JANIK, Izabela, KUŚMIERSKA, Martyna and KUŚMIERSKI, Jakub. The Impact of Creatine Supplementation on Strength Training. , Weronika. The impact of regular yoga practice on the course of endocrinological and diabetological disorders - a literature review. Quality in Sport. 2024;15:51885. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.15.51885
https://apcz.umk.pl/QS/article/view/51885

The journal has had 20 points in 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: 01.06.2024. Revised: 20.06.2024. Accepted: 01.07.2024. Published: 03.07.2024.

The Impact of Creatine Supplementation on Strength Training

Izabela Janik

E-mail: izabelajanik98@gmail.com

ORCID: https://orcid.org/0009-0001-2112-1384

University Clinical Center of the Medical University of Silesia in Katowice named after prof. K. Gibiński, 14 Medyków Street, 40-752 Katowice, Poland

Martyna Kuśmierska

E-mail: lek.martynakusmierska@gmail.com

ORCID: https://orcid.org/0009-0005-5895-2471

Independent Public Health Care Facility, Municipal Hospital Complex in Chorzów, 11 Strzelców Bytomskich Street, 41-500 Chorzów, Poland

Jakub Kuśmierski

E-mail: j.kusmierski@outlook.com

ORCID: https://orcid.org/0009-0003-2031-3071

Medical University of Silesia in Katowice, Faculty of Medical Sciences in Zabrze, Poland, 15 Poniatowskiego Street, 40-055 Katowice, Poland

ABSTRACT:

Introduction: Creatine monohydrate supplementation has become a popular ergogenic aid among athletes and fitness enthusiasts aiming not only to enhance strength and muscle mass but also to augment intense resistance training workouts. This study aims to provide a comprehensive review of the current scientific literature on the effects of creatine supplementation on strength training. What's more, it contains the mechanisms of action, potential benefits, optimal dosing strategies, and safety considerations associated with creatine supplementation in the context of strength training.

Material and Methods of Research: A literature search was conducted on Google Scholar and PubMed using keywords related to the impact of creatine supplementation on strength training.

Results: There is no doubt that creatine supplementation has a positive effect on muscle strength, hypertrophy, exercise recovery, performance and power. Creatine also reduces dehydration and cramping, minimizes muscle tightness (including muscle strains and pulls), preventing severe muscle injuries or reducing the severity of muscle injuries. The benefits of supplementing creatine may, in the long run, help athletes achieve bursts of speed and energy, especially during short bouts of high-intensity activities such as weight lifting or sprinting.

Conclusion: This study confirms that supplementing with creatine is a reliable and safe approach to bolster strength training results for those aiming to enhance muscular strength, power, and hypertrophy. By increasing intramuscular phosphocreatine levels and aiding muscle protein synthesis, creatine supplementation offers notable advantages in exercise performance and recovery, especially during intense resistance training regimens.

Keywords: Creatine, Supplementation, Strength training, Muscle mass, Performance enhancement

I. Introduction

Strength training is a fundamental pillar of athletic performance and fitness programs aimed at improving muscle strength, power, and hypertrophy. In recent decades, the use of dietary supplements to enhance exercise performance has gained considerable attention, with creatine emerging as one of the most extensively studied and widely used supplements. Creatine is a naturally occurring compound synthesized from amino acids in the body, predominantly stored in skeletal muscle as phosphocreatine. It exists in various tautomers in solutions, among which are neutral forms and various zwitterionic forms. Creatine is present in vertebrates, where it plays a crucial role in the recycling of adenosine triphosphate (ATP), particularly within muscle and brain tissue. Its role in energy metabolism, particularly during short-duration, high-intensity activities, makes it a popular choice for athletes and strength trainers seeking to optimize their training outcomes [1, 2].

II. Purpose of the study

This study seeks to conduct a thorough review of the contemporary scientific literature regarding the impacts of creatine supplementation on strength training. Through an investigation into creatine's contributions to hypertrophy, exercise recovery, muscle strength and power, as well as its potential for enhancing musculoskeletal function and reducing injury risk, the aim is to uncover the mechanisms by which creatine influences our health, performance, and ultimately, strength training outcomes. The objective of this research is to establish a scientific rationale for incorporating creatine into daily supplementation routines for individuals involved in sports, whether at a professional or recreational level, with the intent of substantially augmenting performance.

III. Materials and Methodology

The research approach we used was to thoroughly search the literature available on Google Scholar and PubMed, using the keywords “Creatine”, “Supplementation”, “Strenght training”, “Muscle mass” and “Performance enhancement”. This strategy was designed to collect research exploring the effects of creatine supplementation on strength training. To expand the scope of our review, we also examined the references cited in the initially identified articles, thus revealing additional relevant studies. Our search criteria focused on original and review articles that substantially enhance our comprehension of the positive impacts of creatine on strength training. This conscientious approach enabled us to gather and scrutinize data from various studies, elucidating prevailing trends and advantages linked with creatine supplementation.

IV. Description of the state of knowledge

Creatine role in metabolism

Creatine (*N*-aminoiminomethyl-*N*-methyl glycine) is a naturally appearing and nitrogen-containing compound composed from amino acids [3]. It is synthesized endogenously by arginine glycine amidinotransferase from arginine and glycine to guanidinoacetate (GAA). The GAA is then methylated by the enzyme guanidinoacetate N-methyltransferase (GAMT) with S-adenosyl methionine (SAMe) to form the final product - creatine [4]. Creatine and phosphagens play a critical role in providing energy through the creatine kinase (CK) and PCr system [5].

Endogenous creatine supplies about half of the daily need for creatine [6]. The remaining half is obtained from red meat, seafood or dietary supplements [7]. Significant majority of creatine is stored in skeletal muscle with the remaining amount in other tissues for example heart, brain, and testes [8, 9]. Vegetarians have been reported to have muscle creatine and PCr stores about 20–30% lower than non-vegetarians. Increasing availability of creatine in tissue may enhance cellular metabolism and thereby lessen the severity of injury and/or disease conditions, particularly when oxygen availability is compromised [5, 10]. The free energy provided by the enzymatic degradation of adenosine triphosphate into adenosine diphosphate and Pi by creatine kinase operates as a primary fuel to restore ATP for cellular metabolism. Ensuring adequate ATP levels during periods of heightened energy demand, such as vigorous exercise or situations where energy production is compromised (like ischemia or hypoxia), or when demand exceeds supply (such as mental fatigue or certain illnesses), is crucial for sustaining ATP availability [6, 7].

These examples contribute to a vast body of earlier literature detailing the specific cellular localization of glycolytic enzymes or ATP (or GTP) regenerating enzymes, such as adenylate kinase, nucleoside diphosphate kinase, or creatine kinase (CK). Creatine kinase has emerged as a paradigm for this type of compartmentation in energy metabolism. It plays a pivotal role in maintaining cellular energy homeostasis by utilizing creatine (Cr) for reversible phosphoryl transfer between ATP and phosphocreatine (PCr) in the reaction: MgATP + Cr $\leftrightarrow$ MgADP + PCr. PCr serves as an alternative energy carrier that, compared to ATP, is metabolically inert (except for its involvement in the CK reaction), smaller in molecular size, less charged over the physiological pH range, and significantly more diffusible. In a given cell type, at least one dimeric cytosolic isoform of CK is always co-expressed with a predominantly octameric mitochondrial isoform (MtCK). Typically, cytosolic muscle-type CK (MCK) is coupled with sarcomeric MtCK (sMtCK), or cytosolic brain-type CK (BCK) with ubiquitous MtCK (uMtCK) [5]. At the cellular level, CK functions primarily through two mechanisms. Firstly, it facilitates the establishment of a global cellular energy buffer in the form of a large PCr pool, which can regenerate ATP during temporal mismatches between ATP generation and consumption. Secondly, cytosolic and mitochondrial CK isoforms, along with highly concentrated and diffusible PCr, participate in the CK/PCr shuttle to address spatial mismatches between ATP generation and consumption within a cell. The mitochondrial isoforms, and to a lesser extent the cytosolic isoforms, are functionally coupled with either ATP-providing processes (such as oxidative phosphorylation or glycolysis, to generate PCr) or ATP-utilizing processes (such as motor proteins, ion pumps, etc., to regenerate ATP from ADP and PCr). Rapidly diffusing PCr and Cr serve as bridges between these sites [10].

Mechanisms of Action

Creatine supplementation exerts its ergogenic effects through several mechanisms. Firstly, creatine increases intramuscular phosphocreatine stores, thereby enhancing the resynthesis of adenosine triphosphate (ATP) during high-intensity exercise bouts, which may lead to improved performance in activities requiring short bursts of power, such as weightlifting and sprinting [11]. Additionally, creatine supplementation has been shown to promote muscle protein synthesis, reduce muscle protein breakdown, and modulate various signaling pathways involved in muscle growth and repair, thereby contributing to gains in muscle mass and strength over time. Early studies suggested that the osmotic impact of creatine supplementation functions as a cellular stressor, triggering an anabolic response through signaling pathways for protein synthesis. Other research indicated that creatine directly influences muscle protein synthesis by modulating components within the mTOR pathway. Additionally, creatine may impact the formation of muscle tissue, known as the myogenic process, by altering the secretion of myokines such as myostatin and insulin-like growth factor-1, as well as the expression of myogenic regulatory factors. This leads to increased mitotic activities of satellite cells and their differentiation into myofibers [12].

Additional support for the growth-promoting benefits of creatine supplementation surfaced in a recent human study. This study revealed that creatine supplementation led to a significant increase in the mRNA content of genes and proteins associated with regulating protein and glycogen synthesis, satellite cell proliferation and differentiation, DNA replication and repair, RNA transcription control, and cell survival. Moreover, it reduced overall protein breakdown and leucine oxidation in humans. Despite these findings, the precise mechanism of action remains unclear. Nonetheless, some researchers suggest that the retention of water in muscle fibers due to the high intracellular abundance of creatine might serve as a primary anabolic signal for proliferation [13, 14].

Impact on muscle recovery

In the context of creatine supplementation, it is suggested that it might contribute to improved recovery post-exercise. Research investigating the impact of creatine supplementation on exercise-induced muscle damage has yielded mixed results. Some studies indicate a decrease in indicators of muscle damage and inflammation, along with functional markers showing enhanced muscle recovery [15, 16, 17]. A limited body of research has explored the potential contribution of creatine to the rehabilitation process and the restoration of muscle mass and function after brief periods (7 to 14 days) of immobilization in young, healthy individuals and athletes recuperating from injuries. These studies assess parameters such as the extent of muscle mass and strength loss during immobilization, alleviation of pain, and the rate at which muscle mass and strength recover. The majority of studies show that creatine supplementation does not attenuate the loss of muscle mass or power from immobilization [18].

While most studies have focused on the role of creatine during the recovery period post-exercise, there is emerging evidence suggesting a potential beneficial role during exercise itself. The sarcoplasmic reticulum (SR) Ca2+ pump primarily utilizes ATP derived from phosphocreatine (PCr) via the creatine kinase (CK) reaction. Local rephosphorylation of ADP by the CK-PCr system helps maintain a low ADP/ATP ratio near the SR Ca2+ pump, ensuring optimal calcium removal from the cytoplasm [19, 20]. However, during periods of high rates of Ca2+ transport, such as during muscle damage, there is a potential for an increase in ADP concentration, leading to a microenvironment with a high ADP/ATP ratio that impairs ATPase function and diminishes SR Ca2+ pump activity. Additionally, a decrease in PCr concentration below 5 mM, indicative of increased ATPase activity, reduces the local ATP regeneration potential of the CK/PCr system [18, 19]. Supplementing with creatine before and after exercise-induced muscle damage may increase PCr concentrations within the muscle, thereby potentially improving intracellular $Ca2+$ handling ability by enhancing the CK/PCr system and promoting local rephosphorylation of ADP to ATP. This, in turn, helps maintain a high ATP/ADP ratio near the SR $Ca2+$ pump during intense eccentric exercise [19, 20]. However, further investigation is needed to fully elucidate this concept.

Furthermore, oral creatine supplementation may contribute to a decrease in the occurrence of dehydration, muscle cramping, and injuries to the bones, ligaments, tendons, and nerves. However, in the current study, it is apparent that creatine (Cr) is possibly functioning through two distinct mechanisms. Firstly, Cr supplementation before eccentric-induced damage might enhance the muscle's calcium buffering capacity by supporting the sarcoplasmic reticulum (SR) $Ca2+$-ATPase pump, leading to a reduction in intracellular calcium levels and the activation of degradative pathways like calpain. Consequently, a decrease in calcium-activated proteases could mitigate further damage to the sarcolemma and prevent additional calcium influx into the muscle. Secondly, Cr supplementation post-exercise may bolster one or more of the crucial phases involved in the regenerative response to exercise-induced damage. This could involve increasing protein synthesis, decreasing protein degradation, and creating an environment conducive to enhanced satellite cell proliferation, thereby facilitating the formation of new muscle fibers. This combined effect may enable a higher training volume to be sustained during subsequent exercise sessions in resistance training [16].

Effects on Strength and Power

Numerous studies have investigated the impact of oral creatine supplementation on strength and power outcomes in both trained and untrained individuals. Overall, the majority of evidence supports the notion that creatine supplementation can enhance muscle mass, muscular strength, power output, and exercise performance, particularly during repetitive, high-intensity resistance training protocols [21, 22]. After 12 weeks of supplementation, significant ($P <$ or $= 0.05$) increases in body mass and fat-free mass were higher in creatine (6.3% and 6.3%, respectively) than placebo (3.6% and 3.1%, respectively) subjects. Moreover, increases in bench press and squat were greater in creatine (24% and 32%, respectively) than placebo (16% and 24%, respectively) subjects. Compared with placebo, creatine supplementation demonstrated significantly greater increases in Type I (35% vs 11%), IIA (36% vs 15%), and IIAB (35% vs 6%) muscle fiber cross-sectional areas. Muscle creatine was significantly elevated after 1 week in creatine subjects (22%), and values remained significantly greater than placebo subjects after 12 weeks. Average volume lifted in the bench press during training was noticeably higher in individuals who implemented creatine during weeks 5-8. No negative side effects to the supplementation were reported [21]. Meta-analyses and systematic reviews have consistently reported significant improvements in maximal strength, muscular endurance, following creatine supplementation. Average increase in muscle strength (1, 3, or 10 repetition maximum) following creatine supplementation plus resistance training was 8% higher than the average increase in muscle strength following placebo ingestion during resistance training (20% vs. 12%). Similarly, the average raise in weightlifting performance (maximal repetitions at a given percent of maximal strength) following creatine supplementation plus resistance training was 14% greater than the average increase in weightlifting performance following placebo ingestion during resistance training (26% vs. 12%) [1].

It can be concluded that creatine supplementation has been shown to improve fat-free mass, physical performance, and muscle morphology in response to heavy resistance training, likely due to facilitating higher quality training sessions [12]. Several studies have demonstrated that ingesting more than 20 grams of creatine per day for 5-7 days increases both creatine and phosphocreatine concentrations in skeletal muscle [11, 23, 24], leading to enhanced body mass [11, 23] and intermittent high-intensity activity, including resistance exercise [25]. However, there is limited data available on the influence of creatine supplementation on body composition, physical performance, skeletal muscle morphology, and muscle creatine concentrations during longer periods of training. While creatine supplementation combined with resistance training has been shown to increase body mass, fat-free mass, and muscular strength in both men and women , few studies have investigated the total creatine accumulation in muscle and the extent of muscle fiber hypertrophy associated with creatine supplementation [11, 26]. Studies on patients with gyrate atrophy who consumed 1.5 grams of creatine per day for one year demonstrated significant increases in Type II muscle fiber diameter. Additionally, patients undergoing rehabilitation for a fractured thigh who received creatine phosphate (500 mg daily i.m. for 20 days) showed significantly greater recovery in echotomography-assessed muscle mass compared to those not receiving creatine phosphate [29]. These findings suggest a potential role of creatine in muscle fiber hypertrophy in cases of muscle atrophy.

Based on positive results showing enhanced resistance exercise performance after 7 days of creatine supplementation, it was hypothesized that physiological adaptations, such as increases in muscle strength, fat-free mass, and muscle fiber cross-sectional area, to 12 weeks of periodized heavy resistance training and creatine supplementation would be optimized due to an improved capacity to perform individual weight training sessions [23, 24]. In recent studies, researchers have obtained muscle biopsies before training and supplementation, after a 1-week supplement loading period, and after 11 weeks of resistance training with a supplemental maintenance dose. Subsequent analysis of muscle biopsy samples allowed researchers to evaluate changes in muscle creatine and phosphocreatine in response to the supplementation regimen and the resistance training program. Furthermore, scientists quantified the extent of specific muscle fiber hypertrophy, including Type I, IIA, IIAB, and IIB fibers, in response to resistance training using histochemical techniques, which had not been previously performed in creatine supplementation studies [21, 27].

Optimal Dosing Strategies

The optimal dosing strategy for creatine supplementation depends on various factors. Therefore, a normal-sized individual may need to consume 2–3 g/day of creatine to maintain normal creatine stores depending on diet, muscle mass, and physical activity levels. A typical loading phase involves consuming 20-25 grams of creatine monohydrate per day for 5-7 days, followed by a maintenance phase of 3-5 grams per day. Numerous studies have indicated that consuming 20 grams of creatine per day leads to an increase in body mass ranging from 0.5 to 1.0 kilograms. Recently, it was demonstrated that ingesting creatine at a rate of 20 grams per day for 28 days resulted in a 1.7-kilogram increase in body mass, surpassing previous increases observed over a 5- to 6-day period. Researchers attributed this increase in body mass to a rise in fat-free mass. However, whether this increase comprised water or protein has yet to be confirmed. Nevertheless, the experimental group of athletes experienced a decrease in urinary volume by 0.6 liters upon initiating creatine ingestion, suggesting that the acute increase in body mass during creatine feeding is likely due to retention of body water. It is worth noting that the changes in urinary volume followed a similar time course as the documented uptake of creatine by muscles [23, 24].

Alternatively, a lower dose of 3-5 grams per day can be taken consistently without a loading phase, albeit with a longer time frame to achieve maximal muscle creatine saturation [30]. Research findings indicate that the uptake of creatine into muscle is most significant during the initial 2 days of supplementation, amounting to 32% of the administered dose in three subjects who received 6 doses of 5 grams of creatine monohydrate per day. During this period, renal excretion accounted for 40%, 61%, and 68% of the creatine dose in these subjects over the first

3 days. Approximately 20% or more of the creatine taken up was measured as phosphocreatine. Notably, there were no observable changes in muscle ATP content. Additionally, combining creatine with carbohydrate or protein sources may enhance its uptake and retention within muscle tissue, although further research is needed to elucidate the optimal nutrient timing strategies for maximizing creatine efficacy [11, 30].

In conclusion, a rapid method to "load" skeletal muscle with creatine in humans involves consuming 20 grams of creatine daily for 6 days. This regimen leads to a significant increase in tissue creatine concentration, which can then be maintained by ingesting 2 grams per day thereafter. Alternatively, ingesting 3 grams of creatine per day for a minimum of 4 weeks is likely to be equally effective at elevating tissue levels, albeit at a slower pace. Based on the findings of our studies, an effective approach to obtain immediate and sustained benefits of creatine ingestion may involve loading doses of 0.3 grams per kilogram of body weight per day for 5-6 days, followed by a maintenance dose of 0.03 grams per kilogram of body weight per day thereafter [8, 23].

Safety Considerations

Creatine supplementation is generally regarded as safe and well-tolerated when used within recommended dosages. However, individuals with pre-existing medical conditions, such as renal dysfunction, should exercise caution and consult with a healthcare professional before initiating creatine supplementation. Suggestions have been made that adhering to a long-term, nitrogen-rich diet could lead to renal hyperfiltration, potentially contributing to the functional and structural decline of the kidneys. In theory, the elevated nitrogen content (32%) of creatine might impose additional strain on the kidneys if consumed excessively over an extended duration. However, present research findings do not support this notion [31].

Several studies have observed an increase in serum creatinine levels (e.g., from 1.1 to 1.3–1.5 mg/dl) with creatine supplementation during training. However, because creatine naturally degrades into creatinine, the elevated serum creatinine levels are attributed to a higher turnover of creatine post-creatine loading and/or the ability to sustain greater training volume/intensity after creatine supplementation. Recent studies have investigated the impact of creatine supplementation on renal function by evaluating urinary creatinine clearance and using iohexol infusion techniques to assess glomerular filtration [29]. Moreover, concerns have been raised regarding the potential for creatine supplementation to increase muscle and/or liver damage

[32]. This concern stemmed from an initial report suggesting that athletes who took creatine during training might experience slightly elevated levels of muscle and/or liver enzymes. While these levels were within normal ranges for athletes, some have posited that creatine could exacerbate muscle and/or liver damage. However, the results of the current study indicated that athletes engaged in intense training exhibited creatine kinase (CK) levels above the clinical norms for untrained individuals (i.e., >225 IU/L). Nonetheless, the mean values observed fell within the normal ranges for athletes undergoing intense training (typically 250–1,000 IU/L), and no significant differences were observed in CK values between creatine users and non-users. Additionally, no significant differences were noted in lactate dehydrogenase (LDH), aspartate aminotransferase (AST), or alanine aminotransferase (ALT) values between groups using and not using creatine, and all these values remained within normal ranges (i.e., LDH 100–250; AST and ALT < 55 IU/L) for non-athletes. These findings suggest that although these athletes may have exhibited elevated CK levels, there appears to be no disparity in muscle and liver enzyme release between athletes who do and do not use creatine during intense training and competition [29, 31].

Concerns have also been raised regarding the potential of creatine supplementation to impact fluid balance and/or electrolyte status. This concern arose from initial reports indicating a slight decrease in urine output during creatine loading, which suggested that short-term creatine supplementation might lead to increased fluid retention [33]. The findings of the current study contradict this hypothesis. While significant interactions were noted among groups in sodium and chloride levels, the differences observed among groups were minimal (i.e., < 1 meq/L) and held no physiological or clinical significance. Additionally, no significant differences were detected among groups in potassium, calcium, phosphorus, urine output, or urine specific gravity. Furthermore, as detailed in our accompanying paper, creatine supplementation did not heighten the occurrence of dehydration or muscle cramping in the athletes monitored over a 3-year span. These results align with previous research indicating that creatine supplementation does not elevate thermal stress, induce dehydration, cause cramping, or disrupt electrolyte status [26, 27].

The only reproducible side effects that are common are weight gain (1 to 2 kg higher after creatine loading), primarily as a result of water retention, decrease urine output, gastrointestinal discomfort, and muscle cramping, although these are typically mild and transient in nature. As previously mentioned, long-term studies have demonstrated no adverse effects on renal function or markers of hepatic and cardiovascular health with creatine supplementation within the recommended dosage range [18, 34, 35].

Interactions

Given that both creatine and caffeine have been shown to enhance human performance, a subject of interest in the scientific community revolves around examining the potential interaction between creatine and caffeine, as well as their individual or combined effects on the short-term maximum performance and endurance of athletes undergoing training.

The inclusion of both caffeine (CAF) and creatine (CRE) in numerous nutritional supplements is largely supported by extensive evidence demonstrating their ergogenic effects. However, this combination remains controversial. Despite findings suggesting no pharmacokinetic interaction between the two substances [36] and their ability to enhance performance through distinct mechanisms [37], some studies have indicated that caffeine may diminish the efficacy of creatine [38].

For this reason, the research was carried out to explore how physical exercise and the simultaneous intake of CRE and CAF might influence pharmacokinetics of trained athletes, as alterations in caffeine's pharmacokinetics could hold significance in anti-doping measures. For trained athletes engaging in anaerobic exercise, neither creatine, caffeine, nor the combination of creatine and caffeine led to improvements in maximal pedaling speed or the ability to sustain it across three anaerobic bouts. Total work performance and heart rate during both the anaerobic test and the subsequent recovery phase remained similar across all treatments. With each treatment, blood lactate, blood glucose, and serum hypoxanthine levels were notably elevated compared to resting values ($p < 0.05$, Wilcoxon), but no statistically significant differences were observed between the treatments. Subjectively, according to Borg scales, participants reported experiencing very strong breathlessness, extremely strong leg fatigue, and strong to very strong overall fatigue, regardless of the treatment received. In turn, when it comes to aerobic effort for the same group of athletes no differences in heart rate at 15, 30, and 45 min were observed. Blood lactate and serum hypoxanthine levels remained somewhat elevated even after the aerobic test ($p < 0.05$ vs. baseline, Wilcoxon), yet no distinctions between the groups were apparent. Subjectively, participants reported experiencing breathlessness, leg fatigue, and general fatigue ranging from weak to moderate, regardless of the treatment received. [36, 38]. Both caffeine and the combination of caffeine and creatine did not result in improvements in either anaerobic or aerobic performance. This finding is consistent with a recent study where the simultaneous administration of caffeine and creatine failed to enhance maximal intermittent exercise. Notably, there was considerable variability in caffeine elimination among participants, with one subject exhibiting a caffeine elimination half-life as long as 61 hours during the caffeine + creatine session. However, urinary concentrations of caffeine did not surpass the limit set by the International Olympic Committee (IOC) in any of the samples analyzed, suggesting that the potential impact of exercise on single-dose caffeine pharmacokinetics is clinically insignificant in current doping tests. It's important to note that the study involved a small sample size and was conducted as a single-dose study. Therefore, there is a possibility of caffeine accumulation over several days among athletes with slow caffeine elimination and a habit of consuming large quantities of caffeine-containing products [36, 39].

V. Conclusion

In conclusion, creatine supplementation represents a safe and effective strategy for enhancing strength training outcomes in individuals seeking to improve muscular strength, power, and hypertrophy. By augmenting intramuscular phosphocreatine stores and supporting muscle protein synthesis, creatine supplementation can confer significant benefits in terms of exercise performance and recovery, particularly during high-intensity resistance training protocols. When used in conjunction with a structured training program and proper nutrition, creatine supplementation can serve as a valuable adjunct for optimizing athletic performance and achieving training goals. Further research is warranted to elucidate the potential synergistic effects of creatine supplementation with other dietary supplements or exercise interventions, as well as its long-term effects on health and performance outcomes.

DISCLOSURE

Author's contribution:

Conceptualization: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Methodology: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Software: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Check: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Formal Analysis: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Investigation: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Resources: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Data Curation: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Writing-Rough Preparation: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Review and Editing: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Visualization: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Supervision: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

Project Administration: Izabela Janik, Martyna Kuśmierska, Jakub Kuśmierski

All authors have read and agreed with the published version of the manuscript.

Funding Statement: The Study Did Not Receive Special Funding.

Institutional Review Board Statement: Not Applicable.

Informed Consent Statement: Not Applicable

Data Availability Statement: Not Applicable.

Conflict Of Interest: The authors declare no conflict of interest.

References:

1. RAWSON, ERIC S.1; VOLEK, JEFF S.2. Effects of Creatine Supplementation and Resistance Training on Muscle Strength and Weightlifting Performance. Journal of Strength and Conditioning Research 17(4):p 822-831, November 2003.

2. Kreider, R.B. Effects of creatine supplementation on performance and training adaptations. *Mol Cell Biochem* 244, 89–94 (2003).

3. Kreider R.B., Kalman D.S., Antonio J., Ziegenfuss T.N., Wildman R., Collins R., Candow D.G., Kleiner S.M., Almada A.L., Lopez H.L. International Society of Sports Nutrition position stand: Safety and efficacy of creatine supplementation in exercise, sport, and medicine. *J. Int. Soc. Sports Nutr.* 2017;14:18. doi: 10.1186/s12970-017-0173-z.

4. Paddon-Jones D., Borsheim E., Wolfe R.R. Potential ergogenic effects of arginine and creatine supplementation. *J. Nutr.* 2004;134:2888S–2894S. doi: 10.1093/jn/134.10.2888S.

5. Wallimann T., Tokarska-Schlattner M., Schlattner U. The creatine kinase system and pleiotropic effects of creatine. *Amino Acids.* 2011;40:1271–1296. doi: 10.1007/s00726-011-0877-3.

6. Brosnan M.E., Brosnan J.T. The role of dietary creatine. *Amino Acids.* 2016;48:1785–1791. doi: 10.1007/s00726-016-2188-1.

7. Bertin M., Pomponi S.M., Kokuhuta C., Iwasaki N., Suzuki T., Ellington W.R. Origin of the genes for the isoforms of creatine kinase. *Gene.* 2007;392:273–282. doi: 10.1016/j.gene.2007.01.007.

8. Buford T.W., Kreider R.B., Stout J.R., 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. doi: 10.1186/1550-2783-4-6.

9. Kreider R.B., Jung Y.P. Creatine supplementation in exercise, sport, and medicine. *J. Exerc. Nutr. Biochem.* 2011;15:53–69. doi: 10.5717/jenb.2011.15.2.53.

10. Schlattner U., Klaus A., Rios S.R., Guzun R., Kay L., Tokarska-Schlattner M. Cellular compartmentation of energy metabolism: Creatine kinase microcompartments and recruitment of B-type creatine kinase to specific subcellular sites. *Amino Acids.* 2016;48:1751–1774. doi: 10.1007/s00726-016-2267-3.

11. Effect of oral creatine supplementation on skeletal muscle phosphocreatine resynthesis, P. L. Greenhaff, K. Bodin, K. Soderlund, and E. Hultman American Journal of Physiology-Endocrinology and Metabolism 1994 266:5, E725-E730.

12. Farshidfar, Farnaz; A. Pinder, Mark; B. Myrie, Semone, Creatine Supplementation and Skeletal Muscle Metabolism for Building Muscle Mass- Review of the Potential Mechanisms of Action, Current Protein and Peptide Science, Volume 18, Number 12, 2017, pp. 1273-1287(15).

13. Francaux, M., & Poortmans, J. R. (2006). Side Effects of Creatine Supplementation in Athletes. International Journal of Sports Physiology and Performance, 1(4), 311-323. Retrieved Apr 27, 2024, from https://doi.org/10.1123/ijspp.1.4.311.

14. Safdar A, Yardley NJ, Snow R, et al. Global and targeted gene expression and protein content in skeletal muscle of young men following short-term creatine monohydrate supplementation. Physiol Genomics. 2008; 32(2):219–228.

15. Bassit RA, Curi R, Rosa LFBPC. Creatine supplementation reduces plasma levels of pro-inflammatory cytokines and PGE2 after a half-ironman competition. *Amino Acids*. 2008; 35:425–31.

16 Cooke MB, Rybalka E, Williams AD, et al. Creatine supplementation enhances muscle force recovery after eccentrically-induced muscle damage in healthy individuals. *J. Int. Soc. Sports Nutr*. 2009; 6:13.

17. Greenhaff PL, Bodin K, Soderlund K, Hultman E. Effect of oral creatine supplementation on skeletal muscle phosphocreatine resynthesis. *Am. J. Physiol. Endocrinol. Metab*. 1994; 266:E725–30.

18. Hall, Matthew DO, CAQSM; Manetta, Elizabeth MD; Tupper, Kristofer DO. Creatine Supplementation: An Update. Current Sports Medicine Reports 20(7):p 338-344, July 2021. | DOI: 10.1249/JSR.0000000000000863.

19. Duke AM, Steele DS. Mechanisms of reduced SR Ca(2+) release induced by inorganic phosphate in rat skeletal muscle fibers. Am J Physiol Cell Physiol. 2001 Aug;281(2):C418-29. doi: 10.1152/ajpcell.2001.281.2.C418. PMID: 11443041.

20. Duke AM, Steele DS. Effects of creatine phosphate on Ca2+ regulation by the sarcoplasmic reticulum in mechanically skinned rat skeletal muscle fibres. J Physiol. 1999 Jun 1;517 (Pt 2)(Pt 2):447-58. doi: 10.1111/j.1469-7793.1999.0447t.x. PMID: 10332094; PMCID: PMC2269360.

21. Volek JS, Duncan ND, Mazzetti SA, et al. Performance and muscle fiber adaptations to creatine supplementation and heavy resistance training. Medicine and Science in Sports and Exercise. 1999 Aug;31(8):1147-1156. DOI: 10.1097/00005768-199908000-00011. PMID: 10449017.

22. https://www.mayoclinic.org/drugs-supplements-creatine/art-20347591?p=1

23. Hultman E., Soderlund K., Timmons J.A., Cederblad G., Greenhaff P.L. Muscle creatine loading in men. *J. Appl. Physiol.* 1996;81:232–237. doi: 10.1152/jappl.1996.81.1.232.

24. Harris R.C., Soderlund K., Hultman E. Elevation of creatine in resting and exercised muscle of normal subjects by creatine supplementation. *Clin. Sci.* 1992;83:367–374. doi: 10.1042/cs0830367.

25. Birch, R., D. Noble, and P. L. Greenhaff. The influence of dietary creatine supplementation on performance during repeated bouts of maximal isokinetic cycling in man. Eur. J. Appl. Physiol. 69:268-270, 1994.

26. McArthur PD, Webster MJ, Body JC, May RA, Eschbach LD, EimerAF, Angelosoulos TJ, Zoeller RF, Krebs GV: Creatine supplementa-tion and acute dehydration. Med Sci Sports Exerc 31: S263, 1999.

27. Volek JS, Mazzetti SA, Farquhar WB, Barnes BR, Gomez AL, KraemerWJ: Physiological responses to short-term exercise in the heat aftercreatine loading. Med Sci Sports Exerc 33: 1101–1108, 2001.

28. Sipilä, I., J. Rapola, O. Simell, and A. Vannas. Supplementary creatine as a treatment for gyrate atrophy of the choroid and retina. N. Engl. J. Med. 304:867-870, 1981.

29. 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 Feb;244(1-2):95-104. PMID: 12701816.

30. Hultman E., Soderlund K., Timmons J.A., Cederblad G., Greenhaff P.L. Muscle creatine loading in men. *J. Appl. Physiol.* 1996;81:232–237. doi: 10.1152/jappl.1996.81.1.232.

31. POORTMANS, JACQUES R.; FRANCAUX, MARC. Long-term oral creatine supplementation does not impair renal function in healthy athletes. Medicine & Science in Sports & Exercise 31(8):p 1108-1110, August 1999.

32. Kreider R: Creatine supplementation: Analysis of ergogenic value,medical safety, and concerns. J Exerc Physiol Online 1: 7–18, 1998.Available: http://www.css.edu/users/tboone2/asep/jan3.htm

33. Hultman E, Soderlund K, Timmons JA, Cederblad G, Greenhaff PL:Muscle creatine loading in men. J Appl Physiol 81: 232–237, 199.

34. Hultman E, Soderlund K, Timmons JA, et al. Muscle creatine loading in men. *J. Appl. Physiol*. 1996; 81:232–7.

35. Powers ME, Arnold BL, Weltman AL, et al. Creatine supplementation increases total body water without altering fluid distribution. *J. Athl. Train*. 2003; 38:44–50.

36. Vanakoski J, Kosunen V, Meririnne E, Seppälä T. Creatine and caffeine in anaerobic and aerobic exercise: effects on physical performance and pharmacokinetic considerations. Int J Clin Pharmacol Ther. 1998 May;36(5):258-62. PMID: 9629989.

37. Trexler ET, Smith-Ryan AE. Creatine and Caffeine: Considerations for Concurrent Supplementation. Int J Sport Nutr Exerc Metab. 2015 Dec;25(6):607-23. doi: 10.1123/ijsnem.2014-0193. PMID: 26219105.

38. Lee CL, Lin JC, Cheng CF. Effect of caffeine ingestion after creatine supplementation on intermittent high-intensity sprint performance. Eur J Appl Physiol. 2011 Aug;111(8):1669-77. doi: 10.1007/s00421-010-1792-0. Epub 2011 Jan 5. PMID: 21207054.

39. Vandenberghe K. Gillis N. \'an Leemsputte M. \'an Heeke P. Vans/apel F. H espel P 1996 Caffeine counteracts the ergogenic action of muscle creatine loading. J Appi Physiol80: 452-457.