

Fueling Strength and Recovery: Basics of Creatine Monohydrate, Usage, Benefits, Effectiveness and Misconceptions

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ABSTRACT

Creatine monohydrate is the most researched as well as one of the widely used dietary supplements when it comes to the nutrition and fitness. It occurs naturally and is stored primarily in skeletal muscles. It plays an important role in adenosine triphosphate (ATP) regeneration, which is the basic energy provider at the time of high-intensity as well as short-duration activities. Supplementation with creatine monohydrate has consistently demonstrated benefits such as increased muscle mass, improved power output, enhanced recovery. Despite its well-documented safety profile and efficacy, it still remains surrounded by misconceptions, including concerns about kidney damage, dehydration, and cramping which shows lack of scientific and evidence-based knowledge in the society. Creatine which was once common among and limited to professional athletes has now spread to college athletes and weightlifters, Fitness enthusiasts, adult population and beyond. We reviewed the current scientific literature, to provide an accessible yet comprehensive overview of creatine monohydrate, highlighting its value not only as a performance-enhancing aid but also as

a safe and effective supplement for general health. Understanding both the established benefits and the misconceptions surrounding creatine is essential not only for athletes, fitness enthusiasts but also for general public.

This review article explores the fundamental aspects of creatine monohydrate, including its biochemical role, mechanisms of action, and practical applications in enhancing athletic performance, strength, and recovery, its dosage, timing and misconceptions. This review also addresses common myths and clarifies the evidence-based understanding of creatine usage, including optimal dosing strategies such as loading phases, maintenance protocols, and timing considerations.

Key Words: Creatine monohydrate, Weightlifting, Muscle mass, Ergogenic aids, Brain health.

INTRODUCTION

Creatine monohydrate (CM) is the most commonly studied as well as widely used supplement in sports and fitness world, renowned for its ability to enhance muscular strength, power output, as well as exercise performance. It plays an important role in

generation of energy, specifically ATP. ATP serves as the basic source of energy for high-intensity as well as short-duration exercises like sprinting and weightlifting. Creatine monohydrate had been reported to significantly increase the body's stores of phosphocreatine, a high-energy compound that helps regenerate ATP during intense physical exertion (1, 2)

Creatine which one was used by professional athletes has now being widely used by college athletes and weightlifters, fitness seekers, adult population and beyond.(3) Creatine a non-protein nitrogen compound which occurs naturally is found in small quantities in animal products as well as in plant products and synthesized in human body also in liver and kidney from amino acids mainly arginine, glycine, and methionine.(4) Although creatine's ability to enhance performance is well-established, important concerns persist regarding its ideal usage, possible side effects, and the long-term safety of continued supplementation.

Various studies have demonstrated that creatine enhances performance in short bursts of high-intensity activities like sprinting, weightlifting, and resistance-based workouts. It enhances strength, power, muscle mass, and recovery while potentially reducing exercise-induced muscle damage. These benefits are attributed to the increased availability of phosphocreatine for ATP resynthesis, improved cellular hydration, and reductions in muscle acidity during exercise

While the effectiveness of creatine in improving performance is well-documented, questions surrounding round its optimal usage, adverse side effects, and its safety in long term use. By delving into the latest research, this review highlights common misconceptions, clarify the science behind creatine supplementation. The review also evaluates impact of CM on recovery, muscle hypertrophy, and performance, shedding light on the nuanced role creatine plays across different fitness levels and exercise modalities.

Creatine is widely considered safe when used appropriately in this review we reviewed the existing literature for potential side effects and contraindications of creatine monohydrate, providing a balanced perspective on the supplement's usage.

Brief Biochemistry of creatine monohydrate and its mechanism of Action.

Biosynthesis

Creatine a non-protein derivative of amino acid, synthesized mainly in the liver, kidneys as well as in pancreas. It is also synthesized in brain and testes and others tissues in small quantity. It is produced in the body naturally through a reaction involving the arginine and glycine (amino acids), catalyzed by the enzyme L-arginine: glycine amidino transferase (AGAT), which generates guanidinoacetate (GAA). AGAT is primarily located in the kidneys, liver, pancreas, and specific regions of the brain. GAA is mainly synthesized in the kidneys and subsequently converted into creatine in the liver by the enzyme guanidinoacetate methyltransferase (GMAT) (5).

The endogenous synthesis of creatine strats with a ping-pong mechanism in which the amidino group from L-arginine is transferred to the N α -amine group of L-glycine. This reaction is catalyzed by the enzyme AGAT. two-step enzymatic process. (6, 7):

Step 1: Transfer of an amino group from arginine to glycine, forming guanidinoacetate happens and in enzyme AGAT catalyzes the reaction.

Step 2: In second step guanidinoacetate is converted into creatine using S-adenosylmethionine as a methyl donor and the reaction is catalyzed by Guanidinoacetate methyltransferase (GAMT) converts.

Mechanism of Action

ATP Regeneration: The creatine-phosphocreatine (PCr) system acts as a quick energy buffer in muscle cells. Within the cell this binds with inorganic phosphate

to form phosphocreatine and thus acting as a high energy source of phosphate for synthesis of ATP that had been degraded to ADP + Pi as a source of energy to fuel cellular metabolism. When energy is required at higher amounts phosphocreatine donates a phosphate group to ADP, forming ATP, which fuels muscle contraction (8,9)

Increased Phosphocreatine Stores: CrM supplementation enhances phosphocreatine stores, enabling prolonged ATP resynthesis and delaying muscle fatigue during high-intensity exercise (10)

Cell Hydration and Anabolic Signaling: Creatine increases intracellular osmolarity, promoting cellular hydration and potentially stimulating anabolic signaling pathways such as the mTOR pathway, which facilitates muscle protein synthesis (11)

Neuroprotective Effects: The brain relies on PCr for ATP production, and CM has shown good neuroprotective benefits in neurodegenerative diseases e.g., Parkinson's and Alzheimer's (12)

In addition to these functions, creatine is essential for transporting energy-related

intermediates from the mitochondrial electron transport chain to the cytosol.

Physiological Effects of Creatine Monohydrate

Multiple studies have shown that creatine monohydrate (CrM) supplementation enhances performance in exercises involving short, high-intensity bursts, like sprinting and weightlifting. Creatine has been shown to promote muscle hypertrophy through increased training volume and enhanced protein synthesis. Some evidence suggests that creatine supplementation enhances Brain function, especially under sleep-deprived or mentally taxing conditions. (13, 14, 15). From a skeletal muscle standpoint, combining this supplementation with resistance training gives good benefits for older adults by enhancing lean muscle mass, increasing muscle thickness in the limbs, boosting upper as well as lower body strength, and improving overall functional performance. (16).

Table 1: Differences between Creatine and Creatine Monohydrate

Feature	Creatine	Creatine Monohydrate	Reference
Definition	It is naturally occurring compound that supplies energy to muscles and brain	It is a synthetic supplement form of creatine with one water molecule attached	7, 8, 10, 11, 13, 14, 17
Chemical Formula	C ₄ H ₉ N ₃ O ₂ .	C ₄ H ₉ N ₃ O ₂ ·H ₂ O	
Solubility	Poor solubility in water	Higher solubility in water	
Bioavailability	Limited absorption in raw form	Highly bioavailable and efficiently absorbed	
Stability	Less stable and degrades quickly	More stable in storage and supplementation	
Performance Benefits	It gives a natural support for ATP production but limited in quantity	It enhances ATP regeneration, improves strength and exercise performance	
Hydration Effect	Minimal effect on cellular hydration	Increases intracellular water retention, supporting muscle growth	
Common Usage	Naturally present in foods such as meat and fish	Available as a supplement in powder or capsule form.	

Dosage and timing

The recommended dosage of creatine monohydrate varies based body mass and goal of an individual. Many sources, including the International Society of Sports Nutrition (ISSN) and research studies,

suggest a loading phase of 0.3 g per kg per day or 20 g per day for 5 to 7 days, followed by a maintenance phase of 3 to g per day. The common approach used for loading phase is of 20 g of CM per day for at least 5 to 7 days or based on body mass (0.3

g/kg/day) followed by the maintenance phase of 3–5 g/day. Studies also reveal that taking daily dosage without a loading phase (e.g., 3 g / day for at least 28 days) is having similar muscle saturation over time. This protocol is widely accepted for muscle creatine saturation, performance enhancement, and clinical perspective (2, 10, 18, 19, 20,).

Loading Phase involves taking higher doses (e.g., 20 g/day) for 5 to 7 days, this saturates creatine stores of muscle rapidly. After loading, a daily dose of 3 to 5 g helps maintain elevated creatine levels (*i.e.* Maintenance Phase). Dosage may vary based on body weight, muscle mass and specific goals. While loading phases can rapidly increase muscle creatine stores, studies have also suggested that taking 3-5 g of CM per day without a loading phase can also effectively elevate muscle creatine levels over time but responses may vary from individual to individual in both the conditions (2, 10, 18, 19, 20,)

Timing:

Various studies have been done to check whether the timing of CM can influence its effectiveness or not. A recent study concluded that the timing of creatine monohydrate intake had no significant impact on the outcomes measured (21), where as a study done in 2023 by Antonio & Ciccone, suggests that taking creatine immediately after exercise May improve muscle absorption by boosting blood circulation and transporter efficiency (22). While post-workout supplementation may offer some advantages due to increased muscle uptake, the overall consistency of daily creatine intake plays a crucial role in achieving optimal benefits. Regular daily supplementation, regardless of timing, effectively increases muscle creatine stores, emphasizing the importance of consistency over specific timing. Combining creatine with carbohydrates or protein can further enhance its effectiveness

Table 2: Timing Strategy for creatine supplement (23, 24, 25, 26, 27, 28, 29, 30)

Timing Strategy	Details
Post-Workout Supplementation	This meta-analysis showed that taking creatine supplementation right after exercise remained more effective Intake of creatine right after exercise could improve muscle absorption due to enhanced blood circulation and increased transporter activity. Taking creatine immediately after exercise may also enhance strength gains compared to pre-exercise consumption.
Pre-Workout Supplementation	Consuming creatine before exercise ensures availability during the workout, though some studies suggest no significant performance difference compared to post-workout intake.
Pre and Post-Workout Combination	Splitting the daily dose, taking half before and half after exercise may optimize muscle creatine retention and performance gains.
Consistent Daily Intake	Regular daily supplementation, regardless of timing, effectively increases muscle creatine stores over time.
With Carbohydrates/Protein	Co-ingesting creatine with carbs and/or protein can increase creatine uptake because of insulin-mediated transport.

Creatine and Body mass

CM is primarily linked with an increase in body mass, which can be attributed to several mechanisms, such as higher intracellular water content and synthesis of muscle protein (19). In the short term, creatine leads to a rapid increase in total body water, mainly due to enhanced hydration within the cells (10). This initial weight gain typically occurs within the first

week of supplementation and is reversible once creatine intake is stopped (2). With long-term use, creatine promotes an increase in lean body mass through enhanced muscle protein synthesis and the activation of satellite cells (14). The activation of the mTOR pathway by creatine contributes to muscle hypertrophy, particularly in resistance-trained individuals (11). Studies indicate that individuals supplementing with

creatine experience greater strength and hypertrophy than non-users (31, 32). For increasing body mass through multiple physiological mechanisms, it is a well-supported strategy. While short-term gain of weight is primarily due to retention of water, long-term effects involve muscle hypertrophy and enhanced training adaptations.

Rawson & Volek in their study reported notable gains in lean body mass and muscle thickness in athletes using creatine, particularly in strength and power-based sports where as Candow *et al.*, 2019 had reported that Creatine has been shown to counteract age-related sarcopenia, improving muscle mass and functional performance in older adults also. (32, 33)

A recent meta-analysis by Khamene (2024) indicated that creatine supplementation tends to produce a more pronounced increase in fat-free mass in males than in females. The effectiveness of supplementation appeared largely unaffected by variables such as dosage strategies, training experience, or age. The findings revealed that creatine not only contributed to gains in overall body mass and/or fat-free mass but also helped reduce body fat percentage. Moreover, studies incorporating a maintenance phase or combining creatine with resistance training reported greater enhancements in body composition (34). It was also noted that females generally exhibit lower creatine levels in the brain's frontal lobe, and increasing these levels through supplementation may help alleviate symptoms of depression (22).

Who Should Avoid Creatine Monohydrate

CM is a proven aid for improving physical performance as well as muscle growth. However, individuals with kidney or liver disease, hypertension, digestive issues, pregnant women, and adolescents should exercise caution.

As creatine is widely used in sports, adolescents should use with caution and

under the supervision of a medical expert or fitness professional. Rapid muscle mass gains and increased water retention can pose a risk, especially without proper training and hydration (35). Creatine is metabolized into creatinine, a waste product filtered by the kidneys. Individuals with pre-existing kidney dysfunction may struggle with creatinine clearance, potentially exacerbating renal impairment (36). Studies suggest that while creatine does not cause kidney damage in healthy individuals, those with kidney disease should avoid it (37). These studies highlights that Individuals with Pre-Existing Kidney Disease should avoid the supplement.

Liver plays a crucial role in creatine synthesis and metabolism. Liver dysfunction can impair creatine processing, leading to metabolic imbalances (38). Those with conditions like cirrhosis or hepatitis should consult a physician. Moreover, as the supplement may cause water retention, leading to increased blood pressure in sensitive individuals (39). While evidence remains inconclusive, hypertensive individuals should monitor their blood pressure closely when considering creatine. Bloating, cramping, and diarrhea had also been reported after usage of creatine supplementation. These side effects are often dose-dependent and may be exacerbated in individuals with irritable bowel syndrome (IBS) or other digestive conditions (40). In pregnancy it is advised to creatine (41).

Hydration Strategies and precautions during Creatine Monohydrate Supplementation

CM is a supplement best known for its benefit's overall strength, power, and development of muscle mass but proper intake of water i.e., hydration and few precautions are important to get the maximum benefit from supplement without any side effect.

CM increases energy stores of muscles as well as promotes strength gains and improves athletic performance. Usually, it is

considered safe but its ability to draw water into muscle cells needs adequate hydration and thus failure to maintain proper fluid balance can cause dehydration, muscle cramps and other complications (35). As creatine increases intracellular water content in muscles leading temporary weight gain and improved muscle volume. This effect highlights the need for sufficient fluid intake in order to support hydration balance and prevent dehydration-and its related issues (21).

As for as the myths that creatine lead dehydration, studies reveals that improper hydration rather than creatine monohydrate itself may lead to muscle cramps especially during high intensity exercise (42). In order to maintain electrolyte balance (Sodium and potassium especially), electrolytes should be taken along with increased water intake which helps to prevent imbalances which can be due to increased fluid retention and loss during exercise (19).

Phase	Recommendations
Hydration During Maintenance Phase	2.5–3.5 liters of water per day while supplementing with creatine, depending on body weight and activity level (43)
Hydration During Loading Phase	Additional 500–1000 mL of water per day to facilitate proper absorption and distribution (35)

Precautions related to Creatine Supplementation

To remain properly hydrated is most important for optimizing the benefit of creatine and preventing the side effects such as dehydration as well as muscle cramps. Recommended water intake guidelines should be followed and while considering necessary precautions, one can safely maximize the benefits from creatine monohydrate

There are no additional benefits from exceeding recommended doses rather this may lead to gastrointestinal distress and unnecessary water retention thus over dosage should be avoided. Renal function checkup (37, 39). Creatine is often combined with other performance-enhancing supplements one be aware of potential interactions with the combing supplement (38).

Antagonists of Creatine Monohydrate:

Certain factors, compounds, and physiological conditions can act as antagonists, inhibiting its effectiveness

Tarnopolsky, 2015 In a review reported that studies suggest that caffeine may counteract the benefits of creatine by interfering with phosphocreatine resynthesis and muscle relaxation kinetics whereas Trexler &

Smith-Ryan, 2019 conflicting research indicates that moderate caffeine intake may not significantly affect creatine's ergogenic benefits (44, 45)

Antonio et al., 2018 reported that excessive fiber intake may impair creatine absorption by affecting intestinal transit time and reducing bioavailability. Harty et al., 2020 reported that alcohol consumption negatively impacts muscle recovery and protein synthesis, potentially diminishing the benefits of creatine supplementation. Volek et al., 2018 reported that conditions such as insulin resistance and metabolic syndrome may impair creatine uptake and utilization. (23, 46, 47)

Kreider et al., 2017 reported that Diuretics increase fluid excretion, which may lead to dehydration and reduce the intracellular water retention effect of creatine whereas Mishra et al., 2019 reported that Chronic use of NSAIDs may impair muscle adaptation to creatine by interfering with inflammatory pathways necessary for muscle growth (19, 48)

Creatine and Sleep Deprivation

Sleep deprivation impairs cognitive function, reaction time, and muscle recovery. Studies indicate that inadequate sleep reduces ATP availability, which can

negatively affect endurance and strength (49). Literature suggest that CM may help mitigate the negative effects of sleep deprivation. Cook et al. (2017) reported that creatine supplementation improved cognitive performance and reduced fatigue in sleep-deprived individuals (50). Similarly, McMorris et al. in their study found that creatine supplementation enhanced reaction time and working memory after sleep loss. Sleep is essential for muscle recovery and protein synthesis. Creatine has been shown to enhance muscle recovery by reducing inflammation and oxidative stress (51, 52). In a study done by Rahimi et al. (2021), they found that taking the creatine monohydrate improves muscle function and reduces soreness following high-intensity exercises and potentially complementing the restorative effects of sleep. They also reported that besides its benefits, creatine monohydrate may have some effects on sleep regulation. Studies also reported that some of the users report increased alertness when taking creatine close to bedtime (53)

Creatine monohydrate, sunlight and Vitamin D levels.

Studies have reported the important role of vitamin D, synthesized upon the exposure of sunlight, in modulating creatine uptake and muscle function (54). The creatine transporter i.e., CRT1 which is encoded by the SLC6A8 gene is responsible for the uptake of creatine into muscle cells. Researches done, suggest that vitamin D may influence the expression of transport proteins which is involved in absorption

muscle nutrient, including CRT1 (55). Thus, sunlight exposure may indirectly support creatine uptake by enhancing function of muscles and metabolic pathways which are related to production of energy (56).

As sunlight plays an important role in vitamin D synthesis, essential for muscle function and creatine metabolism, Vitamin D also improves the skeletal muscle health by regulating calcium homeostasis, contraction of muscle, and energy metabolism. Studies had reported that good levels of vitamin D can optimize creatine uptake as well as its utilization thus potentially enhancing its ergogenic effects. A deficiency in vitamin D may contribute to diminished muscular strength or development, impaired recovery, and suboptimal creatine efficiency. As sunlight is the basic natural source of vitamin D, persons with limited exposure to sun light may require supplementation of vitamin D to maximize the benefits of creatine monohydrate (54, 55, 56, 57, 58, 59).

Misconceptions about Creatine Monohydrate

CM is a safe and effective supplement with extensive scientific backing but despite its well-documented benefits, several misconceptions still persist related to creatine monohydrate Understanding the facts and relying on evidence-based research can help one to make informed decisions regarding creatine supplementation. The scientific literature based on evidences answer of the of misconceptions are as following given in table.

Table 4: Common Misconceptions and Solutions (2, 19, 22, 59, 60, 61, 62, 63)

Misconception	Explanation	Solution
Creatine causes kidney damage	Studies and controlled experiments show that creatine, when taken at the suggested doses, have no harmful effect on renal system of healthy individuals if taken in appropriate dosage	Those with renal disease are advised to consult a before starting CM.
Creatine leads to dehydration and cramps	Some believe creatine increases water retention, leading to dehydration and muscle cramps. However, research indicates creatine may enhance cellular hydration and reduce the risk of cramps.	Staying adequately hydrated while using creatine ensures optimal performance and lowers any potential risk.
Creatine causes excessive weight	Creatine may cause a slight increase in water weight due to enhanced intracellular hydration, but it does	Weight gain from creatine is primarily from water retention

gain	not lead to fat gain.	and lean muscle mass but not fat.
Creatine is only for bodybuilders	While bodybuilders and weight lifters benefit from creatine, research shows its benefits extend to endurance athletes, older adults, and cognitive function also.	Creatine is beneficial not only for bodybuilders and weight lifters but also for athletes, vegetarians, and those looking to improve brain function.
Loading phase is mandatory	The common belief is that creatine must be loaded (20g/day for 5-7 days) before transitioning to a maintenance dose. However, this is unnecessary for long-term benefits.	A dose of 3-5g per day is sufficient to reach full muscle saturation over a few weeks.
Creatine is a steroid	Creatine is often mistakenly classified as a steroid due to its performance-enhancing effects, but it is a compound that naturally exists in certain foods.	Educating users that creatine is an amino acid-derived compound and not a hormone or steroid can dispel this myth.
Creatine lead to hair loss or baldness	Current evidence from the literature does not suggest that creatine boosts total testosterone, free testosterone, DHT levels, or leads to hair loss or baldness.	A review of scientific studies shows no evidence linking CM to hair loss or baldness. One should look for other factors of also in case of hair loss also.
Creatine is effective only for males	Growing evidence suggests that creatine supplementation could serve as a multifaceted therapeutic approach for women throughout their lifespan, with minimal to no adverse effects.	Women can benefit from creatine for muscle strength, cognitive function, and overall health, particularly during aging and pregnancy.

Other health benefits:

Creatine supplementation has been reported various studies to offer several health benefits, including lowering cholesterol and triglyceride levels, supporting healthy blood lipid profiles, and reducing fat buildup in the liver. It may also help lower homocysteine levels, thereby decreasing the risk of cardiovascular disease. It also acts as an antioxidant, aids in blood sugar regulation, and may slow the progression of certain cancers. Studies have also linked creatine intake to increased muscle strength and mass, reduced bone loss, and improved physical function in individuals with osteoarthritis or fibromyalgia. It may boost cognitive performance, especially in older adults, and in some cases, enhance the effects of antidepressant treatments. These findings support contentions that it is prudent for individuals to consume at least 3 g/day of creatine to support general health as one ages. It may also support mental health, reproductive health as well as skin health of a person (64). It had also been reported increase brain PCr content by 5–15% and thereby enhance brain bioenergetics (65)

CONCLUSION

CM remains one of the best studied and effective dietary supplements in the realm of sports nutrition with strong scientific evidences that creatine supplementation is an effective ergogenic nutrient for athletes as well as individuals starting a health and fitness program. Its benefits in enhancing strength, power output, muscle mass, and recovery has been consistently supported by scientific literature. Moreover, its safety profile, affordability, and accessibility make it a staple for athletes and fitness enthusiasts alike. While misconceptions about creatine, ranging from kidney damage to dehydration still persist, current evidence strongly disproves these claims when the supplement is used responsibly. Understanding the basics of creatine, how to properly incorporate it into a routine, and distinguishing myths from facts empowers one to make informed decisions. As research continues to evolve, creatine’s potential roles beyond performance, such as in cognitive health and disease prevention, thus creates a gap for researcher further exploration.

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