creatine supplementation. J Neurochem. 2001;77(2):383-90.

[203] Ducray AD, Schlappi JA, Qualls R, Andres RH, Seiler RW, Schlattner U, Wallimann T, Widmer HR. Creatine treatment promotes differentiation of GABA-ergic neuronal precursors in cultured fetal rat spinal cord. J Neurosci Res. 2007;85(9):1863-75.

[204] Derave W, Van Den Bosch L, Lemmens G, Eijnde BO, Robberecht W, Hespel P. Skeletal muscle properties in a transgenic mouse model for amyotrophic lateral sclerosis: effects of creatine treatment. Neurobiol Dis. 2003;13(3):264-72.

[205] Shefner JM, Cudkowicz ME, Schoenfeld D, Conrad T, Taft J, Chilton M, Urbinelli L, Qureshi M, Zhang H, Pestronk A, Caress J, Donofrio P, Sorenson E, Bradley W, Lomen-Hoerth C, Pioro E, Rezania K, Ross M, Pascuzzi R, Heiman-Patterson T, Tandan R, Mitsumoto H, Rothstein J, Smith-Palmer T, MacDonald D, Burke D. A clinical trial of creatine in ALS. Neurology. 2004;63(9):1656-61.

[206] Willer B, Stucki G, Hoppeler H, Bruhlmann P, Krahenbuhl S. Effects of creatine supplementation on muscle weakness in patients with rheumatoid arthritis. Rheumatology (Oxford). 2000;39(3):293-8.

[207] Roy BD, de Beer J, Harvey D, Tarnopolsky MA. Creatine monohydrate supplementation does not improve functional recovery after total knee arthroplasty. Arch Phys Med Rehabil. 2005;86(7):1293-8.

[208] Neves M, Jr., Gualano B, Roschel H, Fuller R, Benatti FB, de Sa Pinto AL, Lima FR, Pereira RM, Lancha AH, Jr., Bonfa E. Beneficial Effect of Creatine Supplementation in Knee Osteoarthritis. Med Sci Sports Exerc. 2011.

[209] Wu G, Bazer FW, Davis TA, Kim SW, Li P, Marc Rhoads J, Carey Satterfield M, Smith SB, Spencer TE, Yin Y. Arginine metabolism and nutrition in growth, health and disease. Amino Acids. 2009;37(1):153-68.

[210] Op't Eijnde B, Jijakli H, Hespel P, Malaisse WJ. Creatine supplementation increases soleus muscle creatine content and lowers the insulinogenic index in an animal model of inherited type 2 diabetes. Int J Mol Med. 2006;17(6):1077-84.

[211] Gualano B, V DESP, Roschel H, Artioli GG, Neves M, Jr., AL DESP, ME DAS, Cunha MR, Otaduy MC, C DACL, Ferreira JC, Pereira RM, Brum PC, Bonfa E, Lancha AH, Jr. Creatine in type 2 diabetes: a randomized, double-blind, placebo-controlled trial. Med Sci Sports Exerc. 2011;43(5):770-8.

[212] Gualano B, V DESP, Roschel H, Artioli GG, Neves M, Jr., De Sa Pinto AL, Da Silva ME, Cunha MR, Otaduy MC, Leite Cda C, Ferreira JC, Pereira RM, Brum PC, Bonfa E, Lancha AH, Jr. Creatine in type 2 diabetes: a randomized, double-blind, placebo-controlled trial. Med Sci Sports Exerc. 2011;43(5):770-8.

[213] Earnest CP, Almada A, Mitchell TL. High-performance capillary electrophoresis-pure creatine monohydrate reduced blood lipids in men and women. Clinical Science. 1996;91:113-8.

[214] Jacobs RL, Stead LM, Ratnam S, Brosnan ME. Regulation of homocysteine metabolism-effects of insulin, glucagon and creatine. FASEB Journal. 2001;15(4).

[215] McCarty MF. Supplemental creatine may decrease serum homocysteine and abolish the homocysteine 'gender gap' by suppressing endogenous creatine synthesis. Med Hypotheses. 2001;56(1):5-7.

[216] Taes YE, Delanghe JR, De Vriese AS, Rombaut R, Van Camp J, Lameire NH. Creatine supplementation decreases homocysteine in an animal model of uremia. Kidney Int. 2003;64(4):1331-7.

[217] Taes YE, Delanghe JR, De Bacquer D, Langlois M, Stevens L, Geerolf I, Lameire NH, De Vriese AS. Creatine supplementation does not decrease total plasma homocysteine in chronic hemodialysis patients. Kidney Int. 2004;66(6):2422-8.

[218] Deminice R, Portari GV, Vannucchi H, Jordao AA. Effects of creatine supplementation on homocysteine levels and lipid peroxidation in rats. Br J Nutr. 2009;102(1): 110-6.

[219] Jahangir E, Vita JA, Handy D, Holbrook M, Palmisano J, Beal R, Loscalzo J, Eberhardt RT. The effect of L-arginine and creatine on vascular function and homocysteine metabolism. Vasc Med. 2009;14(3): 239-48.

[220] Deminice R, Vannucchi H, Simoes-Ambrosio LM, Jordao AA. Creatine supplementation reduces increased homocysteine concentration induced by acute exercise in rats. Eur J Appl Physiol. 2011.

[221] Lawler JM, Barnes WS, Wu G, Song W, Demaree S. Direct antioxidant properties of creatine. Biochem Biophys Res Commun. 2002;290(1):47-52.

[222] Rakpongsiri K, Sawangkoon S. Protective effect of creatine supplementation and estrogen replacement on cardiac reserve function and antioxidant reservation against oxidative stress in exercise-trained ovariectomized hamsters. Int Heart J. 2008;49(3):343-54.

[223] Kingsley M, Cunningham D, Mason L, Kilduff LP, McEneny J. Role of creatine supplementation on exercise-induced cardiovascular function and oxidative stress. Oxid Med Cell Longev. 2009;2(4):247-54.

[224] Bermon S, Venembre P, Sachet C, Valour S, Dolisi C. Effects of creatine monohydrate ingestion in sedentary and weight- trained older adults. Acta Physiol Scand. 1998;164(2):147-55.

[225] Parise G, Brose A, McCartney N, Tarnopolsky MA. Creatine monohydrate supplementation in the elderly results in greater increases in fat-free mass and knee strength following resistance exercise training as compared to placebo. Abstracts of 6th Internationl Conference on Guanidino Compounds in Biology and Medicine. 2001.

[226] Rawson ES, Clarkson PM, Price TB, Miles MP. Differential response of muscle phosphocreatine to creatine supplementation in young and old subjects. Acta Physiol Scand. 2002;174(1):57-65.

[227] Stout JR, Sue Graves B, Cramer JT, Goldstein ER, Costa PB, Smith AE, Walter AA. Effects of creatine supplementation on the onset of neuromuscular fatigue threshold and muscle strength in elderly men and women (64-86 years). J Nutr Health Aging. 2007;11(6):459-64.

[228] Greenwood M, Kreider R, Greenwood L, Byars A. Creatine supplementation does not increase the incidence of injury or cramping in college baseball players. Journal of Exercise Physiology online. 2003;6(4):16-22.

[229] 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 Cell Biochem. 2003;244(1-2):83-8.

[230] Greenwood M, Farris J, Kreider R, Greenwood L, Byars A. Creatine supplementation patterns and perceived effects in select division I collegiate athletes. Clin J Sport Med. 2000;10(3):191-4.

[231] Watsford ML, Murphy AJ, Spinks WL, Walshe AD. Creatine supplementation and its effect on musculotendinous stiffness and performance. J Strength Cond Res. 2003;17(1):26-33.

[232] Cooke MB, Rybalka E, Williams AD, Cribb PJ, Hayes A. Creatine supplementation enhances muscle force recovery after eccentrically-induced muscle damage in healthy individuals. J Int Soc Sports Nutr. 2009;6:13.

[233] Greenwood M, Kreider R, Greenwood L. Effects of creatine supplementation on the incidence of cramping/ injury during the collegiate baseball season. J Athletic Train. 2001.;36(2):S82.

[234] Schilling BK, Stone MH, Utter A, Kearney JT, Johnson M, Coglianese R, Smith L, O'Bryant HS, Fry AC, Starks M, Keith R, Stone ME. Creatine supplementation and health variables: a retrospective study. Med Sci Sports Exerc. 2001;33(2):183-8.

[235] Yoshizumi WM, Tsourounis C. Effects of creatine supplementation on renal function. J Herb Pharmcother. 2004;4(1):1-7.

[236] Dalbo VJ, Roberts MD, Stout JR, Kerksick CM. Putting to rest the myth of creatine supplementation leading to muscle cramps and dehydration. Br J Sports Med. 2008;42(7):567-73.

[237] Gualano B, Ferreira DC, Sapienza MT, Seguro AC, Lancha AH, Jr. Effect of short-term high-dose creatine supplementation on measured GFR in a young man with a single kidney. Am J Kidney Dis. 2010;55(3):e7-9.

[238] Gualano B, de Salles Painelli V, Roschel H, Lugaresi R, Dorea E, Artioli GG, Lima FR, da Silva ME, Cunha MR, Seguro AC, Shimizu MH, Otaduy MC, Sapienza MT, da Costa Leite C, Bonfa E, Lancha Junior AH. Creatine supplementation does not impair kidney function in type 2 diabetic patients: a randomized, double-blind, placebo-controlled, clinical trial. Eur J Appl Physiol. 2011;111(5):749-56.