REVIEW ARTICLE

Physical effects of α-methyl guanidine acetic-acid consumption: A systematic review

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ABSTRACT

Creatine, a natural compound extensively studied in exercise physiology and sports medicine, has proven to be effective in enhancing physical performance, especially in high-intensity and short-duration activities. Its supplementation promotes increased muscle strength, power, and accelerates post-exercise recovery. This review aims to analyse the most recent scientific advances regarding the use of creatine in sports, analysing its ergogenic efficacy and exploring its potential to optimize performance and muscle adaptation across many athletic disciplines. A systematic review was conducted on the benefits of creatine in physical performance, using Scopus and Web of Science databases due to their academic rigor and prestige. Starting with 1,696 publications, strict exclusion filters were applied: removal of duplicates, selection of studies from the past five years, filtering by language (English and Spanish), and document type. Ultimately, 9 relevant studies were retained, selected for their quality and ranking in the top quartile of the SJR index. These studies form the final corpus for analysis in this review. Creatine supplementation enhances high-intensity performance by improving ATP regeneration, strength, and endurance. It increases muscle power during fatigue, as observed in young athletes, and boosts performance in resistance exercises like bench press by increasing repetitions and total work. Creatine also reduces fatigue and improves recovery between sets. Additionally, it positively affects body composition and VO2 max, demonstrating its effectiveness in both strength and endurance sports. Creatine supplementation consistently enhances physical performance in high-intensity activities by accelerating ATP regeneration and reducing fatigue. It also increases muscular endurance, aerobic capacity, and muscle mass. These findings position creatine as a safe and effective ergogenic aid, supporting its use to optimize both performance and recovery across various athletic contexts.
Keywords: Creatine supplementation, Physical performance, High-intensity activities, Muscle strength.

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INTRODUCTION

Creatine, also known chemically as N-methyl guanidine acetic acid, has been extensively studied in the fields of biochemistry, exercise physiology, and sports medicine. Although it is a natural compound in the body, its significance goes beyond simply being an energy source. It is primarily known for enhancing physical performance, especially in high-intensity, short-duration activities. Its use has gained popularity among athletes and fitness enthusiasts due to its ergogenic effects, which translate into increased muscle strength, power, and post-exercise recovery (Wax et al., 2021). This compound mainly works by increasing the availability of phosphocreatine in the muscles, enabling faster production of ATP, the primary energy source during anaerobic exercise (Tarnopolsky, 2010; Poli et al., 2019).

Recent research indicates that creatine not only increases maximal strength but also improves muscular endurance, even in the absence of direct changes in maximal strength (Furtado, 2024; Mills et al., 2020). Furthermore, creatine has been observed to mitigate neuromuscular fatigue, allowing athletes to maintain optimal performance during prolonged periods of exercise (Abdalla et al., 2022). The effectiveness of creatine also depends on the timing of its administration. Studies suggest that post-workout consumption may be more beneficial than pre-workout, as it maximizes muscle absorption and utilization (António & Ciccone, 2013); however, these studies are still under debate. It is important to understand that the response to creatine supplementation varies according to individual factors such as diet, training type, and genetics (Vieira et al., 2020). Collectively, research has shown that creatine can significantly improve maximal strength and muscular endurance, especially in high-intensity, short-duration activities (Mielgo-Ayuso et al., 2019), and that a post-workout consumption strategy seems to optimize these benefits, reinforcing the previously mentioned idea. Given the aforementioned, it is necessary to conduct a thorough analysis to confirm the conclusions drawn about this compound.

A recent review of studies helps address and clarify common myths and misunderstandings about creatine, such as its safety and efficacy in different usage contexts (António et al., 2021; Macêdo & Silva, 2023). With the growing interest in nutritional supplementation, it is essential to provide evidence-based information that helps consumers and stakeholders make informed decisions regarding the use of this compound. Conducting an updated review on physical performance when consuming creatine, particularly from a sports perspective, is crucial due to the growing body of scientific evidence supporting its ergogenic effects and its application across various athletic disciplines. Over the past five years, research has advanced significantly, providing new insights into how creatine can optimize physical performance, enhance recovery, and contribute to muscle adaptation in different types of athletes under various modalities (Mielgo-Ayuso et al., 2019; Solis et al., 2021; Stares & Bains, 2020).

METHODS

The project included a systematic review of a variety of studies published to date, focusing on the scientifically evidenced benefits of creatine (α-methyl guanidino-acetic acid) consumption in relation to physical performance. For data collection, the two most recognized scientific databases, Scopus and Web Of Science, were used due to the rigor of their academic indexing and the inclusion of high impact journals, which makes them highly prestigious databases. In both cases, the following search commands were applied: in Scopus, "*creatine*" OR "*N-methyl guanidine acetic acid*" AND "*performance*" AND "*effects*" AND "*physical*," which resulted in 1,246 publications; and in Web of Science, ("*creatine*" OR "*N-methyl guanidine acetic acid*") AND "*performance*" AND "*effects*" AND "*physical*," with a total of 450 publications.

For this review, a total of 1,696 publications were initially identified. During the filtering process, strict exclusion criteria were applied to ensure the relevance and quality of the final content. First, 241 duplicate publications were removed. Next, 860 publications older than five years were discarded, as the nature of this review seeks to provide a scientific update on results, hence the five-year filter. A language filter was also applied, retaining only publications in English and Spanish, leading to the exclusion of an additional 15 documents. Finally, the document type was limited to academic articles, resulting in the elimination of 127 publications.

As a result of these filters, 453 publications remained, which were subjected to a detailed analysis of their abstracts, keywords, themes, and areas of research, leading to the exclusion of an additional 436 publications. Ultimately, 17 publications were considered relevant in terms of thematic focus, relevance, and objective results. From this group, and applying a strict criterion based on the quality of the journal and its ranking in the top quartile of the Scimago SJR index, 9 publications were selected to constitute the final corpus for this review.

Figure 1 shows the PRISMA flowchart that summarizes the study selection process. From an initial search of 1,696 publications, exclusion filters reduced the number of studies to 9 selected for this review. The diagram provides a clear visual representation of the systematic approach followed to ensure the quality and relevance of the included articles.

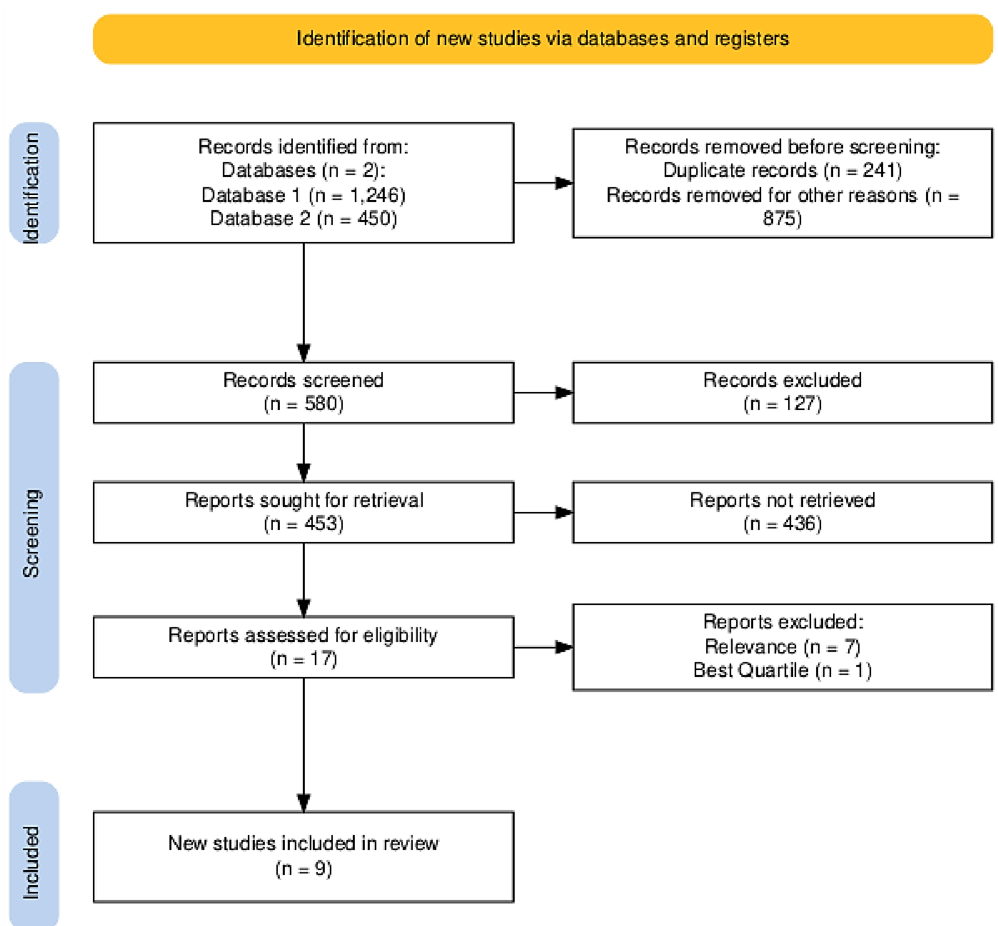

Figure 1. PRISMA flowchart - Inclusion research.

Table 1. Summary of the key reviewed studies.

Authors	Titles	Source/Scimago Best Quartile	Year	Dose	Performance
Ojeda, AH; Jofré-Saldía, E; Torres-Banduc, M; Maliqueo, SG; Barahona-Fuentes, G; Acevedo, CC; Romero, GL; Garduño, RD; Vera, GR; Paredes, PV; Avalos, BB; Serey, TM; Yeomans-Cabrera, MM and Jorquera-Aguilera, C	"Effects of a Low Dose of Orally Administered Creatine Monohydrate on Post-Fatigue Muscle Power in Young Soccer Players".	"Nutrients"/Q1	2024	The creatine (Cr) dose was 0.3 g per kilogram of body weight per day, dissolved in 200 mL of water, and taken between 18:00 and 20:00 h for 14 days. Participants were instructed to consume it with a carbohydrate-rich meal to optimize absorption.	Creatine supplementation, at a dose of 0.3 $g \cdot kg^{-1} \cdot day^{-1}$ for 14 days, significantly improved muscle power, particularly under conditions of acute intra-session fatigue, by enhancing the ability to maintain and generate strength and power. This effect was driven by increased intramuscular phosphocreatine saturation, which enabled faster ATP regeneration, leading to improved overall physical performance in young soccer players.
Maicas-Pérez, L; Hernández-Lougedo, J; Heredia-Elvar, JR; Pedauyé-Rueda, B; Cañuelo-Márquez, AM; Barba-Ruiz, M; Lozano-Estevan, MD; Garcia-Fernández, P and Maté-Muñoz, JL	"Effects of Creatine Supplementation after 20 Minutes of Recovery in a Bench Press Exercise Protocol in Moderately Physically Trained Men".	"Nutrients"/Q1	2023	The doses used were 0.3 $g \cdot kg^{-1} \cdot day^{-1}$ of creatine monohydrate for the creatine group and 0.3 $g \cdot kg^{-1} \cdot day^{-1}$ of placebo (maltodextrin) for the placebo group.	The creatine (CR) group showed a significant increase in repetitions during Sets 1 (14.8 vs. 13.6) and 2 (8 vs. 6.7) compared to the placebo (PLA) group, with no difference in Set 3. Blood lactate levels increased significantly at 10, 15, and 20 minutes post-exercise in the CR group. Additionally, mean propulsive velocity (MPV) was higher in the CR group at these points. Overall, creatine supplementation improved strength performance but resulted in greater metabolic stress and muscle fatigue during recovery.
Furtado, ETF; De Oliveira, JPL; Pereira, ISB; Veiga, EP; Da Silva, SF and De Abreu, WC	"Short term creatine loading improves strength endurance even without changing maximal strength, RPE, fatigue index, blood lactate, and mode state".	"Anais da Academia Brasileira de Ciencias"/Q2	2024	The dosing protocol for the creatine group involved a loading phase for five days, with participants receiving a total of 100 grams of micronized creatine monohydrate (20 grams per serving, spread across five pots). Additionally, they consumed 10 grams of dextrose per serving. Participants were instructed to take four servings of 7.5 grams each per day, diluted in about 400 mL of water after meals.	Creatine supplementation (20 g/day for five days) significantly improved performance in resistance exercises, specifically in the bench press. There was a 14.7% increase in the total number of repetitions and an 11.1% increase in total work compared to the placebo group, which only showed marginal increases of 1.2% and 1.4%, respectively. Creatine enhanced the ability to perform more repetitions and total work, suggesting it may increase endurance and training capacity in the bench press. Creatine also appears to contribute to better phosphocreatine regeneration and improved energy supply during exercise. Overall, the benefits of creatine include an increase in strength endurance and total work during resistance training, which could facilitate muscle mass gain.
Almeida, D; Pereira, R; Borges, EQ; Rawson, ES; Rocha, LS and Machado, M	"Creatine Supplementation Improves Physical Performance, Without Negative Effects on Health Markers, in Young Weightlifters".	"Journal of Science in Sport and Exercise"/Q2	2022	The doses used for creatine in this study involved two phases: a loading phase and a maintenance phase. Participants in the creatine group received 0.3 g/kg of body mass for 7 days (loading phase), followed by a maintenance dose of 0.03 g/kg for 21 days.	Creatine supplementation significantly improved physical performance in the creatine group compared to the placebo group. Specifically, there were notable increases in body weight and one-repetition maximum (1RM) across all evaluated exercises. Additionally, while some blood and urine health markers showed differences between groups, these variations were small and remained within clinical reference ranges. Overall, the results suggest that the dosing scheme used for creatine, in conjunction with resistance training, enhances physical performance without evident health risks for young weightlifters.
Tayebi, MM; Yousefpour, M and Ghahari, L	"Effects of creatine hydrochloride supplementation on physical performance and hormonal changes in soldiers".	"Physical Activity Review" /Q3	2021	The dose for the Cr group consisted of consuming 3 g of CrHCl mixed with 200 ml of juice, once a day, for 2 weeks. The Pl group (placebo group) consumed 3 g of dextrose in the same manner. Both supplements were premixed and distributed in resealable bags with instructions for consumption. Participants were instructed to follow the dosage without making any changes in their diet or daily activity.	Creatine hydrochloride (CrHCl) supplementation led to significant improvements in vertical jump, power performance and one-repetition maximum (1RM) in the back squat. However, CrHCl loading was not sufficient to improve 1RM in the bench press or fatigue index (FI). In addition, after 2 weeks of CrHCl supplementation, there were significant changes in testosterone and cortisol levels compared to the placebo group. The study recommends that military soldiers use CrHCl supplementation for 2 weeks to improve strength, power performance, and hormonal variables.

Authors	Titles	Source/Scimago Best Quartile	Year	Dose	Performance
Samadi, M; Askarian, A; Shirvani, H; Shamsoddini, A; Shakibaee, A; Forbes, SC and Kaviani, M	"Effects of Four Weeks of Beta-Alanine Supplementation Combined with One Week of Creatine Loading on Physical and Cognitive Performance in Military Personnel.	"International Journal of Environmental Research and Public Health"/Q2	2022	Participants were randomly assigned in two groups and instructed to take 6.4 g of beta-alanine (BA) daily for four weeks, divided into 8 capsules (3 with breakfast, 3 with lunch, and 2 with dinner). In the final week, the BA + Cr group added creatine monohydrate (Cr) at a dose of 0.3 g per kg of body weight per day, which was split into 3 portions and consumed with meals, while the BA + PL group received an isocaloric placebo of rice flour.	Mixing one week of creatine loading with four weeks of beta-alanine supplementation significantly improved vertical jump performance (indicating enhanced leg power) and increased resting testosterone levels compared to beta-alanine alone. Furthermore, the combination led to greater physical and cognitive performance improvements within the group that received both supplements. These results suggest that creatine supplementation can effectively enhance hormonal levels and physical performance, which is beneficial for military personnel facing high physical and cognitive demands.
Bernat, P; Candow, DG; Gryzb, K; Butchart, S; Schoenfeld, BJ and Bruno, P	"Effects of high-velocity resistance training and creatine supplementation in untrained healthy aging males".	"Applied Physiology, Nutrition and Metabolism"/Q1	2019	Participants supplemented with 0.1 g of creatine per kilogram of body weight per day, mixed with 0.1 g of maltodextrin per kilogram per day, while the placebo group received 0.2 g of maltodextrin per kilogram per day.	The study found significant improvements in muscle thickness, muscle strength, and some measures of peak torque and physical performance in untrained healthy aging males who participated in high-velocity resistance training (HVRT) for 8 weeks. Specifically, all measures of muscle strength showed a significant increase ($p < 0.001$), as did muscle thickness ($p < 0.001$). Some peak torque measures, such as knee flexion at 1.05 and 3.14 rad/s, also increased significantly ($p < 0.001$). Notably, there was a group × time interaction for leg press strength ($p = 0.044$) and total lower-body strength ($p = 0.039$), indicating that the creatine group experienced greater gains in leg press and total lower-body strength compared to the placebo group. Overall, HVRT combined with creatine supplementation led to enhanced strength outcomes in the participants.
Mills S.; Candow D.G.; Forbes S.C.; Neary J.P.; Ormsbee M.J. and Antonio J.	"Effects of creatine supplementation during resistance training sessions in physically active young adults".	"Nutrients"/Q1	2020	The dosage of creatine used was $0.1\ g \cdot kg^{-1} \cdot d^{-1}$. The creatine (Creapure® AlzChem) and the placebo (Globe® Plus 10 DE maltodextrin) were in powder form, similar in taste, color (white), texture, and appearance. Participants consumed the creatine mixed with water (900 mL), taking 50 mL of the solution containing $0.0055\ g \cdot kg^{-1}$ of creatine or placebo immediately after each set of resistance training (18 sets per training day).	Improved muscle strength and endurance, with significant increases observed in leg press strength (Δ 43 ± 32 kg) and chest press strength (Δ 13 ± 11 kg). Males showed enhanced chest press strength over time, while the supplementation was well-tolerated with minimal adverse effects reported. Additionally, creatine reduced the fatigue index after 7 days of use, indicating better resistance to fatigue during workouts. These results highlight creatine's effectiveness in enhancing strength among physically active individuals. Additionally, creatine supplementation is associated with elevated intramuscular phosphocreatine (PCr) levels, which may facilitate faster ATP resynthesis and recovery between sets, contributing to enhanced endurance and overall performance over time.
Bogdanis G.C.; Nevill M.E.; Aphamis G.; Stavrinou P.S.; Jenkins D.G.; Giannaki C.D.; Lakomy H.K.A. and Williams C.	"Effects of Oral Creatine Supplementation on Power Output during Repeated Treadmill Sprinting".	"Nutrients"/Q1	2022	The dosage for creatine (Cr) supplementation was set at 75 mg of Cr monohydrate per kilogram of body mass per day. This dosing regimen was applied after an initial 5-day period of placebo supplementation, during which participants received 75 mg of glucose per kilogram of body mass per day.	Cr supplementation significantly improved sprint endurance and total work output during repeated 10-second sprints, as evidenced by increased mean power output (MPO) and running speed in the latter part of the exercise session. Importantly, while aerobic contributions to energy supply, indicated by VO2 levels, remained unchanged, Cr supplementation led to a notable 20.1% reduction in plasma ammonia levels post-exercise. This reduction suggests enhanced ATP turnover and less metabolic stress, likely due to an increased reliance on phosphocreatine (PCr) for energy production. Overall, the study highlights that creatine not only boosts performance in weight-bearing activities but also facilitates faster recovery during repeated sprints by optimizing energy availability and reducing metabolic byproducts associated with fatigue.

Note. The information in this table has been collected and synthesized from the key findings of nine scientific articles. It is used solely for the purpose of conducting a literature review, respecting copyright and properly acknowledging the original sources. This synthesis is not intended to plagiarize, but to contribute to scientific knowledge through comparative analysis and discussion.

RESULTS

Table 1 summarizes the key reviewed studies, providing an overview of the creatine doses used and the observed effects on physical performance. Through this table, the most relevant conclusions from each investigation are highlighted, facilitating a direct comparison between different approaches and obtained results.

DISCUSSION

Creatine supplementation has been the subject of numerous studies evaluating its impact on physical performance, especially in high-intensity activities. The results shown in the "*performance*" column of the document consistently demonstrate that creatine administration, across various doses and protocols, generates significant improvements in subjects' ability to perform strength and endurance exercises. These findings are mainly related to the role of phosphocreatine in the rapid regeneration of ATP, the primary energy source for muscle contraction during high-demand exercises.

One of the main benefits observed is creatine's ability to improve performance under fatigue conditions. In young soccer players, 14 days of supplementation at a dose of 0.3 g/kg/day resulted in a significant increase in muscle power, allowing participants to maintain their ability to generate force despite intra-session fatigue. This outcome is attributable to higher phosphocreatine saturation in the muscles, which facilitates faster ATP regeneration and, consequently, better response in repetitive high-intensity activities.

Furthermore, in resistance exercises such as bench presses, creatine supplementation not only increased muscle strength, but also allowed for a greater number of repetitions and an increase in total work performed. In one specific study, participants supplemented with creatine showed a 14.7% increase in the number of repetitions and 11.1% increase in total work performed compared to a placebo group. This finding highlights the role of creatine not only in improving maximal strength, but also in maintaining repetitive efforts, which is crucial in sports and training that require multiple high intensity sets.

Creatine has also been shown to be effective in improving recovery parameters between sets, significantly decreasing fatigue levels. For example, in repeated treadmill sprints, creatine supplementation improved both endurance and recovery speed between efforts. This effect was observed along with a 20.1% reduction in plasma ammonia levels, suggesting a reduced accumulation of metabolic by products associated with fatigue, thus improving energy regeneration capacity.

At last, it is important to emphasize that creatine supplementation not only affects strength and endurance, but also positively influences body composition and VO2 max, as was observed in youth wrestlers. Combining strength training with creatine supplementation resulted in significant increases in muscle mass and VO2 max, indicating improvements in aerobic capacity. These results highlight the versatility of creatine as a supplement for both strength and endurance sports.

CONCLUSION

The studies analysed showed that creatine supplementation has positive and consistent effects on physical performance, especially in high-intensity and repetitive activities. The underlying mechanisms of these benefits are related to the increase in intramuscular phosphocreatine saturation, allowing a faster regeneration of ATP, which facilitates a better muscular response in exercises involving fast and explosive movements. In addition, creatine has shown a significant ability to reduce metabolic fatigue levels, improve muscular endurance and accelerate recovery between complex sets, which is essential in sports and training that require high energy expenditure. The benefits of creatine are not limited to anaerobic performance but also extend to improvements in aerobic capacity and body composition, with observed increases in VO2 max and muscle mass. These metabolic and physiological adaptations position creatine as a key ergogenic supplement, not only for high-performance athletes, but also for more general populations seeking to optimize their physical capacity in endurance and strength exercises. Current evidence strongly supports the use of creatine as an effective and safe agent for enhancing both performance and recovery in a variety of athletic contexts.

AUTHOR CONTRIBUTIONS

Conceptualization, Zevallos-Aquije, Axel.; methodology, Zevallos-Aquije, Anneliese and Zevallos-Aquije, Axel; software, Zevallos-Aquije, Axel; validation, Salas-Bolaños, Rosa Alejandra; formal analysis, Maravi-Cardenas, Alvaro Jose; investigation, Zevallos-Aquije, Axel; resources, Zevallos-Aquije, Axel; data curation, Palomino-Salcedo, Karen; writing—original draft preparation, Zevallos-Aquije, Anneliese; writing—review and editing, Salas-Bolaños, Rosa Alejandra; visualization, Maravi-Cardenas, Alvaro Jose; supervision, Salas-Bolaños, Rosa Alejandra; project administration, Palomino-Salcedo, Karen. All authors have read and agreed to the published version of the manuscript.

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