Review Paper

Effects of oral capsaicinoids and capsinoids supplementation on resistance and high intensity interval training: A systematic review of randomized controlled trials

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ABSTRACT

Oral capsaicinoids and capsinoids supplementation has been studied recently for a plausible ergogenic impact on sports performance. However, non-aggregated literature has focused on the impact of this substances in healthy humans' performance. The aim of the present systematic review was to explore the effects of capsaicinoids and capsinoids on resistance training (RT) and HIIT exercise. Studies searches were performed in the PubMed/MEDLINE, Scopus and Web of Science electronic databases. Studies where healthy subjects consumed capsaicinoids or capsinoids acutely or chronically compared to placebo before a RT or HIIT intervention were included. The methodological quality of the included studies was assessed with PEDro checklist. A total of 7 excellent-good quality placebo-controlled trials (i.e., 5 RT and 2 HIIT experiments) were included. The most prevalent protocol used capsaicin (i.e., 6 capsacin and 1 capsiate studies) and acute (i.e., 5 of 7 interventions) supplementation designs. Positive effects were only noted for capsaicin in repetitions until failure (+14.4 to +21.7%), total weight lifted (+13.0 to +23.3%), perceived effort (-6.4%), fatigue index (+15.0%) and peak torque (+6.1%) compared to placebo. Neuromuscular HIIT variables (e.g., total and medium sprint time) were not highly affected by capsaicin except the time to reach 90% VO_2 peak (+61.2%) and the number of efforts performed (+14.7%). Collectively, our findings suggest a positive effect of 12 mg of capsaicin on strength endurance, total weight lifted and perceived effort variables in healthy males after acute (i.e., 45 minutes pre-exercise) supplementation.
Keywords: Sports nutrition; Sports performance; Resistance training; Human physical conditioning.

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INTRODUCTION

Dietary supplements are legal complements (i.e.., nonmedical prescription or banned substances) which in conjunction with a healthy diet can improve wellbeing and sports performance (Maughan et al., 2018). These products are free-sale and widely popular between athletes (Jes et al., 2021; Knapik et al., 2016; Mata et al., 2021), a target group for this kind of compounds. In recent years, supplements market has grown with the addition of new nutraceuticals (Kamiński et al., 2020; Piccolella et al., 2019), some of them without strong scientific research to support their recommendation (Alali et al., 2021; Schmitt & Ferro, 2013).

Capsaicinoids are a group of compounds naturally found in spicy fruits like chili peppers. Due to their potential clinical and sports applications, new scientific research have emerged around this topic in recent years (Hayman & Kam, 2008; Zhang et al., 2020). The most abundant capsaicinoid in peppers is capsaicin (trans-8-methyl-N-vanillyl-6-nonenamide), a vanilloid found in the placental tissue of *Capsicum* (Basith et al., 2016). The vanillyl moiety is the responsible of capsaicin´s pungency and some of its pharmacological effects in health, pain relief, weight loss and sports performance (Luo et al., 2011; Sharma et al., 2013).

Over the last decade, another group of capsaicinoids analogues called capsinoids, has been studied (Lang et al., 2009; Luo et al., 2011). Capsinoids are mainly found in CH-19 Sweet which is a non-pungent modification of the traditional peppers (Lang et al., 2009). Although structural similarities between both active principles exist (an aliphatic hydroxyl group in vanillyl alcohol with a fatty acid), their central linkages are different, changing an amide moiety for an ester moiety (Luo et al., 2011).

Capsaicinoids and capsinoids interact with the transient receptor potential vanilloid 1 (TRPV1) (Hayman & Kam, 2008; Vriens et al., 2009), which exerts the most important physiological functions of this substances. TRPV1 agonists play an important role in the management of perceived heat and analgesia due to the downregulation of the voltage activated calcium channels and the reduction of inflammatory hyperalgesia states (Baamonde et al., 2005; Hayman & Kam, 2008).

These mechanisms could exert relevant functions in sports performance. Accordingly, de Moura e Silva et al. (2021a) performed a systematic review where some possible performance-enhanced pathways of capsaicin are presented. Between the proposed ergogenic effects of capsaicinoids and capsinoids are found: (a) An increase in the calcium released by sarcoplasmic reticulum; (b) a rise in fatty acid oxidation; (c) an analgesic effect; (d) an increase in glycogen efficiency; and (e) a positive effect around the acethylcoline levels.

Moreover, resistance training (RT) and interval training performance depend on both peripheral and central fatigue (Froyd et al., 2013; Márquez et al., 2017; Zając et al., 2015). Capsaicinoids and capsinoids target neuromuscular processes involved in resistance and interval training-induced fatigue. In fact, as mentioned above, the TRPV1 activity of this active principles can modulate critical pathways in short-term-high-intensity modalities (de Moura e Silva, Cholewa, Billaut, Jäger, de Freitas, Lira, & Rossi, 2021a; Hayman & Kam, 2008). Although previous research has focused on topical clinical capsaicin applications (e.g., capsaicin topical cream) (Chrubasik et al., 2010; Mason et al., 2004), more recent studies discussed its plausible oral dietetic supplementation (e.g., capsules and gummies) as ergogenic aid (Cross et al., 2020; de Moura e Silva, Cholewa, Billaut, Jäger, de Freitas, Lira, & Rossi, 2021a). While there is growing research exploring this topic (de Freitas et al., 2018; de Moura e Silva, Cholewa, Jäger, Zanchi, de Freitas, de Moura, Barros, Antunes, Caperuto, Ribeiro, Lira, et al., 2021; Opheim & Rankin, 2012), there is no systematic review specifically looking at this question on high intensity training. Therefore, the purpose of this review was to explore the effects and applications of oral capsaicinoids and capsinoids supplementation on short-term-high intensity exercises, including resistance and interval training, in young males.

METHODS

Experimental approach to the problem

To test the authors´ hypothesis, a systematic review of capsaicinoids or capsinoids effects on high intensity exercise was performed. This systematic review of the literature was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA-P) guidelines (Shamseer et al., 2015; Urrutia & Bonfill, 2010).

Subjects

The pooled participants from all studies included 102 subjects (median = 15; range = 9-20). All studies included healthy young participants (range = 18-30 years), most of them were conducted among trained individuals, only one intervention was performed on untrained subjects (35).

Procedures

Search strategy

On December 6th 2021, and up to December 30th 2021, the search for studies was conducted, without date or language restrictions, on the online databases PubMed/MEDLINE, Scopus, and Web of Science. The syntax used was: ((Capsaicin) OR (Capsaicinoid) OR (Capsinoids) OR (Capsiate)) AND ((Resistance training) OR (strength training) OR (strength exercise) OR (resistance exercise) OR (weight training) OR (hypertrophy training) OR (weightlifting) OR (HIIT) OR (Interval training) OR (high intensity interval training) OR (non-continuous training) OR (high intensity interval exercise) OR (high intensity intermittent exercise) OR (high intensity intermittent exercise) OR (sprint interval training) OR (HIIE)).

The first literature search was conducted by the lead author (PJM). The study selection and secondary searches examining references of main intervention articles and published reviews were carried out by two authors (PJM and CAF).

Inclusion criteria and study selection

Studies were included in the present systematic review if they fulfil the following criteria: (a) conducted in humans (healthy subjects between 15 and 70 years), (b) capsaicinoids or capsinoids were acutely or chronically consumed by the subjects, (c) comparison on the effects of capsaicinoids or capsinoids with placebo and randomization, (d) outcomes analysed included muscle maximal strength (e.g., 1RM; maximal torque), muscle endurance (e.g., total work capacity; total repetitions; fatigue index), perceived exertion, or related outcomes, obtained after acute or chronic resistance training or HIIT interventions. Studies that did not satisfy any of the selected criteria were automatically excluded.

Data extraction

Two authors (PJM and EBV) extracted the following data: (a) author´s names and publication date (year); (b) subject´s characteristics (gender and main age); (c) exercise type; (d) exercise protocol; (e) supplemental protocol; and (f) main outcomes regarding de impact of capsaicinoids or capsinoids on resistance or interval training.

If the data needed were not available in the original documents, we tried to obtain them contacting with researchers. If data could not be obtained, means and standard deviations were extracted from the originals figures and graphics using the validated software (r = 0.99, p < .001) "*Web Plot Digitizer*" (https://apps.automeris.io/wpd/) (Drevon et al., 2017).

Methodological quality assessment
For evaluating the methodological quality of the included studies, the Physiotherapy Evidence Database (PEDro) checklist scale was used. It includes 11 items which must be response with a "*Yes/No*" criteria by researchers (Maher et al., 2003), obtaining a point for every positive answer. Items consist of a selection of methodological key aspects of the experiment, such as, randomization, blinding, attrition, and the reporting data. Additionally, its agreement with other scales (e.g., Cochrane risk of bias tool) has been reported (Moseley et al., 2019) and validated for pharmacological and non-pharmacological randomized controlled trials (Foley et al., 2006). The summary score does not include the first item, therefore, only 10 points can be achieved. PEDro scale classify the obtained score as "*poor*" (0-3), "*fair*" (4-5), "*good*" (6-8) and "*excellent*" (9-10) the methodological quality. The methodological quality assessment was performed independently by two researchers (EBV and CAF). When a discrepancy in the scale criteria appeared, it was discussed with a third author (PJM) until agreement was reached.

RESULTS

Study selection

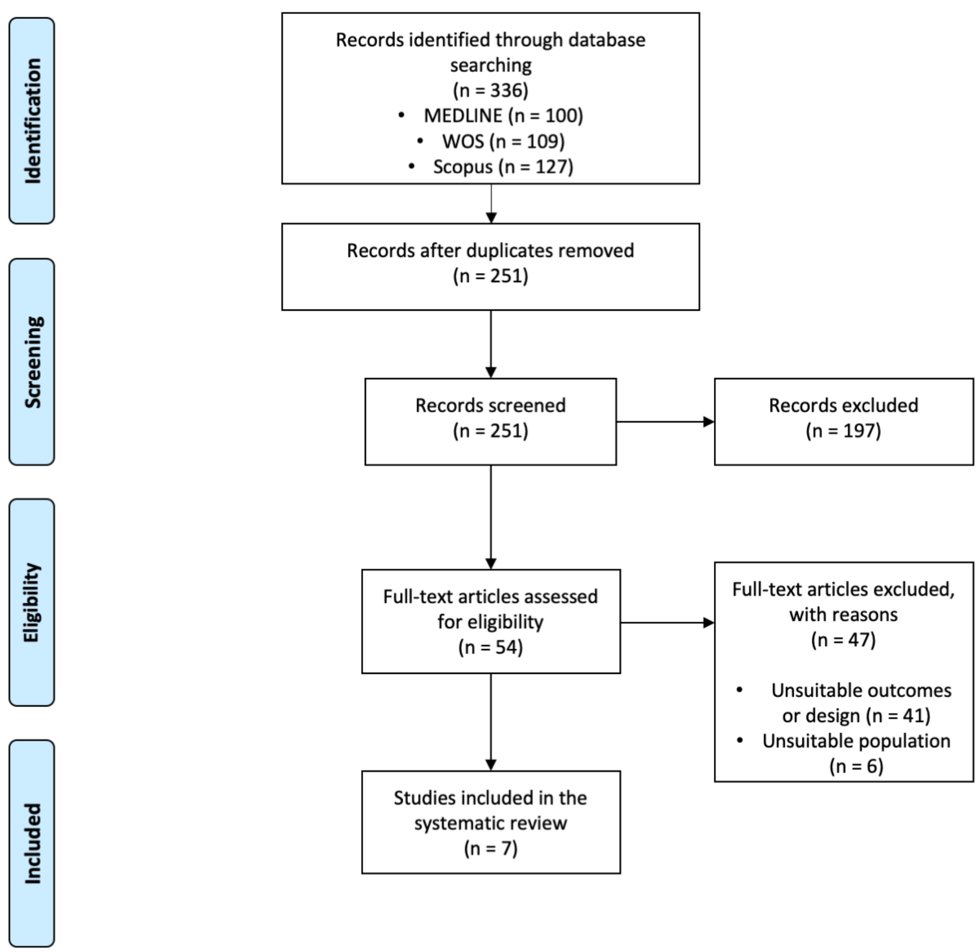


Figure 1. Flow diagram of the literature search.

Table 1 Effects of capsaicin on maximal strength endurance, total weight lifted, total and medium sprint time, RPE, fatigue index, peak torque and time to reach 90% VO_2 after resistance and interval training.

Study	Sample	Training status	Type of exercise	Exercise protocol	Supplemental protocol	Main Outcomes (post)	Control group	Supplemented group
Walter et al. (2009)	20 (20M) 21.5 ± 1.4 years	Recreationally active	Resistance training after graded cycling exercise	Graded 25 W incremental test every 2 min until exhaustion. 1-RM in bench press and leg press	Acute SUP: 200 mg caffeine, 33.34 mg capsaicin, 5 mg bioperine, 20 mg niacin CON: 175 calcium carbonate, 160 mg microcrystalline cellulose, 5 mg stearic acid, 5 mg magnesium stearate	Bench press (kg): Leg press (kg):	82.3 (±5.1) 225.8 (±12.5)	82.7 (±5.4) 224.0 (±12.9)
Opheim et al. (2012)	19 (9M) 22.6 ± 2.6 years	Experienced athletes	Repeated Sprint	15x30-m sprints on 35 s intervals	One week SUP: capsaicin, 6 capsules of 4.3 mg) CON: 6 gelatine capsules of 500 mg of toasted wheat flour	Medium sprint time (s): Total sprint time (s):	4.8 (±0.2) 71.9 (±3.5)	4.7 (±0.2) 71.1 (±3.6)
de Freitas et al. (2018)	10 (10M) 22.7 ± 4.0 years	Young men. At least 1 year experience.	Resistance training	4 sets of back squats until muscular failure with 70% 1RM/ 90 s rest.	Acute SUP: 12 mg of purified capsaicin CON: 50 mg of starch	Total weight lifted (kg): Total repetitions until failure: RPE:	3,179.6 (±942.4) 34.8 (±14.8) 18.3 (±1.7)	3,919.4 (±1,227.4) 42. 3 (±14. 7) 17.2 (±1.0)
de Freitas et al. (2019)	13 (13 M) 24.4 ± 4.0 years	Active men. At least 6 months experience	HIIE	15 s at 120% of sVO_2 peak/ 15 s of passive recovery until exhaustion	Acute SUP: 12 mg of purified capsaicin CON: 12 mg of starch	Time to reach 90% VO_2 peak (s): Number of efforts performed: RPE:	165 (±138) 89 (±30) 18 (±1)	266 (±204) 102 (±34) 18 (±1)
de Freitas et al. (2019)	11 (11 M) 23.3 ± 2.2 years	At least 1 year experience in resistance training.	Concurrent HIIE and resistance training	5-km intermittent run in 1:1 effort and pause ratio; 10 minutes passive rest and 4x70% 1RM back squats until failure.	Acute SUP: 2 dose of 12 mg of purified capsaicin CON: 2 dose of 12 mg of starch	RPE: Total repetitions until failure: Total weight lifted (kg):	8.1 (±1.3) 30.5 (±10.2) 1,838.9 (±624.1)	6.9 (±0.9) 34.9 (±8.2) 2,077.6 (±465.2)
Cross et al. (2020)	9 (5F/4M) 23.6 ± 1.5 years	Recreationally active subjects.	Resistance training	120 maximal isokinetic knee extensions at 120º per second with passive flexion at 240º per second	Acute SUP: 1.2 mg of capsaicin containing gummy. CON: eucaloric placebo	Peak torque (N·m-1): Summed torque (N·m-1): Fatigue index (%):	118.8 (±41.3) 7823 (±2611) 48.7 (±21.0)	126.0 (±40.4) 8012 (±2771) 56.0 (±17.1)
de Moura et al. (2021)	20 (M) 18-30 years	Young untrained males	Resistance training	3 sets of 45º leg press, 3 sets of bench press until failure with 70% of 1RM and 90s rest between sets.	Chronic (6 weeks)/ mixed SUP: 12 mg of capsiate capsules CON: Starch capsules	Muscle strength at 45 leg press (kg) Muscle strength at bench press (kg) Total weight lifted at 45 leg press (kg): Total repetitions until failure at 45 leg press: Total weight lifted at bench press (kg): Total repetitions until failure at bench press: Peak power for 3 sets (W):	388.9 (±56.0) 63.9 (±15.1) 20,675.0 (±5036.7) 53.0 (±9.7) 1,912.8 (±458.2) 30.3 (±5.6) 3,514.4 (±1073.2)	380.6 (±86.5) 61.7 (±16.4) 21,962.3 (±5497.7) 58.1 (±8.5) 1,787.0 (±614.0) 28.8 (±4.8) 3,753.1 (±715.9)

Abbreviations ordered alphabetically: BL: Baseline; F: Female; M: Male; RPE: Rating of perceived exertion; sVO_2: Speed associated with VO_2; data are presented as mean ± SD.

Our initial search included a total of 336 studies, of which 251 were available after eliminating duplicates. After title and abstract screening only 54 documents were suitable for full read selection. Finally, 7 studies met all the inclusion criteria and were included in this systematic review. Included research are expressed accordingly to PICOs criteria on Table 1.

The flow diagram of the study selection is depicted in Figure 1.

Study characteristics
Capsaicinoids or capsinoids administration followed an acute protocol (i.e., 45 minutes pre-exercise) in 5 of the 7 studies (Cross et al., 2020; de Freitas, Billaut, et al., 2019a; de Freitas, Cholewa, et al., 2019; de Freitas et al., 2018; Walter et al., 2009), a chronic/mixed six-weeks protocol (de Moura e Silva, Cholewa, Jäger, Zanchi, de Freitas, de Moura, Barros, Antunes, Caperuto, Ribeiro, Pereira dos Santos, et al., 2021) and a 1-week intervention (Opheim & Rankin, 2012). Although the most common dose was 12 mg of purified capsaicin (de Freitas, Billaut, et al., 2019b; de Freitas, Cholewa, et al., 2019; de Freitas et al., 2018; de Moura e Silva, Cholewa, Jäger, Zanchi, de Freitas, de Moura, Barros, Antunes, Caperuto, Ribeiro, Pereira dos Santos, et al., 2021), reported protocols range between 1.2 and 33.34 mg of capsaicin (Cross et al., 2020; Walter et al., 2009).

Out of a multicomponent supplemental protocol study (Opheim & Rankin, 2012), the other 6 interventions used mono ingredient capsaicinoids or capsinoids products. Between the 7 studies selected, only one of them chose a capsiate supplemental protocol (de Moura e Silva, Cholewa, Jäger, Zanchi, de Freitas, de Moura, Barros, Antunes, Caperuto, Ribeiro, Pereira dos Santos, et al., 2021), the other 6 interventions were performed with capsaicin products.

The application vehicle were capsules in 6 of the 7 studies, despite of that Cross et al., (2020), selected a gummy low dose administration (1.2 mg of capsaicin), which was compared with a eucaloric placebo. Dosages ranged from 33.34 mg of capsaicin in the multi-ingredient protocol to 12 mg of capsaicin or capsiate in the most study selection. Only one study used a different dose of 25.8 mg capsaicin (Opheim & Rankin, 2012).

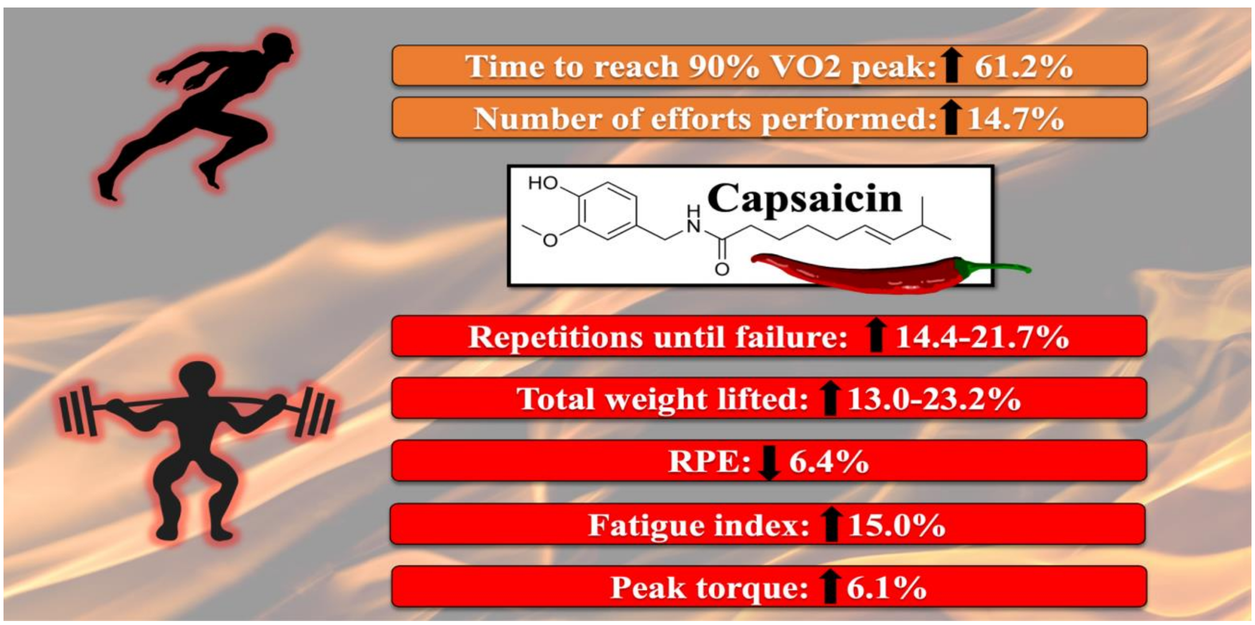
Methodological quality assessment
The mean score on the PEDro scale was 8.3 ± 1.4 (Table 2). Three studies scored 10 points and were classified as being of excellent methodological quality. Four studies scored 7, or 8 points and were classified as being of good methodological quality.

Effects of capsaicinoids and capsinoids on sports performance
Of the 7 studies included in this review, 3 included resistance training interventions, 2 included concurrent training protocol (i.e., resistance training + aerobic training), and 2 included high-intensity-interval training. This data is summarized in Table 1 and Figure 2.

Effects of capsaicinoids and capsinoids on resistance training
From the 7 studies included in this review, 5 of them applied a RT protocol. Walter et al., (2009) elucidated the effects of a multicomponent capsaicin-rich formula in 1-RM leg press and bench press after a 25 W graded incremental test until exhaustion. In this case, there were no differences between supplementation and placebo control group (i.e., 175 calcium carbonate, 160 mg microcrystalline cellulose, 5 mg stearic acid, 5 mg magnesium stearate) in 1-RM (kg) strength in bench press (CON: 82.4 ± 5.1; SUP: 82.7 ± 5.3) or leg press (CON: 225.8 ± 12.5; SUP: 224.0 ± 12.9).

Table 2. Results from the PEDro checklist.

Study	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Total score
Cross et al. (2020)	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	7
de Freitas et al. (2018)	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
de Freitas et al. (2019a)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
de Freitas et al. (2019b)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
de Moura e Silva et al. (2021)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Opheim et al. (2012)	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	7
Walter et al. (2009)	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8



Note. Orange boxes: denotes HIIT outcomes. Red boxes: denotes resistance training outcomes. Black arrows represent positive increments or reductions of the selected. outcome. Range values: represent the results from two or more studies.

Figure 2. Positive effects of capsaicin supplementation on resistance training and HIIT variables compared to controlled placebo.

Other 3 studies evaluated the impact of capsaicin supplementation on maximal effort strength endurance training. The 3 protocols included were performed in multi-joint exercises. One of the interventions used a pre-exhaustion high-intensity-interval-exercise task before resistance training (de Freitas, Cholewa, et al., 2019). After 5-km intermittent run with a 1:1 work to rest ratio, a 4x70% RM in back squats until failure was performed. A significant improvement in total repetitions until failure (CON: 30.5 ± 10.2; SUP: 34.9 ± 8.2), total weight lifted (kg) (CON: 1,838.9 ± 624.1; SUP: 2,077.6 ± 465.2) and a lower RPE between conditions (CON: 8.1 ± 1.3; SUP: 6.9 ± 0.9) was observed in favour of the capsaicin group.

Previous research (de Freitas et al., 2018) investigated the impact of a 12 mg purified capsaicin formula in 4 sets of back squats with 70% RM in young men. In this study a positive raised in total weight lifted (CON: 3,179.6 ± 942.4; SUP: 3,919.4 ± 1,227.4) and repetitions until failure (CON: 34.7 ± 14.8; SUP: 42.3 ± 14.7) was observed in capsaicin condition respect to placebo group. A lower increment in rated of perceived exertion (RPE) was also documented in capsaicin supplemental group (SUP: 17.2 ± 1.0) versus placebo condition (CON: 18.3± 1.7).

In 2021, one study (de Moura e Silva, Cholewa, Jäger, Zanchi, de Freitas, de Moura, Barros, Antunes, Caperuto, Ribeiro, Pereira dos Santos, et al., 2021) compared the impact of a mixed (6 weeks chronic and acute) capsiate supplementation protocol versus placebo in bench press and 45º leg press. After the intervention, a significant strength improvement was observed in upper body strength in favour of supplemental group (CON: Δ% = 5.8 ± 5.2 %; SUP: Δ% = 13.4 ± 9.1 %) but not in lower body strength, peak power, or total repetitions until failure.

Finally, another investigation (Cross et al., 2020) explored the impact of a low dose capsaicin gummy on isokinetic knee extension exercise. In this case, knee extensor peak torque was significantly greater in the capsaicin condition (SUP: 126.0 ± 40.4 N·m-1; CON: 118.8 ± 41.3 N·m-1). However, no significant differences were detected in summed torque (SUP: 8012 ± 2771; CON: 7823 ± 2611 N·m-1) or fatigue index (SUP: 56.0 ± 17.1; CON:48.7 ± 21.0).

Effects of capsaicinoids and capsinoids on high intensity interval training

Only two studies were exclusively focused in high intensity interval training (HIIT). Both experiments used a repeated sprint until exhaustion design. First, (Opheim & Rankin, 2012) did not observed a significant improvement on medium sprint time (s) (SUP:4,7 ± 0.24; CON: 4.8 ± 0.23) or total sprint time (s) (SUP:71.1 ± 3.6; CON: 71.9 ± 3.5) with a high dose capsaicin supplementation (25.8 mg) for one week.

On the other hand, on a 15 s at 120% sVO_2 peak exercise/ 15 s passive recovery protocol (de Freitas, Billaut, et al., 2019b), 12 mg capsaicin supplementation showed a significant improvement in time to reach 90% VO_2 peak (s) (SUP:266 ± 204; CON: 165 ± 138) and the number of efforts performed (SUP:102 ± 34; CON: 89 ± 30).

DISCUSSION

The aim of this systematic review was seeking to outline the current evidence of capsaicinoids and capsinoids supplementation on short-term-high-intensity-exercise modalities (resistance training and HIIT). Our findings suggest some interesting results: (a) capsaicinoids and capsainoids benefit significantly repetitions until failure in 2 of the 3 studies analysed; (b) while maximum strength and weight lifted evidence is mixed, total volume and total weight lifted is increased after capsaicin consumption; (c) Most studies where RPE is examined show a positive effect of capsaicin, nevertheless, not in fatigue index; (d) Capsaicin has a mix impact in high-intensity-interval-training performance, with a positive effect on number of efforts performed and 90% VO_2 peak reach time. However, supplementation does not influence medium sprint time and total sprint time versus placebo in the study where this data is examined.

Supplementation and resistance training

To date, only 5 studies have investigated the effects of capsaicin supplementation in humans developing a resistance training. Of the collected data some methodological differences must be consider for a practical application of our findings.

Our findings suggest a positive impact of capsaicinoids and capsinoids as "*counter-fatigue*" elements due to their positive impact on maximal efforts until failure and rate of perceived effort (de Freitas, Cholewa, et al., 2019; de Freitas et al., 2018). As a TRPV1 agonist, capsaicin mechanisms are linked to an incremental of analgesia and a positive improvement in pain tolerance and nociception (Knotkova et al., 2008; Lebovitz et al., 2012; Ota et al., 2013) which can modify calcium released channels dynamic (Ito et al., 2013; Mahmmoud, 2008; Zhai et al., 2020). For example, in de Freitas et al., (2018) capsaicin group (12 mg) performed more repetitions in all the sets of a 4x70% RM back squats protocol until muscular concentric failure which finally increased significantly total volume (measured as total weight lifted).

These positive effects were also observed in other study (de Freitas, Cholewa, et al., 2019) where capsaicin supplementation was included in a HIIT and resistance training concurrent design. In this experiment, resistance training consisted of 4 sets of 70% RM in back squats where muscular concentric failure was achieved in every set after a 5-km 1:1 work to rest ratio HIIT until exhaustion. To date, this is the unique study where a mono-ingredient capsaicin supplemental protocol (12 mg of capsaicin) examined its effect on concurrent HIIT and resistance training. These effects show a potential strength endurance benefit of capsaicin, due to a lower increment in RPE during sets and the whole session, impacting positively on total weight lifted and repetitions until failure.

Of note, one study (de Moura e Silva, Cholewa, Jäger, Zanchi, de Freitas, de Moura, Barros, Antunes, Caperuto, Ribeiro, Pereira dos Santos, et al., (2021) could not find a significant improvement in lower body strength, peak power, inflammatory response to exercise or total repetitions until failure with a mixed (acute and chronic) capsiate supplementation (12 mg). However, upper body strength and fat-free mass changes were augmented significantly in the supplemental group. These results could be explained by the impact of a chronic TRPV1 stimulation on its physiological dynamics. As a consequence of long term TRPV1 agonists use, a reduction, endocytosis and lysosomal degradation of TRPV1 receptors have been observed (Sanz-Salvador et al., 2012). This mechanism may explain a potential not beneficial effect in non-acute capsaicin supplementation and suggests a potential intermittent or washout benefit in its use.

All studies mentioned above recruited at least 1-year experienced athletes except one (de Moura e Silva, Cholewa, Jäger, Zanchi, de Freitas, de Moura, Barros, Antunes, Caperuto, Ribeiro, Pereira dos Santos, et al., 2021). Curiously, the only other experiment in which capsaicin supplementation did not show a positive effect on resistance training was also performed in non-trained men (Walter et al., 2009). Therefore, training status and experience could be an important variable in TRPV1 agonists supplementation as they modify the capacity of effort application in maximal intensity exercise protocols as we discuss above. On the other hand, this hypothesis should be kept in mind carefully because of Walter et al., (2009) include a multi-ingredient supplemental protocol (200 mg caffeine, 33.34 mg of capsaicin, 5 mg piperine, 20 mg niacin) instead of a purify capsaicin or capsiate form. These findings are also observed in (Cross et al., 2020) where recreationally active subject did not obtain a beneficial response to capsaicin low dose (1.2 mg) administration on summed torque and fatigue index.

Although capsaicin can modulate TRPV1 activity and nociception (Knotkova et al., 2008; Vianna et al., 2018), our data suggest that its supplementation seems safe and does not increase injury risk in exhaustion resistance training tasks (de Freitas, Cholewa, et al., 2019; de Freitas et al., 2018; de Moura e Silva, Cholewa, Jäger, Zanchi, de Freitas, de Moura, Barros, Antunes, Caperuto, Ribeiro, Pereira dos Santos, et al., 2021). As a consequence, capsaicin may improve neuromuscular fatigue perception without a total disinhibition of nervous system alert mechanisms.

Besides some heterogeneity in protocols, results presented herein hypothesize the positive impact of capsaicin supplementation in strenuous resistance training tasks performed by subjects with at least one year experience.

Supplementation and high intensity interval training

As previously note, only 2 studies have explored the impact of capsaicin supplementation on high-intensity-interval training. On the one hand, Opheim et al. (Opheim & Rankin, 2012) did not show an improvement in medium sprint time or total sprint time with 25.8 mg of capsaicin versus placebo. The selected protocol included a 15x30-m interval repeated sprint design with experienced athletes. Unlike resistance training, where experienced subjects benefit from capsaicin supplementation, in this case there were not anyone. One possible reason could be linked to rest intervals. While resistance training studies include efforts with a usual 90 s rest between "*all-out*" sets, sprints protocols used 35 seconds, which could modify energetic dynamic contributions (Neufer, 2018; Ulupınar et al., 2021). Other reason could be related to discomfort of capsaicin supplementation intake in gastrointestinal tract reported in the cited study where 13.5% of participants of withdraw before the end (Opheim & Rankin, 2012). Intestinal cramps, diarrhoea, nausea, flatulence and stomach discomfort were also reported in significant higher rate in capsaicin supplementation group. These findings suggest that high capsaicin dosages (25.8 mg capsaicin) could be deleterious on sports performance. Discomfort data have not been reported in the only other study where capsaicin was supplemented in a high dose way (33.34 mg) (Walter et al., 2009) and the rest data.

Nevertheless, de Freitas et al. (de Freitas, Billaut, et al., 2019a) show and improvement in neuromuscular performance, number of efforts performed, and time to reach 90% of VO_2 peak without changes in VO_2 values. In fact, these results found an increment of 13 extra efforts in capsaicin group which means a 188 s extra activity. In this study was also noticed that total RPE was equivalent between groups, which possibly means that capsaicin group could performed more sets until exhaustion or they could put up with more sets in maximal intensity threshold (RPE = 18). As mentioned by de Freitas, Billaut, et al., (2019b) in their study, capsaicin did not result in an increment in energy cost, EPOC effect or a change in energetic systems as noticed before in rodent research (Luo et al., 2011). Despite the positive effect of capsaicin in peripheral neuromuscular performance, more research in capsaicin bioenergetics mechanisms is needed to understand its impact on human sports metabolism.

Overall, although the current literature on this topic is promising, the low number of studies make necessary future large research to elucidate its real impact.

Potential mechanisms for the ergogenic effects of capsaicinoids and capsinoids

Capsaicinoids and capsinoids supplementation have demonstrated to reduce RPE while enhancing physical performance in humans (de Freitas, Billaut, et al., 2019a; de Freitas, Cholewa, et al., 2019). In this sense, although possible mechanisms such as increased calcium release, acetylcholine levels or available energy have been associated to capsaicinoids and capsinoids ergogenic effects (de Moura e Silva, Cholewa, Billaut, Jäger, de Freitas, Lira, & Rossi, 2021b), physiological changes related to perceptions could play a key role.

As mentioned above, resistance and interval training performance depend on both muscular and neural factors (Froyd et al., 2013; Márquez et al., 2017; Zając et al., 2015). During high-intensity exercise, afferents III and IV seem to contribute to the development of central fatigue (Collins et al., 2018). These small-diameter muscle afferents contribute to the cardiorespiratory and perceptual responses during exercise (de Freitas, Billaut, et al., 2019a; de Freitas, Cholewa, et al., 2019). The increased firing from afferents III and IV is related to higher levels of exercise-related discomfort (Taylor et al., 2016) and RPE (Amann et al., 2010). Feedback from these muscle afferents during fatiguing exercise could directly or indirectly reduce motoneuron firing, which can impair exercise performance by deteriorating motor unit recruitment (Taylor et al., 2016). Besides, they contain TRPV1 receptors, with group IV afferents being the most affected by capsaicin (Kaufman et al., 1982). Knowing that these metabo-sensitive afferents respond to TRPV1 agonists (Kaufman et al., 1982; Mannozzi et al., 2021), capsaicinoids and capsinoids supplementation could have analgesic effects and increase pain tolerance during exercise. Consequently, physical performance could be enhanced by modulating exercise related RPE and/or discomfort levels.

Limitations

All included studies were classified as being of "*excellent*" or "*good*" methodological quality, however, while capsaicinoids and capsinoids supplementation shows an interesting positive effect on maximal efforts until failure performance, some limitations need to be mentioned. First, the low sample of some studies and the low number of total publications make difficult to obtain strong recommendations and extrapolations protocols should be cautiously interpreted. Second, these data where capsaicin supplementation shows an increment in sports performance is mainly reported in experienced resistance trained men, as a consequence, future research in women and novice athletes must elucidate its impact in other populations. Third, although capsaicin is well-tolerated in moderate oral dose (i.e., 1.2-12 mg) long-term studies are required to determine precise future practical applications. To date, capsaicin and capsinoids studies as ergogenic aids range between acute and only 6 weeks of chronic use. On the other hand, HIIT recommendations are low in quantity and mixed in quality, for this reason more studies are needed to assess more precise interventions with capsaicin supplements. Given capsaicin evidence, future research needs to explore and verify the positive findings in larger studies in different training models.

CONCLUSION

Capsaicin may exert a favourable acute effect (i.e., 45 minutes after consumption) in maximal efforts until failure, total load-work, and RPE during training sessions such as resistance training and HIIT. Of note, long-term capsaicin intake might reduce its effect. Collectively, due to the effect of capsaicinoids and capsinoids on neuromuscular performance, rated of perceived effort and the available mechanism's literature about this topic, these compounds could be considered as promising nutraceuticals which could modulate maximal intensity exercise.

AUTHOR CONTRIBUTIONS

The study idea and methodology was conceived by JCC, PJM and CAF. RRC, JF, JCC, CAF and EBV were involved in data collection and/or data treatment. Initial manuscript writing was conducted by CAF and PJM, and all authors critically reviewed the manuscript and approved the final version.

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