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CREATINE: NOT JUST FOR ATHLETES - A MULTI-SYSTEM HEALTH SUPPLEMENT

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ABSTRACT

Background: Creatine is one of the most comprehensively studied nutritional compounds in human physiology. While historically regarded as an ergogenic aid for sport performance, evidence accumulated over the last three decades demonstrates that creatine functions as a multisystem bioenergetic molecule with relevance for skeletal muscle, the central nervous system, cardiovascular tissues, metabolic regulation and aging. Recent systematic reviews and meta analyses highlight substantial clinical potential, yet creatine remains underused in general health and preventive medicine due to persistent misconceptions regarding safety and applicability.

Aims: This narrative review synthesizes advances in creatine research from 1992 to 2025, integrating data across neurology, cardiometabolic health, endocrinology, inflammation and aging. The review evaluates population specific responses in older adults, women, adolescents and vegetarians, outlines mechanistic pathways underlying systemic effects and clarifies the contemporary safety profile. Additionally, it identifies gaps in translational application and discusses the growing relevance and novelty of creatine as a broad spectrum health supplement.

Methods: Literature published between 1992 and 2025 was identified through PubMed, Embase, Scopus and the Cochrane Library using terms related to creatine metabolism, bioenergetics, neurology, cardiology, endocrinology and aging. Randomized controlled trials, systematic reviews, meta analyses and mechanistic human studies were prioritized.

Results: Creatine supplementation increases intramuscular phosphocreatine by 20 to 40 percent, enhances high intensity performance, improves cognitive function under metabolic stress, supports neuroprotection, improves

glycaemic control in type two diabetes and reduces inflammatory markers. Evidence demonstrates benefits in aging adults, women, adolescents and individuals following vegetarian diets. Cardiovascular studies indicate improved energetic buffering and microvascular function. Across populations, creatine monohydrate remains the most validated form with a consistent safety record, including long term trials in both healthy and clinical groups.

Conclusion: Creatine has expanded from a sport oriented ergogenic aid into a versatile, evidence based health compound with relevance for neurology, cardiometabolic medicine, endocrinology, aging physiology and preventive care. Its favourable safety profile and physiological rationale support broader use in clinical and public health contexts. Further long term studies in diverse populations are needed to refine dosing strategies and optimise translational implementation.

Keywords: creatine, phosphocreatine, atp regeneration, neuroprotection, cognitive function, metabolism, aging, supplement safety.

INTRODUCTION

BACKGROUND AND RATIONALE

Creatine is widely recognized as one of the most effective and well validated nutritional supplements. Historically, its development as an ergogenic aid began with the landmark work of Harris and colleagues in 1992, who demonstrated that oral creatine monohydrate supplementation markedly increases intramuscular phosphocreatine content in healthy adults and enhances high intensity exercise capacity [1]. Subsequent studies in the 1990s confirmed its role in skeletal muscle energetics and established creatine monohydrate as the reference form for human supplementation [2–4].

Over the past three decades, research has shifted from a narrow focus on sport performance to a broader view of creatine as a systemic bioenergetic compound. In skeletal muscle, recent systematic reviews and meta analyses show consistent gains in strength, power and lean mass when creatine is combined with resistance training in adults under and over fifty years of age [20,24–26]. In the central nervous system, human trials and meta analytic data indicate that supplementation increases brain creatine content, improves working and episodic memory, and enhances cognitive performance particularly under conditions of sleep deprivation and metabolic stress [30–33,53].

Cardiovascular research has identified creatine as an important component of myocardial energy transfer through the creatine kinase shuttle, with reductions in creatine and phosphocreatine documented in heart failure and associations with impaired ventricular function [54–56]. Experimental and early clinical work suggests that supplementation can improve exercise capacity, microvascular function and resistance to ischemic injury in cardiac patients [57–59].

At the metabolic level, creatine influences glucose homeostasis and inflammatory pathways. Controlled trials in type 2 diabetes report improvements in glycaemic control when creatine is used alongside standard care, while studies in athletes demonstrate reductions in key pro inflammatory markers after strenuous exercise [63,64,67]. In aging populations, narrative reviews, clinical trials and meta analyses show that creatine, especially in combination with resistance training, can attenuate age related loss of muscle mass and strength, influence bone turnover and help preserve functional capacity in older adults [68,72–74].

Several high quality systematic reviews and position stands published between 2015 and 2024 summarise these multisystem effects and address the long term safety of creatine use in healthy individuals, women, older adults and clinical populations [7,22,26,30,54,68,74,97,98]. These works consistently conclude that recommended doses do not impair renal function or cause clinically relevant adverse effects in people without pre existing severe kidney disease.

Despite this extensive evidence, creatine remains underused outside athletic contexts. Misconceptions about renal toxicity, fluid retention and sex specific risks persist among clinicians, patients and the general public, which limits its adoption in geriatrics, neurology, endocrinology and preventive cardiology. At the same time, important questions remain insufficiently integrated in the literature. Existing reviews often focus on a single domain such as sport performance, brain health, cardiovascular disease, aging muscle or safety, without providing a unified view of creatine as a multi system health supplement. Data on population specific responses in women, vegetarians and adolescents are scattered across specialised publications, and the translational implications for routine clinical practice are not consistently synthesised.

The present narrative review addresses these gaps by bringing together mechanistic, physiological and clinical findings from 1992 to 2025 across muscle, brain, cardiovascular and metabolic systems, with a specific focus on aging adults, women, adolescents and plant based populations, and by integrating contemporary safety data relevant to everyday clinical decision making.

RELEVANCE

The relevance of this topic is determined by the rapid expansion of scientific data on the non strength related and non

classical effects of creatine, which is clearly reflected in the literature of the past decade. Creatine is no longer viewed solely as a sports supplement. Accumulated evidence demonstrates its significant role in neuroenergetics, cardiometabolic regulation, glucose homeostasis, anti inflammatory mechanisms and the prevention of sarcopenia. Systematic reviews and meta analyses confirm its multisystem impact, including improvements in cognitive function, increased resistance to metabolic stress, reductions in inflammatory markers and enhanced functional mobility in older adults. Given the global rise in metabolic disorders, age related diseases and cognitive impairments, investigating creatine as a universal nutritional tool has become clinically important and timely.

NOVELTY

The novelty of this approach lies in the integration of data from neurology, endocrinology, gerontology and sports medicine, which makes it possible to consider creatine as a multisystem compound with a wide spectrum of biological effects. Recent years have seen the publication of studies demonstrating its influence on cognitive processes in older adults, vegetarians and individuals under high cognitive load, as well as its potential role in mitochondrial protection and maintenance of neuronal energy balance. New literature highlights its clinical relevance in traumatic brain injury, chronic inflammation, sarcopenia, postmenopausal muscle loss and reductions in bone mineral density. These areas had not previously been adequately addressed outside the athletic context. Thus, the relevance is defined by the expanding clinical fields of creatine application, while the novelty lies in a comprehensive analysis of its systemic effects, which goes beyond traditional athletic use and reflects current trends in medicine and human physiology.

AIMS

This review aims to summarize current evidence on creatine's physiological and biochemical effects, highlight emerging applications in neurology, cardiometabolic disease, inflammation, and aging, evaluate responses across specific populations such as older adults, women, adolescents, and vegetarians, assess safety and persistent misconceptions, and explore integration of creatine supplementation into broader health and clinical practice.

RESEARCH QUESTIONS

This review addresses several key questions: what recent findings refine the understanding of creatine's systemic biological effects; how creatine influences skeletal muscle, the brain, cardiovascular tissues, metabolic pathways, and inflammatory processes; which populations benefit most and why; what current evidence shows regarding the safety profile of creatine; and how creatine may be incorporated into preventive and clinical strategies.

METHODS

SEARCH STRATEGY

A literature search of PubMed/MEDLINE, Embase, Scopus, and the Cochrane Library identified studies from January 1992 to September 2025. Search terms included: "creatine", "creatine monohydrate", "phosphocreatine", "ATP regeneration", "muscle energetics", "neuroprotection", "cognitive function", "cardiometabolic health", "type 2 diabetes", "inflammation", "aging", "sarcopenia", "women", "adolescents", "vegetarians", and related terms. Approximately 100 publications were included based on relevance, methodological quality, and contribution to the aims of the review.

The table below presents a summary of inclusion and exclusion criteria applied in the literature selection process for this reviw

Table 1. Inclusion and Exclusion Criteria

Category	Criteria
Inclusion	• Human clinical trials (RCTs, crossover, cohort, controlled); • Systematic reviews and meta-analyses; • Mechanistic studies related to human creatine metabolism; • Studies involving athletes, older adults, women, adolescents, vegetarians/vegans, and relevant clinical groups
Exclusion	• Non-English publications; • Case reports without broader applicability;

	• Animal studies lacking translational value; • Commentary or narrative opinions without primary data

RESULTS

1. HISTORICAL AND METHODOLOGICAL FOUNDATION

Creatine, first identified in 1832 by Chevreul and later linked to muscle energetics in the early 20th century, emerged as a research focus following the pivotal findings of Harris et al. (1992) demonstrating that exogenous creatine monohydrate (CM) increases intramuscular phosphocreatine (PCr) content [1]. Since then, scientific interest has expanded substantially, shifting from sport performance toward broader physiological, clinical, and metabolic applications. Today, CM is considered the gold-standard form due to its high bioavailability, consistent efficacy, and robust evidence base [4,7–9].

2. MECHANISTIC OVERVIEW AND BIOLOGICAL FUNDAMENTALS

Creatine is a nitrogen-containing compound synthesized endogenously in the liver and kidneys from arginine, glycine, and methionine, and obtained exogenously from foods such as meat and fish or through supplementation [2]. Approximately 95% of total body creatine is stored in skeletal muscle, where it exists as free creatine (~40%) and phosphocreatine (PCr; ~60%), forming a key component of the creatine kinase system that supports rapid ATP regeneration during high-intensity exertion [3,4]. Endogenous production provides roughly 1 g/day, while typical omnivorous diets contribute an additional 1–2 g/day- insufficient to fully saturate muscular stores [5,6]. Supplementation effectively increases intramuscular creatine by 20–40%, elevating creatine and PCr content by 15–20% within five days of loading or approximately 30 days of low-dose intake, with levels returning to baseline within 5–8 weeks after cessation [7,14]. By expanding the available pool of creatine and PCr, supplementation enhances the capacity for rapid energy turnover during repeated or demanding physical effort. Beyond its canonical role in muscle energetics, creatine also influences cellular hydration, bone metabolism, and neurocognitive processes, contributing to growing interest in its applications across performance, rehabilitation, and preventive health domains.

Table 2 compares major creatine forms: properties, advantages, and limitations based on literature data[4,7,8,9,10,11,12,13]

Table 2. Types of Creatine

Creatine Form	Key Properties	Advantages	Limitations / Notes	References
Creatine Monohydrate (CM)	Most studied; highest bioavailability	Gold standard; 20–40% ↑ PCr; strong RCT/ meta-analysis support	Temporary water retention	[4, 7, 8, 9]
Creatine Ethyl Ester (CEE)	Esterified form claimed to improve permeability	None proven	Lower bioavailability; converts faster to creatinine; not recommended for pregnancy, children, kidney/liver disease	[10, 11]
Creatine Gluconate	Creatine bound to glucose	Theoretical ↑ uptake via insulin-mediated pathways	No evidence of superiority over CM	[12]
Creatine Citrate	Highly soluble; Gastrointestinal (GI) friendly	Better solubility; potentially less GI discomfort	Similar bioavailability and effectiveness to CM; higher cost	[12]

Magnesium Creatine Chelate	Creatine + magnesium (cofactor for creatine kinase)	Theoretically improved uptake/stability	Limited evidence; no clear advantage over CM	[13]

3.EFFECTS ON PERFORMANCE AND MUSCULOSKELETAL PHYSIOLOGY

Creatine is among the most widely used ergogenic aids worldwide, with substantial adoption among NCAA athletes (14%), adolescents (~34%), and military personnel (~27%) [17-19]. Its popularity increased markedly after the 1992 Olympic Games and continues to grow, with annual U.S. sales exceeding $400 million [16].

3.1 Mechanism of Ergogenic Action

During high-intensity efforts, the ATP-PCr system provides rapid ATP resynthesis but can sustain maximal output for only ~10 seconds. Supplementation increases intramuscular PCr availability, thereby enhancing ATP turnover, delaying fatigue, and improving high-intensity performance [15].

3.2 Dosing Strategies

Loading protocols typically use 20–25 g/day for 5–7 days or ~0.3 g/kg/day for ≥3 days, followed by maintenance doses of ~3–5 g/day (~0.03 g/kg/day). Although loading accelerates saturation, similar tissue levels are achieved over time with lower daily dosing [20]. As supplements are not strictly regulated by the FDA, product variability remains a concern [21].

3.3 Performance Outcomes

Creatine is consistently shown to increase lean body mass, strength, muscular power, and performance in short-duration, high-intensity activities [15,22,23]. Meta-analyses indicate significant improvements in both upper- and lower-body strength, with particularly notable gains in bench press performance [24-25]. Approximately 64% of studies report a measurable increase in lean mass, largely attributable to intracellular water shifts [26]. It is important to note that this compound is used widely across both individual sports, such as swimming, combat sports and team-based disciplines, including football, soccer, and other high-intensity field sports. Individual variability also exists: athletes with low baseline creatine stores benefit most, while "nonresponders" tend to already have high muscle creatine content [27].

3.4 Regulatory status

Creatine is legal and not banned by WADA, the IOC, or the NCAA. However, because supplements are not tightly regulated, they may contain variable amounts of creatine or unintended substances [28].

4. NEUROCOGNITIVE AND NEUROLOGICAL EFFECTS

Creatine is traditionally associated with muscle performance and athletic training, but emerging evidence highlights its equally important role in brain energy metabolism. Despite accounting for only about 2% of total body mass, the brain consumes nearly 20% of the body's resting energy, relying heavily on rapid ATP resynthesis to sustain neurotransmission, ion transport, and synaptic function. Creatine and phosphocreatine form a crucial energy-buffering system, and supplementation has been shown to increase cerebral creatine stores, albeit to a lesser extent than in skeletal muscle [29]. Notably, enhancing brain creatine availability may support cognitive performance, particularly under conditions of elevated metabolic stress such as sleep deprivation or aging. Systematic reviews indicate that creatine supplementation can improve memory-most prominently in older adults-underscoring its role as a neuroenergetic and neuroprotective agent rather than merely a tool for muscular enhancement. Beyond cognitive function, creatine has demonstrated potential benefits in several neurological and clinical contexts, including mild traumatic brain injury, concussion recovery, depression, and certain neuromuscular and neurodegenerative disorders. By stabilizing cellular energy homeostasis, reducing oxidative stress, and supporting mitochondrial function, creatine may help mitigate the consequences of metabolic disruption commonly seen in these conditions. Collectively, this growing body of research positions creatine as a multifunctional compound with significant implications for brain health, cognitive resilience, and neurological recovery.

The following table summarizes neurocognitive and neurological effects of creatine based on literature data [30,31,32,33,34,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53]

Table 3. Neurocognitive and neurological effects

Brain energy metabolism	• Creatine increases brain creatine and phosphocreatine levels (↑3–10%) [30] • Enhances ATP buffering and supports neuronal energy during metabolic stress [31]
Cognitive function	• Improves cognitive performance in people with creatine deficiency syndromes [32,52]. • Enhances cognitive performance during sleep deprivation [33,34]. • Improves short-term and working memory in older adults and vegetarians. improves memory performance in healthy individuals, with particularly strong benefits in older adults [53] • Creatine also enhances cognitive function specifically in vegetarians-memory [50] and working memory plus intelligence [51]
• Mental health • Traumatic brain injury (TBI) & concussion	• Provides neuroprotection after brain trauma-maintains mitochondrial function and reduces oxidative damage, may be effective at reducing the severity of, or enhancing recovery from mild traumatic brain injury [39,40]. • Reduces cortical damage size in animal TBI models by 21–50%. [39] • Improves symptoms after concussion in preliminary human studies. [41] • May aid neurological recovery after TBI. [42]
Neurodegenerative diseases	• Shows metabolic benefits in Huntington's disease (improved ATP/PCr, lower lactate)[43] • Large clinical trials show mixed results-no confirmed disease modification. [44] • Demonstrates neuroprotection in animal models of Parkinson's and Huntington's disease. [45]
Anxiety & PTSD	• Altered creatine metabolism observed in GAD (generalized anxiety disorder) and PTSD (post traumatic stress disorder) patients [46] • Small clinical studies show improvements in mood and sleep [47]
Muscle–brain disorders	• Improves strength, fatigue resistance, and bone density in Duchenne muscular dystroph. [48]
Metabolic brain disorders	• Effective treatment for cerebral creatine deficiency syndromes (significant neurological improvement) [49]

5.CARDIOVASCULAR IMPLICATIONS

Creatine plays a key role in cardiac energy metabolism [54], as the phosphocreatine system enables rapid ATP regeneration during myocardial contraction, as described by Ingwall and Wallimann [55]. In cardiomyocytes, the

phosphocreatine–creatine kinase (PCr–CK) shuttle functions as a critical intracellular energy-transfer system, rapidly regenerating ATP at sites of high demand and maintaining contractile efficiency during periods of metabolic stress. In heart failure, levels of creatine and phosphocreatine are reduced due to decreased creatine transporter expression; the phosphocreatine/ATP ratio correlates with ejection fraction and serves as a predictor of mortality, as shown by Neubauer and colleagues [56]. Creatine supplementation may be beneficial for patients with heart failure by improving aerobic capacity or muscle strength, according to findings from Ahmed et al. [57]. Animal studies also demonstrate that creatine increases resistance to ischemia and may protect against anthracycline cardiotoxicity, partly through antioxidant mechanisms and effects on the creatine transporter, as demonstrated by Gupta [58]. Creatine improves microvascular function, increasing capillary density and enhancing vessel recruitment during reactive hyperemia, which directly supports better tissue perfusion [59] . Supplementation can additionally lower homocysteine levels, an important cardiovascular risk factor [100] . Creatine shows strong antioxidant and endothelial-protective effects, neutralizing ROS and stabilizing endothelial membranes, thereby reducing vascular permeability and oxidative damage [60,61] . It also helps maintain mitochondrial function, reducing mitochondrial ROS - a key mechanism in protecting cardiac and vascular cells [62]

6.ANTI-INFLAMMATORY AND METABOLIC EFFECTS

6.1 Anti-inflammatory Actions

Several studies indicate that this compound can attenuate the inflammatory response following intense exercise [62], primarily through reductions in key pro-inflammatory markers such as TNF-α, IL-1β, and PGE2. This effect has been demonstrated in work by Santos et al. (2004) [63] and Bassit et al. (2008) [64].

Additionally, this compound exhibits anti-catabolic properties, as shown by reduced muscle protein breakdown and decreased leucine oxidation in young men, according to Walzel et al. [65].

6.2 Endocrine Effects: Testosterone and DHT

Evidence suggests that short-term loading with this compound may influence androgen metabolism. Specifically, levels of dihydrotestosterone (DHT) increased by 56% after 7 days of loading and remained 40% above baseline after 14 days of maintenance supplementation [66].

While these findings are notable, the physiological relevance and long-term implications remain unclear and require further investigation.

6.3 Effects on Glucose Metabolism and Type 2 Diabetes

Type 2 Diabetes Mellitus (T2DM) represents the most prevalent form of diabetes worldwide.

Supplementation with this compound appears to reduce fasting glucose and HbA1c concentrations when compared to placebo, with no significant differences relative to standard pharmacological treatments such as metformin or glibenclamide [67].

All treatment modalities-creatine, metformin, and glibenclamide-were effective in lowering blood glucose levels, and importantly, no major adverse effects were reported.

Based on currently available but low-certainty evidence, creatine may serve as a potential hypoglycemic adjunct therapy for patients with T2DM, though additional high-quality trials are warranted [67].

7.POPULATION-SPECIFIC OUTCOMES

7.1 Older Adults

Sarcopenia, commonly defined as the age-related decrease in strength, muscle mass and functionality, is associated with osteoporosis, frailty and cachexia [68,69] Furthermore, sarcopenia increases the risk of falls, injuries, fractures and premature mortality [70]. Sarcopenia occurs in 5–17 % of community-dwelling aging adults and 14–85 % in those residing in long-term care facilities. With estimates that by the year 2050 there will be 1.5 billion adults ≥65 years of age [71], the prevalence of sarcopenia will continue to rise for the foreseeable future. Therefore, identifying treatments to overcome sarcopenia and associated age-related conditions is critically important from a global health perspective.

We have previously discussed and summarized the small body of research showing some favorable effects of creatine monohydrate supplementation on indices of aging muscle and bone [68], [72] Overall, creatine (primarily when combined with resistance training) has been shown to increase measures of muscle accretion, strength and functionality [74]. Creatine has also been shown to increase bone area [73], and strength [74], attenuate the rate of bone mineral loss [73] and influence bone turnover in older adults [73]. Based on these musculoskeletal benefits, it is highly plausible that creatine may be an effective intervention to treat frailty (characterized by muscle weakness) and

cachexia (characterized by rapid muscle wasting).

7.2 Adolescents and children

Research in youth athletes shows that creatine improves strength and sport performance, particularly in swimming and soccer, with benefits observed after both loading doses (20 g/day for 4 days) and low daily doses (3–5 g/day) [75-77]. Yanez-Silva et al. [76] reported improvements in peak and mean power output as well as total work completed during a Wingate anaerobic capacity test. Clinical pediatric studies also report improvements in muscle strength, neuromuscular symptoms, and fat-free mass in conditions such as muscular dystrophy when using doses of 3–5 g/day or 0.1 g/kg/day [78]. Creatine has also shown therapeutic benefits in rare metabolic disorders (GAMT/AGAT deficiency, gyrate atrophy), cystic fibrosis and more [75]. Safety data from numerous adolescent studies show no significant adverse events, and creatine is well tolerated when used under supervision [80]. The FDA has classified creatine as GRAS. (generally recognized as safe) for older children and adolescents [79]. Safe creatine use mainly applies to adolescents (≈13+, especially 16+), provided there is supervision and ISSN guidelines are followed. For children under 13, creatine is not routinely recommended, except for medical conditions treated under professional care [75].

7.3 Women

Creatine is especially relevant for women because they naturally have 70–80% lower endogenous creatine stores than men, making supplementation more impactful [81]. In premenopausal women, creatine improves strength, power, and exercise performance without causing significant weight gain, with strong evidence from multiple trials using doses of 20 g/day for 4–7 days (loading) followed by 3–5 g/day [82,83,]. Among postmenopausal women, high-dose short-term supplementation (0.3 g/kg/day ≈ 20 g/day) enhances fat-free mass, strength, and functional performance [84], and when combined with resistance training, creatine increases lean mass, improves strength, and slows bone mineral loss [85,86]

7.4 Vegans & vegetarians

Vegans have significantly lower creatine intake, as plant foods contain almost no creatine, leading to reduced creatine levels in serum, plasma, red blood cells and muscle [87,88]. Supplementation rapidly increases muscle creatine and phosphocreatine stores, with vegans and vegetarians often showing greater increases (“super-compensation”) than omnivores-e.g. 25% in vegetarians after supplementation [89]. These increases translate into improvements in lean mass, muscle fiber size, work output and anaerobic performance, especially during high-intensity exercise [90]. Even very small doses (1 g/day) effectively prevent declines in muscle creatine when switching to a vegetarian diet. [91]

8. SAFETY PROFILE

Controlled human studies consistently demonstrate that recommended doses of creatine (3–5 g/day maintenance; 20 g/day loading) increase muscle creatine stores without harming kidney function-most trials show no negative changes in mGFR, cystatin C, proteinuria, albuminuria, or electrolytes, even during long-term use. Slight increases in serum creatinine may appear, but this reflects normal creatine → creatinine conversion, not kidney damage. Importantly, multiple randomized controlled trials in both healthy individuals and clinical populations (diabetes, osteoarthritis, fibromyalgia, postmenopausal women, youth with SLE) show kidney function remains stable during supplementation. [92-97,99] Despite several unproved allegations, liver (enzymes, urea) and kidneys (glomerular filtration urea and albumin excretion rates) show no change in functionality in healthy subjects supplemented with creatine, even during several months, in both young and older populations. The International Society of Sports Nutrition concludes that no scientific evidence supports renal dysfunction, dehydration, heat intolerance, or increased cramping associated with creatine use in appropriate doses. Overall, the evidence strongly supports that creatine monohydrate is safe for the kidneys when used within recommended doses in healthy people and most clinical groups, with the only caution applying to individuals with pre-existing severe kidney disease, who should avoid supplementation [98,99]

DISCUSSION

Creatine has transitioned from an ergogenic supplement to a multi system bioenergetic compound with clinically meaningful effects across multiple domains of human health. Its capacity to stabilise ATP availability and sustain cellular energy reserves in high demand tissues is repeatedly demonstrated in physiological and clinical studies [3,4,7,14,31,54].

This mechanism explains its broad spectrum of benefits.

In skeletal muscle, supplementation increases phosphocreatine stores and enhances strength, power and functional recovery according to numerous controlled trials and meta analyses [15,22,23,24,25,26].

In the brain, creatine contributes to cognitive resilience during sleep deprivation, improves memory in older adults and vegetarians, and demonstrates neuroprotective effects in traumatic brain injury models and early clinical studies

[30,31,33,34,39,40,41,42,50,51,52,53].

Cardiac data indicate improved energetic buffering and microvascular function with relevance for patients with compromised myocardial metabolism [54,55,56,57,58,59,60,61].

Metabolic findings show better glycaemic control in type two diabetes and reductions in inflammatory markers after strenuous exercise [62,63,64,67].

In aging, creatine combined with resistance training mitigates sarcopenia, slows bone mineral loss and improves functional performance in older adults [68,72,73,74,85,86].

Despite a strong safety record supported by controlled long term studies [92,93,94,95,96,97,99], creatine remains underused outside athletic populations.

Misconceptions concerning renal safety are widespread, particularly among older adults, women and individuals on plant based diets, although available evidence does not support these concerns [87,88,89,90,91,98].

The reviewed data support the integration of creatine into broader nutritional and clinical strategies as a low cost and physiologically justified intervention.

CLINICAL IMPLICATIONS

Creatine may be clinically relevant for:

- aging adults to mitigate sarcopenia [68,72,74]
- patients with type two diabetes [67]
- post concussion and traumatic brain injury recovery [39,40,41,42]
- individuals under high cognitive load [33,34,50,52]
- perimenopausal and postmenopausal women [81,82,83,85,86]
- vegetarians and vegans [87,88,89,90,91]
- cardiac rehabilitation [54,55,57,59]
- chronic inflammatory conditions [62,63,64]
- Its safety profile, accessibility and biological rationale support broader clinical adoption.

CONCLUSION

The presented evidence shows that creatine is a key bioenergetic compound influencing the function of skeletal muscle, the brain, the cardiovascular system and metabolic pathways. Mechanistic studies confirm that its ability to support ATP regeneration and stabilize cellular energy metabolism underlies its effects in muscle tissue, neuronal structures and the myocardium. Clinical findings demonstrate improvements in high intensity performance, increased cognitive resilience, elements of neuroprotection, better glycaemic control in type 2 diabetes and a moderate reduction in inflammatory markers.

Research in specific populations highlights the particular relevance of creatine for older adults, women with lower baseline creatine stores, adolescents when used under supervision and vegetarians who exhibit reduced phosphocreatine pools. Clinical data and meta analyses indicate a stable safety profile at recommended doses in healthy individuals and most clinical groups with preserved renal function.

The overall analysis confirms that creatine extends far beyond the scope of a traditional ergogenic supplement and is emerging as a versatile nutrient with potential applications in neurology, geriatrics, endocrinology, cardiology and rehabilitative medicine. Several questions require further investigation, including long term use in clinical populations, optimization of dosing strategies for different groups and evaluation of its role in chronic neurodegenerative conditions.

DISCLOSURE

AUTHORS' CONTRIBUTIONS

Project administration: Zuzanna Muszkiet, Michał Bar, Damian Truchel, Dominik Poszwa

USE OF AI

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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