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Creatine in adult health and performance: A literature review

Marcin Migiel

ORCID: https://orcid.org/0009-0003-3562-5051

Private Health Care Facility in the Commune of Nowy Targ, 2 Podhalańska Street, 34-471 Ludźmierz, Poland

Email: migielmarcin@gmail.com

Izabela Brynczka

ORCID: https://orcid.org/0009-0002-1527-5659

Ludwik Rydygier Specialist Hospital, 1 Złota Jesień Street, 31-826 Kraków, Poland

Email: iza.brynczka@gmail.com

Natalia Siuta

ORCID: https://orcid.org/0000-0001-8441-5382

Private Health Care Facility in the Commune of Nowy Targ, 2 Podhalańska Street, 34-471 Ludźmierz, Poland

Email: natalia.siuta.99@gmail.com

Joanna Rypel-Bośka

ORCID: https://orcid.org/0009-0002-2380-571X

Klara Helska Specialist Hospital of Lung Diseases „Odrodzenie”, 1 Gładkie Street, 34-500 Zakopane, Poland

Email: joanna.rypel1999@gmail.com

Jakub Miaśnikiewicz
ORCID: https://orcid.org/0009-0003-3186-010X
Central Teaching Hospital of the Medical University of Lodz, 251 Pomorska Street, 92-213 Łódź, Poland
Email: j.miasnikiewicz@gmail.com

Klaudia Goleniewska
ORCID: https://orcid.org/0009-0002-1597-9699
University Clinical Hospital No. 2 of Medical University of Łódź, 113 Żeromskiego Street, 90-549 Łódź, Poland
Email: kla.goleniewska@gmail.com

Aleksandra Stupecka
ORCID: https://orcid.org/0009-0004-3585-9664
University Clinical Hospital No. 1 named after Norbert Barlicki, 22 Dr. Stefama Kopcinskiego Street, 90-153 Łódź, Poland
Email: aleksandragieras@gmail.com

Wiktoria Cecuła
ORCID: https://orcid.org/0009-0005-8749-2312
Central Clinical Hospital of the Medical University of Łódź, 251 Pomorska Street, 92-213 Łódź, Poland
Email: wiktoria.cecula@stud.umed.lodz.pl

Kamil Ciechomski
ORCID: https://orcid.org/0009-0002-0049-2714
Healthcare Service Center in Łowicz, 28 Ułańska Street, 99-400 Łowicz, Poland
Email: kamil.ciechomski@stud.umed.lodz.pl

Corresponding author:
Marcin Migiel
Email: migielmarcin@gmail.com

Abstract

Introduction and Purpose: Creatine is a naturally occurring compound widely used as a supplement to enhance high-intensity exercise performance and increase muscle mass. Beyond its muscular benefits, creatine plays a key role in cellular energy homeostasis. There is growing interest in its potential cognitive and therapeutic applications, but several misconceptions about its safety and effects persist.

Research Objective: The role of this article is to summarize current evidence on creatine supplementation in adults, focusing on its efficacy for physical performance, its safety profile and emerging roles in cognitive and other health domains.

Materials and methods: A literature review of studies published from 2019–2024 in the PubMed database analyzed clinical trials, meta-analyses, and systematic reviews on the effects of PA, using the following keywords: „creatine” ; „performance” ; „aging” ; „cognitive function” ; „depression”.

Conclusions: Creatine monohydrate is recognized as the most effective supplement for increasing muscle strength and muscle mass, with consistent benefits observed in both athletes and older adults. Long-term use of recommended doses is well-tolerated. Emerging evidence suggests creatine may also support cognitive function and brain health. Future research should prioritize human studies exploring neurological and mental health applications.

Keywords: creatine; performance; aging; cognitive function; depression

1. Introduction

Creatine is a nitrogen-containing compound that is not part of proteins, which is synthesized in the human body from three amino acids: arginine, glycine and methionine. This process occurs mainly in the liver and kidneys, and subsequently creatine is transported to target tissues, mainly to skeletal muscles [1,2]. An additional source of creatine is the diet – the largest amounts are found in red meat and fish, which means that individuals who do not consume animal products generally have lower levels of muscle creatine [1]. About 95% of the total creatine pool is located in muscles, where it is present in the form of free creatine and phosphocreatine (PCr), while the remaining 5% is distributed in the heart, brain, and testes [1,3,4].

The primary role of creatine is to rapidly supply energy to cells, especially in situations of increased demand, such as intense physical exercise or hypoxia. This occurs through the creatine kinase system, which allows for rapid regeneration of ATP from ADP by using the phosphate group from PCr [1,3,4]. This system not only facilitates ATP resynthesis but also participates in the transport of energy from mitochondria to sites of its consumption in the cytoplasm, which is particularly significant in cells with high energy metabolism, such as myocytes and neurons [4].

Creatine supplementation, most often in the form of creatine monohydrate, can increase phosphocreatine content in muscles by as much as 20–40%, which translates into improved exercise capacity, increased strength, muscle mass, and accelerated post-exercise recovery [1,5]. Importantly, the benefits of supplementation are not limited solely to the muscular system – a positive effect of creatine on protecting brain and heart function has also been demonstrated, through its involvement in maintaining energy homeostasis and reducing oxidative stress [3,4].

2. Misconceptions about creatine

Although scientific understanding has considerably progressed and many studies have demonstrated the effectiveness and safety of creatine supplementation, many unwarranted misconceptions about it remain in the public sphere. One of the most frequently repeated myths is the alleged nephrotoxic effect of creatine supplementation. In contrast to these concerns, current scientific data do not indicate that using creatine at recommended doses (3–5 g/day) leads to kidney damage in healthy individuals. An increased serum creatinine level, sometimes

observed during supplementation, results from creatine metabolism rather than from impaired glomerular filtration [2,6,7].

Another common error is equating creatine with anabolic steroids. Creatine is not a hormonal substance – it does not affect levels of testosterone or other sex hormones, and its effect is based solely on improving ATP availability, which in turn allows for an increase in training intensity and volume [2]. Another widespread belief is that creatine causes hair loss. This claim is not supported by well-designed clinical studies, and the only source of this hypothesis comes from isolated, poorly documented observations [2].

Also raising concerns has been the issue of water retention and dehydration. Although short-term supplementation may lead to a temporary elevated intracellular water volume, no long-term water retention or increased risk of dehydration has been reported [2]. Research also shows that creatine is safe in both women and men, as well as in older individuals and children – of course at appropriate doses and under clinical supervision [2,3].

3. Forms and bioavailability of creatine

Creatine as a supplement is available in numerous forms, of which the most widespread and best-researched is creatine monohydrate (CrM). Studies have shown that CrM is characterized by almost 100% bioavailability, is not degraded to creatinine in the gastrointestinal tract, and effectively increases creatine concentration in plasma and in target tissues such as muscle and brain [8].

Alternative forms of creatine are also available on the market, such as creatine hydrochloride (CrHCl), creatine citrate, creatine ethyl ester, and creatine free acid. However, there is a lack of convincing scientific evidence confirming their superior bioavailability or efficacy compared to CrM [9]. In reality, many of these forms have not undergone rigorous clinical trials, and their marketing claims of higher effectiveness often find no support in the scientific literature [9].

Innovative approaches, such as lipid-based formulations (LMP) aimed at increasing creatine bioavailability, have shown initially promising results in preclinical studies, suggesting a potential increase in plasma creatine concentration at lower doses [10]. However, further clinical studies are needed to confirm their efficacy and safety in humans.

In summary, despite the availability of various forms of creatine, creatine monohydrate remains the most effective and safe supplement option, supported by the largest number of scientific

studies. Alternative forms may offer certain advantages in terms of solubility or consumption comfort, but their superiority over CrM in terms of bioavailability and efficacy has not been clearly confirmed in scientific studies.

4. **Creatine can support cognitive function**

Creatine plays a key role in maintaining energy homeostasis in the central nervous system, acting through the phosphocreatine system, which enables rapid ATP resynthesis during sudden increases in neuronal energy demand. Energy deficits in the brain can lead to cognitive impairment, therefore increasing the availability of creatine may beneficially affect the maintenance of mental performance, particularly in situations of metabolic deficit, such as sleep deprivation, aging, or oxidative stress [11,12].

In one recently published study, it was shown that even a single dose of creatine may help counteract certain negative metabolic alterations and impairments in cognitive function associated with sleep deprivation, which represents an important and unique observation in the context of the neuroprotective properties of this substance. Participants in the study, after taking creatine, exhibited increased performance in tasks requiring working memory, executive function, and information processing speed. This improvement was correlated with an elevated level of phosphocreatine in the brain, suggesting that creatine may support cognitive functions by increasing energy availability in neurons. This mechanism relies on the ability of creatine to rapidly regenerate ATP from ADP, which is crucial for maintaining an adequate energy level in nerve cells, especially during intense mental activity. Additionally, the increased availability of phosphocreatine may support the brain's energy stability, which is crucial for maintaining optimal cognitive performance [13]. It should be noted that a high dose of creatine (0.35 g/kg) was used in the study, whereas typically 3–5 g is recommended for an adult, and that the experiment involved only a small number of participants (15). It is undoubtedly necessary to conduct studies on larger populations to draw more conclusive inferences. Nevertheless, the results of the discussed study appear to be consistent with observations from other recently published work suggesting that creatine supplementation can support cognitive functions. However, only studies with larger statistical power will allow for the formulation of more definitive clinical recommendations in this area.

5. Potential therapeutic support in neurodegenerative diseases

In the context of neurodegenerative diseases, creatine demonstrates neuroprotective potential primarily due to its effect on energy metabolism of neurons and modulation of NMDA receptor signaling. In vitro studies conducted on hippocampal cell cultures have shown that creatine supplementation increased intracellular levels of adenosine triphosphate (ATP), the major source of energy for cellular reactions, and phosphocreatine, which translated to an enhanced resistance of the cells to the excitotoxic effects of glutamate. Creatine also prevented excessive increases in calcium concentration in the cytoplasm following NMDA receptor stimulation, suggesting its direct effect on the excitotoxic cascade [14,15]. Despite earlier assumptions, creatine did not exhibit a direct antioxidant effect – it did not neutralize reactive oxygen species generated by the xanthine system, and at high H_2O_2 concentrations its presence could even exacerbate cytotoxicity [14]. Thus, the protective action of creatine is primarily associated with the improvement of neuronal energy balance and the limitation of secondary glutamate release, which may constitute a significant therapeutic mechanism in diseases such as Alzheimer's disease.

An additional neuroprotective mechanism of creatine may be its influence on the functioning of mitochondria in nerve cells. Brain tissue, due to its high energy demand, is particularly sensitive to disturbances in ATP production, oxidative stress and mitochondrial damage. Creatine facilitates the regeneration of ATP during energy deficiency by transporting high-energy phosphate groups, while also helping to limit intracellular calcium buildup and oxidative stress in neuronal cells. Preclinical studies have shown that creatine supplementation reduces mitochondrial membrane depolarization, delays the opening of mitochondrial permeability transition pores, and limits protein nitration and mitochondrial DNA damage. Moreover, creatine may act as a regulator of glutamatergic neurotransmission and exhibits anti-inflammatory properties, e.g., by inhibiting the expression of adhesion molecules and Toll-like receptors. In result, improved survival of nerve cells was observed in models of Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis. Although most data come from in vitro studies and animal models, and clinical trial results are less conclusive, it is suggested that appropriately early supplementation intervention may slow the neurodegenerative process in patients from at-risk groups [16,17,18].

6. Creatine and physical activity

Among various strategies supporting the physical health of older individuals and patients with decreased mobility, creatine supplementation stands out as a safe and effective means of promoting both gains in muscle mass and improvements in functional capacity. Multiple studies consistently demonstrate that creatine use in individuals aged 50 and above, combined with resistance training, leads to increases in lean body mass and muscle strength [19,20,21]. Simultaneously, a reduction in body fat content was observed, which may beneficially affect metabolic homeostasis and reduce the risk of sarcopenia. These benefits result not only from increased phosphocreatine levels and improved ATP resynthesis capacity in muscle cells, but also from creatine's influence on molecular anabolic pathways, for example, by increasing the expression of IGF-1 and activating kinases in the mTOR pathway, which promotes muscle protein synthesis [19,20,22].

An important aspect of creatine intervention is its beneficial effect on bone health. It has been shown that creatine supplementation may help maintenance or even increase bone mineral density in older individuals, especially when accompanied by resistance training [19,23]. This mechanism is likely related to an improvement in mechanical loading of the bone due to increased muscle strength and mass, as well as a reduction in a bone resorption marker, namely the excretion of N-telopeptides [19,22]. Additionally, some studies suggest a potential influence of creatine on the functioning of the neuromuscular system, which may translate into improved motor coordination and a reduced frequency of falls [19,20,24]. Within this framework, creatine constitutes an important link in the prevention of age-related disability, as improvements in dynamic balance, lower limb explosive strength, and the ability to perform daily activities can significantly increase the independence of patients [19,25].

The muscle atrophy mass and deterioration of neuromuscular coordination, which are typical phenomena of aging, significantly increase the risk of falls in elderly individuals. An animal model has shown that long-term creatine supplementation can modulate the expression of genes related to neuroprotection and neuronal growth, resulting in improved motor function, as measured by an increase in locomotor activity [26,27]. Among elderly, improvements in motor coordination and lower limb strength can play a key role in gait stabilization and reducing the frequency of falls. An updated meta-analysis of six interventional studies, involving individuals

aged 57–69 undergoing resistance training programs and simultaneously supplemented with creatine (at doses of 5 g/day, in some cases with a loading phase of 20 g/day for 5 days), demonstrated a significant improvement in the chair stand test, which is one of the established predictors of fall risk. This improvement was 23% in the creatine group compared to 16% in the placebo group [25]. Earlier analyses have also confirmed that creatine supplementation leads to a significant increase in lower limb strength, which further reinforces its role in fall prevention [26]. Despite the inclusion of other measures, such as the timed up-and-go, did not show significant differences between groups, and the direct number of falls has not yet been subject to evaluation, these results nevertheless suggest that creatine can be an effective component of interventions aimed at reducing fall risk in older adults.

In the clinical context, it is also significant that creatine supplementation may improve quality of life in patients with frailty and sarcopenia by enhancing their ability to function independently [28]. Studies have also observed that creatine can mitigate the molecular mechanisms associated with age-related muscle degradation, such as increased oxidative stress, mitochondrial dysfunction, and chronic inflammation typical of sarcopenia pathophysiology [29].

7. Creatine in sports

Creatine monohydrate is widely used for years to support athletes' exercise performance – particularly in improving adaptation to strength training and performance during short-term, high-intensity anaerobic efforts. An increasing amount of data also indicates its beneficial effect on aerobic endurance in endurance sports, especially by extending time to exhaustion during prolonged high-intensity efforts and improving results in events requiring repeated bursts or final sprints [30]. The mechanism of action of creatine is related to the increase of intramuscular phosphocreatine stores, which enables faster ATP resynthesis and delays the onset of fatigue during intense effort [30,31]. Studies have shown that creatine supplementation leads to significant gains in muscle strength and power, as well as increased lean body mass, and improves the ability to perform repeated high-intensity efforts. Moreover, this supplement is considered safe for long-term use at typical doses (~3–5 g per day) [31]. Benefits from its use have been observed in various regularly exercising individuals: in older individuals, the addition of creatine to a resistance training program resulted in a greater increase in muscle strength than training alone [32], whereas in postmenopausal women, a sustained two-year regimen of creatine supplementation during regular exercise caused an improvement in some

measures of bone strength and a greater increase in lean body mass compared to placebo [33]. Furthermore, studies indicate potential positive effects observed in premenopausal women – it has been shown that a 5-day creatine (20 g/day) during the luteal phase of the menstrual cycle reduced the fatigue index during repeated sprints, thus mitigating the performance decline characteristic of this phase [34]. Creatine supplementation is also applied during recovery periods. It has been demonstrated that taking creatine during immobilization caused by injury helps limit skeletal muscle atrophy and maintain muscle mass and metabolic fitness, hence its use is recommended as a form of support during the rehabilitation of athletes returning to health [35]. Creatine significantly improves the capacity for repeated intense efforts: studies have recorded that creatine supplementation enabled the maintenance of higher average power and speed during successive treadmill sprints with less decline in speed at the end of the effort, despite a slight accompanying increase in body mass [36]. Additionally, a 4-week creatine supplementation before an intense eccentric exercise accelerated post-exercise recovery – shortening the time to regain muscle strength, reducing swelling, and improving range of motion within a few days after exercise compared to placebo [37]. Moreover, even short-term creatine "loading" translates into increased strength endurance: it has been shown that 5-day supplementation (20 g/day) allowed a significantly greater number of repetitions at 70% of maximal weight (1RM) in a set of exercises to muscular failure, thereby increasing the total work volume without affecting 1RM or perceived exertion [38].

8. **Creatine in depression**

While creatine is predominantly recognized and researched for its effects on physical performance and muscle development, there is a growing scientific interest in its potential applications beyond sports-related contexts, particularly in the management of psychiatric conditions such as depression. In an 8-week randomized pilot study involving 100 adult patients with depression, it was shown that adding creatine monohydrate (5 g/day) to cognitive-behavioral therapy (CBT) led to a significantly greater reduction in the severity of depressive symptoms than CBT with placebo, with no difference in the incidence of adverse effects [39]. At the same time, preclinical studies confirm the antidepressant potential of creatine. In the study by Aliomrani et al. on a mouse model, cyclosporin A (CYA) induced depressive behaviors, which were effectively prevented by co-administration of creatine with alpha-lipoic acid – indicating the involvement of mitochondrial mechanisms in the antidepressant action [40]. Another study on an animal model of treatment-resistant depression (high-altitude

hypoxia) revealed significant sex-dependent differences: creatine supplementation induced a pronounced antidepressant effect in female rats (including a reduction in immobility time in the forced swim test and reversal of anhedonia) and normalized energy deficits and brain serotonin levels, whereas no significant improvement was observed in males [41]. Clinical data from preliminary studies are also promising. In an open-label pilot study by Hellem et al. (2015) involving women with depression and coexisting methamphetamine dependence, it was found that 8-week creatine supplementation (5 g/day) caused a rapid (as early as 2 weeks) and sustained reduction in the severity of depressive and anxiety symptoms, accompanied by an increase in brain phosphocreatine levels [42]. In summary, available preclinical and clinical evidence indicates that creatine may represent a safe and effective adjunctive treatment for depression, which requires confirmation in further, larger-scale studies [39,40,41,42].

Conclusion

Creatine (especially in the form of monohydrate) is a well-studied, safe, and effective supplement that improves physical performance, strength, and lean body mass in various groups (both in athletes and in older individuals), especially in conjunction with resistance training. Long-term supplementation at typical doses (3–5 g/day) is considered safe, and numerous studies have debunked persistent myths: no evidence has shown that creatine damages the kidneys, has anabolic hormonal effects, accelerates hair loss, or causes chronic excessive water retention. Creatine monohydrate remains the gold standard of supplementation due to its highest bioavailability and proven efficacy, whereas alternative forms (e.g., hydrochloride, citrate, esters) have not yet demonstrated greater effectiveness. Increasing evidence indicates that creatine has a beneficial effect not only on the muscular system but also on the central nervous system – it can support cognitive functions (e.g., mitigating the effects of sleep deprivation) and exert neuroprotective effects by improving neuronal energy metabolism and reducing excitotoxicity. For this reason, its potential adjunctive role in neurodegenerative diseases is being investigated, although current human results are inconclusive and require further research. Moreover, preliminary studies suggest that creatine supplementation may exhibit antidepressant effects as an adjunctive therapy, opening a new direction for potential clinical applications. Creatine is a versatile supplement with a proven safety profile and a wide spectrum of benefits. These include improvements in physical performance and muscle function in people of different ages, as well as potential support for neurological and mental health; however, fully realizing its therapeutic potential requires further research.

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Authors's contribution

Conceptualization: Marcin Migiel, Izabela Brynczka

Methodology: Joanna Rypel-Bośka, Natalia Siuta

Formal analysis: Kamil Ciechomski, Jakub Miaśnikiewicz

Invastigation: Klaudia Goleniewska, Aleksandra Stupecka

Writing-rough preparation: Wiktoria Cecuła, Marcin Migiel

Writing-review: Marcin Migiel, Izabela Brynczka

Supervision: Joanna Rypel-Bośka, Natalia Siuta

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References:

[1] Kreider RB, Kalman DS, Antonio J, Ziegenfuss TN, Wildman R, Collins R, et al. International Society of Sports Nutrition position stand: safety and efficacy of creatine

supplementation in exercise, sport, and medicine. J Int Soc Sports Nutr. 2017 Feb;14:18. doi:10.1186/s12970-017-0173-z. PMID: 28615996; PMCID: PMC5469049.

[2] Antonio J, Candow DG, Forbes SC, Gualano B, Jagim AR, Kreider RB, et al. Common questions and misconceptions about creatine supplementation: what does the scientific evidence really show? J Int Soc Sports Nutr. 2021 Feb;18:13. doi:10.1186/s12970-021-00412-w. PMID: 33602135; PMCID: PMC7881130

[3] Roschel H, Gualano B, Ostojic SM, Rawson ES. Creatine supplementation and brain health. Nutrients. 2021 Feb;13(2):586. doi:10.3390/nu13020586. PMID: 33578876; PMCID: PMC7916590.

[4] Balestrino M. Role of creatine in the heart: health and disease. Nutrients. 2021 Apr;13(4):1215. doi:10.3390/nu13041215. PMID: 33924425; PMCID: PMC8069213.

[5] Ribeiro F, Longobardi I, Perim P, Duarte B, Ferreira P, Gualano B, et al. Timing of creatine supplementation around exercise: a real concern? Nutrients. 2021 Aug;13(8):2844. doi:10.3390/nu13082844. PMID: 34444299; PMCID: PMC8402496.

[6] Poortmans JR, Auquier H, Renaut V, Durussel A, Saugy M, Brisson GR. Effect of short-term creatine supplementation on renal responses in men. Eur J Appl Physiol Occup Physiol. 1997;76(6):566-7. doi: 10.1007/s004210050291. PMID: 9404870.

[7] Persky AM, Rawson ES. Safety of creatine supplementation. Subcell Biochem. 2007;46:275-89. doi: 10.1007/978-1-4020-6486-9_14. PMID: 18652082.

[8] Kreider RB, Kalman DS, Antonio J, Ziegenfuss TN, Wildman R, Collins R, Candow DG, Kleiner SM, Almada AL, Lopez HL. Bioavailability, efficacy, safety, and regulatory status of creatine and related compounds: a critical review. Nutrients. 2022 Feb;14(5):1035. doi:10.3390/nu14051035. PMID: 35268011; PMCID: PMC8912867.

[9] Jagim AR, Stecker RA, Harty PS, Erickson JL, Kerksick CM. Analysis of the efficacy, safety, and cost of alternative forms of creatine available for purchase on Amazon.com: are label claims supported by science? Nutrients. 2022 Dec;14(24):5192. doi:10.1016/j.heliyon.2022.e12113. PMID: 36544833; PMCID: PMC9761713.

[10] Fielding RA, Rivas D, Grosicki GJ, Ezzyat Y, Ceglia L, Price LL, Orhan C, Sahin K, Fowler K, White T, Durkee S, Kritsch K, Bellamine A. Effects of low doses of L-carnitine tartrate and lipid multi-particulate formulated creatine monohydrate on muscle protein synthesis in myoblasts and bioavailability in humans and rodents. Nutrients. 2021 Nov 9;13(11):3985. doi:10.3390/nu13113985. PMID: 34836240; PMCID: PMC8625796.

[11] Prokopidis K, Giannos P, Triantafyllidis KK, Kechagias KS, Forbes SC, Candow DG. Effects of creatine supplementation on memory in healthy individuals: a systematic review and meta-analysis of randomized controlled trials. Nutr Rev. 2023 Mar;81(4):416–427. doi:10.1093/nutrit/nuac064. PMID:35984306; PMCID:PMC9999677.

[12] Snow WM, Cadonic C, Cortes-Perez C, Roy Chowdhury SK, Djordjevic J, Thomson E, Bernstein MJ, Suh M, Fernyhough P, Albensi BC. Chronic dietary creatine enhances hippocampal-dependent spatial memory, bioenergetics, and levels of plasticity-related proteins associated with NF-κB. Learn Mem. 2018 Jan 16;25(2):54-66. doi: 10.1101/lm.046284.117. PMID: 29339557; PMCID: PMC5772392.

[13] Gordji-Nejad A, Matusch A, Kleedörfer S, Patel J, Drzezga A, Elmenhorst D, Binkofski F, Bauer A. Single dose creatine improves cognitive performance and induces changes in cerebral high energy phosphates during sleep deprivation. Sci Rep. 2024 Feb;14:4937. doi:10.1038/s41598-024-54249-9. PMID: 38418482; PMCID: PMC10902318.

[14] Genius J, Geiger J, Bender A, Möller HJ, Klopstock T, Rujescu D. Creatine protects against excitotoxicity in an in vitro model of neurodegeneration. PLoS One. 2012;7(2):e30554. doi:10.1371/journal.pone.0030554. PMID: 22347384; PMCID: PMC3275587.

[15] Stout AK, Raphael HM, Kanterewicz BI, Klann E, Reynolds IJ. Glutamate-induced neuron death requires mitochondrial calcium uptake. Nat Neurosci. 1998 Sep;1(5):366-73. doi: 10.1038/1577. PMID: 10196525.

[16] Chang H, Leem YH. The potential role of creatine supplementation in neurodegenerative diseases. Phys Act Nutr. 2023 Dec;27(4):48-54. doi: 10.20463/pan.2023.0037. Epub 2023 Dec 31. PMID: 38297476; PMCID: PMC10844727.

[17] Leland KM, McDonald TL, Drescher KM. Effect of creatine, creatinine, and creatine ethyl ester on TLR expression in macrophages. Int Immunopharmacol. 2011 Sep;11(9):1341-7. doi: 10.1016/j.intimp.2011.04.018. Epub 2011 May 14. PMID: 21575742; PMCID: PMC3157573.

[18]Nomura A, Zhang M, Sakamoto T, Ishii Y, Morishima Y, Mochizuki M, Kimura T, Uchida Y, Sekizawa K. Anti-inflammatory activity of creatine supplementation in endothelial cells in vitro. Br J Pharmacol. 2003 Jun;139(4):715-20. doi: 10.1038/sj.bjp.0705316. PMID: 12812994; PMCID: PMC1573908.

[19] Candow DG, Forbes SC, Kirk B, Duque G. Current evidence and possible future applications of creatine supplementation for older adults. Nutrients. 2021;13(3):745. doi:10.3390/nu13030745.

[20] Harmon KK, Stout JR, Fukuda DH, Pabian PS, Rawson ES, Stock MS. The application of creatine supplementation in medical rehabilitation. Nutrients. 2021;13(6):1825. doi:10.3390/nu13061825.

[21] Forbes SC, Candow DG, Krentz JR, Roberts MD, Young KC. Changes in fat mass following creatine supplementation and resistance training in adults ≥50 years of age: a meta-analysis. J Funct Morphol Kinesiol. 2019;4(3):54. doi:10.3390/jfmk4030054.

[22] Candow DG, Vogt E, Johannsmeyer S, Forbes SC, Farthing JP. Strategic creatine supplementation and resistance training in healthy older adults. Appl Physiol Nutr Metab. 2015;40(7):689–694. doi:10.1139/apnm-2014-0498.

[23] Chrusch MJ, Chilibeck PD, Chad KE, Davison KS, Burke DG. Creatine supplementation combined with resistance training in older men. Med Sci Sports Exerc. 2001;33(12):2111–2117. doi:10.1097/00005768-200112000-00025.

[24] Eijnde BO, Van Leemputte M, Goris M, et al. Effects of creatine supplementation and exercise training on fitness in men 55–75 yr old. J Appl Physiol. 2003;95(2):818–828. doi:10.1152/japplphysiol.00910.2002.

[25] Chilibeck PD, Kaviani M, Candow DG, Zello GA. Effect of creatine supplementation during resistance training on lean tissue mass and muscular strength in older adults: a meta-analysis. Open Access J Sports Med. 2017;8:213–226. doi:10.2147/OAJSM.S123529.

[26] Candow DG, Forbes SC, Chilibeck PD, Cornish SM, Antonio J, Kreider RB. Effectiveness of Creatine Supplementation on Aging Muscle and Bone: Focus on Falls Prevention and Inflammation. J Clin Med. 2019 Apr 11;8(4):488. doi: 10.3390/jcm8040488. PMID: 30978926; PMCID: PMC6518405.

[27] Bender A, Beckers J, Schneider I, Hölter SM, Haack T, Ruthsatz T, Vogt-Weisenhorn DM, Becker L, Genius J, Rujescu D, Irmler M, Mijalski T, Mader M, Quintanilla-Martinez L, Fuchs H, Gailus-Durner V, de Angelis MH, Wurst W, Schmidt J, Klopstock T. Creatine improves health and survival of mice. Neurobiol Aging. 2008 Sep;29(9):1404-11. doi: 10.1016/j.neurobiolaging.2007.03.001. Epub 2007 Apr 9. PMID: 17416441.

[28] Rizzoli R, Reginster JY, Arnal JF, et al. Quality of life in sarcopenia and frailty. Calcif Tissue Int. 2013;93(2):101–120. doi:10.1007/s00223-013-9758-y.

[29] Ogawa S, Yakabe M, Akishita M. Age-related sarcopenia and its pathophysiological bases. Inflamm Regen. 2016;36:17. doi:10.1186/s41232-016-0022-5.

[30] Forbes SC, Candow DG, Falk Neto JH, Kennedy MD, Forbes JL, Machado M, et al. Creatine supplementation and endurance performance: surges and sprints to win the race. J Int Soc Sports Nutr. 2023;20(1):2204071.

[31] Antonio J, Pereira F, Curtis J, Rojas J, Evans C. The top 5 can't-miss sport supplements. Nutrients. 2024;16(19):3247.

[32] Amiri E, Sheikholeslami-Vatani D. The role of resistance training and creatine supplementation on oxidative stress, antioxidant defense, muscle strength, and quality of life in older adults. Front Public Health. 2023;11:1062832.

[33] Chilibeck PD, Candow DG, Gordon JJ, Duff WR, Mason R, Shaw K, et al. A 2-year randomized controlled trial on creatine supplementation during exercise for postmenopausal bone health. Med Sci Sports Exerc. 2023;55(10):1750-1760.

[34] Gordon AN, Moore SR, Patterson ND, Hostetter ME, Cabre HE, Hirsch KR, et al. The effects of creatine monohydrate loading on exercise recovery in active women throughout the menstrual cycle. Nutrients. 2023;15(16):3567.

[35] Turnagöl HH, Koşar ŞN, Güzel Y, Aktitiz S, Atakan MM. Nutritional considerations for injury prevention and recovery in combat sports. Nutrients. 2022;14(1):53.

[36] Bogdanis GC, Nevill ME, Aphamis G, Stavrinou PS, Jenkins DG, Giannaki CD, et al. Effects of oral creatine supplementation on power output during repeated treadmill sprinting. Nutrients. 2022;14(6):1140.

[37] Yamaguchi S, Inami T, Ishida H, Morito A, Yamada S, Nagata N, et al. The effect of prior creatine intake for 28 days on accelerated recovery from exercise-induced muscle damage: a double-blind, randomized, placebo-controlled trial. Nutrients. 2024;16(6):896.

[38] Furtado ETF, de Oliveira JPL, Pereira ISB, Veiga EP, da Silva SF, de Abreu WC. Short term creatine loading improves strength endurance even without changing maximal strength, RPE, fatigue index, and mood state. An Acad Bras Cienc. 2024;96(2):e20230559.

[39] Sherpa NN, De Giorgi R, Ostinelli EG, Choudhury A, Dolma T, Dorjee S. Efficacy and safety profile of oral creatine monohydrate in add-on to cognitive-behavioural therapy in

depression: an 8-week pilot, double-blind, randomised, placebo-controlled feasibility and exploratory trial in an under-resourced area. Eur Neuropsychopharmacol. 2025;90:28–35.

[40] Aliomrani M, Mesripour A, Saleki Mehrjardi A. Creatine and alpha-lipoic acid antidepressant-like effect following cyclosporine A administration. Turk J Pharm Sci. 2022;19(2):196–201.

[41] Kanekar S, Ettaro R, Hoffman MD, Ombach HJ, Brown J, Lynch C, et al. Sex-based impact of creatine supplementation on depressive symptoms, brain serotonin and SSRI efficacy in an animal model of treatment-resistant depression. Int J Mol Sci. 2021;22(15):8195.

[42] Hellem TL, Sung YH, Shi XF, Pett MA, Latendresse G, Morgan J, et al. Creatine as a novel treatment for depression in females using methamphetamine: a pilot study. J Dual Diagn. 2015;11(3–4):189–202.