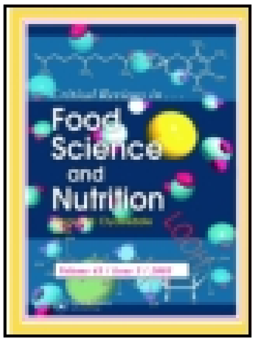

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REVIEW

Is caffeine mouth rinsing an effective strategy to improve physical and cognitive performance? A systematic review

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ABSTRACT

The aim of this study was to perform a systematic review on the effects of caffeine mouth rinsing on physical and cognitive performance. Following a search through 4 databases, 18 studies were found meeting the inclusion criteria (15 for physical performance and 3 for cognitive performance). All selected studies found an improvement in cognitive performance with caffeine mouth rinse. Four studies found positive effects of caffeine mouthwash on physical performance when repeated during exercise, while one study detected a positive effect with a single mouthwash before exercise, but only in a fasted state. Among these studies that showed positive effects, however, three (2 for physical performance and 1 for cognitive performance) presented fair methodological quality. There was also a variety of methodological approaches in the studies that showed no improvement in physical performance with caffeine mouth rinse, which may have influenced the potential to detect the ergogenic effect of caffeine mouth rinse. Thus, the effects of caffeine mouth rinse on physical performance are mixed, but a potential ergogenic effect might be present in a fasted state and when mouthwash is repeated during exercise. Concerning cognitive performance, caffeine mouth rinse seems to be a beneficial strategy.

KEYWORDS
Bitter tastant; cognition; ergogenic aids; exercise; sports nutrition

Introduction

Caffeine is one of the most ergogenic aids used by athletes via different forms of administration such as capsules, tablets, coffee, energy drinks, gels, bars, and gums. After remotion of caffeine from the prohibited substances list of the World Anti-Doping Agency in 2004, the use of caffeine by athletes have considerably increased (Chester and Wojek 2008). However, scientific evidence of caffeine's ergogenic effects on physical performance is known since the 1970s (Costill, Dalsky, and Fink 1978; Ivy et al. 1979). Costill, Dalsky, and Fink (1978) found an increase in time to exhaustion during constant-load exercise (80% of VO_2max) in humans after caffeine intake when compared with the ingestion of a placebo. Since this pioneering study, a growing number of studies investigating the effects of caffeine intake on physical performance have been published and summarized in a recent umbrella meta-analysis that indicated an ergogenic effect of caffeine on a broad range of exercise modes, such as aerobic endurance, anaerobic power, muscular strength, muscle endurance, exercise speed, and vertical jump height (Grgic et al. 2020).

In addition to physical performance, it has been suggested that caffeine ingestion also appears to enhance cognitive performance. A recent meta-analysis (Lorenzo-Calvo et al. 2021) examining the impact of different sources of caffeine (capsules, gums, and drinks) demonstrated that caffeine improves performance (e.g., response accuracy) in different cognitive tests. Caffeine ingestion has also been beneficial during actions of sports involving cognitive aspects (e.g., ball passing accuracy) (Foskett, Ali, and Gant 2009; Stuart et al. 2005). Cognitive and physical performance improvement with caffeine ingestion is currently explained mainly by its antagonist action on adenosine receptors (Guest et al. 2021). Caffeine is similar in structure to adenosine and can bind to its receptors, blocking the action of adenosine at central level. As adenosine inhibits the release of excitatory neurotransmitters in the brain (i.e., dopamine, norepinephrine), caffeine ingestion increases the release of these neurotransmitters, exerting their ergogenic action at central level (Fredholm 1995).

Although caffeine improves physical and cognitive performance, side effects such as anxiety, headaches, and increased blood pressure may be prevalent in some individuals after caffeine ingestion (Pallarés et al. 2013). Therefore, new forms of caffeine administration that may mitigate its side effect would be relevant. In this context, caffeine mouth rinsing has been proposed as an effective alternative to improving both physical and cognitive performance without

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promoting side effects (Best et al. 2021; Wickham and Spriet 2018). Another advantage of this alternative form of caffeine administration would be its immediate action, enabling repeated use during sports competitions and cognitive tasks. Mouth rinsing strategy involves the mouth rinse caffeine for few seconds (5–20 seconds) without further ingestion (Wickham and Spriet 2018). Although the buccal mucosa can absorb caffeine, increased plasma caffeine concentration was not found after caffeine mouth rinsing, probably due to the short time (10 seconds) of the mouth rinse (Doering et al. 2014). The mechanisms involved in a potential ergogenic effect of mouth rinse with caffeine are not entirely known, but two possible mechanisms have been proposed. The first mechanism involves caffeine binding with adenosine receptors located in the oral cavity, promoting an increase in neurotransmitters' release and muscle firing rates (Kamimori et al. 2002). The second mechanism refers to bitter taste receptors located in the mouth directly connected to regions of the brain related to information processing and reward (Gam, Guelfi, and Fournier 2014; Zald, Hagen, and Pardo 2002). These receptors, in turn, are activated when exposed to caffeine, improving mental alertness through dopamine transmission by activation of sensory neurons in the mouth, starting a cascade of transduction events toward the brain (Pickering 2019).

Systematic reviews addressed to investigate the effects of alternative forms of caffeine administration (i.e., chewing gum, mouth rinse, and nasal aerosol) on physical performance are scarce. Only a systematic review examined the effects of caffeine mouth rinsing on physical performance and found a mixed result (Ehlert, Twiddy, and Wilson 2020), possibly due to different methodological approaches adopted in the included studies (e.g., different caffeine concentrations, exercise modes and nutritional state). Since this systematic review, other studies have been published (Barbosa et al. 2020; Figueiredo et al. 2021; Melo et al. 2021; Pak et al. 2020; Karuk, Rudarli Nalcakan, and Pekünlü 2021); therefore, given the current lack of scientific consensus on the effects of caffeine mouth rinsing on physical performance, an updated systematic review would assist to elucidate the potential of caffeine mouth rinsing in sport. On the other hand, the effect of caffeine mouth rinsing on cognitive performance has not been critically reviewed. Thus, this systematic review aims to summarize the studies investigating the effects of caffeine mouth rinsing on physical and cognitive performance.

Material and methods

The present study' protocol was designed following PRISMA (Preferred Reporting Items for Systematic Review, and Meta-Analysis) guidelines. Systematic research literature was performed in March 2021 in the databases of Pubmed, Web of Science, Science Direct and Cochrane to identify original research. The search strategy was performed using the terms and operators "caffeine mouth rinse" OR "caffeine mouthwash" AND "performance" OR "exercise" OR "cognitive performance" OR "physical performance." The analysis was restricted to "English language" and original research articles published in the peer-review journal. Besides, a review of the selected articles' references was performed, and there was no year restriction applied to the search.

Table 1. Description of the PICOS strategy.

PICOS Components	Detail
Participants	Healthy humans
Intervention	Caffeine mouth rinse before and/or during exercise and/or cognitive task
Comparison	Placebo condition
Outcome	Physical and/or cognitive performance (time-based, mean of power/velocity, strength, speed, reaction time, mental fatigue and cognitive control)
Study design	Single and double-blind, randomized controlled trials with crossover design or counterbalanced

Eligibility criteria

Inclusion and exclusion criteria were determined through the PICOS (Participants, Intervention, Comparison, Outcome, and Study Design) application. The PICOS strategy utilized is reported in Table 1.

Study selection and data collection

Two researchers (W.F.S. and J.P.L.S.) independently reviewed the titles, abstracts, and full texts of the selected articles to check eligibility criteria. Any disagreements between these two researchers were resolved through discussion or by majority (M.D.S.C.). The data extraction process was focused on the following information: (1) title, type of publication (original), information on publication (year, country, research center, or department), funding statement, and disclosure of potential conflicts of interest; and (2) design and methods of the study, participants selected (sample size, age, sex of participants), control condition (randomization, type of placebo), intervention (concentration of caffeine solution), and outcomes reported (time, mean power, strength, speed, reaction time, mental fatigue and cognitive control).

Quality assessment

The Physiotherapy Evidence Database (PEDro) scale was used to assess the quality of the articles. Due to the specificity of this review, the PEDro scale was modified as previously suggested (Grgic 2018) and the following question (item 12) was added: "Did the study assess the effectiveness of the blinding to the caffeine condition(s)?." Since the first item is not scored, the total score ranged from 0 to 11. Articles with a total score of 10–11 were classified as excellent, 7–9 as good, 5–6 as fair, and less than 5 as poor methodological quality. Two researchers (WFS and JPLS) independently conducted the quality assessment and disagreement resolved through discussion. A third reviewer was asked (M.D.S.C.) when disagreements remained unsolved.

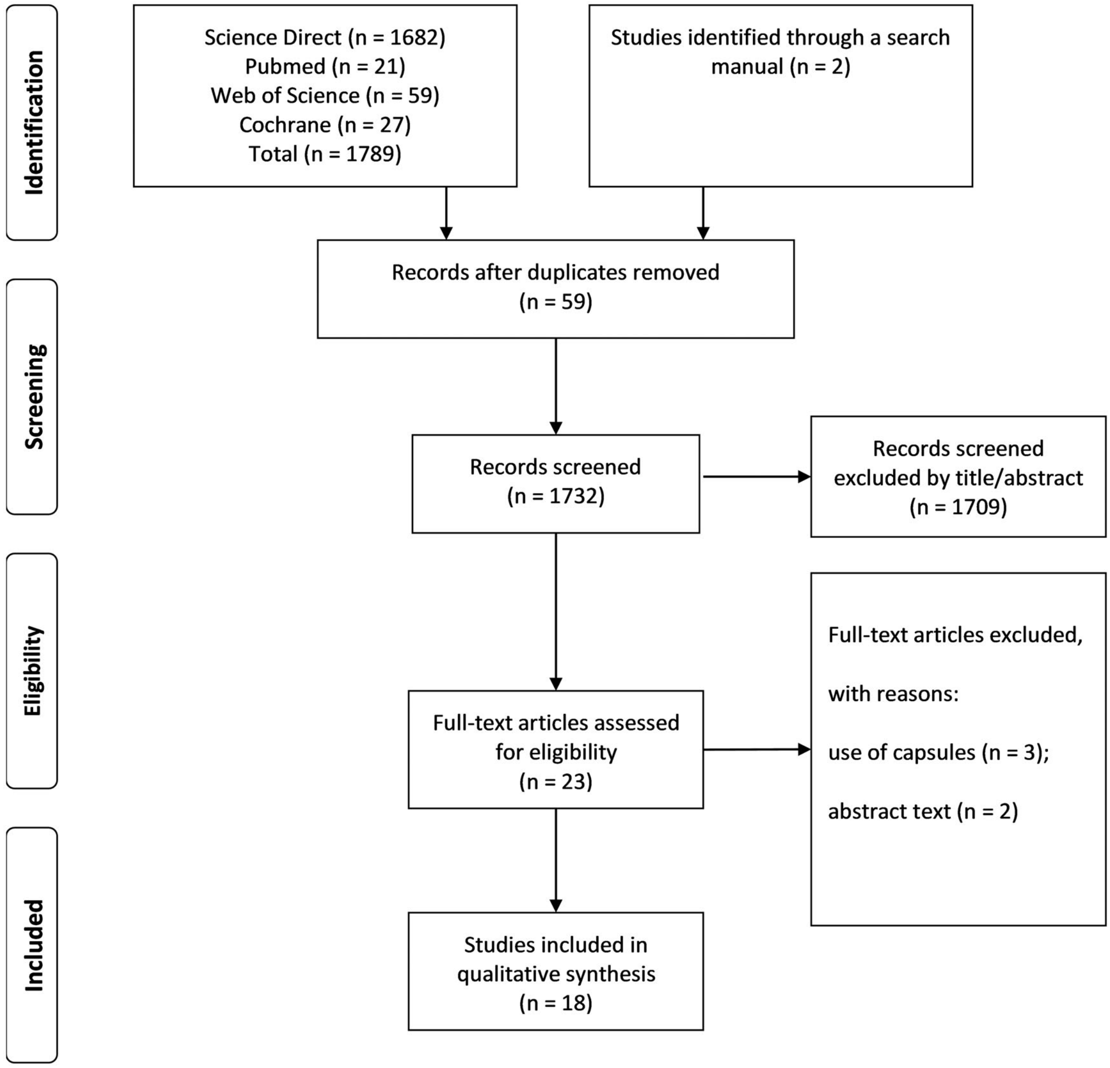

Figure 1. Flowchart of search strategy and selection of studies.

Results

Study selection

A total of 1791 articles were initially identified. Of 1732 that remained after removing 59 duplicates, 1709 articles did not fit with the purpose of the present review. Thus, we evaluated 23 full-text articles, and after applying inclusion and exclusion criteria, we included 18 articles in qualitative synthesis (Figure 1).

Study methodological quality

Among the studies that evaluated physical performance, two articles reached 10–11 points (Clarke, Kornilios, and Richardson 2015; Doering et al. 2014), ten studies 7–9 points (Barbosa et al. 2020; Beaven et al. 2013; Bottoms et al. 2014; Dolan et al. 2017; Figueiredo et al. 2021; Kizzi et al. 2016; Marinho et al. 2020; Karayiğit et al. 2017; Pataky et al. 2016; Sinclair and Bottoms 2014) and three studies 5–6 points (Melo et al. 2021; Karuk, Rudarli Nalcakan, and Pekünlü 2021; Pak et al. 2020) in PEDro scale (Table 2). Concerning studies that verified cognitive performance, two studies reached 9–10 points (De Pauw et al. 2015; Van Cutsem et al. 2018), while a study scored 5–6 points (Pomportes et al. 2017) in PEDro scale (Table 2). None of the 18 selected studies reported conflicts of interest or funding related to commercial interest. The medium PEDro score was 9, with the values ranging from 6 to 10 among studies. However, three studies that showed a positive effect of caffeine mouth rinsing presented fair quality (5–6 points in PEDro scale), being two investigating the effect of caffeine mouth rinsing on physical performance (Melo et al. 2021; Pak et al. 2020) and one on cognitive performance (Pomportes et al. 2017).

Study characteristics

Of the 18 studies selected, 15 studies evaluated the effects of caffeine mouth rinsing on performance. The total of participants was 205, where 183 were men; the remaining 22 were women and included into an unique study (Pak et al. 2020). A total of nine studies performed the caffeine mouth rinsing before exercise (Barbosa et al. 2020; Clarke, Kornilios, and Richardson 2015; Dolan et al. 2017; Figueiredo et al. 2021;

Table 2. Quality score for eligible studies.

Study	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Total
Barbosa et al. 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Beaven et al. 2013	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	9
Bottoms et al. 2014	No	Yes	No	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	7
Clarke, Kornilios, and Richardson 2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10
De Pauw et al. 2015	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Nos	Yes	Yes	No	9
Doering et al. 2014	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	10
Dolan et al. 2017	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	9
Figueiredo et al. 2021	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Karayiğit et al. 2017	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	9
Karuk, Rudarli Nalcakan, and Pekünlü 2021	No	Yes	No	Yes	Yes	No	No	Yes	No	Yes	Yes	No	6
Kizzi et al. 2016	No	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Marinho et al. 2020	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	8
Melo et al. 2021	No	Yes	No	Yes	Yes	No	No	No	No	Yes	Yes	No	5
Pak et al. 2020	No	Yes	No	Yes	Yes	No	No	Yes	No	Yes	Yes	No	6
Pataky et al. 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9
Pomportes et al. 2017	No	Yes	No	Yes	Yes	No	No	Yes	No	Yes	Yes	No	6
Sinclair et al. 2014	No	Yes	No	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	7
Van Cutsem et al. 2018	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	9

Karayiğit et al. 2017; Karuk, Rudarli Nalcakan, and Pekünlü 2021; Marinho et al. 2020; Pak et al. 2020; Pataky et al. 2016), four studies during exercise (Beaven et al. 2013; Bottoms et al. 2014; Kizzi et al. 2016; Sinclair and Bottoms 2014) and two studies in both before and during exercise (Doering et al. 2014; Melo et al. 2021). These solutions were rinsed for 5-second in five studies (Beaven et al. 2013; Bottoms et al. 2014; Pak et al. 2020; Pataky et al. 2016; Sinclair and Bottoms 2014) and 10-second in ten studies (Barbosa et al. 2020; Clarke, Kornilios, and Richardson 2015; Doering et al. 2014; Dolan et al. 2017; Figueiredo et al. 2021; Karayiğit et al. 2017; Karuk, Rudarli Nalcakan, and Pekünlü 2021; Kizzi et al. 2016; Marinho et al. 2020; Melo et al. 2021). Regarding to the mode of exercise, two studies utilized a repeated maximal sprint test [5×6 maximal sprints (24 seconds active recovery)] (Beaven et al. 2013; Kizzi et al. 2016), six studies utilized a time trial protocol (Barbosa et al. 2020; Bottoms et al. 2014; Doering et al. 2014; Figueiredo et al. 2021; Pataky et al. 2016; Sinclair and Bottoms 2014), whereas others utilized Yo-Yo Intermittent Recovery Test Level 1 (Dolan et al. 2017), Wingate test (Karayiğit et al. 2017; Marinho et al. 2020), Taekwondo Anaerobic Intermittent Kick Test (Pak et al. 2020), repeated vertical jump (Karuk, Rudarli Nalcakan, and Pekünlü 2021), maximal strength and resistance exercise (Clarke, Kornilios, and Richardson 2015) and time exhaustion (Melo et al. 2021).

Three studies evaluated the effects of caffeine mouth rinse on cognitive performance (De Pauw et al. 2015; Pomportes et al. 2017; Van Cutsem et al. 2018). The total number of participants was 42, and only one study included women (6 participants) (Pomportes et al. 2017). One study used a single mouth rinse immediately before cognitive task (De Pauw et al. 2015) and other two studies performed repeated mouth rinses before and during cognitive task (Pomportes et al. 2017; Van Cutsem et al. 2018). Regarding the mouth rinse protocol, two studies used 20-second mouth rinse (De Pauw et al. 2015; Pomportes et al. 2017) and one study used 10-second mouth rinse (Van Cutsem et al. 2018). Cognitive performance was assessed using the Stroop task (De Pauw et al. 2015), Flanker task (Van Cutsem et al. 2018), Simon task and duration-production task (Pomportes et al. 2017).

Caffeine solution concentration ranged from 0.032 (Doering et al. 2014) to 2% (Kizzi et al. 2016). The placebo condition included microcrystalline cellulose (Barbosa et al. 2020; Figueiredo et al. 2021), water (Karayiğit et al. 2017), flavored water (Beaven et al. 2013; Gam, Guelfi, and Fournier 2014; Pomportes et al. 2017), artificial saliva (Van Cutsem et al. 2018), distilled water (De Pauw et al. 2015), non-caloric mint essence (Melo et al. 2021) and decaffeinated diet cola (Doering et al. 2014).

Physical performance

Five out of 15 selected studies involving physical performance found a positive effect with caffeine mouth rising compared to placebo (Bottoms et al. 2014; Kizzi et al. 2016; Melo et al. 2021; Pak et al. 2020; Sinclair et al. 2014) (Table 3). Of these studies, four used repeated caffeine mouth rising (Bottoms et al. 2014; Kizzi et al. 2016; Melo et al. 2021; Sinclair et al. 2014) and one used single mouth rinsing before exercise (Pak et al. 2020). In contrast, from the ten studies that found no improvement in physical performance with caffeine mouth rinse, eight used a single mouth rising before exercise (Barbosa et al. 2020; Clarke, Kornilios, and Richardson 2015; Dolan et al. 2017; Figueiredo et al. 2021; Karayiğit et al. 2017; Karuk, Rudarli Nalcakan, and Pekünlü 2021; Marinho et al. 2020; Pataky et al. 2016) and two adopted repeated caffeine mouth rising strategy (Beaven et al. 2013; Doering et al. 2014).

Cognitive performance

All studies found positive effects of caffeine mouth rinse on cognitive performance (Table 4). When compared to placebo, caffeine mouth rinse promoted a decrease in mental fatigue (Van Cutsem et al. 2018) and reaction time (De Pauw et al. 2015), and an increase in cognitive control (Pomportes et al. 2017).

Table 3. Summary and results of the studies reviewed assessing the effect of caffeine mouth rinsing on physical performance.

Study	Study design	N/Sample	Age (years) (mean ± SD)	PEDro Scale	Exercise protocol	Mouth rinse protocol	Mouth rinsing time	Control	Performance improvement
Barbosa et al. 2020	DB	7 M/ recreationally trained	24.6 ± 11.5	9/10	800-m running TT	CAF 0.6% MR (300 mg) immediately before test	10 s	PLA (300 mg of microcrystalline cellulose (0.6%))	↔ any of the performance variables examined
Beaven et al. 2013	DB	12 M/ recreationally trained	32 ± 7.5	10/10	5 × 6 maximal sprints (24 s active recovery)	CAF 1.2% MR prior each sprint	5 s	PLA (non-caloric saccharin solution)	↔ any of the performance variables examined
Bottoms et al. 2014	SB	12 M/healthy active	20.5 ± 0.7	7/10	30-min cycling TT	CAF (128 mg) 0.032% MR every 6 min of exercise	5 s	PLA (water bolus)	↑ distance covered in CAF
Clarke, Kornilios, and Richardson 2015	DB	15 M/recreationally resistance-trained	21 ± 2	10/10	Leg Press 1 RM + 60% of 1 RM to failure	CAF (300 mg; 0.3 g/kg) 1.2% MR before test	10 s	PLA (water)	↔ any of the performance variables examined
Doering et al. 2014	DB	10 M/trained cyclists	32.9 ± 7.5	10/10	0.75 × Wmax × 3.600 kJ cycling TT	CAF (35 mg) MR before and every 12.5% of exercise completion	10 s	PLA (diet cola beverage decaffeinated and decarbonated)	↔ any of the performance variables examined
Dolan et al. 2017	DB	14 M/competitive lacross players	19.9 ± 1.3	10/10	Yo-Yo Intermittent Recovery Test-Level 1	CAF 1.2% MR before test	10 s	PLA (flavored water)	↔ any of the performance variables examined
Karayiğit et al. 2017	DB	10 M/ recreationally active	20.50 ± 1.58	5/10	Wingate test	CAF 2% MR before test (500 mg)	10 s	PLA (water)	↔ any of the performance variables examined
Karuk, Rudarli Nalcakan, and Pekünlü 2021	SB	8 M/athletes	22.3 ± 4.2	8/10	Repeated vertical jump	CAF 1.2% (300 mg) MR 10 s before the test	10 s	PLA (non-caloric sweetener)	↔ any of the performance variables examined
Kizzi et al. 2016	DB	8 M/ recreationally active	23 ± 2	8/10	5 × 6 maximal sprints (24 s active recovery)	CAF 2% MR prior each sprint	10 s	PLA (non-caloric solution)	↑ mean power output in CAF
Marinho et al. 2020	DB	10 M/healthy	24.8 ± 3.7	10/10	Wingate test	CAF 1.2% MR (300 mg) before test	10 s	PLA (non-caloric mint essence solution)	↔ any of the performance variables examined
Pak et al. 2020	SB	18 M and 9 F/ taekwondo athletes	17 ± 3	5/10	Taekwondo anaerobic intermittent test	CAF (6 mg/kg) MR before test	5 s	PLA (25 ml water containing sweetener)	↑ success full kicks
Pataky et al. 2016	DB	25 M and 13 F/ recreationally trained 13 F	21 ± 1	10/10	3-km TT	CAF 1.14% MR before test	5 s	PLA (flavor-matched placebo containing 6 g of saccharine)	↔ any of the performance variables examined
Sinclair et al. 2014	SB	12 M/ND	21.54 ± 1.28	5/10	30-min arm crank TT	CAF 0.032% MR every 6 minutes of exercise	5 s	PLA (water bolus)	↑ distance covered in CAF
Melo et al. 2021	SB	12 M/ physically active	22 ± 2.8	9/10	Cycling TE	CAF 1.2% MR before the test and every 15 minutes during the trial	10 s	PLA (non-caloric mint essence)	↑ TE
Figueiredo et al. 2021	DB	10 M/trained healthy subjects	30.1 ± 6.4	10/10	10-km running TT	CAF 1.2% (300 mg) MR 10 s before the test	10 s	PLA (300 mg of microcrystalline cellulose)	↔ any of the performance variables examined

CAF, caffeine; DB, double-blinded; SB, single-blinded; ES, Effect size; F, females; M, males; MR, mouth rinse; MD, maltodextrin; NR, not reported; RM, repetition maximum; PLA, placebo; PT, peak torque; TE, time exhaustion; TT, time trial.

Table 4. Summary and results of the studies reviewed assessing the effect of caffeine mouth rinsing on cognitive performance.

Study	Study design	N/Sample	Age (years) (mean ± SD)	PEDro Scale	Task	Mouth rinse protocol	Mouth rinsing time	Control	Performance improvement
De Pauw et al. 2015	DB	10 M/ healthy subjects	27 ± 3	10/10	Stroop task (90 min)	CAF 1.2% MR before test	20 s	Artificial saliva	↓ reaction time
Pomportes et al. 2017	SB	16 M 6 F/ physically active	26 ± 8	6/10	Simon task (3 × 3 min) and duration-production task (3 × 3 min)	CAF 67 mg before and twice during the exercise	20 s	Tap water added orange sugarless sirup	↑ temporal performance and cognitive control
Van Cutsem et al. 2018	DB	10 M/ healthy subjects	23 ± 2	10/10	Flanker test (2 × 3 min) and Stroop task (90 min)	CAF 1.2% + MD 6.4% MR before the Stroop test and every 12.5% of completion	10 s	Artificial saliva	↓ mental fatigue

CAF, caffeine; DB, double-blinded; F, females; MD, maltodextrin; M, males; MR, mouth rinse; SB, single-blinded.

Discussion

The present systematic review investigated the effects of caffeine mouth rinsing on physical and cognitive performance. The main finding of the present systematic review was that the effects of caffeine mouth rinse on physical performance are mixed, showing positive effects only in 5 of 15 studies reviewed. In contrast, all studies assessing cognitive performance showed improvement with caffeine mouth rinse.

Although the results of the studies with physical performance included in this review are mixed, we found some similarities in the methodological approach across the studies that showed positive effects on physical performance. Most of these studies used repeated caffeine mouth rising during exercise (Bottoms et al. 2014; Kizzi et al. 2016; Sinclair and Bottoms 2014; Melo et al. 2021). It seems important since improvements in physical performance were obtained when long (10 seconds) but not short (5 seconds) exposure to carbohydrate mouth rising was applied (Sinclair et a. 2014). These findings suggest that for better activation of mouth receptors, more frequent and/or prolonged exposures to caffeine in the oral cavity are needed during exercise to promote a cumulative effect on improving exercise performance. However, further studies combining single vs. multiple and long vs. short caffeine mouth rising during exercise are needed to confirm this hypothesis. In addition, 2 of 5 studies with positive effects presents fair quality, mainly due to adopt a single-blind design, no control condition, and no assessment of blinding effectiveness (Melo et al. 2021; Pak et al. 2020). Therefore, some caution should be employed when interpreting their findings.

Similar to mouthwash with carbohydrate (Ataide-Silva et al. 2016; Lane, Bird, et al. 2013), the magnitude of physical performance improvement promoted by caffeine mouth rinse may also be related to endogenous glycogen stores (i.e., liver and muscle) (Lane, Areta, et al. 2013). While Beaven et al. (2013) found no improvement on repeated-sprint performance using a short period of fasting before exercise (2 hours), Kizzi et al. (2016) observed an increase in both peak and mean power during maximal sprint cycling, but under low muscle glycogen availability. Pak et al. (2020) observed that a single exposure to caffeine mouth rinse before exercise improved performance of successful kicks compared to glucose and placebo during a taekwondo test in a fasted but not in a fed state. It is also important to note that most studies with no caffeine mouth rinse effect on physical performance were performed in individuals under a fed state (Clarke, Kornilios, and Richardson 2015; Doering et al. 2014; Dolan et al. 2017; Marinho et al. 2020; Pataky et al. 2016). From an evolutionary viewpoint, bitter taste receptors may respond better in conditions where muscle and liver glycogen stores are depleted since such receptors' sensitivity may be reduced in a fed state (Beelen et al. 2009). In support of this assumption, increased activation of the primary taste cortex (i.e., insular cortex) with the presence of caffeine in the mouth has been found in a hunger condition (i.e., fasted state), but not in a satiety condition (i.e., fed state) (Haase, Cerf-Ducastel, and Murphy 2009). Interestingly, while participants from Doering's study performed a cycling time trial 1 hour after the last meal, other studies found improvement in physical performance with caffeine mouth rinsing 4 hours postprandial (Bottoms et al. 2014; Sinclair and Bottoms 2014). One possible explanation is that a prolonged period between the last meal and exercise (∼4 hours) may have increased the bitter taste receptors' sensitivity contributing to a beneficial effect of caffeine mouth rinsing on physical performance. Therefore, caffeine mouth rinsing seems to be effective in improving physical performance to a greater extent under low carbohydrate availability or fast state.

As caffeine mouth rinse effects are probably mediated by activation of reward and pleasure circuitry impacting perception of effort (Carter, Jeukendrup, and Jones 2004), a non-improvement during high-intensity exercise after caffeine mouth rinse may be due to this mode of exercise already be performed near-maximal perception of effort. This characteristic decreases the possibility of improving in physical performance via reduction of effort perception (i.e., ceiling effect). Furthermore, activation of brain areas associated with reward and pleasure promoted by caffeine mouth rinse may be insufficient to enhance anaerobic performance because this exercise mode is more dependent on intramuscular factors. This is in line with previous data demonstrating a greater magnitude of the effect of caffeine on performance in aerobic than anaerobic exercise (Grgic et al. 2020). Finally, the use of a fixed torque factor ($0.75\,N{\cdot}m{\cdot}kg^{-1}$) in studies with Wingate test may have influenced the lack of beneficial effect of caffeine mouth rinse (Karayiğit et al. 2017; Marinho et al. 2020). Peak power during all-out exercise using low torque factor depends on cycling velocity; as maximal pedaling speed is reached, the beneficial effect of caffeine via increased neural drive may be missed (Glaister et al. 2015). According to this assumption, an increase in peak power with caffeine ingestion was found only when torque factor was increased to $1.15\,N{\cdot}m{\cdot}kg^{-1}$ (Glaister et al. 2015). Thus, further studies should compare the ergogenic effect of caffeine mouth rinse on high-intensity and submaximal exercise tests, and use different torque factors during all-out tests to test these assumptions.

Although the effects of caffeine ingestion on physical performance are well established (Grgic et al. 2020), some findings suggest that there is interindividual variation in response to caffeine ingestion (Del Coso et al. 2019). This interindividual variation seems to be explained by CYP1A2 gene polymorphism that encodes the cytochrome P450 1A2 enzyme, found mainly in the liver, responsible for caffeine's metabolism (Rahimi 2019). Individuals with the AC or CC genotype are categorized as slow metabolizers, whereas those with the AA genotype are fast metabolizers (Guest et al. 2018). However, mouth rinse avoids hepatic metabolism, giving an advantage to some individuals. Only two studies (Figueiredo et al. 2021; Pataky et al. 2016) have evaluated caffeine mouth rinse effect on physical performance in individuals with different CYP1A2 genotypes. Pataky et al. (2016) verified that caffeine mouth rinses no promoted physical performance improvement during a 3-km cycling time trial regardless of CYP1A2 polymorphism. Figueiredo et al. (2021) also did not find an effect of caffeine mouth rinse on performance during a 10-km running trial or a vertical jump in individuals CC homozygotes or AC heterozygotes. Thus, these results suggest that the effects of caffeine mouth rinse on physical performance are independent of the CYP1A2 genotype.

While the studies involving caffeine mouth rinse to improve physical performance showed a mixed effect, studies investigating the effect of caffeine mouth rinse on cognitive performance have successfully demonstrated the effectiveness of caffeine mouth rinse. A more powerful impact on cognitive performance may be expected because the ergogenic effects of caffeine are primarily mediated by central mechanisms. This statement is consistent with the most evident improvement with caffeine mouth rinse in the complex cognitive tests than simple response tests (Hogervorst et al. 1999), which suggest that the effects of caffeine are centrally rather than peripheral sensorimotor mediated. It is important to highlight, however, that all studies investigating the effects of caffeine mouth rinse on cognitive performance did not assess the blinding effectiveness. Given that expectancy concerning the nature of the substance might exert an influence on cognitive task performance (Shabir et al. 2018), future research should quantify the blinding effectiveness for better control of this confounding factor between trials. Despite these issues and the reduced number of studies, the findings of the present review indicate, however, that caffeine mouth rinse is a promising strategy to improve cognitive performance. This strategy may have the potential to benefit sports where success depends on quick decision making (e.g., soccer and basketball). Further studies exploring this last question will be necessary.

Limitations and future studies

It is necessary to acknowledge some of the limitations of the studies selected in the present systematic review. Starting with the sample of studies summarized here, we can observe a high prevalence of males. Therefore, the results presented in this systematic review cannot be generalizable to women, making it necessary to address this question in further studies. Another factor that may interfere with the effectiveness of the caffeine mouth rinse would be the habitual consumption of caffeine; however, only 5 studies (Barbosa et al. 2020; Dolan et al. 2017; Figueiredo et al. 2021; Pataky et al. 2016) reported participant's habitual caffeine intake. The expectancy (placebo effect) cannot be ruled out since those physiological permutations (e.g., changes in motivation and mood states) associated with an expectancy of caffeine use may influence physical and cognitive performance (Shabir et al. 2018). Only four studies selected reported blinding effectiveness (Beaven et al. 2013; Bottoms et al. 2014; Kizzi et al. 2016; Sinclair and Bottoms 2014). Concerning cognitive performance improvement, it is important to highlight the small number of studies found in this area. Therefore, more studies must be carried out to confirm these findings. Finally, future studies should evaluate the influence of other factors on the effectiveness of the caffeine mouth rinse, such as optimal dose, ideal frequency of rinses, sex, habitual caffeine consumption, inter-individual variation in the ability to detect a bitter taste, training level, and different periods between the last meal and exercise.

Conclusion

The findings summarized in the present review suggest that the effectiveness of caffeine mouth rinse on physical performance is mixed. However, a potential ergogenic effect might be present when exercise is performed in a fasted state, and/or caffeine mouth rinse is long and/or repeated during exercise. Finally, our results suggest that beneficial effect of caffeine mouth rinse on cognitive performance is more prominent than on physical performance.

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Authors' contributions

W.F.S. and M.D.S.C. conceived the idea for the review, conducted the study selection, data extraction, methodological quality assessment and drafted the initial manuscript. J.P.L.S. contributed to search strategy, methodological quality assessment and writing the manuscript. L.J.C.F., G.A.F., and A.E.L.S. contributed to data interpretation, writing the manuscript, and its revisions. All authors read and approved the final manuscript.

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