WYDRA-ROJEK, Aleksandra, ŁAKOMA, Aleksandra, MARZEC, Weronika Zofia, CHOIŃSKI, Maciej, WASIEWICZ-CIACH, Paulina, KUCZYŃSKI, Piotr, MARSZAŁEK, Anna, MARZEC, Marcelina Teresa, KUTYŁA, Katarzyna and MOKOT, Wojciech Jan. Creatine - the impact of supplementation on the human body. Quality in Sport. 2024;20:54004. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.20.54004
https://apcz.umk.pl/QS/article/view/54004

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 01.08.2024. Revised: 20.08.2024. Accepted: 21.08.2024. Published: 22.08.2024.

Creatine - the impact of supplementation on the human body

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Abstract

Introduction

Creatine is an endogenously occurring compound in the human body and one of the most extensively studied dietary supplements used worldwide. It is synthesized in the human body, primarily in the kidneys and liver, and is supplied through a diet rich in animal-based foods. Creatine is a nitrogenous compound composed of three amino acids: glycine, arginine, and methionine. It plays a crucial role in the body's metabolism, and therefore, the function of many organs and systems depends on its levels.

Aim of the study

The aim of this study was to discuss the role that creatine plays in the body. A summary of the effects of creatine supplementation in sports and various disease conditions was provided. The study also explored the metabolism of creatine and focused on the best available form of creatine and its dosing regimen.

Materials and methods

The study was based on articles searched in the PubMed database, published between 2006 and 2023. The following keywords were used for the search: "creatine," "creatine supplementation," "creatine monohydrate," "creatine supplement," and "creatine effects."

Conclusion

Creatine is one of the most popular chemical compounds that occur endogenously in the muscle cells of the body. It is a nitrogenous compound primarily produced in the liver, and its levels can be further increased with creatine supplements. The most widely available and well-studied form on the market is creatine monohydrate. Until recently, creatine supplementation was only associated with sports, but it is now used in various disease conditions and supports the function of many organs.

Keywords :

"creatine," "creatine supplementation," "creatine monohydrate," "creatine supplement".

Introduction

Creatine is a nitrogenous compound, with as much as 98% stored in the muscle cells of the human body. It is composed of three amino acids: arginine, glycine, and methionine. The human body produces about 1 gram of creatine daily, with this synthesis occurring in the liver, kidneys, pancreas, and brain. The remaining amount of creatine is supplied through diet, primarily from animal-based products. Its sources include dairy, white and red meat, and fish. In the body, creatine exists in two forms: free creatine, which constitutes about 40% of the stores, and creatine phosphate, which makes up approximately 60%. A person weighing around 70 kg has a creatine pool of approximately 120-140 grams, although this amount varies depending on muscle mass. Free creatine, when combined with a phosphate group, forms creatine phosphate, which is essential for the production of adenosine triphosphate (ATP), the primary source of energy. Recent studies indicate that creatine affects the function of many organs and systems [1,2,3,21].

Creatine Metabolism

Creatine is a vital compound for optimal metabolism. The enzyme creatine kinase phosphorylates creatine to form creatine phosphate. The breakdown of creatine phosphate back to creatine occurs through the cleavage of the phosphate bond, releasing a substantial amount of energy that enables the conversion of adenosine diphosphate (ADP) to adenosine triphosphate (ATP). Consequently, creatine serves as an energy reserve for the synthesis of ATP molecules under anaerobic conditions. [20].

The synthesis of creatine occurs in two stages:

1. The first stage occurs in the kidneys:
    - Guanidinoacetic acid is produced from glycine and arginine.
2. The second stage occurs in the liver:
    - Guanidinoacetic acid is transported to the liver and converted into creatine with the help of the methyl donor S-adenosylmethionine [20].

Creatine synthesis can also occur in other organs such as the brain and testes. There is evidence that cardiac muscle cells also possess the ability to produce creatine [20].

Effects on the Body

Nervous System

Creatine has a beneficial impact on brain function, as it is a neuroprotective compound with antioxidant properties for brain cells. Its influence on the course of psychiatric and neurological disorders has also been proven [2]. High levels of creatine in body tissues alleviate the course of injuries and disease conditions, especially those involving hypoxia [16]. A creatine deficiency accompanies many neurodegenerative diseases and disrupts the proper functioning of brain tissue. It is an essential chemical compound for the proper functioning of the body [4]. Creatine has a wide range of applications: in addition to improving athletic performance, it offers neuroprotection in brain and spinal cord injuries, reducing their severity and leading to better rehabilitation outcomes [17].

The brain can produce endogenous creatine, making it independent of creatine produced by the liver or kidneys. This is crucial during states of increased demand for creatine by brain tissue, as it enables the resynthesis of adenosine triphosphate (ATP).

ATP is necessary for the proper functioning of nerve cells. Creatine can also cross the blood-brain barrier via specific transporters, though this transport is limited, and in states of increased demand for creatine by brain tissue, more time and higher doses are required compared to skeletal muscles. This is particularly significant in disease states with impaired brain energy metabolism, such as brain injury, hypoxia, or performing complex cognitive tasks. When brain tissue lacks creatine, there are issues with many developmental and mental disorders [5,6].

Creatine deficiency states, which involve problems with information assimilation, learning difficulties, or seizures, confirm that it plays a significant role in cognitive functions [5]. It affects memory, particularly when the supplement is taken by older individuals [7]. Considering that information processing and memory are energy-intensive processes, increasing creatine levels in brain tissue improves its energetic state and memory function [14]. Studies indicate a positive effect of creatine supplementation on sleep deprivation. Among those studied who were deprived of sleep, it was noted to have a beneficial impact on mood, reaction time, and balance [18]. It has been observed that in vegetarians, who avoid primary dietary sources of creatine, cognitive function improved after creatine supplementation [8]. It has also been proven that creatine taken by athletes to enhance their physical performance also improved their cognitive abilities [9].

Brain injury is a state of increased ATP demand by nerve cells, coupled with reduced blood flow. Creatine, involved in energy homeostasis, helps regenerate ATP despite the accompanying hypoxia of the injuries. Additionally, it improves neurotransmission, reduces inflammation, and decreases brain tissue swelling. Given that creatine levels drop in the case of brain injury, supplementation accelerates brain tissue regeneration and enables a quicker recovery [10,20].

Due to creatine's known impact on central nervous system homeostasis, it is believed that its supplementation may benefit the course of neurodegenerative diseases through its antioxidant action and ATP regeneration capability. One such disease is Duchenne muscular dystrophy, caused by a dystrophin gene mutation. It has been shown that creatine intake by patients with this disease improves their muscle strength and bone density [5].

2. Creatine and the Female Body

Pregnancy, a state of increased metabolic demand due to the growth and development of the fetus and placenta, causes changes in creatine homeostasis. The intake of creatine by pregnant women to protect against perinatal fetal injury is the subject of numerous studies. There is evidence that creatine supplementation during pregnancy reduces the risk of perinatal hypoxia and brain damage in the fetus. However, there is still no clear consensus on whether its supplementation is essential for successful reproduction. Since it has been shown that creatine supplementation improves cellular bioenergetics under ischemic conditions and possesses neuroprotective properties, interest has increased in using creatine during pregnancy to promote neuronal development and reduce complications arising from perinatal hypoxia. The decrease in estrogen levels in women during menopause contributes to the loss of muscle mass and bone tissue. It has been shown that creatine intake by women during this period reduces inflammation, decreases bone resorption markers, stimulates bone formation, and thus limits muscle mass loss [11,23].

3. Anti-inflammatory and Anticatabolic Effects

It has been documented that creatine supplementation has anti-inflammatory and anticatabolic effects. This is significant for individuals engaging in intense exercise, patients with inflammatory diseases, and those susceptible to bone and muscle loss. Evidence shows that creatine intake reduces inflammatory markers and decreases bone catabolism [15]. Limited use of skeletal muscles leads to a reduction in their mass and strength, protein degradation within the muscles, and disturbances at the neuromuscular level [12]. It has been demonstrated that creatine supplementation positively impacts immobilized patients by enhancing muscle strength, mass, and endurance [13].

4. Creatine and Physical Performance

Creatine supplementation is one of the most effective and well-researched substances for enhancing athletic performance. Numerous studies have shown that it improves overall physical performance by increasing endurance during intense exercise [16]. Combining creatine with training leads to enhanced physical endurance, improved muscle composition, and reduced body fat [21].

Creatine can enhance overall functionality by improving strength and extending the time to fatigue. It also has the potential to improve the performance of daily activities and increase muscle mass in older adults [22].

5. Carbohydrate Metabolism

It is also known that creatine supplementation affects carbohydrate metabolism. Its use improves glucose tolerance in patients with type 2 diabetes when combined with physical activity [19].

6. Impact on Cardiomyocytes

Creatine influences the bioenergetics of the heart muscle. This is particularly significant in patients with coronary artery disease, where the heart muscle receives a limited amount of blood and is particularly vulnerable to ischemia. Researchers report that creatine supplementation protects against heart ischemia and reduces the frequency of arrhythmias. There is evidence that creatine supplementation supports metabolism and proper heart function, especially in patients suffering from ischemic heart disease [16,20].

Which Form of Creatine is Best?

The most extensively studied form of creatine is creatine monohydrate. Its effectiveness is documented by numerous studies, it has high bioavailability, and it benefits from low production and supplementation costs. Considering its physical and chemical properties, as well as the volume of human studies, it can be confidently stated that, despite other forms of creatine available on the market, monohydrate remains the most effective. Research on other forms such as creatine nitrate, creatine salts, creatine dipeptides, or ethyl ester creatine has not produced results as favorable as those for monohydrate [22].

Regarding dosing, the optimal scheme for saturating the body with creatine involves a supplementation of 20 grams per day divided into 4 doses over a week. Alternatively, an individual daily dose can be calculated using the formula 0.3 grams per kilogram of body weight per day, divided into 4 doses. This scheme allows for proper saturation of the body, followed by maintenance doses of 0.03 grams per kilogram of body weight per day [1,22].

Conclusion

Creatine is an endogenous nitrogenous compound primarily found in muscle cells. In recent years, its supplementation has become increasingly popular. The most studied and well-absorbed form of creatine is creatine monohydrate. While it was once primarily associated with enhancing athletic performance, extensive research has revealed its significant role in the body and a range of benefits from its supplementation. Exogenous creatine supplementation increases the overall creatine pool in the body, contributing to various positive effects. It is essential for proper nervous system function and exhibits neuroprotective properties. It supports the normal functioning of nerve tissue, reduces the severity of central nervous system injuries, and may positively impact the treatment of neurological disorders. Creatine improves cognitive functions, memory, and information processing. It has been proven to support successful reproduction and reduce complications associated with perinatal hypoxia. Additionally, creatine has anti-inflammatory and anticatabolic properties. It enhances muscle performance, increases endurance, accelerates ATP resynthesis, boosts muscle mass, and speeds up recovery after exercise. It also supports metabolism in cardiomyocytes and improves glucose tolerance.

Disclosure

Author's contribution

Author's contribution Conceptualization: Aleksandra Wydra-Rojek and Marcelina Teresa Marzec; Methodology: Paulina Wasiewicz- Ciach; Software: Weronika Zofia Marzec; Check: Aleksandra Łakoma and Katarzyna Kutyła; Formal analysis: Anna Marszałek and Piotr Kuczyński; Investigation: Anna Marszałek and Wojciech Jan Mokot; Resources: Piotr Kuczyński; Data curation: Katarzyna Kutyła; Writing - rough preparation: Aleksandra Wydra-Rojek and Weronika Zofia Marzec; Writing - review and editing: Marcelina Teresa Marzec and Paulina Wasiewicz-Ciach; Visualization: Wojciech Jan Mokot; Supervision: Maciej Choiński; Project administration: Aleksandra Łakoma and Maciej Choiński ; Receiving funding - no specific funding. All authors have read and agreed with the published version of the manuscript.

Financing statement

This research received no external funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Conflict of interest

The authors deny any conflict of interest.

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