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HUMAN NUTRITION

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

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THE CREATINE FACTOR

Creatine supplementation burst onto the nutrition scene a few years back, and its popularity has been quite phenomenal. It has been called the ultimate ergogenic aid. As a supplement, creatine is believed to exert its influence by increasing muscle creatine and phosphocreatine concentrations, creating a higher rate of ATP resynthesis, resulting in a delay in an onset of muscle fatigue and facilitating more rapid recovery during repeated rounds of high intensity exercise.

Approximately 95% of the body's total creatine/phosphocreatine (also called phosphorylcreatine) pool is found in muscle, with the majority being located in skeletal muscle rather than in smooth muscle. Tissues that contain creatine are: skeletal muscle, heart muscle, all smooth muscles, sperm and neural tissue, including the brain. On the average, there are about 120 grams of creatine/phosphocreatine in a typical 70-kilogram male. Of this, 72 to 80.4 grams exist as the phosphocreatine form in resting muscle.[1]

Creatine and phosphocreatine undergo irreversible cyclization and dehydration to form creatine at a rate of approximately two grams of creatine per day in the typical adult male.[2] This would then represent the amount of creatine that must be obtained from dietary sources or endogenous synthesis of creatine takes place in the liver and kidney, and this creatine is then released into the bloodstream to be actively taken up by the muscle cells. Glycine, arginine and methionine are the three amino acids used to synthesize of creatine. The body can produce from 1 to 2 grams of creatine per day.[2]

According to Clark's review (Nutrition 14:322-324, 1998), the supplementation of creatine at a rate of 2 to 5 grams per day will increase muscle creatine and phosphocreatine. Dosing at a rate of 20 grams per day for two weeks has lead to marked increases in muscle creatine, which can be maintained with a continued daily dose of five grams. The ingestion of 20 to 30 grams of creatine per day, for up to three weeks, has been seen to increase muscle creatine about 20%.[3] The general finding has been that 20 grams per day is the loading dose that is used for a period of 6 to 14 days, followed by a maintenance dose of five grams per day which was continued throughout the training period. It has been found by green, et al, that: creatine absorption is most efficient in a low-fat, high carbohydrate diet.[4] About 70% of the population who has taken supplemental creatine demonstrated increases in total muscle creatine. Individuals who have low muscle creatine at the start of a creatine supplementation program usually produce the most striking increases in muscle creatine.[3]

A single dose of five grams of creatine has raised creatine plasma levels to a peak in one hour, with a return to pre-supplement levels observed five hours after dosing. This would indicate that the serum half-life of creatine is probably about two hours. According to the laws of pharmacokinetics, this would give the dose of supplemented creatine a serum life span of about 14 hours in the body. Typically, this is determined by multiplying the serum half-like by a factor of seven, provided the administered agent is following first-order kinetics. As mentioned earlier, under normal circumstances the body will turnover about two grams of creatine/phosphocreatine per day. Creatine retention has been found to be maximal (about 32%) in the first two days of supplementation. Caffeine may negate the effects of creatine supplementation by inhibiting the resynthesis of phosphocreatine.[5] It has been reported that athletes consuming 20 grams of creatine daily suffer from water retention, and it may be that some reported muscle cramping and heat intolerance have resulted from this effect. In addition, there have been reports of muscle strains and diarrhea with oral creatine, as well.

In the muscle, creatine is reversibly converted to phosphocreatine, which is the chief store of high-energy phosphates in the muscle. Studies have shown a more rapid resynthesis of phosphocreatine following exercise in athletes who are supplementing their diets with creatine, due to creatine's ability to increase overall phosphocreatine levels and stimulate its regeneration. Creatine has been found to

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be most effective as an ergogenic aid for athletes engaging in repeated bouts of brief strenuous, high-intensity, maximal exercise. It may enhance strength and power performances, leading to increased repetitions and power output.

In a study conducted by Albion Laboratories, test animals were swam to exhaustion and then allowed to rest for 20 minutes before swimming them to exhaustion a second time. In each instance, the animals that received a supplement of a patents pending magnesium creatine chelate were able to swim for a longer period of time.

Creatine's Future?

In view of the extensive usage of creatine as a nutritional supplement over the last few years, along with the publicity it has received from professional sports, it is easy to see why there has been a large influx of research interest and in this substance and its related forms. Since creatine is inherently involved in the core energy generating system of the most active tissues, it could have beneficial effects above and beyond those found in the area of athletic performance.

In a recent double blind, placebo controlled study, [Ferraro S, et al, Clin Cardiol, 19(9):699-703, 1996 Sep], the hemodynamic effects of the phosphate form of creatine on human patients suffering from congestive heart failure was investigated. The patients were all on conventional pharmacologic therapy at the time of the study. The cardiac function of the patients who were on conventional pharmacological agents plus the placebo showed no significant change during the study. The patients who were on the drug therapy plus creatine showed significant improvement, in several different measures of cardiac function, that reflected an overall better force of heart contraction and a more complete output of blood from the heart.

A closely related finding was observed in another study on a group of patients suffering from heart failure (Cafiero M, et al; Clin Ter, 144(4):34-8, 1994, Apr). In this study, 23 patients with hear failure were given a 5-gram dose of creatine (as phosphate) and significant improvement was seen in the ejection volume of their hearts, as well as other measures of heart contractility. Once these improvements of heart contractility were seen in the acute treatment, the creatine therapy was continued for six more days and further improvement was observed for a variety of cardiac parameters that indicated overall improvement in the performance of the muscle of the patient's hearts.

The replacement of heart valves via surgery is rather commonplace today. The recovery of cardiac function and the incidence of arrhythmias after such surgery can cause problems. In a study of 50 patients undergoing such surgery [Chambers DJ, et al; Ann Thorac Surg, 6(1):67-75, 1996 Jan], the addition of creatine (as phosphate) to the normal treatment was shown to provide myocardial protection to the patients by reducing postoperative arrhythmias and decreasing the need for other supportive measures.

Along these lines, Guichard P, Burkhardt JE and Seidler NW [Med Hypotheses, 45 (1):41-44, 1995 Jul] have proposed that the maintenance of high intracellular concentration of unphosphorylated creatine could help fight against the incidence of diabetic heart disease through its ability to neutralize diabetes associated toxic sugar metabolites seen in these individuals.

Magnesium and Energy

In the January 1997 issue of Albion's Research Notes, we presented an extensive review of magnesium's role in energy metabolism. All energy for muscle contraction is derived from the hydrolysis of ATP. Magnesium is intimately linked to the metabolic cycle of ATP production and hydrolysis. There are three overlapping mutually supportive energy systems that provide the ATP needed for physical exercise:

1. Immediate
2. Nonoxidative (glycolytic)
3. Oxidative. High intensity exercises are anaerobic and they rely on the immediate energy system, which gets its ATP from:

    a. ATP existing in muscle sarcoplasm
    b. Myokinase reaction (ADP + Inorganic Phosphate)
    c. CPK Reaction (see Figure 1)

The CPK and Myokinase Reactions create the vast majority of ATP needed for high intensity, anaerobic activity.

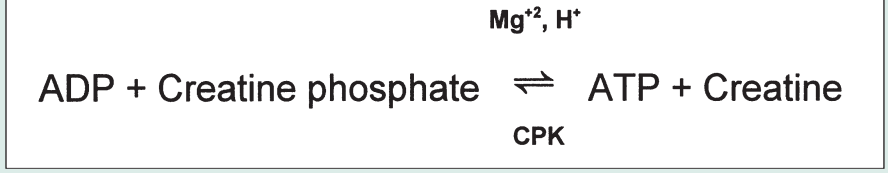

Figure 1

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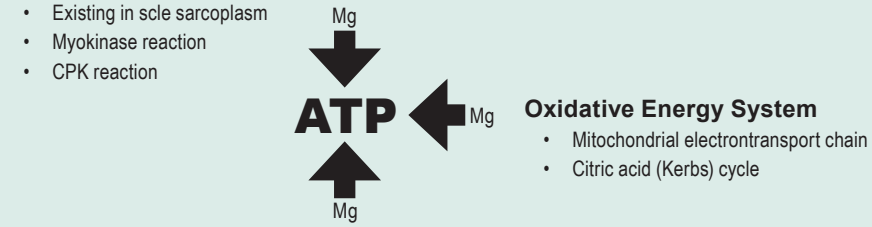
The formation of ATP via the Myokinase Reaction requires magnesium to catalyze the formation of ATP and the CPK reaction cycle requires magnesium to proceed in its energy producing system, as well.

In other words, the ability of creatine to cycle the use and regeneration of ATP for the energy of muscle contractions requires magnesium. In the presence of a magnesium deficiency, no energy can be obtained from creatine! This is why the scientists at Albion Laboratories have developed a patents pending form of creatine in which the creatine in which the creatine is actually chelated to magnesium to form a magnesium creatine molecule – not an admixture. The result is a bioavailable molecule that has two essential components for the generation of energy in the muscle: creatine and magnesium!

Figure 2, below, depicts the energy systems needing magnesium:

Figure 2

Magnesium: The key factor in all the components of these energy producing systems.



Magnesium is involved in more energy producing systems than creatine and creatine requires magnesium for its energy producing cycle. It would seem to follow that the co-supplementation of magnesium and creatine is a very logical choice. Albion is the only company to offer magnesium and creatine in a single molecule.

Other Notable Findings with Magnesium

Electrolyte balance is important to cardiovascular stability, particularly in congestive heart failure. The electrolyte magnesium is essential as a co-factor in several reactions that contribute to stable cardiovascular hemodynamics and electrophysiological functioning. Its deficiency is common and can be a risk factor to heart failure. Magnesium therapy, both for deficiency replacement and in higher pharmacologic doses, is helpful in improving hemodynamics and treating arrhythmias found in patients with congestive heart failure.

"Significance of Magnesium in Congestive Heart Failure", Douban S, et al., Am Heart J, 132 (3):664-71, 1996 Sep)

The purpose of this study was to assess whether magnesium supplementation reverses or attenuates the cardiac dysfunction found with chronic alcohol intake, both at tissue and cellular levels. In the study, the effects of magnesium supplementation during chronic ethanol ingestion on the mechanical properties of the heart were studied. In addition, the acute effects of ethanol on the cardiac muscle of the chronic alcohol exposed, in the absence and presence of magnesium supplementation were also examined. Chronic alcohol exposure caused significant changes in the rate and force of cardiac muscle contraction and relaxation that lead to enlargement in heart size and increase in systolic blood pressure. Magnesium supplementation normalized heart size and blood pressure in those chronically exposed to alcohol. In addition, magnesium supplementation normalized ethanol induced changes in cardiac contractive force and relaxation. Researchers conclude that magnesium supplementation can help normalize the hearts' mechanical function in the face of chronic ethanol exposure.

"Dietary Magnesium Supplementation Attenuates Ethanol-Induced Myocardial Dysfunction", Brown RA, et al, Alcohol Clin Exp Res, 22(9):2062-72, 1998 Dec)

Mitral Valve Prolapse (MVP) is frequent disorder characterized by a number of complaints which lessen the quality of life. Magnesium deficiency has been one of the chief causes of MVP syndrome suggested. This study attempted to assess whether magnesium supplementation alleviates symptoms of MVP. In the study, out of 141 patients, 60% had low serum magnesium. These were subjected to magnesium or placebo supplementation in a double-blind, crossover fashion. Symptoms of MVP (weakness, chest pain, difficulty in breathing, palpitations, anxiety and adrenergic activity). The incidence of MVP symptoms were cut in half for patients who received magnesium supplementation and the magnitude

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of MVP associated adrenergic activity was cut by about 75%. The researchers concluded that many patients with heavily symptomatic Mitral Valve Prolapse are low in magnesium and that magnesium supplementation improves most symptoms and favorably adjusts adrenergic activity.

"Clinical Symptoms of Mitral Valve Prolapse are related to Hypomagnesium and Attenuated by Magnesium Supplementation", Lichodziewska B, et al; Am J Cardiol, 79(6):768-72, 1997 March 15)

There have been many additional studies that report on the cardioprotective, antiarrhythmic or positive ionotropic benefits of magnesium. There is no question, based on the accumulating body of research, that magnesium has a positive impact on heart function. More recently, creatine's positive effects on cardiac function have also been reported, as noted above.

Magnesium and creatine have been proven to provide beneficial effects in the same diverse areas of physiological activities. Since their biochemical roles are also closely interlaced in very specific reactions, isn't it logical for Albion to attempt to unite these two into a single Albion chelate force? The result is a new magnesium creatine chelate molecule that is the subject of several pending patents. It is not a mixture – it is a totally reacted product.

The Need for Albion Chelate Technology

The loading dose for creatine is a very large one; and even its subsequent maintenance dose remains quite high. The studies reviewed have pointed out that about 20 grams per day for 2 weeks will increase muscle creatine by about 20%. Assuming an average body creatine content (range 72-80.4 grams in a 70 kg male) is about 76 grams, a 20% increase would be about 15.2 grams. There is an average loss of 2 grams of creatine per day. This would come to 28 grams over the span of 2 weeks. So a 15.2 gram increase in net body creatine would translate into a net increase in uptake of 15.2 plus 28 to equal 43.2 grams. At an intake of 20 grams per day, this would provide a relative creatine absorption of 43.2 grams/280 grams of 15.4%.

Granted, these numbers are extrapolated, but they do get their basis in the substantial research data of the leading researchers in the area of creatine loading. Harris, et al, found the maximal creatine absorption to about 32%, and this occurred in the first two days of supplementation.[3]

Given the low relative absorption rate for creatine, it is believed that by using Albion's chelate technology, the formation of a patents pending Magnesium Creatine Chelate will improve the absorption characteristic for the creatine. This molecule is unique – not only in structure, but also in safety. Toxicology studies have proven that there are no side effects in animals when they receive magnesium creatine chelate supplemented up to 2,000 mg of this magnesium creatine chelate per kg of body weight. That is about 160 mg of magnesium per kg of body weight!! And this is the only product of its kind that has kosher approval.

In addition, the combining of magnesium and creatine will finally harness together two separate nutritional forces that have been shown to have positive effects of the heart, energy and muscular performance.

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