CREATINE SUPPLEMENTATION ENHANCES THE PROTECTIVE EFFECT OF THE LOAD AND REDUCES MUSCLE DAMAGE IN STRENGTH TRAINING PRACTITIONERS

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ABSTRACT

Creatine supplementation (Cr) has been widely used by athletes and practitioners of resistance exercises to improve physical performance and muscle recovery. Despite this, not all of its effects are completely known, especially in the context of the protective effect of cargo (EPC). This study investigated whether Cr supplementation can enhance CPE and reduce markers of muscle damage in 20 healthy men who had been practicing bodybuilding for more than six months (age: 26 ± 7 years; body mass: 81.3 ± 9.2 kg; height: 177 ± 0.07 cm). Participants were randomly divided into two groups: creatine supplementation (CRE) and placebo (PLA). The CRE group received 20 g of creatine monohydrate per day (4 doses of 5 g), while the PLA group received maltodextrin at the same dosage. The experimental protocol was conducted over 25 days and included strength tests (1RM in the bicep curl exercise on the Scott bench), blood collection for creatine kinase (CK) analysis, and evaluation of delayed muscle soreness (DOM) perception. The results showed that Cr supplementation significantly reduced the perception of pain after the first and second exercise sessions, in addition to promoting a more attenuated response of CK levels compared to the PLA group. The CRE group also showed a significant increase in total body mass (TCM), which was not observed in the PLA group. These findings indicate that Cr supplementation can potentiate EPC, reducing exercise-induced muscle damage and aiding in the continuity of strength training programs. Future studies are needed to investigate the mechanisms associated with these effects.

Keywords: Creatine. Strength training. Protective effect of the load. Muscle recovery. Creatine kinase.

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INTRODUCTION

Creatine supplementation has gained increasing prominence in the field of sports and physical activity, consolidating itself as one of the most used and researched supplements (MAUGHAN *et al*., 2018; DO NASCIMENTO *et al*., 2020). Its popularity extends from high-performance athletes to regular practitioners of physical exercise, all seeking to improve their performance (KREIDER *et al*., 2017; IWATA, 2019). Creatine (Cr), chemically known as α-methyl guanidine acetic acid, is a nitrogenous compound that can be obtained through the diet or synthesized endogenously from the amino acids glycine, methionine, and arginine (CANDOW *et al*., 2019).

Endogenous creatine synthesis occurs mainly in the kidneys, liver, and pancreas, with a lower production in the brain (KREIDER *et al*., 2017). Its primary function is related to the rapid supply of energy during muscle contraction, through phosphorylcreatine (CrP), in a reaction catalyzed by the enzyme creatine kinase (CK) (GUALANO *et al*., 2019; ROSCHEL *et al*., 2021). This process is essential for the immediate resynthesis of ATP, especially in high-intensity and short-duration exercises (KREIDER *et al*., 2017).

Recent studies such as de Miranda *et al*. (2025) have broadened our understanding of creatine's mechanisms of action. In addition to its energetic role, Cr supplementation has shown potential to increase muscle hydration, modulate gene expression, reduce oxidative stress, and improve post-exercise recovery (CANDOW *et al*., 2019; GUALANO *et al*., 2019; ROSCHEL *et al*., 2021). These multifaceted effects contribute to its effectiveness not only in sports performance but also in therapeutic contexts (KREIDER *et al*., 2017; MIRANDA *et al*., 2025).

The ATP-CP system, in which creatine plays a central role, is crucial for high-intensity activities. Hydrolysis of CrP releases the energy needed to phosphorylate adenosine diphosphate (ADP), generating ATP (GUALANO *et al*., 2019; ROSCHEL *et al*., 2021). This process not only provides energy quickly but also contributes to the regulation of intracellular pH, potentially delaying muscle fatigue (KREIDER *et al*., 2017; SILVA; ALMEIDA and FACCIN, 2022).

An interesting phenomenon associated with strength training is the load protective effect (EPC). This phenomenon is characterized by a muscle adaptation that reduces damage in subsequent exercises of the same nature (HYLDAHL *et al*., 2017). Delayed-onset muscle soreness (DOMS), often experienced after intense or unusual exercise, especially those with a significant eccentric component, is an indirect indicator of muscle damage (PEAKE *et al*., 2017).

Recent research has suggested a possible interaction between creatine supplementation and EPC. Studies indicate that Cr can potentiate this protective effect, possibly through mechanisms involving cell membrane stabilization, increased buffering capacity, and reduced oxidative stress (VEGGI *et al*., 2013; GUALANO *et al*., 2019; ROSCHEL *et al*., 2021).

Serum creatine kinase (CK) has been widely used as an indirect marker of muscle damage. Its elevation after intense exercise, especially those with a significant eccentric component, may persist for several days (AOKI, 2004; PEAKE *et al*., 2017). However, the interpretation of CK levels should be cautious, considering individual factors and the type of exercise performed (BAECHLE *et al*., 2000; ROSCHEL *et al*., 2021).

Despite the extensive body of research on creatine, there are still controversies regarding its effects on the integrity of muscle macrostructure and its interaction with EPC. This knowledge gap justifies the need for further investigations, especially considering the potential benefits for athletes and physical exercisers (GUALANO *et al*., 2019; ROSCHEL *et al*., 2021; MIRANDA *et al*., 2025).

In this context, the present study seeks to investigate whether creatine supplementation can modulate serum concentrations of Creatine Kinase (CK) in men who practice strength training, evaluating its influence on the protective effect of the load. We hypothesize that Cr supplementation may accentuate EPC, offering additional protection against exercise-induced muscle damage.

This research not only contributes to the advancement of scientific knowledge in the area of sports nutrition and exercise physiology, but also has significant practical implications for athletes, exercisers, and healthcare professionals involved in prescribing supplements and strength training programs.

METHODOLOGY

SAMPLE

The study included the participation of 20 physically active male volunteers, with a mean age of 26 ± 7 years, body mass of 81.3 ± 9.2 kg, and height of 177 ± 0.07 cm. The inclusion criteria were: weight training for at least six months, with a minimum frequency of three times a week, eutrophic nutritional status, and non-use of nutritional supplements or drugs. Participants were instructed not to participate in other training programs during the study period.

All volunteers were informed in detail about the objectives and procedures of the study and signed an informed consent form. The study was approved by the institution's

ethics committee (CAAE number 39730114.0.0000.5254), following the guidelines of Resolution 466/2012 of the National Health Council (BRASIL, 2012).

EXPERIMENTAL DESIGN

The study was conducted in a double-blind, randomized, placebo-controlled design. Participants were randomly divided into two groups: creatine supplementation (CRE, n=10) and placebo (PLA, n=10). The CRE group received creatine monohydrate, while the PLA group received maltodextrin, both at a dosage of 20 grams daily, divided into four doses of 5 grams (KREIDER *et al*., 2017).

TRAINING AND EVALUATION PROTOCOL

The experimental protocol was conducted over 25 days, as shown in the following table I:

Table 1. Experimental protocol

Day	Activity
1	Performing the 1RM test (one repetition maximum) on the bicep curl exercise on the Scott bench.
2 to 3	Rest
4	Retest of the 1RM to confirm the values obtained.
5 to 9	Rest period
10 to 14	Beginning of the supplementation protocol
15	Blood collection, evaluation of pain perception, exercise session consisting of four sets until failure in the biceps curl exercise on the Scott bench with a load corresponding to 75% of 1RM, followed by a new evaluation of pain perception
16 to 18	Blood draws and daily assessments of pain perception.
19 to 21	Continuation of supplementation
22	Blood collection, evaluation of pain perception, exercise session consisting of four sets until failure in the biceps curl exercise on the Scott bench with a load corresponding to 75% of 1RM, followed by a new evaluation of pain perception
23 to 25	Blood draws and daily assessments of pain perception.

The 1RM test was performed according to the protocol of estimated maximum repetitions, described by Dohoney (2002). The participants performed up to 10 repetitions maximums with a previously estimated load, and the 1RM values were calculated using specific software for this purpose.

BLOOD SAMPLE COLLECTION AND ANALYSIS

Samples of approximately 5 ml of venous blood were collected from the forearm of each participant by a qualified professional, following biosafety standards. The blood was centrifuged to separate the serum, which was used to measure the enzyme Creatine Kinase (CK). CK analysis was performed by spectrophotometric method, using a Bio Plus

- Bio 200F spectrophotometer (Brazil) and LabTest kit (Brazil), with a reading at 340 nm wavelength (BRANCACCIO et al., 2010).

ASSESSMENT OF PAIN PERCEPTION

The subjective perception of muscle pain was assessed using a visual analog scale (VAS) of 0-10, where 0 represents "no pain" and 10 represents "maximum pain" (CLARKSON and HUBAL, 2002).

STATISTICAL ANALYSIS

Data were analyzed using SPSS software (version 25.0, IBM, USA). The normality of the data was verified by the Shapiro-Wilk test. To compare the variables between the groups and over time, repeated measures analysis of variance (ANOVA) was used. Tukey's post-hoc was applied to identify specific differences. The level of significance was set at $p<0.05$. In addition, the effect size was calculated using Cohen's d, interpreted as small (0.2-0.5), medium (0.5-0.8) or large (>0.8) (COHEN, 1988).

RESULTS

CHARACTERISTICS OF THE SUBJECTS

Table 2 presents the characteristics of the subjects in the creatine (CRE) and placebo (PLA) groups. No significant differences were observed between the groups for age, total body mass (MCT), height, and maximum strength (1RM) indicating sample homogeneity.

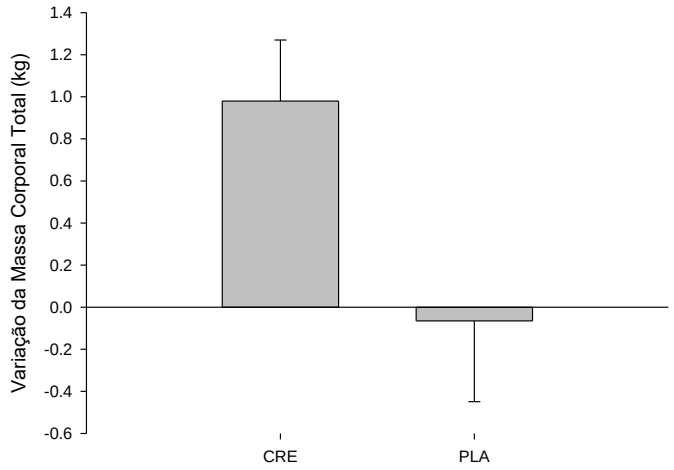
Table 2. Subject characteristics (mean ± standard deviation)

Variables	CRE Group	PLA Group	P
	Mean ± Standard Deviation	Mean ± Standard Deviation	P-value
Age	27.7 ± 1.6	27.6 ± 1.6	0,86
MCT	81.0 ± 8.1	74.6 ± 10.3	0,46
Stature	178 ± 8	176 ± 9	0,14
1 RM	50.2 ± 8.0	45.2 ± 4.3	0,10

CHANGE IN TOTAL BODY MASS

The analysis of the variation in total body mass (MCT) revealed a significant increase of approximately 1 kg in the CRE group throughout the study, while the PLA group did not show significant changes ($p<0.05$) (Graph 1).

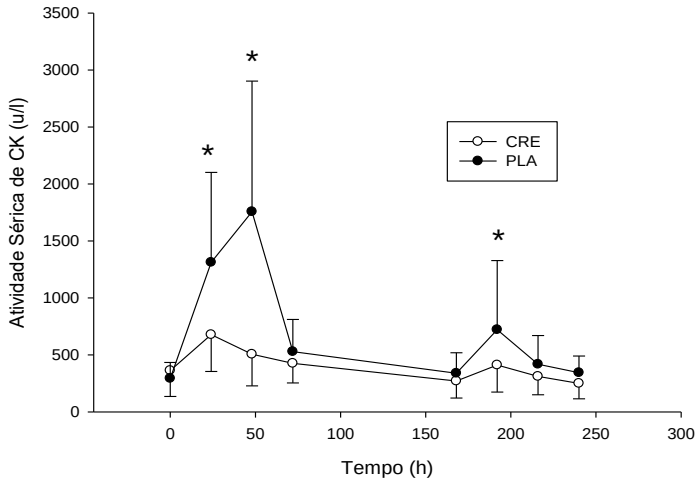
Graph 1. Change in total body mass (Kg)



SERUM CREATINE KINASE (CK) ACTIVITY

Graph 2 illustrates the variation in serum CK activity after exercise in the CRE and PLA groups during the two weeks of testing. It was observed that:

Graph 2. Variation in serum CK activity



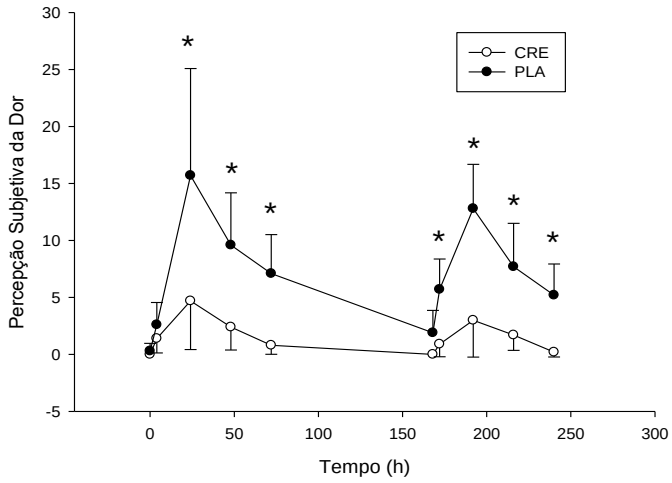
The PLA group showed an increase in CK concentration in both weeks, peaking at 48 hours in the first week and at 24 hours in the second week, with the increase in the second week being less pronounced.

The CRE group also showed an increase in CK concentration in both weeks, but to a lesser extent compared to the PLA group. The peak of CK in the CRE group occurred consistently at 24h post-exercise.

SUBJECTIVE PERCEPTION OF PAIN

Graph 3 shows the variation in the subjective perception of pain in the biceps brachii during elbow extension.

Graph 3. Variation in subjective pain perception



Based on the results, we can observe that the PLA group had higher pain levels in the first week compared to the second week, peaking at 24 hours after the test.

When analyzing the CRE group, we observed that it demonstrated lower pain levels in the first week compared to the PLA group. Where the peak of pain also occurred at 24 hours post-test.

In the second week, pain values were lower than those in the first week for both groups, with the CRE group showing no significant increases.

Thus, these results suggest that creatine supplementation may have positively influenced both the serum CK response and the perception of muscle pain, indicating a possible protective effect against exercise-induced muscle damage and potentiation of the load-protective effect (CPE).

DISCUSSION

The main finding of this study was that creatine supplementation significantly reduced delayed onset muscle soreness (DOMS) after both the first and second exercise sessions. This effect was accompanied by additional protection against increased creatine kinase (CK) levels, especially in the creatine-supplemented group (CRE) when compared to the placebo group (PLA). In addition, a significant increase in total body mass (MCT) was observed in the CRE group, a result not identified in the PLA group. These findings

reinforce the potential role of creatine in mitigating markers of muscle damage and improving muscle adaptation during exercise.

Similar results were reported by Veggi *et al*. (2013), who also observed a reduction in CK levels in participants supplemented with creatine after exercise sessions involving the biceps muscle. This pattern indicates that creatine supplementation can act as a protective agent, attenuating the effects of intense exercise on muscle integrity.

In the present study, CK levels increased significantly 48 hours after exercise in the PLA group, corroborating the findings of Queiroz *et al*. (2013), who reported a sustained increase in this enzyme in the two weeks of testing. The increase in CK in the blood is a classic indicator of muscle damage since this enzyme is present mainly inside muscle cells and is released into the bloodstream in response to muscle injuries (BARROSO *et al*., 2005; SILVA, 2007; BRANCACCIO *et al*., 2010; MIRANDA *et al*., 2025). In contrast, in the CRE group, CK concentrations did not show a significant increase in the two sessions, suggesting a protective effect of supplementation.

Comparing the results with previous studies, such as the one by Machado *et al*. (2007), some methodological differences may explain the divergences in reported CK levels. In the study by Machado (2007), the participants were sedentary and performed five different exercises in three sets of 10 repetitions at 85% of 1RM, while in the present study, the individuals were physically active and performed a single exercise in four maximum sets. The distinct characteristics of the samples and the protocols used may have influenced the results, making a direct comparison difficult.

Another relevant finding was the progressive reduction of CK concentrations in the second week of testing in both groups, but more markedly in the CRE group, evidencing the protective effect of the load (EPC). This phenomenon, described in the literature as the adaptive capacity of the muscle to minimize damage in subsequent exercise sessions, was also observed by Kamandulis *et al*. (2010), who reported a decrease in CK levels after repeated exercise sessions. Additional studies, such as those by Chen *et al*. (2007); Ferreira *et al*. (2012), and Miranda *et al*. (2025), reinforce this hypothesis, highlighting the importance of EPC in muscle recovery.

Regarding delayed onset muscle soreness, the present study demonstrated a significant reduction in pain perception in the second week in both groups, with the CRE group presenting consistently lower values. This may be related to the indirect anti-inflammatory effect of creatine since muscle damage induces inflammatory responses that are closely linked to the sensation of pain (SILVA, 2007; AZEVEDO *et al*., 2012). This pattern was similar to that observed by Queiroz *et al*. (2013), who reported persistent

muscle soreness up to 96 hours after exercise in protocols with higher training volume. However, the difference in pain assessment time (72 hours in this study versus 96 hours in the study by Queiroz *et al*. (2013) may explain part of the discrepancies found.

Another important effect of creatine supplementation was the increase in total body mass (MCT), with an average gain of 1 kg in the CRE group after the test weeks. This result corroborates the findings of Volek *et al*. (1997) and Warber *et al*. (2002), who reported increases in MCT of 1.4 kg after five days of supplementation with high doses of creatine. A similar study conducted by Izquierdo *et al*. (1998) observed an increase of 0.6 kg in MCT in individuals undergoing creatine supplementation. This increase in mass can be attributed, at least partially, to greater intramuscular water retention, as described by McBride and Gregory (2002), who highlighted the role of creatine in cellular osmoregulation and increased muscle volume.

Thus, the results of this study reinforce the efficacy of creatine supplementation not only in reducing markers of muscle damage and alleviating pain but also as a potential strategy to promote short-term body mass gains.

CONCLUSION

The results of this study confirm the hypothesis initially proposed, demonstrating that creatine supplementation exerts a significant protective effect against exercise-induced muscle damage. This effect was evidenced by the reduction in CK levels, the lower perception of delayed muscle soreness, and the consistent increase in total body mass in the supplemented group, especially in the second week of training. These findings reinforce the role of creatine as an effective strategy to mitigate markers of muscle injury and improve recovery by enhancing the protective effect of load (EPC).

In this way, creatine supplementation can be considered a useful tool for physical activity practitioners and athletes who want to maintain the continuity and quality of training, reducing the risk of muscle fatigue and facilitating recovery between consecutive sessions. However, future studies are needed to further explore the mechanisms that regulate this protective effect and investigate the long-term response in different populations and training protocols. The inclusion of additional inflammatory markers and histological analyses could enrich the understanding of these processes.

CONFLICT OF INTEREST STATEMENT AND FUNDING SOURCES

The authors declare that there is no conflict of interest of a personal, commercial, academic, political, or financial nature in this manuscript. This study did not receive specific funding from public, commercial, or non-profit sector funding agencies.

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