INTERNATIONAL SEVEN JOURNAL
OF MULTIDISCIPLINARY
ISSN: 2764-9547

The interaction of caffeine on creatine absorption

A interação da cafeína na absorção da creatina

DOI: 10.56238/isevmjv1n1-002
Receiving the originals: 02/01/2023
Acceptance for publication: 23/01/2023

Iara Rodrigues dos Santos
Nutrition undergraduate student at UMA University Center

Karine Amâncio dos Reis
Nutrition undergraduate student at UMA University Center

Rafaela de Jesus Santos Lucas
Nutrition undergraduate student at UMA University Center

Eunice da Silva Barros
Nutritionist and Professor at UNA Barreiro University Center; Master in Dental Clinics, PUC-MINAS; Institution: UNA Barreiro University Center
Address: Av. Afonso Vaz de Melo, 465 - Barreiro, Belo Horizonte - MG, 30640-070
E-mail: eunice.barros@prof.una.br

ABSTRACT

Introduction: Creatine and caffeine are food supplements used as ergogenic resources by athletes and practitioners of physical activity. In sports, caffeine has been commercialized because, besides inhibiting pain, it also helps in the development of muscle strength and improves sports performance. Creatine tends to improve high intensity and short duration exercise in sports performance and helps in the recovery period. Objective: To analyze and investigate the interaction of caffeine on creatine absorption. Methods: This article was developed from a bibliographic review in Medline, Lilacs, Ebsco and Google Academic databases, where books, magazines and articles were read. Result: The findings are mixed and may be strongly influenced by the type of training, supplementation dose, exercise time, ingested schedule, and genetic influence that acts on fast or slow metabolization regarding the interaction of caffeine on creatine absorption. Conclusion: Despite the justifications for combined creatine and caffeine supplementation, research directly investigating caffeine consumption during creatine loading suggested that caffeine may attenuate the effect of creatine when supplemented simultaneously. Future research with assessment intervals, the influence of the CYP1A2 gene on caffeine metabolization, and different dosages of ergogenic resources should be conducted to further clarify the issue.

Keywords: Caffeine, Creatine, Nutritional supplementation, Sports nutrition.

1 INTRODUCTION

In sports performance and strength exercise, some athletes seek improvements for health and physical performance. Physical activity is pertinent to ensure muscle strength and sports

performance and individuals engage in different sports and varied nutritional strategies to increase power (BENJAMIN Wax et al, 2021).

One of the strategies to increase strength and performance is the use of ergogenic resources. The ergogenic resources consist of substances used with the purpose of increasing the capacity of physical power, aiming at improving performance. In this sense, they can be classified into five different categories: pharmacological, physiological, psychological, biomechanical or mechanical, and nutritional (EDMARA Luzia dos Reis et al, 2017). Creatine and caffeine are food supplements used as one of the ergogenic resources chosen by athletes and practitioners of physical activity (BENJAMIN Wax et al, 2021).

Creatine is called methyl guanidine-acetic acid, and is formed endogenously by living beings from reactions involving the essential amino acids: arginine, glycine, and methionine, through the liver and kidneys (JOSE Antonio et al, 2021).

Currently, there are 17 types of creatine, monohydrate is the most marketed, but there is little or no evidence that any of the other newer forms of creatine are more effective and/or safer than creatine monohydrate, whether taken alone and/or in combination with other nutrients. Furthermore, considering that the safety, efficacy, and regulatory status of creatine monohydrate are clearly defined in almost all global markets, among other forms of creatine present in the current market as a dietary or food supplement, creatine monohydrate is less clear (RALF J sesame et al,2011).

There are different forms in the marketing of creatine in the form of tablets, liquids, gels, powders or bars (DAMARES Bernardino et al, 2014). The powder version of creatine monohydrate has been extensively studied and the most widely used form since the 1990s. Studies prove that the creatine monohydrate form, ingested orally at a dosage of 3 to 5g/day, increases blood concentration over a period of 3 to 4h after its ingestion (JOSÉ Antônio et al, 2021).

Regarding renal dysfunction, the literature has provided no support that creatine promotes altered renal function or has long-term detrimental effects. Prolonged intake of high doses of creatine (up to 30 g/d for up to 5 years) in patient populations has not been associated with an increased incidence of this dysfunction. Although some have suggested that individuals with pre-existing kidney disease should consult their physician prior to creatine supplementation with great caution (RICHARD B. Kreider et al, 2017).

Caffeine is a psychoactive substance that belongs to the trimethylxanthine group (CRAIG Pickering et al, 2019). It is an odorless white powder that is soluble in water and lipids and has a

bitter taste (NANCI S et al, 2021). It can be rapidly absorbed in the small intestine, but also in the stomach (CRAIG Pickering et al, 2019).

Caffeine is a central nervous system (CNS) stimulant, triggering excitement, alertness, mood improvement, concentration, and may dissipate drowsiness. In sports, caffeine is an ergogenic aid that has been marketed by practitioners of physical activity because, in addition to inhibiting pain, it also helps in the development of muscle strength, thus improving physical performance (NICOLUMAS Contreras Barraza et al, 2021).

Along with natural sources such as coffee, tea and cocoa, caffeine is also added to many foods, beverages and novelty products such as jerky, peanut butter and candy. Currently, it is widely consumed in coffee, tea, cocoa, soda, energy drinks, and some medicines. Alternative sources of caffeine such as chewing gum, mouthwash, and energy gels have also been shown to improve sports performance (NANCI S et al, 2021).

According to the International Olympic Committee and the International Society of Sports Nutrition, at least 3 to 6 mg/kg of caffeine is recommended to improve physical performance (VERÔNICA Giraldez Costa et al, 2022). However, according to the study by Nicolumas Contreras Barraza (et al, 2021), supplementation of 6 mg of caffeine per kilogram can be considered to maximize physical performance in sports with high endurance demands.

Caffeine is monitored by the World Anti-Doping Agency (WADA) and the International Olympic Committee (IOC), and athletes are encouraged to maintain a urine caffeine concentration below a limit of 12 μg/ml, which corresponds to 10 mg/kg of body mass ingested orally over several hours, and which is more than three times the reported performance-enhancing intake (NANCI S et al, 2021, WADA 2022).

CYP1A2 gene coding has been used to characterize individuals as fast or slow metabolizers of caffeine. Over 95% of caffeine is metabolized by the CYP1A2 enzyme. It has been assessed, according to a study by (NANCI S et al, 2021), that individuals with the AA genotype who engage in regular physical activity and individuals with the AC or CC genotype (slow metabolizers) have an increased risk of heart attack, hypertension, pre-diabetes, and appear to have an increase in blood pressure with increased caffeinated coffee consumption, while those with the AA genotype have no such risk. Furthermore, regular physical activity seems to attenuate the increase in blood pressure induced by caffeine intake, but only in individuals with the AA genotype.

In view of the above, in this study we intend to analyze and investigate the interaction of caffeine in the absorption of creatine. As there seems to be a demand for studies about the factors

that interfere in the action of creatine together with caffeine, in a second moment, we intend to expand the corpus of the research and evaluate the genetic factors related to it.

2 METHODS

The search was conducted in the Medline, Lilacs, Ebsco, and Google Academic databases from 2011 to 2022, using the following descriptors: caffeine, creatine, nutritional supplementation, and sports nutrition. The eligibility criteria used were original articles and free review articles available in full, in English, Spanish and Portuguese, published between 2011 and 2022 that addressed the proposed theme. After searching the databases, 70 articles were found, 54 of which were excluded and the others were used for our research.

3 DEVELOPMENT

In different sports modalities, nutritional supplements are widely used by athletes and practitioners of physical activity. The influence on supplement choice is for a number of different reasons, as each product has a different function within a performance plan, such as direct activity enhancement, physique manipulation, pain relief, musculoskeletal, rapid recovery from injury, and mood enhancement (MAUGHAN RJ et al, 2018).

Among these supplements, caffeine is a stimulant that improves athletic performance in endurance-related situations such as exercise time, fatigue, and competitive contests, where the winner is the one who finishes the course in less time while maintaining pace (MAUGHAN RJ et al, 2018).

With the use of creatine, performance in sports tends to improve in high-intensity, short-duration exercises, such as in anaerobic exercises in jumping sports, short runs, weightlifting, throwing and throwing, short activities in which there is the adenosine triphosphate (ATP) energy system (MAUGHAN RJ et al, 2018).

The use ratio between anaerobic metabolism increases, favoring the production of energy by a greater formation of ATP. In summary, these changes contribute both to favor the supply of O^2 to the muscles and also to stimulate the amount of energy generated by the metabolism (SIMONE Biesek et al. 2015). Consequently, the result will be a greater gain in lean mass, strength and muscle power (MAUGHAN RJ et al, 2018).

According to the study Nanci S et al, 2021 it was reported that the often positive ergogenic effect of acute caffeine ingestion before exercise is not affected by creatine when a previous experimental creatine loading protocol was completed by the participants. It was also shown in the

study by Eric T. Trexler et al, 2015, that prior creatine loading does not influence the ergogenic potential of acute caffeine supplementation. While this research suggests that creatine does not influence the efficacy of caffeine, any influence that chronic caffeine consumption may exert on creatine supplementation is not addressed.

However, there is some ambiguity regarding caffeine ingestion during a creatine loading phase. The studies available to date suggest that chronic ingestion of high doses of caffeine (> 9 mg/kg) and creatine should be employed with caution, as opposing mechanisms in Ca2+ clearance and release and muscle relaxation time have been hypostatinized (NANCI S et al, 2021).

As pointed out by (SCOTT C Forbes et al 2020), the hypothesis that the combination of caffeine and creatine may be counterproductive, which produces opposite results than expected, due to high levels of caffeine greater than > 5 mg/kg. Sprint exercise, is an anaerobic endurance training of short duration (up to 20", 100m, 200m, 110m with barrier) that includes periods of maximal muscular effort and intensity, interspersed with a short distance. Caffeine consumption at a dosage of 5-6 mg/kg when evaluated around the most exertional exercise (sprint), does not appear to have an ergolytic effect, because, the creatine dose has been shown to increase the performance of high intensity, long duration exercise.

According to the study by the author Felipe Pedrosa (et al 2019) was conducted with sample number of 30 men, aged between 18 and 40 years, who were not using any type of dietary supplement or pharmacological resource. These were divided into 4 distinct groups, being: the control group n=8 without supplementation use; creatine group n=7; caffeine group n=7; creatine+caffeine group n=8. During the 28-day creatine supplementation period, each research participant ingested 5 grams of creatine every day right after lunch. The caffeine supplementation group received manipulated capsules in an individualized amount, receiving 5mg/kg/weight. Each individual consumed the supplement 1 hour before training.

Creatine supplementation generally results in increases in total body water, with many studies reporting 1-2 kg of weight gain with creatine loading. On the other hand, high doses (> 250-300 mg) of caffeine induce diuresis in participants who have never taken caffeine. While the diuretic effect of caffeine is largely attenuated in habitual drinkers, opposing effects on hydration status may be an important consideration for combination supplementation, particularly in studies that restrict caffeine intake prior to initiation of supplementation. The contribution of this potential interaction mechanism is speculative, as previous studies have not measured hydration status or reported pre- and post-test body weight data for each treatment group. Ergogenic mechanisms and potential sources of interference between creatine and caffeine (ERIC T Trexler et al, 2015).

According to the author (FELIPE Pedrosa et al 2019), until it is well clarified, it seems consistent to avoid the association of both supplementations when the goal is to increase strength. In this study, a negative influence of the associated supplementation of creatine and caffeine on lower limb strength occurred, since the isolated supplementation was able to increase strength at 7 days, while the association of both did not promote the same outcome. These findings cannot be extrapolated to the population because the sample size is small. Until further clarification is obtained, it seems to be consistent to avoid the association of both supplementations when the goal is to increase strength.

Another point that should be taken into consideration would be the wide variety of differences in experimental protocols, such as dosage, type of exercise, intensity of exertion, training status of the individual, diet prior to exercise, and habitual consumption of caffeine, which complicate the interpretation of results (FELIPE Pedrosa et al 2019).

Eric T. Trexler (et al, 2015) suggests that muscle relaxation time may explain how chronic caffeine ingestion attenuates the ergogenic effect of creatine. The combination of caffeine and creatine may imply gastrointestinal discomfort impacting the lack of performance improvement. Research has shown that between 3 of 7 study participants reported gastrointestinal discomfort in response to concomitant creatine and caffeine supplementation, although there do not appear to be any pharmacokinetic interactions between the two.

The relationship between the studies and the authors who evaluated the interaction of caffeine on the action of creatine is presented in Table 1 below:

Table 1: Characterization of the studies

AUTHOR/YEAR	ARTICLE	RESULT	INTERACT
Nanci S. et al, 2021	**International society of sports nutrition position stand: caffeine and exercise performance**	This author's study, to date, suggests that chronic intake of high doses of caffeine and creatine should be employed with caution, as opposing mechanisms in Ca2+ clearance and release and muscle relaxation time have been hypostatinized. Until future research is available, it may be prudent to consume caffeine and creatine separately, or avoid high caffeine intakes when using creatine for muscle benefits.	There have been no reports of caffeine interacting with creatine absorption.
Eric T. Trexler et al, 2015	**Creatine and Caffeine: Considerations for Concurrent Supplementation**	Combining caffeine with creatine may imply gastrointestinal discomfort impacting the lack of performance improvement. More research is needed to determine if caffeine reduces performance improvements from creatine	There was interaction in people with gastrointesti-nal discomfort.

		loading. Until future controlled research refutes the existence of interference between the ingredients, or identifies doses of caffeine at which no interference is identified.	
Scott C. Forbes et al 2020	**Supplements and Nutritional Interventions to Augment High-Intensity Interval Training Physiological and Performance Adaptations-A Narrative Review**	When evaluated around high intensity *sprint* exercise, there does not appear to be an ergolytic effect, as caffeine consumption after creatine loading has been shown to increase high intensity exercise performance.	There was no interaction in high-intensity exercise.
Felipe Pedrosa et al 2019	**Effects of creatine supplementation combined with caffeine on the strength of bodybuilders**	It seems to be consistent to avoid the association of both supplementations when the goal is to increase strength. In this study there was a negative influence of creatine and caffeine supplementation on strength, since the isolated supplementation was able to increase strength after 7 days, while the association of both did not promote the same outcome. Future researches with different evaluation intervals and dosages should be carried out to better clarify the subject.	There was a negative influence of the supplementation tion together.

Source: Nanci S. et al, 2021, International society of sports nutrition position stand: caffeine and exercise performance; Eric T. Trexler et al, 201, Creatine and Caffeine: Considerations for Concurrent Supplementation; Scott C. Forbes et al 2020, Supplements and Nutritional Interventions to Augment High-Intensity Interval Training Physiological and Performance Adaptations-A Narrative Review; Felipe Pedrosa et al 2019, Effects of creatine supplementation conciliated with caffeine on strength in bodybuilders.

4 CONCLUSION

Through the analysis of the data presented by the current studies, the findings are mixed and may be strongly influenced by the training of the physical activity practitioner, depending also on the dosage, the type of training, the time of exercise, the supplementation schedule, and the fast or slow metabolism in relation to the interaction of caffeine on creatine absorption.

Despite the justifications for combined supplementation, research directly investigating chronic caffeine consumption during creatine loading has suggested that caffeine may attenuate the effect of creatine when supplemented simultaneously. Since the interaction of caffeine and creatine together is absorbed in an individualized manner, each person will have a different absorption. The supplement taken separately, on the other hand, will be better absorbed.

Future researches with different evaluation intervals and dosages should be carried out to better clarify the subject. And as a proposal, we suggest epigenetic studies related to the CYP1A2 gene in the influence of the rapid metabolization of caffeine interaction on the action of creatine.

REFERENCES

ANTONIO, Jose; CANDOW, Darren G.; FORBES, Scott C.; GUALANO, Bruno; JAGIM, Andrew R.; KREIDER, Richard B.; RAWSON, Eric S.; SMITH-RYAN, Abbie E.; VANDUSSELDORP, Trisha A.; WILLOUGHBY, Darryn S.. Common questions and misconceptions about creatine supplementation: what does the scientific evidence really show?. Journal Of The International Society Of Sports Nutrition, Santana de Parnaiba, v. 18, n. 1, p. 1-17, 2 jan. 2021. Informa UK Limited. http://dx.doi.org/10.1186/s12970-021-00412-w.

BIESEK, Simone; ALVES, Letícia Azen; GUERRA, Isabela (Org.). Estratégias de nutrição e suplementação no esporte. 3.ed. rev. e atual. Barueri: Manole, 2015. xii, 454 p. ISBN 9788520438589.

CONTRERAS-BARRAZA, Nicolás; MADRID-CASACA, Héctor; SALAZAR-SEPðLVEDA, Guido; GARCIA-GORDILLO, Miguel Ángel; ADSUAR, José C.; VEGA-MUÑOZ, Alejandro. Bibliometric Analysis of Studies on Coffee/Caffeine and Sport. Nutrients, [S.L.], v. 13, n. 9, p. 3234, 17 set. 2021. MDPI AG. http://dx.doi.org/10.3390/nu13093234.

CORRÊA, Damares Bernardino; NAVARRO, Antônio Coppi. Distribuição de resposta dos praticantes de atividade física com relação à utilização de suplementos alimentares e o acompanhamento nutricional em uma academia de Natal/RN. Revista Brasileira de Nutrição Esportiva, v. 8, n. 43, p. 5, 2014.

GIRÁLDEZ-COSTAS, Verónica; AGUILAR-NAVARRO, Millán; GONZÁLEZ-GARCÍA, Jaime; COSO, Juan del; SALINERO, Juan José. Acute caffeine supplementation enhances several aspects of shot put performance in trained athletes. Journal Of The International Society Of Sports Nutrition, [S.L.], v. 19, n. 1, p. 366-380, 6 jul. 2022. Informa UK Limited. http://dx.doi.org/10.1080/15502783.2022.2096415.

JÄGER, Ralf; PURPURA, Martin; SHAO, Andrew; INOUE, Toshitada; KREIDER, Richard B.. Analysis of the efficacy, safety, and regulatory status of novel forms of creatine. Amino Acids, [S.L.], v. 40, n. 5, p. 1369-1383, 22 mar. 2011. Springer Science and Business Media LLC. http://dx.doi.org/10.1007/s00726-011-0874-6.

MAUGHAN, Ronald J.; BURKE, Louise M.; DVORAK, Jiri; LARSON-MEYER, D. Enette; PEELING, Peter; PHILLIPS, Stuart M.; RAWSON, Eric S.; WALSH, Neil P.; GARTHE, Ina; GEYER, Hans. IOC Consensus Statement: dietary supplements and the high-performance athlete. International Journal Of Sport Nutrition And Exercise Metabolism, [S.L.], v. 28, n. 2, p. 104-125, mar. 2018. Human Kinetics. http://dx.doi.org/10.1123/ijsnem.2018-0020.

GUEST, Nanci S.; VANDUSSELDORP, Trisha A.; NELSON, Michael T.; GRGIC, Jozo; SCHOENFELD, Brad J.; JENKINS, Nathaniel D. M.; ARENT, Shawn M.; ANTONIO, Jose; STOUT, Jeffrey R.; TREXLER, Eric T.. International society of sports nutrition position stand: caffeine and exercise performance. Journal Of The International Society Of Sports Nutrition, [S.L.], v. 18, n. 1, p. 1-37, 2 jan. 2021. Informa UK Limited. http://dx.doi.org/10.1186/s12970-020-00383-4.

PEDROSA, Felipe; SOUZA, Ana Caroline Pereira Ferreira de; LEAL, José Carlos; MARQUES-OLIVEIRA, Gleuber Henrique. EFEITOS DA SUPLEMENTAÇÃO DE CREATINA CONCILIADA A CAFEÍNA NA FORÇA DE PRATICANTES DE MUSCULAÇÃO. Revista

Brasileira de Nutrição Esportiva: Periódico do Instituto Brasileiro de Pesquisa e Ensino em Fisiologia do Exercício, São Paulo, v. 13, n. 81, p. 739-748, set/out. 2019.

PICKERING, Craig; GRGIC, Jozo. Caffeine and Exercise: what next?. Sports Medicine, [S.L.], v. 49, n. 7, p. 1007-1030, 11 abr. 2019. Springer Science and Business Media LLC. http://dx.doi.org/10.1007/s40279-019-01101-0.

REIS, Edmara Luzia dos; CAMARGOS, Gustavo Leite; OLIVEIRA, Renata Aparecida Rodrigues; DOMINGUES, Sabrina Fontes. UTILIZAÇÃO DE RECURSOS ERGOGÊNICOS E SUPLEMENTOS ALIMENTARESPOR PRATICANTES DE MUSCULAÇÃO EM ACADEMIAS. Revista Brasileira de Nutrição Esportiva: Periódico do Instituto Brasileiro de Pesquisa e Ensino em Fisiologia do Exercício, São Paulo, v. 11, n. 62, p. 219-231, abr. 2017.

KREIDER, Richard B.; KALMAN, Douglas S.; ANTONIO, Jose; ZIEGENFUSS, Tim N.; WILDMAN, Robert; COLLINS, Rick; CANDOW, Darren G.; KLEINER, Susan M.; ALMADA, Anthony L.; LOPEZ, Hector L.. International Society of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine. Journal Of The International Society Of Sports Nutrition, [S.L.], v. 14, n. 1, p. 1-18, 3 jan. 2017. Informa UK Limited. http://dx.doi.org/10.1186/s12970-017-0173-z.

FORBES, Scott C.; CANDOW, Darren G.; SMITH-RYAN, Abbie E.; HIRSCH, Katie R.; ROBERTS, Michael D.; VANDUSSELDORP, Trisha A.; STRATTON, Matthew T.; KAVIANI, Mojtaba; LITTLE, Jonathan P.. Supplements and Nutritional Interventions to Augment High-Intensity Interval Training Physiological and Performance Adaptations—A Narrative Review. Nutrients, [S.L.], v. 12, n. 2, p. 390, 31 jan. 2020. MDPI AG. http://dx.doi.org/10.3390/nu12020390.

WORLD ANTI-DOPING CODE. INTERNATIONAL. STANDARD. PROHIBITED LIST. 2022. This List shall come into effect on 1 January 2022.

TREXLER, Eric T.; SMITH-RYAN, Abbie E.. Creatine and Caffeine: considerations for concurrent supplementation. International Journal Of Sport Nutrition And Exercise Metabolism, [S.L.], v. 25, n. 6, p. 607-623, dez. 2015. Human Kinetics. http://dx.doi.org/10.1123/ijsnem.2014-0193.

WAX, Benjamin; KERKSICK, Chad M.; JAGIM, Andrew R.; MAYO, Jerry J.; LYONS, Brian C.; KREIDER, Richard B.. Creatine for Exercise and Sports Performance, with Recovery Considerations for Healthy Populations. Nutrients, [S.L.], v. 13, n. 6, p. 1915, 2 jun. 2021. MDPI AG. http://dx.doi.org/10.3390/nu13061915.