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How Does Creatine Supplementation Affect Physical Performance and Muscle Recovery? - A Literature Review of Its Effects, Mechanisms of Action, Safety and Side Effects

Martyna Pacanowska
Jagiellonian University Medical College
Świętej Anny 12, 31-008 Cracow, Poland
martyna.pacanowska@gmail.com
https://orcid.org/0000-0002-5803-548X

Małgorzata Blecharczyk
Medical University of Warsaw
Żwirki i Wigury 61, 02-091, Warsaw, Poland
gosia.blech20@gmail.com
https://orcid.org/0009-0009-1146-7662

Igor Zydlewski
Medical University of Warsaw
Żwirki i Wigury 61, 02-091, Warsaw, Poland
igorzydlewski@op.pl
https://orcid.org/0009-0009-5053-8910

Martyna Mrozek
Medical University of Warsaw
Żwirki i Wigury 61, 02-091, Warsaw, Poland
mrozekmartyna99@gmail.com
https://orcid.org/0009-0004-1678-4054

Alicja Nowik
Military Institute of Medicine – National Research Institute
Szaserów 128, 04-141 Warsaw, Poland
alicja.nowik@outlook.com
https://orcid.org/0009-0004-0446-0116

Marcin Sękulski
Medical University of Warsaw
Żwirki i Wigury 61, 02-091 Warsaw, Poland
marcin.sekulski1@gmail.com
https://orcid.org/0009-0004-7164-5938

Maciej Kosiński
University Clinical Centre of the Medical University of Warsaw
Banacha 1A, 02-097 Warsaw, Poland
maciej.kosinski.11@gmail.com
https://orcid.org/0009-0003-6171-236X

Paweł Jakubiec
Lazarski University,
Świeradowska 43, 02-662 Warsaw, Poland
pawel.jakubiec@hotmail.com
https://orcid.org/0009-0002-0101-7878

ABSTRACT

Introduction: Creatine is a naturally occurring compound that plays a primary role in energy metabolism, particularly within muscle cells. Its main sites of synthesis include the liver, kidneys, and pancreas [1,2]. This compound is crucial for muscle recovery following exercise. Creatine's ability to rapidly replenish ATP stores reduces fatigue and muscle soreness, thereby accelerating the recovery process. By increasing the availability of phosphocreatine in muscle cells, creatine significantly enhances the capacity to perform both short-duration and high-intensity exercises [4,8]. This allows athletes to complete more repetitions per set and recover faster between sets. Consequently, creatine supplementation has gained increasing popularity, particularly among athletes and physically active individuals. Additionally, creatine's influence on muscle protein synthesis is also linked to its ability to improve muscle cell hydration [15].

Aim of the Study: The aim of this study is to evaluate the impact of creatine supplementation on physical performance and muscle recovery, as well as to review its efficacy, safety, and potential side effects.

Material and Methods: A review and analysis of randomized clinical trials and clinical studies from 2010 to 2025 available in PubMed and Google Scholar.

Conclusions: Research findings indicate that long-term creatine use does not cause significant adverse side effects. Individuals supplementing with creatine have shown an increase in lean body mass without any undesirable effects on liver and kidney function. By improving muscle strength and endurance, creatine helps stabilize joints, thereby reducing the risk of

musculoskeletal injuries [13]. From a practical perspective, these findings provide valuable insights for athletes, coaches, and physically active individuals striving to enhance both short-term and long-term training outcomes through creatine supplementation.
Keywords: creatine supplementation, physiscal performance, muscle recovery, phosphocreatine, body composition, muscle physiology, injury prevention

INTRODUCTION

Biochemical pathways

To understand the role of creatine in muscle physiology, it is necessary to delve into the biochemical pathways involved in its synthesis. Creatine synthesis is a two-step process that occurs primarily in the liver, kidneys, and pancreas. The first step involves the transfer of the amidino group from arginine to glycine, resulting in the formation of guanidinoacetate and ornithine. This reaction is catalyzed by the enzyme L-arginine:glycine amidinotransferase (AGAT).

The second step involves the methylation of guanidinoacetate by S-adenosylmethionine (SAM), leading to the formation of creatine. This reaction is catalyzed by the enzyme guanidinoacetate N-methyltransferase (GAMT) [6], [11]. The next step is the transport of the synthesized creatine through the bloodstream to various tissues, including skeletal muscles, where it plays a key role in energy metabolism. Within muscle cells, creatine undergoes phosphorylation, forming phosphocreatine (PCr) through the action of the enzyme creatine kinase (CK). The role of phosphocreatine is crucial during periods of high energy demand, such as intense physical activity, as it serves as a rapid reserve of high-energy phosphates that can be utilized for the regeneration of adenosine triphosphate (ATP) [4], [14]. This rapid process is essential for maintaining muscle contraction and performance during short-term, high-intensity exercise.

Several factors influence the storage of creatine and phosphocreatine in muscle tissue, including dietary intake, muscle fiber type, and the presence of specific creatine transporters. These transporters facilitate the uptake of creatine into muscle cells, ensuring appropriate intracellular concentrations for optimal performance and recovery [4], [6].

Storage

The majority of creatine in the human body is stored in skeletal muscles, which is essential for meeting the energy demands of muscle contractions. It has been demonstrated that creatine supplementation promotes muscle hypertrophy and increases strength. This effect is attributed to creatine's role in enhancing water content within muscle cells, which may contribute to their volumetric growth, the creation of an anabolic environment, and increased protein synthesis. Studies indicate that individuals who supplement with creatine experience greater gains in lean muscle mass and strength compared to those who do not [2], [14].

Creatine is also stored in other tissues, including the brain and various organs. The brain, in particular, exhibits a high energy demand, and the storage and utilization of creatine within the brain are crucial for cognitive function and proper neuronal activity [9], [11]. Research suggests that creatine supplementation may enhance cognitive abilities, especially in tasks requiring short-term memory and rapid thinking [4], [15]. Additionally, by mitigating oxidative stress and supporting mitochondrial function, creatine exhibits neuroprotective properties, which may reduce the risk of neurodegenerative diseases [15].

Creatine is also stored in the heart, kidneys, and liver. Studies indicate that, particularly under conditions of increased energy demand, such as physical exertion or heart disease, creatine supplementation improves cardiac performance [5], [11]. The initial stage of creatine synthesis from amino acids occurs in the liver, after which creatine is transported to other tissues. The kidneys play a role in creatine resorption and excretion, helping to maintain its balance within the body [18].

Factor affecting storage

Creatine storage in the human body is multifaceted and involves various physiological and biochemical mechanisms. A key determinant of creatine storage capacity is the initial concentration of creatine in muscles. Individuals with lower baseline muscle creatine levels typically experience a greater increase in creatine storage following supplementation compared to those whose creatine levels are already high [2], [4]. This phenomenon is attributed to the saturation effect, where muscles with high creatine concentrations have a limited ability to store additional amounts.

The dosage regimen and duration of creatine supplementation also play a crucial role. One supplementation strategy involves a loading phase, which consists of consuming 20 grams of creatine daily for 5–7 days, followed by a maintenance dose of 3–5 grams per day. This approach leads to a more rapid increase in muscle creatine stores compared to lower doses without a loading phase [11], [17]. The loading phase facilitates the rapid saturation of muscle creatine stores, which can then be maintained with lower daily doses in subsequent days. Another important factor is the timing of creatine intake in relation to physical exercise. Studies have demonstrated that consuming creatine immediately before or after training may enhance its absorption and storage in muscles, likely due to increased blood flow and heightened muscle insulin sensitivity during and after exercise [7].

Furthermore, co-ingestion of creatine with carbohydrates enhances its muscle uptake, which may be attributed to insulin-mediated stimulation of creatine transport into muscle cells [2], [17]. Insulin increases the activity of sodium-dependent creatine transporters in the muscle cell membrane, thereby facilitating creatine transport. Additionally, genetic factors may influence an individual's ability to store creatine. Variations in the expression and activity of creatine transporters, as well as differences in muscle fiber composition, can significantly affect creatine storage efficiency [17]. For instance, individuals with a higher proportion of type II muscle fibers have a greater capacity for phosphocreatine storage and may derive greater benefits from creatine supplementation.

REVIEW OF LITERATURE

Effet on physical performance

Aerobic capacity, also referred to as aerobic endurance, is the ability to sustain prolonged physical effort without a significant increase in fatigue. It is influenced by various factors, including creatine supplementation. Creatine supplementation has been shown to enhance performance during submaximal aerobic efforts, such as treadmill running interspersed with high-intensity intervals. This improvement is attributed to creatine's role in energy metabolism—facilitating the rapid regeneration of adenosine triphosphate (ATP) during intense exertion, thereby delaying fatigue and increasing overall endurance [17, 20].

Moreover, creatine has the ability to reduce muscle damage and inflammation, further supporting its role in improving aerobic performance. This enables athletes to engage in more demanding and intense training sessions while enhancing recovery [22]. Research has demonstrated the beneficial effects of creatine supplementation in repeated sprint tests, such as six maximal 15-meter sprints with 30-second rest intervals, as well as in sport-simulating tests and repeated 20-meter sprint performance [4]. However, since individual responses to creatine may vary, its potential benefits should be assessed in relation to the specific demands of a given sport or physical activity [7].

Effect on power and strenght

Maximal strength is the greatest amount of force that a muscle or muscle group can generate during a maximal contraction. It is a key determinant in assessing athletic performance and overall physical fitness. Research has shown that creatine supplementation (20 g per day) during resistance training significantly increased maximal strength in cyclists and collegiate football players in exercises such as bench press and squats [4]. In a study evaluating the effects of creatine on peak torque and the fatigue index, researchers found that after seven days of supplementation, individuals taking creatine exhibited a lower fatigue index compared to the non-supplemented group [10].

However, exceptions exist, such as a study involving Brazilian jiu-jitsu and wrestling athletes. This study found that short-term creatine supplementation did not significantly improve peak and mean power output or the fatigue index during repeated sprints [4]. This suggests that the effectiveness of creatine may depend on the type of sport, the duration of supplementation, and the nature of the physical effort performed.

In a study involving older adults, creatine supplementation combined with resistance training led to a significant increase in muscle mass compared to the placebo group [11]. Supplementation with creatine monohydrate, in conjunction with a structured resistance training program, may reduce the loss of lean body mass and muscle strength typically associated with aging [15]. This indicates that creatine may support the maintenance of muscular endurance in older individuals, improving their overall physical fitness and quality of life.

Effect on muscle recovery

Muscle protein synthesis (MPS) is a crucial process in muscle recovery and growth, particularly following physical exercise. Researchers [6] have demonstrated that, in terms of enhancing high-intensity exercise performance and increasing lean body mass, creatine monohydrate is the most effective form of creatine. This effect is largely attributed to its role in promoting muscle protein synthesis, which is essential for muscle regeneration and hypertrophy. Amino acids serve as the monomeric building blocks of proteins, and their increased availability within muscle cells can contribute to higher rates of MPS. This has significant implications for post-exercise muscle recovery, as the demand for amino acids rises to facilitate tissue repair and the formation of new muscle fibers [7].

Additionally, creatine influences the expression of certain genes associated with muscle growth. Creatine supplementation has been shown to upregulate myogenic regulatory factors (MRFs), such as MyoD and myogenin, which play a fundamental role in muscle differentiation and growth. This gene expression modulation further supports creatine's role in enhancing muscle protein synthesis and promoting muscle hypertrophy [21].

Effect on injury prevention

Muscle damage is a critical factor to consider when assessing the impact of creatine supplementation on injury prevention. Research suggests that creatine supplementation can significantly reduce markers of muscle damage following intense exercise. This effect is attributed to creatine's role in muscle cell metabolism, where it helps maintain ATP levels during high-intensity exercise while simultaneously mitigating muscle cell damage and inflammation [5], [11]. The protective effects of creatine are also linked to its ability to buffer hydrogen ions and stabilize cell membranes. Studies indicate that creatine supplementation can modulate the expression of genes associated with oxidative stress and inflammatory responses, thereby fostering a more favorable environment for muscle recovery [5], [11], [14].

In a study involving Ironman triathletes, participants who supplemented with creatine exhibited lower levels of muscle damage markers, including creatine kinase, lactate dehydrogenase, and aldolase, after competition [4]. This finding suggests that creatine may help attenuate the inflammatory response associated with intense physical exertion.

Furthermore, creatine has been shown to influence biomarkers of apoptosis. A study conducted on young athletes demonstrated that short-term creatine monohydrate supplementation significantly reduced levels of the p53 protein, which is associated with apoptosis, following intense aerobic exercise [24]. The reduction in p53 levels indicates that creatine may have potential anti-inflammatory properties that contribute to minimizing muscle damage and enhancing recovery.

Safety and side effect

The potential side effects of creatine supplementation have been extensively studied. One of the most frequently reported effects is weight gain, primarily due to an increase in lean muscle mass. This effect offers significant benefits for athletes aiming to enhance strength and muscle mass, as well as for patients suffering from muscle-wasting conditions. However, weight gain is typically temporary, as it largely results from increased water retention within muscle cells [20].

Another commonly reported side effect is gastrointestinal discomfort, including bloating, cramps, and diarrhea. These symptoms can often be mitigated by adjusting the dosage or timing of creatine intake and are frequently dose-dependent [12,13]. In most cases, these effects are mild and resolve spontaneously.

Concerns have also been raised regarding creatine's impact on kidney function. However, research confirms that creatine supplementation does not have adverse effects on kidney health in healthy individuals—even with long-term use, there is no evidence of kidney damage. While creatine supplementation may lead to an increase in serum creatinine levels, this does not indicate impaired kidney function [9]. Similarly, studies investigating creatine's effects on liver health have found no significant impact on liver enzyme levels or overall liver function, even in individuals with pre-existing conditions [14]. The U.S. Food and Drug Administration (FDA) has classified creatine as "generally recognized as safe" (GRAS) [5].

Although most side effects are minimal, individual responses to creatine may vary. Factors such as dosage, frequency of use, and overall health status can influence the likelihood and severity of side effects.

CONCLUSIONS

Analyzing the extensive body of research on the role of creatine in muscle physiology, the metabolic pathways it is involved in, its function, and the process of its storage, it becomes clear that creatine supplementation plays a significant role in both overall health and athletic performance. The target group- athletes- derive particular benefits from creatine supplementation, as it improves training outcomes, aerobic and anaerobic endurance, aids recovery, and reduces muscle damage after exertion. Creatine supplementation significantly supports muscle hypertrophy through various mechanisms, including increased muscle protein synthesis, expression of certain genes, reduced protein degradation, enhanced muscular strength, and improved recovery after exercise. These properties highlight its value not only as a physical performance aid but also as a tool that ensures the maintenance of muscle health.

The safety of creatine supplementation is well-documented, and its consumption at recommended doses is associated with minimal side effects. The most commonly reported effect is water retention, which causes a transient increase in body weight. Although long-term studies conducted to date confirm the safety of creatine, further analysis is needed regarding its impact on different demographic groups, and future studies should focus on the effects of various doses and supplementation protocols. Research involving a broader range of participant groups will help better understand the full spectrum of creatine's benefits for diverse populations. In summary, creatine is a versatile supplement whose application extends beyond conventional sports supplementation, encompassing overall health and cognitive functions. Undoubtedly, further research will reveal additional uses for creatine supplementation, solidifying its position as a key ingredient for enhancing both physical performance and neurological health.

Disclosure

Author's contribution

Conceptualization, M. Pacanowska; methodology, M. Mrozek and M. Blecharczyk; software, M. Kosiński; check, M. Sękulski, and P. Jakubiec; formal analysis, A. Nowik and I. Zydlewski; investigation, M. Blecharczyk; resources, I. Zydlewski; data curation, M. Sękulski and M. Kosiński; writing - rough preparation, P. Jakubiec; writing - review and editing, A. Nowik; visualization, M. Mrozek; supervision, M. Pacanowska; project administration, M.Pacanowska; All authors have read and agreed with the published version of the manuscript.

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The authors deny any conflict of interest.

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