This manuscript is a preprint and has not been peer-reviewed.

Title of the Manuscript: Higher Relative Doses of Acute Capsaicin Supplementation Enhance the Performance of Trained Men in Resistance Training

Authors:

Matheus Dias Mendes[a,*], Brena de Oliveira[b], Marcos Antonio Pereira dos Santos[c],

Fernando Vitor Lima[d], Marcos Daniel Motta Drummond[a,*]

Affiliations:

[a,b] Laboratory of Nutrition and Sports Training, Federal University of Minas Gerais, Belo Horizonte, Brazil.

[c] Center for Studies in Exercise Physiology Applied to Performance and Health, Federal University of Piauí, Teresina, Brazil.

[d] Strength Training Laboratoty, Federal University of Minas Gerais, Belo Horizonte, Brazil.

Corresponding Authors:

Name: Matheus Dias Mendes and Marcos Daniel Motta Drummond

Email: nutrimatheusmendes@gmail.com, zangmarcos@gmail.com

Andress: Laboratory of Nutrition and Sports Training, Federal University of Minas Gerais, Av. Presidente Carlos Luz, 6627, Pampulha, Belo Horizonte, MG, 31310-250, Brazil.

Word Count: 4456

Number of Tables: 2
Number of Figures: 4

Short Title:
Capsaicin Supplementation and Strength Training

Keywords:
Nutritional Supplements, Performance-Enhancing Substances, Strength Training, TRPV Cation Channels.

Acknowledgments:
This study received no external funding. The authors thank all volunteers for their participation.

Conflicts of Interest:
The authors declare no conflict of interest.

Higher Relative Doses of Acute Capsaicin Supplementation Enhance the Performance of Trained Men in Resistance Training

Abstract

Objectives: This study aims to compare the efficacy of acute capsaicin supplementation on strength tests and psychophysiological parameters using different doses, relative to total body mass. **Methods:** The sample consisted of 19 male volunteers with a mean age of 23.4±3.2 years. The volunteers consumed either a lower dose of capsaicin (0.15 mg/kg) (LCAP), a higher dose of capsaicin (0.35 mg/kg) (HCAP), or a placebo (PLA). After 45 minutes, the volunteers performed four sets of the back squat exercise. The first set was performed until concentric failure to determine the number of maximum repetitions (NRM). In the following three sets, a maximum of 12 repetitions was performed at an intensity of 70% of 1RM, with a two minute rest between sets. Total volume (TV), movement speed (MS), lactate concentration, and rating of perceived exertion (RPE) were evaluated. **Results:** The results showed a significant increase in TV with HCAP ($p=0.019$) compared to LCAP and PLA, while LCAP showed no significant difference compared to PLA ($p=1.00$). Additionally, there were no changes in MS ($p=0.495$), lactate concentration ($p=0.733$), or RPE ($p=0.554$), regardless of the capsaicin dose. **Conclusion:** Acute capsaicin supplementation can increase TV, but only at high doses, without causing significant changes in MS, lactate concentration, or RPE.

Keyworks: Nutritional Supplements, Performance-Enhancing Substances, Strength Training, TRPV Cation Channels.

1. Introduction

Nutritional ergogenic aids are used in various sports and training protocols[1,2] to enhance performance, reduce the perception of fatigue, and improve recovery between training sessions[1]. Among the nutritional substances with ergogenic potential, capsaicin (CAP), a compound found in peppers, has shown promising results in strength training[3]. Capsaicin is a transient receptor potential vanilloid 1 (TRPV1) agonist, present in various body tissues, such as skeletal muscle and the nervous system[4,5]. By activating TRPV1 receptors, capsaicin can enhance muscle contractions by inducing calcium influx into the sarcoplasmic reticulum[6,7], possibly increasing the interaction between actin and myosin. Additionally, TRPV1 receptor activation in afferent nerve fibers III and IV may attenuate their signaling to the central nervous system (CNS) in response to exercise, potentially reducing the Rating of Perceived Exertion (RPE)[9,10]. Thus, these effects on skeletal muscle and the CNS can improve strength endurance[10], as well as movement speed and muscle power[11].

Some studies on capsaicin supplementation or its capsiate analogue have shown an ergogenic effect in strength training protocols with a dosage of 12 mg of this substance[10,11,13].

However, other studies have reported discrepant results with the same dosage[14-16], even when using similar test protocols and sample populations. Some authors[15,16] have suggested that the absence of the expected ergogenic effect may be due to an insufficient dose. However, the literature indicates that different doses, considered low, have shown effective results in improving performance in strength training protocols[17,18]. On the other hand, no benefits have been observed with a dosage described as high (25.8 mg)[19]. In summary, such discrepancies may suggest a dose-response relationship regarding acute capsaicin supplementation.

Due to the individual pharmacokinetics and pharmacodynamics, may be an individual variability in response to the dose administered[20], which may be related to the individual's total body mass. Thus, by using personalized dosages, greater efficacy can be obtained when administering the substance used[20]. However, the human studies presented in the literature evaluated the efficacy of supplementation with an absolute dosage, not respecting the biological individuality of the participants. Thus, it is necessary to investigate the effect of the administration of different doses of capsaicin, being relativized by body mass, on performance in strength training and psychophysiological variables.

Also, it is known that each individual has unique pharmacokinetics and pharmacodynamics, which may lead to variability in response to the administered dose[20]. Thus, by using personalized dosages relative to body mass, the supplemented substance may promote greater ergogenic effects[20]. However, studies in humans reported in the literature have evaluated the efficacy of capsaicin supplementation using absolute dosages, without accounting for individual variability. Therefore, it is necessary to investigate the effects of administering different capsaicin doses relative to body mass on strength performance and psychophysiological variables, allowing for potential individual responses.

Therefore, the aim of this study was to compare the potential effects of acute capsaicin supplementation, with different dosages relative to total body mass, in a resistance training protocol using the back squat exercise, as well as its possible impacts on RPE, lactate concentration, and movement speed. The hypothesis is that only higher dosages will be effective in increasing strength performance, without inducing changes in psychophysiological parameters or movement speed.

2. Materials and Methods

2.1. Sample

The sample consisted of 19 males, with a mean age of 23.4±3.2 years and 4.4±3 years of experience in resistance training, with an average frequency of 5±1 training sessions per week. The volunteers were also characterized according to their ability to perform the 1RM in the back squat (156.8±20.1 kg), as well as the ratio between maximum strength and total body mass (2.1±0.3). Additionally, the volunteers were characterized by total body mass (76.1±8.9 kg), height (1.73±0.62 m), muscle mass (37.2±4.0 kg), fat mass (11.1±4.4 kg), body fat percentage (14.3±4.4%), intracellular water (30±3.0 L), and extracellular water (17.5±2.0 L). To evaluate and characterize the body composition of the volunteers, the bioimpedance method was used, with an instrument validated for this procedure (Inbody 570® bioimpedance scale; Inbody Co., Ltda., Korea)[21].

The sample size was determined using data obtained from the main variable in a pilot study, in which the statistical test ANOVA for repeated measures was used. The statistical significance level was set at $\alpha = 0.05$, the ANOVA effect size at $\eta^2 = 0.082$, and the power obtained as a result of the test was $\beta = 0.104$. Based on this, the sample size of 19 volunteers was estimated using the G Power software (version 3.1.9.4).

To be included in the study, the volunteers had to be between 18 and 40 years old, with at least 12 consecutive months of experience in resistance training and performing the back squat exercise, with a minimum regular training frequency of three times per week[14]. Volunteers were excluded if they had food allergies, joint, muscle, or bone injuries in the lower limbs, or any clinical condition that could compromise the performance of the strength tests. Additionally, they were instructed to abstain from any substance with potential ergogenic capacity during the study and not consume spicy foods or caffeine-based stimulant drinks on the day of the experimental sessions[16].

After being informed about the procedures, as well as the potential risks and benefits, the volunteers agreed to participate in the study and signed the informed consent form. This study complied with all the standards established by the National Health Council (Res 466/2012) and was approved by the Federal University of Minas Gerais (UFMG) Research Ethics Committee (CAAE: 67972323.9.0000.5149).

2.2. Experimental Design

This is a cross-sectional experimental study with a randomized, double-blind, crossover placebo-controlled design. Blinding and randomization were performed by an external researcher who was not directly associated with the research data. Each volunteer participated in eight experimental sessions, with an interval of 72 to 96 hours, and all sessions were conducted at the same time of day. The first session aimed to present the research and characterize the sample. In the second session, the participants became familiar with the environment and procedures that would be applied in the experimental sessions. In the third and fourth sessions, the individuals performed the 1RM test and retest, respectively. The following session was devoted to familiarization with the resistance training protocol. In the next three experimental sessions, the volunteers randomly and blindly consumed either a low dose of capsaicin (LCAP), a high dose of capsaicin (HCAP), or a placebo (PLA) before performing the strength tests, resistance training protocol, and monitoring psychophysiological parameters and movement speed. The study design is shown in Figure 1.

During the experimental sessions, food consumption from the previous day and the last meal before the experimental session were monitored using the 24-hour food recall (R24h)[16]. This was done to compare and monitor the calories (kcal) and macronutrient (carbohydrates, fats, and proteins) intake throughout the study. All volunteers were instructed to eat their last meal 120 minutes before the experimental sessions. In addition, they were advised by a qualified professional to maintain their usual food consumption and replicate the pre-effort meal performed in the first experimental session.

2.3. Familiarization

In the 1RM test familiarization, the volunteer was asked about the usual weight lifted in the back squat exercise and the number of maximum repetitions that can be performed, in order to then be tested in a set[22]. In association with the 1RM test familiarization, the RPE anchoring was performed through a visual cognitive procedure. The volunteers were instructed to perform a repetition with only the weight of the barbell and associate the RPE with the anchor as "extremely easy." Then, when the volunteers performed the maximum repetition, they were instructed to establish a consonance between that effort and the anchor described as "extremely difficult"[23].

To perform the back squat and standardize the range of motion, all volunteers performed the movement until knee flexion reached a position of 90º [24], using a digital goniometer to measure this amplitude. The procedures followed the same parameters adopted by Simões et al.,[14]. Subsequently, the volunteers performed the resistance training protocol to familiarize themselves with the parameters, which will be described later in the text.

2.4. Procedures

Supplementation was performed 45 minutes before the resistance training protocol[25] (Figure 02). Regarding the dosage of capsaicin, a dosage relative to the individual's total body mass was used, with a low dosage selected from the study by Freitas et al.[10], which corresponded to approximately 0.15 mg/kg (LCAP). Thus, the average consumption for the sample in the present study was 11.4±1.3 mg. Regarding the high dosage (HCAP), it was determined based on a study by Opheim and Rankin [19], in which they used a dosage of approximately 0.35 mg/kg. Therefore, the average dosage consumed by the volunteers in the present study was 26.6±3.1 mg. The placebo capsules contained starch. All capsules were identical, and both the evaluators and participants were unaware of what was being consumed. Prior to the resistance training protocol, the volunteers performed a five-minute passive warm-up on the stationary bicycle at low intensity and constant speed[14].

2.5. One-repetition maximal test (1RM)

The volunteer started the 1RM test according to the weight estimated in the familiarization[22]. Subsequently, a progressive increase of 10% to 15% was applied in each attempt, based on the subjective perception of both the volunteer and the evaluator, with a five-minute interval between each attempt[26]. When the volunteer was unable to perform a single complete repetition, the weight lifted in the previous successful attempt was considered the 1RM[22].

2.6. Resistance Training Protocol

The volunteers performed four sets, with the first set aimed at determining the number of maximum repetitions (NRM). They were then instructed to perform as many repetitions as possible until momentary concentric failure, which was determined when the volunteer voluntarily interrupted the execution, did not complete the full range of motion, or involuntarily altered the movement pattern[16]. Regarding the execution of the exercise, the volunteers were instructed to maintain the pattern described during the 1RM test familiarization.

In the following three sets, a maximum of 12 repetitions or voluntary interruption were performed, at an intensity of 70% of 1RM, with a two-minute interval between each set. Participants were instructed to perform the exercise until the established repetition limit or based on their perception of exhaustion. The total volume (TV) was determined after all the sets were performed and was calculated by multiplying the total number of repetitions by the lifted mass (total repetitions × lifted mass)[14,16].

2.7. Movement Speed

During the resistance training protocol, movement speed was monitored. To perform this procedure, a linear position transducer with cable extension was used, with the bar positioned vertically and fixed by a Velcro strap. This instrument has been validated and is considered reliable for this procedure (Ergonauta I, version 1.1). The displacement data in relation to time were transmitted to a smartphone application via Bluetooth connection, with a sampling rate of 1000 Hz. The average movement speed across the four sets was then calculated[28].

2.8. Blood Lactate Concentration

To analyze blood lactate concentration, a fingertip blood sample was collected immediately after capsule consumption and again 120 seconds after the resistance training protocol[29]. A disposable lancet (Accu-Chek Safe-T-Pro Uno, 28g / 0.36mm – Roche Diagnostics) was used to puncture the skin, which was immediately and properly discarded. After this procedure, a dry gauze was used to wipe away the first drop of blood before transferring the sample to a reagent strip (Lactate Test Strip, Detect/BM-Lactate - Roche Diagnostics), allowing for analysis by a portable lactate meter (Accutrend® Plus - Roche Diagnostics)[16].

2.9. Rating of Perceived Exertion (RPE)

The RPE scale was applied during passive rest intervals between sets in the resistance training protocol[16]. Using the OMNI-Resistance Exercise Scale (OMNI-RES), volunteers provided their ratings based on their subjective perception of effort during the training session[23].

2.10. Statistical analysis

To assess the normality of the data, the Shapiro-Wilk test was used, and to assess the sphericity of the data, the Mauckly test was used. Variables with normal distribution, for TV, movement speed, RPE and food recall, were compared using repeated measures ANOVA. To evaluate lactate concentration, mixed ANOVA with repeated measures was used. When necessary, the *Bonferroni post-hoc* test was used to identify differences. The significance level adopted in all analyzes was $\alpha=0.05$. To determine the effect size (d), the calculation and classification proposed by Rhea[30] for resistance training was used, considered as trivial (<0.25), small (0.25-0.50), moderate (0.50-1.00) and large (>1.0). All statistical analyses performed using SPSS software (version 29.0, IBM, NY, USA), and the graphs were design using R studio software (version 4.3.3).

3. Results

The variables had normal distribution and sphericity ($p>0.05$), only the variable RPE was determinate by the *Greenhouse-Geisser* correction for sphericity. Regarding TV, a statistically significant difference was observed between the mean of the experimental conditions ($p=0.019$; $F=4.451$). The *post hoc* test reported that the HCAP condition (6,208.4±1232.7kg) presented a higher total volume when compared to the LCAP condition (5,826.4±1,154.2kg) ($p= 0.042$; 95%CI=12–751.8; $d=0.32$), with effect size considered small. There was also a higher total volume for the HCAP condition (6,208.4±1,232.7) than for the PLA condition (5,700.9±1,051.3) ($p=0.033$; 95%CI=34.1–980.8; $d=0.44$), with effect size considered small. However, there was no statistical difference between the LCAP

(5,826.4±1,154.2) and PLA (5,700.9±1,051.3) conditions (p= 1.00; 95%CI = - 417.6–668.7; *d*=0.11*),* with a trivial effect size. The individual's results of TV in relation with the mean are represented in Figure 3.

There was no statistically significant difference in the movement speed between the conditions (p=0.495; F=0.718). Therefore, when comparing separately, the conditions are considered statistically equal, HCAP (0.38±0.05 m/s) and LCAP (0.37±0.05 m/s) (p=1.00; 95%CI=-0.02–0.03; *d*=0.20*),* as well as between the HCAP (0.38±0.05 m/s) and PLA (0.39±0.07 m/s) conditions (p=1.00; 95%CI=-0.04–0.03; *d=0.16),* both presenting trivial effect size. Likewise, there was no statistical difference in the mean velocity between the LCAP (0.37±0.05 m/s) and PLA (0.39±0.07 m/s) conditions (p=0.57; 95%CI= -0.04–0.01; *d*=0.32), however, with a small effect size favoring the PLA condition. The individual's movement speed in relation with the mean are represented in Figure 4.

Regarding lactate concentration during exercise, there was no statistical difference for the interaction between the factors condition x time (p=0.733; F=0.313). However, there was a statistically significant difference for the time factor (p < 0.001; F=199.4). Therefore, it is observed that lactate concentration was higher in the post-exercise period when compared to the pre-exercise moment, regardless of the condition (p<0.001; 95%CI= 7.1–9.5; *d*=20), with large effect size, descrition in Table 1.

No statistically significant difference in the RPE was observed between the experimental conditions (p=0.554; F=0.600). Thus, the comparison between the conditions evidences this result, thus there is no difference between the HCAP (8.4±0.84) and LCAP (8.4±0.75) conditions (p=1.00; 95%CI= -0.4–0.5; *d*=0.0), as well as HCAP (8.4±0.84) and PLA (8.2±0.7) (p=1.00; 95%CI= -0.31–0.68; *d*=0.25), in addition, the effect size was considered trivial and small, respectively. Finally, the comparison between the LCAP (8.4±0.75) and PLA (8.2±0.7) conditions also did not show significant difference (p=1.00; 95%CI= -0.27–0.56; *d*=0.27*),* with a small effect size.

The volunteers nutritional profile showed no difference in energy intake (kcal) between the experimental conditions (p=0.205). Also, nutrient intake (g) was similar between conditions carbohydrate (p=0.522), protein (p=0.219) and lipid (p=0.386). Similarly, the pre-exercise meal showed no difference in energy (kcal) (p=0.860) and macronutrients (g) intake carbohydrate (p=0.884), protein (p=0.326), lipid (p=0.579) between the experimental conditions.

4. Discussion

The aim of this study was to evaluate the effect of acute capsaicin supplementation at different doses, relative to total body mass, on performance and psychophysiological parameters in a resistance training protocol. The hypothesis was that higher doses of capsaicin would be more effective in increasing performance without inducing changes in psychophysiological parameters or movement speed. The main finding of this study was a significant increase in TV, but only in the HCAP condition, compared to LCAP and PLA. Additionally, the results showed no significant changes in movement speed or psychophysiological parameters with capsaicin supplementation at either dosage. Therefore, the hypothesis was confirmed.

Regarding TV, the results indicate that larger doses are needed to promote performance improvement. Considering the administration of the LCAP dosage, the results found by Simões et al.,[14] corroborate the present study, in which supplementation with 12 mg of CAP did not show a significant increase in TV in a similar resistance training protocol[22]. Cruz et al.,[16] and Moura et al.,[15] also did not observe an increase in total volume with the 12 mg CAP dosage; however, both protocols performed in these studies were in the upper limbs[22]. In the present study, the measurements were relative to total body mass, and the condition supplemented with HCAP would be more similar to the absolute doses used in the other cited studies. Therefore, the administration of low doses of capsaicin, either in a relativized or absolute manner, is possibly not efficient in increasing TV.

The response dependent on higher doses may be justified by the fact that TRPV1 receptors are located mainly in muscle fibers[6]. Thus, individuals with a greater amount of muscle tissue may have a greater number of receptors and, therefore, would need a higher dose to achieve the same physiological response[32]. Another possibility is related to the level of training of the individuals. However, no data were found in the literature regarding the number of receptors in trained subjects[32]. Above all, another hypothesis is the existence of a dose-response relationship concerning the level of physical fitness[32]. Therefore, further studies are needed to investigate the relationship between dosage and the subject's fitness and sports training level.

However, Freitas et al.,[10] observed significant positive results with the absolute dosage of 12 mg regarding the increase in TV in a similar resistance training protocol[33]. Freitas et al.,[33] also found an increase in the number of repetitions in a resistance training protocol for the back squat exercise[33]. However, in this study, the resistance training protocol was performed after a High Intensity Interval Training (HIIT) session on the treadmill, and an absolute dosage of 24 mg was used[33]. Both studies were conducted on men with more than one year of experience in resistance training, and the protocol was performed at 70% of 1RM[33]. Therefore, the results differed from the present study, in which only the higher dose showed a positive effect on TV[33].

Moura et al.,[15] observed an increase in TV in the bench press exercise[33]. As in the present study, they observed a dose-response relationship regarding capsaicin supplementation, but the low dosage (6 mg) was effective[33]. Therefore, it is possible that, in association with the dose-response effect, there may also be a muscle-dependent relationship[33]. In an in vivo study conducted by Zhou et al.,[34], a higher number of TRPV1 receptors was reported in the gastrocnemius muscle compared to the soleus, which has a greater amount of fast-twitch fibers[33]. However, they observed greater activation of receptors in the soleus muscle when supplemented with capsaicin, demonstrating greater sensitivity to supplementation[33]. Therefore, the relationship between the number and distribution of TRPV1 receptors according to the muscle group stimulated is not yet clear in the literature, requiring further studies to understand this phenomenon[33].

Possibly, the increase in TV and the capacity for strength endurance is related to the increase in calcium influx into the sarcoplasm[6]. By stimulating the activation of CamK through the activation of TRPV1 receptors and the consequent influx of Ca^{2+}, there was possibly an increase in the interaction between ryanodine and dihydropyridine receptors, thus enhancing the ability to form cross-bridges[35,38]. This was demonstrated in the study conducted by Arkhipov et al.,[36], which reported an increase in strength production with continuous skeletal muscle stimulation within 60 seconds of muscle contraction, with the greatest difference occurring at approximately 30 seconds of contraction[35]. Therefore, according to the findings of Arkhipov et al.,[36] the duration of the stimulus is a primary factor for greater efficiency with capsaicin supplementation[35]. A limitation of the present study is that the stimulus duration was not monitored[35]. However, only the first set of the resistance training protocol required a longer time under tension because the NRM was performed, whereas the other sets were limited to 12 repetitions, possibly not exceeding a contraction time of 60 seconds[35].

Regarding movement speed, the results found by Jiménez-Martínez et al.,[37] do not fully corroborate the present study. The authors observed an increase in the mean movement speed across the three sets, along with a reduction in the percentage of speed loss throughout the sets, indicating a decrease in neuromuscular fatigue. The protocol was performed in the back squat exercise, with eight repetitions per set across three sets at 70% of 1RM, and the sample consisted of trained individuals. This result was obtained using the supplementation of 2.5 mg of phenylcapsaicin compared to a placebo, with the low dosage considered to be 0.625 mg. Similarly, Silva et al.,[11] observed an increase in peak speed in the bench press exercise in Jiu-Jitsu athletes. In their study, supplementation with 12 mg of capsaicin was administered; however, the strength training session protocol was based on a load relative to total body mass. The differences in results indicate the need for more studies about movement speed and capsaicin supplementation.

Mean movement speed may be one of the parameters indicating neuromuscular fatigue, as it is related to the decline in strength production[28]. In the present study, an increase in TV was observed in the HCAP condition without promoting significant changes in movement speed. These results may indicate reduced neuromuscular fatigue and an increased ability to perform work. Therefore, the findings partially corroborate those of Jiménez-Martínez et al.,[37] who demonstrated an increase in movement speed during a resistance training protocol, but with similar TV between compared conditions. Possibly, the mechanism explaining the absence of changes in movement speed in the present study is related to the activation of TRPV1 receptors in afferent nerve fibers III and IV. Activation of these receptors attenuates the response of afferent nerves III and IV to the CNS, leading to desensitization and prolonging the stimuli in the motor cortex[39].

Lactate concentration in the present study increased after exercise, regardless of the experimental condition. This result was also observed by Freitas et al.,[10] who demonstrated that there was no difference in lactate concentration between conditions, either between sets or after exercise. Jiménez-Martínez et al.,[37], Moura et al.[15], and Cruz et al.,[16] also did not observe a statistically significant difference in lactate concentration between capsaicin supplementation and placebo after a resistance training protocol. Therefore, the results regarding the influence of capsaicin supplementation suggest that this substance does not alter lactate production in resistance training.

Additionally, in the present study, the subjective perception of effort was similar between the experimental conditions. Corroborating the results of the present study, Simões et al.,[14] did not observe changes in RPE with isolated capsaicin supplementation, nor when combined with caffeine, in a similar resistance training protocol. Similarly, Cruz et al.,[16] demonstrated that there was no change in RPE with capsaicin supplementation alone (12 mg), as well as when combined with caffeine. Jiménez-Martínez et al.,[38] also demonstrated similar results, observing no changes in RPE regardless of the administered dosage of phenylcapsaicin in a resistance training protocol. Likewise, the results found by Moura et al.,[18] corroborate the present study, where no significant changes were observed in RPE regardless of the dose administered; however, it presented a small effect size with the HCAP dose (12 mg). Thus, the possible peripheral analgesic or central stimulant effect of capsaicin may not be sufficient to reduce RPE in resistance training.

Regarding the dietary profile, no significant changes were observed in caloric or macronutrient intake either prior to exercise or on the day preceding the experimental session. Consequently, dietary intake was unlikely to have influenced the study outcomes[11,16].

The present study has some limitations, among others already presented earlier in the text, which do not impact the reliability of the study. Initially, the results cannot be extrapolated to other populations, such as females or beginners in strength training. In addition, it is not possible to infer that capsaicin supplementation would be efficient in increasing performance in a complete lower and/or upper limb strength training session. Thus, it is recommended that future research investigate the limitations presented.

5. Conclusion

Acute high-dose capsaicin supplementation, relativized to the individual's total body mass, is effective to increase the performance in resistance training. Furthermore, this effect occurs without affect negatively the RPE and inducing others changes in the individual's psychophysiological parameters.

6. Aplication Pratics

As for the practical applications, the results showed that resistance-trained men can improve strength performance in the lower limbs with a dosage of 0.35 mg/kg. In addition to improving performance, they presented the same perception of fatigue, as indicated by the psychophysiological parameters. Thus, a multidisciplinary approach is necessary to ensure that supplementation is applied according to the adopted and prescribed resistance training protocol.

Financing

This study was not funded.

Authors' contributions

MATHEUS participated in all stages of the study, MARCOS contributed to the writing of the study, study design, and interpretation of the results, BRENA contributed to data collection. FERNANDO and MARCOS contributed to the writing of the study. All authors read and agreed with the final version of the study, as well as the order and presentation of the authors.

Conflicts of interest

The authors declare that there is no conflict of interest.

References

1. Kerksick CM, Wilborn CD, Roberts MD, et al. ISSN exercise & sports nutrition review update: research & recommendations. *J Int Soc Sports Nutr.* 2018;15(1):38. doi:10.1186/s12970-018-0242-y.

2. Peeling P, Binnie MJ, Goods PSR, Sim M, Burke LM. Evidence-based supplements for the enhancement of athletic performance. *Int J Sport Nutr Exerc Metab.* 2018;28(2):178-187. doi:10.1123/ijsnem.2017-0343

3. Grgic J, Mikulic P, Schoenfeld BJ, et al. Effects of capsaicin and Capsiate on endurance performance: A meta-analysis. *Nutrients.* 2022;14(21):4531. doi:10.3390/nu14214531
4. Matta JA, Ahern GP. TRPV1 and synaptic transmission. *Curr Pharm Biotechnol.* 2011;12(1):95-101. doi:10.2174/138920111794295725
5. Hudson ASR, Hudson MC, Hudson MP, Oliveira AA, Costa NCS. Involvement of the TRPV1 channel in the modulation of spontaneous locomotor activity, physical performance, and physical exercise-induced physiological responses. *Braz J Med Biol Res.* 2016;49(6):e5235. doi:10.1590/1414-431x20165235
6. Lotteau S, Ducreux S, Romestaing C, et al. Characterization of functional TRPV1 channels in the sarcoplasmic reticulum of mouse skeletal muscle. *PLoS One.* 2013;8(3):e58673. doi:10.1371/journal.pone.0058673
7. Vahidi Ferdowsi P, de Souza JM, Hargraves TL, et al. TRPV1 activation by capsaicin mediates glucose oxidation and ATP production independent of insulin signaling in mouse skeletal muscle cells. *Cells.* 2021;10(6):1560. doi:10.3390/cells10061560
8. Taylor JL, Amann M, Duchateau J, Meeusen R, Rice CL. Neural contributions to muscle fatigue: from the brain to the muscle and back again. *Med Sci Sports Exerc.* 2016;48(11):2294-2306. doi:10.1249/MSS.0000000000000923
9. Butenas AL, Saito A, Mizuno M, Ichinose M, Homma S. Sex-dependent attenuating effects of capsaicin administration on the mechanoreflex in healthy rats. *Am J Physiol Heart Circ Physiol.* 2023;325(2):H372-H384. doi:10.1152/ajpheart.00169.2023
10.Freitas MC, Azevedo LM, Moreira SB, et al. Acute capsaicin supplementation improvises resistance training performance in trained men. *J Strength Cond Res.* 2018;32(8):2227-2232. doi:10.1519/JSC.0000000000002381
11. Silva BVC, Sousa M, Franco-Alvarenga PE, et al. Acute supplementation with capsaicin enhances upper-limb performance in male Jiu-Jitsu athletes. *Sports.* 2022;10(8):120. doi:10.3390/sports10080120
12.Gomes WDS, Almeida JA, Souza DB, et al. Effects of Capsiate supplementation on maximal voluntary contraction in healthy men. *Int J Sports Med.* 2021;42(6):548-555. doi:10.1055/a-1335-7871
13.Grgic J, Mikulic P, Schoenfeld BJ, et al. Effects of capsaicin and Capsiate on endurance performance: A meta-analysis. *Nutrients.* 2022;14(21):4531. doi:10.3390/nu14214531
14.Simões CB, Moreira SB, Cavalcante T, et al. Acute caffeine and capsaicin supplementation and performance in resistance training. *Motriz: J Phys Educ.* 2022;28:e1022008. doi:10.1590/S1980-657420220081022
15.Moura HPSN, Esteves GP, De Souza Neto AV, et al. Acute low-dose Capsiate supplementation improves upper body resistance exercise performance in trained men: A randomized, crossover and double-blind study. *Int J Exerc Sci.* 2022;15(2):1007-1018.
16.Cruz VM, Jiménez-Martínez P, Peinado AB, et al. Combined caffeine-capsaicin supplementation does not enhance the performance of trained men in a resistance session. *Muscles Ligaments Tendons J.* 2023;13(4):645-652. doi:10.32098/mltj.04.2023.12
17.Cross BL, Gallego J, Rivera M, et al. Effect of a commercially available low-dose capsaicin supplement on knee extensor contractile function. *Int J Exerc Sci.* 2020;13(2):312-322.
18.Moura e Silva VEL, de Souza Neto AV, Moreira SB, et al. Capsaicinoids and Capsinoids as an ergogenic aid: a systematic review and the potential mechanisms involved. *Int J Sports Physiol Perform.* 2021;16(4):464-473. doi:10.1123/ijspp.2020-0308
19.Opheim MN, Rankin JW. Effect of capsaicin supplementation on repeated sprinting performance. *J Strength Cond Res.* 2012;26(2):319-326. doi:10.1519/JSC.0b013e31821a413d
20.Al-Metwali B, Mulla H. Personalized dosing of medicines for children. *J Pharm Pharmacol.* 2017;69(5):514-524. doi:10.1111/jphp.12695
21.Karelis AD, Chamberland G, Aubertin-Leheudre M, Duval C, Ecological validity of a portable bioelectrical impedance analyzer for the assessment of body composition. *Appl Physiol Nutr Metab.* 2013;38(9):999-1004. doi:10.1139/apnm-2013-0027

22.Fonseca ICS, Silva LB, Carvalho JF, et al. Subsequent performance of two 1RM tests in the same session reduces 1RM and consequently the volume load of strength training session. *J Exerc Physiol Online.* 2020;23(5):65-75.

23.Robertson RJ, Goss FL, Rutkowski J, et al. Concurrent validation of the OMNI perceived exertion scale for resistance exercise. *Med Sci Sports Exerc.* 2003;35(2):333-341. doi:10.1249/01.MSS.0000048831.15016.2A

24.Esformes JI, Bampouras TM. Effect of back squat depth on lower-body postactivation potentiation. *J Strength Cond Res.* 2013;27(11):2997-3000. doi:10.1519/JSC.0b013e31828a1f93

25.O'Neill J, Brock C, Olesen AE, Andresen T, Nilsson M, Dickenson AH. Unraveling the mystery of capsaicin: a tool to understand and treat pain. *Pharmacol Rev.* 2012;64(4):939-971. doi:10.1124/pr.112.006163

26.Drake D, Kennedy R, Wallace E. Familiarization, validity and smallest detectable difference of the isometric squat test in evaluating maximal strength. *J Sports Sci.* 2018;36(18):2087-2095. doi:10.1080/02640414.2018.1439872

27.Pérez-Castilla A, Jiménez-Reyes P, González-Badillo JJ. Reliability and concurrent validity of seven commercially available devices for the assessment of movement velocity at different intensities during the bench press. *J Strength Cond Res.* 2019;33(5):1258-1265. doi:10.1519/JSC.0000000000002015

28.Sanchez-Medina L, González-Badillo JJ. Velocity loss as an indicator of neuromuscular fatigue during resistance training. *Med Sci Sports Exerc.* 2011;43(9):1725-1734. doi:10.1249/MSS.0b013e318216eb99

29.Garnacho-Castaño MV, Domínguez R, Mate-Muñoz JL. Acute physiological and mechanical responses during resistance exercise at the lactate threshold intensity. *J Strength Cond Res.* 2015;29(10):2867-2873. doi:10.1519/JSC.0000000000000965

30.Rhea MR. Determining the magnitude of treatment effects in strength training research through the use of the effect size. *J Strength Cond Res.* 2004;18(4):918-920. doi:10.1519/14403.1

31.Cohen J. *Statistical Power Analysis for the Behavioral Sciences.* 2nd ed. Elsevier; 1988.

32.Li S, Zheng J. The capsaicin binding affinity of wild-type and mutant TRPV1 ion channels. *J Biol Chem.* 2023;299(11):102968. doi:10.1016/j.jbc.2023.102968

33.Freitas MC, Moreira SB, Moura e Silva VEL, et al. Acute capsaicin supplementation improved resistance exercise performance performed after a high-intensity intermittent running in resistance-trained men. *J Strength Cond Res.* 2022;36(1):130-134. doi:10.1519/JSC.0000000000003587

34.Zhou G, Su Y, Fa S, et al. Diversity effect of capsaicin on different types of skeletal muscle. *Mol Cell Biochem.* 2018;443:11-23. doi:10.1007/s11010-017-3211-6

35.Chin ER. Intracellular Ca2+ signaling in skeletal muscle: decoding a complex message. *Exerc Sport Sci Rev.* 2010;38(2):76-85. doi:10.1097/JES.0b013e3181d496d5

36.Arkhipov AY, Shilnikov VV, Chistopol'skii IA, et al. Activation of TRPV1 channels inhibits the release of acetylcholine and improves muscle contractility in mice. *Cell Mol Neurobiol.* 2023;43(8):4157-4172. doi:10.1007/s10571-023-01364-w

37.Jiménez-Martínez P, Peinado AB, Garnacho-Castaño MV, et al. Effects of different phenylcapsaicin doses on resistance training performance, muscle damage, protein breakdown, metabolic response, ratings of perceived exertion, and recovery: a randomized, triple-blinded, placebo-controlled, crossover trial. *J Int Soc Sports Nutr.* 2023;20(1):2204083. doi:10.1080/15502783.2023.2204083

38.Jiménez-Martínez P, Peinado AB, Garnacho-Castaño MV, et al. Effects of different phenylcapsaicin doses on neuromuscular activity and mechanical performance in trained male subjects: a randomized, triple-blinded, crossover, placebo-controlled trial. *Front Physiol.* 2023; 14:1149320. doi:10.3389/fphys.2023.1149320

39. Mannozzi J, Groebe B, Hellsten Y, Leicht AS, Green S. Chronic ablation of TRPV1-sensitive skeletal muscle afferents attenuates the muscle metaboreflex. *Am J Physiol Regul Integr Comp Physiol.* 2021;321(3):R385-R395. doi:10.1152/ajpregu.00052.2021

Table 1 – The lactate concentration mean of the experimental conditions

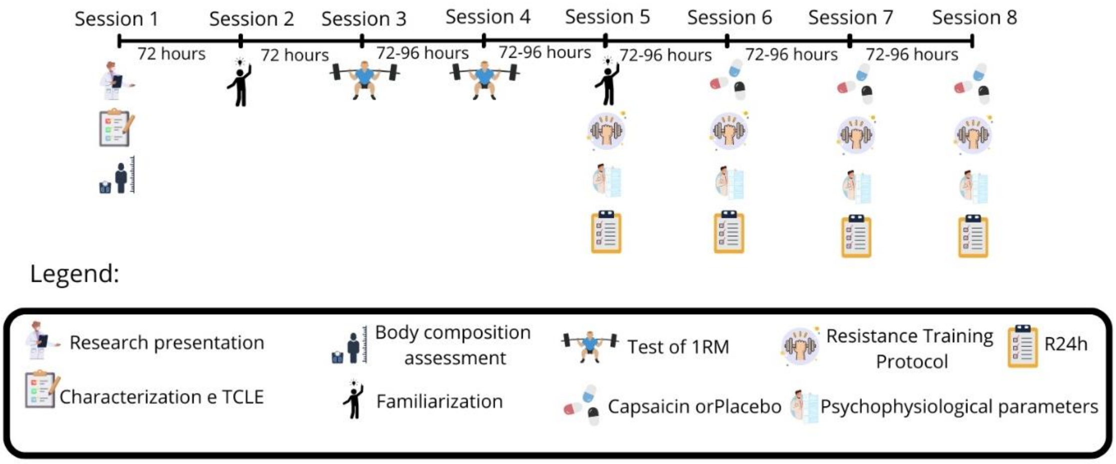
	CONDITION			
Time lactate (mmol/L)	HCAP	LCAP	PLA	Total mean
Pré-session	1,7±0,615	2,1±0,607	1,7±0,561	1.8±0.086
Pós-session	9,8±2,433	10,4±2,928	10,2±3,435	10.1±0.578*

* Statistically significant difference compared to the pre-exercise and post-exercise.

Table 2 – Food consumption

	CONDITION			Value *p*
R24h	ACAP	BCAP	PLA	
KCAL	2594±684	2805±761	2851±726	0,205
CHO (g)	368±115	395±135	372±124	0,522
PTN (g)	141±50	148±54	161±47	0,219
LIP (g)	67±20	77±30	81±43	0,386
Experimental Session				
KCAL	522±169	518±180	504±211	0,860
CHO (g)	79±33	77±25	80±34	0,884
PTN (g)	30±15	27±16	24±17	0,326
LIP (g)	13±14	13±9	10±7	0,579

Legend: Kcal: calories; CHO: carbohydrates; PTN: protein; LIP: lipids.



APPENDIX – FIGURES

Figure 1 - Study design

Figure 2 – Procedures in the experimental session

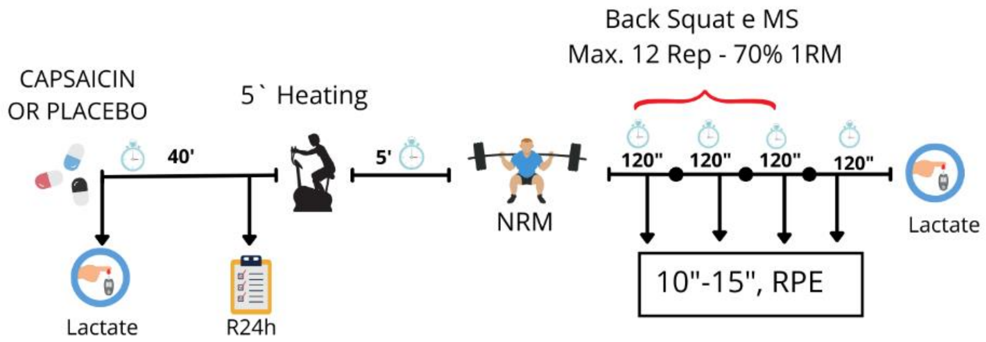
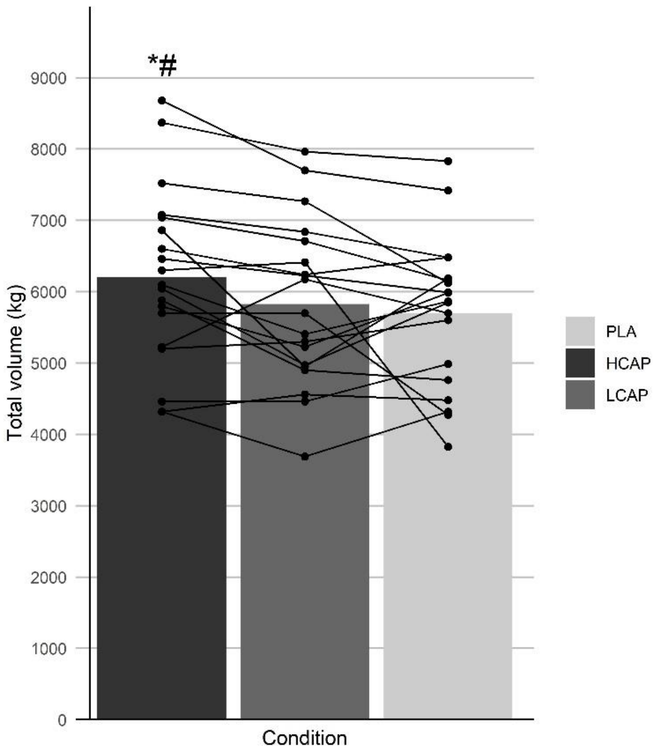


Figure 3 – The mean and individual's values of TV.



*Statistically significant difference compared to the PLA condition. #Statistically significant difference compared to the LCAP condition.

Figure 4 – Individual's and movement speed means