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Creatine monohydrate: A potent dietary supplement

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Abstract
Creatine monohydrate, a dietary supplement, improves muscular function during short and high intensity of resistance training that depend on the phosphocreatine shuttle for adenosine triphosphate. The most effective dosage for creatine supplementation consists of loading for 5–7 days at 0.3 g/kg/d, then maintaining for 4–6 weeks at 0.03 g/kg/d. To raise the intramuscular creatine reserves, however, loading doses are not required. The most researched type of creatine is creatine monohydrate; creatine ethyl ester has not demonstrated any further advantages. With few recorded negative effects, creatine is a relatively safe dietary supplement. Transient water retention during the initial phases of supplementing is the most frequent adverse effect. There have been incidences of liver and kidney problems with creatine when it was taken with other supplements or at doses greater than advised for several months. To assess the long-term and potential negative effects of sustained creatine administration, more research is required.

Keywords: Creatine monohydrate, metabolism, consumption, health implications

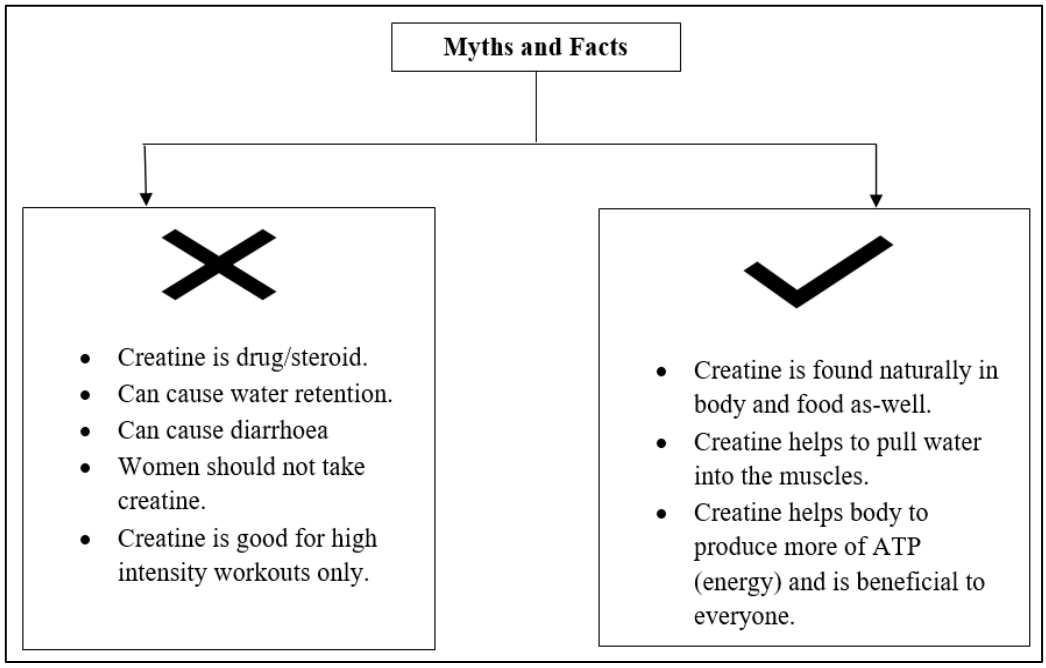
Introduction
Creatine is one of the natural sources of energy for muscle contraction in the body [1]. The body gets about half of its supply from eating meat, and the other half is created in the liver and kidneys before being used by the skeletal muscles [2]. Skeletal muscles store about 95% of the creatine that is utilised during physical activity. By sustaining production in active muscles, creatine aids in ensuring a steady supply of energy to working muscles [3]. Furthermore, heart, brain, and other tissues also contain creatine in little amounts. Creatine supplements (CrS) gained popularity in early 1990's when it was believed by athletes that their performance had benefited from consumption of CrS by competing in sprint and power events in Olympics in Barcelona. Along with this, CrS became more popular among athletes when studies showed some benefits with strength training and it became one of the most extensively studied supplements [4]. Over 300 researches have looked at the effects of creatine on resistance training, and 70% of them found increases in strength. There are several different types of creatine; however, creatine monohydrate has received the most research and has demonstrated advantages in short-duration, high-intensity weightlifting and cycling [5]. After that, many athletes started to consume CrS in order to enhance physical performance and build mussels. In healthy individuals, supplements are generally harmless [6]. Creatine boosts performance but has little impact on aerobic endurance since it produces "quick burst" energy and improves strength. Male athletes that participate in power sports like football, wrestling, hockey, and bodybuilding are at the top for consuming CrS [1].

Creatine metabolism
Creatine is primarily found in two forms in the human body: the phosphorylated form, which accounts for 60% of stores, and the free form, which accounts for 40% of stores [7]. The typical skeletal muscle fibre type and total amount of muscle mass-dependent creatine pool for a 70 kg young male differs between individuals [2]. The rate of creatinine generation from the breakdown of phosphocreatine and creatine is matched by endogenous production and dietary intake at 2.6 percent and 1.1 percent/day, respectively. In general, taking oral creatine supplements raises the body's level of creatine [4]. It can be removed from the blood through renal filtration or saturation into different organs and cells. It is produced by the combination of three amino acids—glycine, arginine, and methionine—and three enzymes—L-arginine: glycine amidinotransferase, guanidinoacetate methyltransferase, and methionine adenosyltransferase [8]. Adults' glycine metabolism is not significantly affected by creatine production, whereas arginine and methionine metabolism are more significantly affected. Only CreaT1 transports creatine consumed by supplementation into cells [9].

Another creatine transporter, called Crea T2, is found and largely active in the testes. Phosphorylation, glycosylation, extracellular, and intracellular amounts of creatine are some of the mechanisms that control creatine uptake. The extracellular and intracellular levels of creatine have been particularly triggered when total creatine concentration inside the cell falls, and Crea T1 has demonstrated to be extremely sensitive to both levels [10]. Additionally, it has been shown that the presence of a mitochondrial isoform of Crea T1 enables creatine to be carried into the mitochondria in addition to cytosolic creatine. indicating the presence of an additional intra-mitochondrial pool of creatine, which appears to be crucial for the phosphatetransport mechanism that moves phosphate from the mitochondria to the cytosol [9]. Patients with myopathy have shown decreased levels of total creatine, phosphocreatine, as well as decreased amounts of the supposedly harmful CreaT1 protein principal cause of these reduced levels [11].

Consumption of creatine

Since creatine is abundantly present in food, no athletic organisation has a policy against its use, though some organisations do forbid teams from giving athletes certain kinds of dietary supplements [12]. In these situations, athletes are free to purchase and consume creatine on their own without facing consequences or breaking any rules regarding the use of prohibited substances. Creatine usage worldwide is substantially more than the four million kilogrammes (kg) consumed annually by Americans [13]. In survey-based research, the prevalence of creatine use among athletes and military people has often been estimated to be between 15-40%, with use being more prevalent among male strength/power athletes. Similar prevalence of creatine use has been documented among high school athletes. The National Collegiate Athletic Association (NCAA) reported that in 2014, creatine was one of the most popular dietary supplements used by their male athletes (e.g., baseball - 28.1%, basketball - 14.6%, football - 27.5%, golf - 13.0%, ice hockey - 29.4%, lacrosse - 25.3%, soccer - 11.1%, swimming-19.2%, tennis - 12.9%, track and field - 16.1%) [14]. In comparison, these NCAA athletes reported moderate use of androgenic anabolic steroids, significant use of alcohol (83%) and cigarettes (10–16%), and low use of marijuana (22%). No study has documented any negative or ergolytic effects of short- or long-term CrS, whereas other studies have documented the improvement in athletic performance and/or health in people with various conditions [1, 5]. Therefore, athletes consuming creatine would not be as much of a health risk as the incidence of alcohol, cigarette, and drug use among NCAA athletes [15].



(Source: Jager *et al*., 2011; Roelands *et al*., 2020; Forbes *et al*., 2022**)**

Fig 1: Myths and Facts

Health implications of creatine supplementation

The majority of early studies on creatine concentrated on how it affected exercise performance, training adaptations, and safety in both trained and untrained healthy people. Acute exercise capacity, training adaptations, and muscle creatine and PCr levels have all been shown to rise with creatine supplementation [16]. On a variety of high-intensity exercise tasks, such as fitness/weight training, golf, volleyball, soccer, softball, ice hockey, running, and swimming, among others, the improvement in performance has typically been 10–20%. Although the majority of research has been done on men but ergogenic advantages have been observed in both men and women from young infants to elderly populations [17]. The International Society of Sports Nutrition (ISSN) determined after thoroughly analysing the research that creatine is "now accessible to athletes in terms of ergogenic nutritional supplements boosting lean body mass and high-intensity exercise capacity throughout training". Dietitians of Canada, the American College of Nutrition, and the American Dietetic Association are at similar conclusions and have been reached by Sports Medicine in support of their stance [18]. Thus, the use of creatine supplements as an efficient ergogenic aid is widely accepted by scientists. Evidence that creatine supplementation may provide some health and/or therapeutic

benefits as we age, started to gather as performance-related research evaluated health and safety markers [11, 18]. In this regard, CrS has been shown to help lower cholesterol, triglycerides, and/or manage blood lipid levels, reduce the buildup of fat on the liver, decrease homocysteine thus reducing risk of heart disease, serve as an antioxidant, enhance glycemic control, reduce the progress of some forms of cancer, increase strength and muscle mass, minimise bone loss in some studies, and improve functional capacity in osteoarthritic and fibromyalgia patients [17, 19]. These results reinforce the idea that, in order to maintain overall health as one ages, it is important for people to consume at least 3 g of creatine daily. Therefore, despite the need for additional research, it is reasonable to infer from the available data that taking supplements of creatine can improve overall health, fitness, and wellbeing over the course of a person's lifetime and increase the amount of cellular energy available [19].

With few documented adverse effects, creatine is generally safe. However, you should be aware that if you use creatine supplements, your body's muscles may retain water, which could lead to weight gain [20]. Depending on how much creatine your body currently contains, it may take seven to 28 days to notice an increase in energy. When you are genuinely dehydrated or trying to reduce weight, taking creatine pills could be risky [9]. The International Society of Sports Nutrition recently concluded that there is no scientific proof that either short- or long-term use of creatine monohydrate on otherwise healthy people results in any negative effects [20]. But before taking supplements, like creatine, make sure you speak with your doctor. Although your body already contains some creatine, taking additional supplements seems to be generally safe. But be aware that the American Food and Drug Administration does not control dietary supplements [6, 9]. The amount of creatine supplement, the quality, and the other ingredients in creatine products that are offered in stores can vary. Standards for purity and safety are also uncontrolled [2, 18]. The safety of creatine supplementation in pregnant or nursing mothers is not well understood. Before using, discuss with your healthcare professional if you have kidney problems [1]. Your kidney illness could get worse if you take the supplement. Your kidneys might be harmed by several drugs. If you use any medications, be sure to see your doctor first as the combination of pharmaceuticals and creatine supplements may cause kidney damage [15, 19]. The consequences of mixing creatine supplements with over-the-counter pharmaceuticals, prescription prescriptions, vitamins, and energy drinks are unknown to doctors, as are the effects on the heart, brain, kidneys, liver, and reproductive organs [21].

Conclusion

Numerous studies on the use of creatine supplements have been released. When muscle creatine levels are markedly raised, ergogenic effects on performance have been seen in a considerable proportion of these trials. It is now clear that the buildup of creatine in skeletal muscle or other tissues has an impact on a number of cellular functions, which may explain its ergogenic and therapeutic potential. Recent research has begun to paint a clearer picture of the physiological processes through which creatine supplementation impacts the protein and glucose metabolism in skeletal muscle. There is still uncertainty on the precise traits of nonresponders and the best dosing methods.

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