Effects of Combining Caffeine and Sodium Bicarbonate on Exercise Performance: A Review with Suggestions for Future Research

Effects of combining caffeine and sodium bicarbonate on exercise performance: a review with suggestions for future research

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Abstract

This paper aimed to: (a) critically review studies that explored the isolated and combined effects of caffeine and sodium bicarbonate ingestion on exercise performance; (b) discuss some of the possible reasons for the discrepancy in findings; and, (c) provide suggestions for future studies. Out of the eight studies that examined this topic, only one reported that the combined ingestion of both supplements provided additive effects. In other studies, the following findings were observed: (a) only caffeine was ergogenic; (b) isolated and combined ingestion of both supplements was comparably ergogenic; (c) neither isolated nor combined ingestion of caffeine and sodium bicarbonate provided a performance-enhancing effect; and, (d) caffeine and caffeine plus sodium bicarbonate improved performance compared to sodium bicarbonate (but not as compared to placebo). Even though studies used currently recommended protocols of caffeine supplementation and exercise tasks for which the isolated ergogenic effects of caffeine and sodium bicarbonate are already established, the response to sodium bicarbonate supplementation was very variable, which might largely explain the discrepancies in the findings. The protocols of sodium bicarbonate ingestion generally resulted in high incidence and severity of side-effects, which might have had a negative effect on exercise performance. Future studies that optimize protocols of sodium bicarbonate supplementation are needed to fully explore if combining caffeine and sodium bicarbonate indeed provides any additive effects on exercise performance.

Introduction

Caffeine is one of the most commonly ingested psychoactive substances in the world and a highly popular ergogenic aid (Graham, 2001; Mitchell et al. 2014). Current evidence indicates that acute ingestion of caffeine may be ergogenic for aerobic and muscle endurance, muscle strength, power, as well as jumping and sprinting performance (Grgic 2018, Grgic et al. 2018; Grgic, Grgic, et al. 2020; Polito et al. 2016; Southward et al. 2018; Warren et al. 2010). For those interested in supplementing with caffeine, contemporary recommendations are to ingest caffeine in the doses from 3 to 6 mg per kg of body mass 30 to 60 minutes before the start of the exercise session (Grgic, Grgic, et al. 2020; McLellan et al. 2016). After oral ingestion, the time to reach peak plasma concentrations is generally 60 minutes (Graham, 2001). Initially, it was suggested that caffeine increases performed through enhanced fat oxidation and sparing of muscle glycogen, but this hypothesis received little support in the literature (Costill et al. 1978; Graham, 2001). Caffeine's ergogenic potential was also associated with its effects on intracellular calcium ion (Ca^{2+}) release (Fredholm, 1995). However, such effects are generally observed in studies using animal models and doses that would be toxic to humans (Fredholm, 1995). Currently, it is believed that the ergogenic effects of caffeine are explained by its tendency to bind to adenosine receptors (McLellan et al. 2016). Caffeine's molecular structure is similar to that of adenosine. After ingestion, caffeine binds to adenosine A_1 and A_{2A} receptors, subsequently promoting wakefulness, reducing perceived exertion, and ultimately enhancing exercise performance (McLellan et al. 2016). Some of the most common side-effects of caffeine intake include anxiety, tremor, insomnia, elevated heart rate, and headache (Spriet, 2014). The incidence and severity of side-effects associated with caffeine ingestion can be minimized by providing caffeine in lower doses (≤3 mg/kg) (Spriet, 2014).

Another supplement that has been shown to provide performance-enhancing effects is sodium bicarbonate. Current findings indicate that sodium bicarbonate may be acutely ergogenic for several high-intensity tasks, such as intermittent sprints, swimming, boxing, rowing, and muscle endurance (Artioli et al. 2007; Bishop and Claudius, 2005; Carr, Hopkins, et al. 2011; Grgic, Garofolini, et al. 2020; Grgic, Rodriguez, et al. 2020; Lindh et al. 2008; McNaughton and Cedaro, 1991; Siegler and Hirscher, 2010). The most profound effects of sodium bicarbonate are observed for high-intensity tasks that last between 30 seconds and 10 minutes (Heibel et al. 2018; Lancha Junior et al. 2015). Generally, sodium bicarbonate is effective when ingested in the dose of 0.3 g per kg of body mass, approximately 60 to 120 minutes before exercise (Heibel et al. 2018; Lancha Junior et al. 2015). The primary mechanism by which sodium bicarbonate increases exercise performance is related to its effects on dynamic buffering capacity. During high-intensity exercise, there is an increased accumulation of hydrogen ions (H^+). Increased accumulation of H^+ may lead to intramuscular acidosis (i.e., decrease in pH), and acidosis has been identified as a factor that contributes to fatigue and performance decrements (Heibel et al. 2018; Lancha Junior et al. 2015). Additionally, acidosis may impair muscle contraction, given that H^+ may compete with Ca^{2+} for the troponin binding site (Donaldson et al. 1978). The primary aim of supplementation with sodium bicarbonate is to increase blood bicarbonate levels. Under resting conditions, the circulating concentrations of bicarbonate generally range between 23 and 27 mmol/L (Heibel et al. 2018; Lancha Junior et al. 2015). Studies that provide sodium bicarbonate in doses of 0.2 to 0.3 g/kg commonly report increases in blood bicarbonate by 5 to 6 mmol/L (Bishop and Claudius, 2005; Heibel et al. 2018). This increase in blood bicarbonate is coupled with an increase in extracellular buffering, leading to a greater efflux of H^+ out of the muscles active during exercise into the circulation (Heibel et al. 2018; Lancha Junior et al. 2015). An increase in the rate at which accumulating H^+ is removed from muscles active during exercise may contribute to intramuscular pH maintenance, which may ultimately prevent performance loss. Even though a well-established ergogenic aid, there are some side-effects to sodium bicarbonate supplementation that should be considered. Side-effects associated with sodium bicarbonate supplementation vary between individuals, but they most commonly include stomach cramps, nausea, diarrhea, and vomiting (Froio de Araujo Dias et al. 2015; Pruscino et al. 2008; Saunders et al. 2014).

When provided in isolation, both caffeine and sodium bicarbonate may be ergogenic for several exercise tasks. For example, one recent meta-analysis reported that isolated ingestion of caffeine and sodium bicarbonate enhanced performance in the Yo-Yo test, with similar overall effectiveness (Grgic, Garofolini, et al. 2020). In the level 2 Yo-Yo test, effect size of caffeine was 0.31 (95% confidence interval [CI]: 0.12, 0.51; percent change: +14.4%), whereas the effect size for sodium bicarbonate amounted to 0.39 (95% CI: 0.08, 0.70; percent change: +17.5%). Sodium bicarbonate was also reported to enhance muscular endurance by an effect size of 0.37 (95% CI: 0.15, 0.59), which is very similar to the effect size of caffeine for the same muscular quality (effect size: 0.38; 95% CI: 0.29, 0.48) (Grgic, Rodriguez, et al. 2020; Polito et al. 2016). Finally, there is also data that speed (i.e. decreased performance times in events lasting between 45 seconds and 8 minutes) is enhanced with isolated ingestion of caffeine (effect size: 0.41; 95% CI: 0.15, 0.68) and sodium bicarbonate (effect size: 0.40; 95% CI: 0.27, 0.54) (Christensen et al. 2017). It is interesting to note that the effectiveness of caffeine and sodium bicarbonate is similar, even though these supplements enhance performance through different mechanisms. While isolated ingestion of both supplements has been associated with an increase in glycolytic energy contribution during exercise, this effect may or may not be associated with enhanced performance (da Silva et al. 2019; Lopes-Silva et al. 2015, 2018). As noted previously, caffeine primarily acts as an adenosine receptor antagonist, while sodium bicarbonate improves performance due to its effects on H^+ buffering and pH maintenance. Therefore, it is reasonable to speculate that the combined ingestion of both supplements would produce additive effects. Even though this idea has been explored in several studies, the evidence remains largely conflicting and unclear (Carr, Gore, et al. 2011; Christensen et al. 2014; Felippe et al. 2016; Ferguson, 2010; Higgins et al. 2016; Kilding et al. 2012; Pruscino et al. 2008; Rezaei et al. 2019).

Burke (2017) provided an overview of studies that explored supplement interaction. However, the effects of combining caffeine and sodium bicarbonate on exercise performance have only been briefly reviewed, as much of the focus was directed towards repeated use of supplements and individual responses. Additionally, since the review by Burke (2017), additional research has been published (Higgins et al. 2016; Rezaei et al. 2019). Therefore, the aims of this paper were to: (a) critically review studies that explored the isolated and combined effects of caffeine and sodium bicarbonate ingestion on exercise performance; (b) discuss some of the possible reasons for the discrepancy in findings; and, (c) provided suggestions for future research.

Methods

Literature search methodology

To identify studies relevant to this review, literature searches of PubMed/MEDLINE, Scopus, SPORTDiscus, and Open Access Theses and Dissertations databases were undertaken. The following search syntax was used in all databases: “caffeine” AND (“sodium bicarbonate” OR “NaHCO3”). In addition to the main searches, reference lists of the included studies were examined, and forward citation tracking was conducted (i.e., checking the papers that cited the included studies) using the Google Scholar and Scopus databases.

Inclusion criteria

Studies were included in this review if they satisfied the following criteria:

1. Explored the effects of isolated and combined ingestion of caffeine and sodium bicarbonate ingestion on exercise performance
2. Utilized a crossover, placebo-controlled study design
3. Included humans as study participants

Data extraction

From all included studies, the following data were extracted:

1. Study authors and year of publication
2. Sample characteristics
3. Exercise test
4. Sodium bicarbonate and caffeine supplementation protocol
5. pH and blood bicarbonate values (if measured)
6. Side-effects associated with supplementation
7. Main study findings

Methodological quality

Study quality was assessed using the PEDro checklist (Maher et al. 2003). This checklist has 11 items that refer to eligibility criteria, randomization, allocation concealment, blinding of participants, therapists, and assessors, attrition, and data reporting. Each item is scored with a "1" if the criterion is satisfied or with a "0" if the criterion is not satisfied. Even though this checklist has 11 items, the first item is not included in the total score. Therefore, the maximum possible score on the checklist was 10 points. Based on the total score, studies were classified as "excellent methodological quality" (9–10 points), "good methodological quality" (6–8 points), "fair methodological quality" (4–5 points), and "poor methodological quality" (≤3 points).

Results

Search results

A total of 897 potentially relevant references was screened. After excluding the documents based on title, abstract, or full-text, eight studies were included in the review (Carr, Gore, et al. 2011; Christensen et al. 2014; Felippe et al. 2016; Ferguson, 2010; Higgins et al. 2016; Kilding et al. 2012; Pruscino et al. 2008; Rezaei et al. 2019). The flow diagram of the search is depicted in Figure 1.

Summary of the included studies

A detailed summary of each included study is provided in Table 1. All studies utilized a randomized, double-blind design. The sample size in these studies ranged from 6 to 16 participants. Exercise performance was evaluated using a rowing task (two studies), a 3-km cycling time trial (two studies), 200-m swimming, "Special Judo Fitness Tests" (SJFT), cycling to volitional exhaustion, and Karate-specific aerobic test (one study for each task). Caffeine supplementation was provided in the doses from 3 to 6 mg/kg, 30 to 60 minutes before exercise. Sodium bicarbonate was provided in the dose of 0.3 g/kg in all studies and was commonly ingested in several smaller doses. Supplementation started up to three days before the exercise task, or as close as 60 minutes pre-exercise. All studies included a minimum of four trials, namely, a caffeine trial, sodium bicarbonate trial, caffeine plus sodium bicarbonate trial, and a placebo trial. One study also included a control trial where no supplementation was provided (Rezaei et al. 2019). Two studies reported that only caffeine ingestion was ergogenic (Carr, Gore, et al. 2011; Christensen et al. 2014), two reported that isolated and combined ingestion of both supplements was comparably ergogenic (Kilding et al. 2012; Rezaei et al. 2019), and two studies did not find any ergogenic effects (Ferguson, 2010; Pruscino et al. 2008). Additionally, one study (Higgins et al. 2016) reported that caffeine and caffeine plus sodium bicarbonate improved performance compared to sodium bicarbonate (but not placebo), and one study (Felippe et al. 2016) reported that only combined ingestion of caffeine and sodium bicarbonate enhanced performance as compared to placebo. As compared to placebo, effect size of caffeine, sodium bicarbonate, and caffeine plus sodium bicarbonate ranged from 0.09 to 0.92 (median: 0.21), –0.05 to 1.70 (median: 0.22), and 0.05 to 1.26 (median: 0.30), respectively.

Methodological quality

Five studies were categorized as being of excellent methodological quality and three studies were classified as being of good methodological quality (Table 2). None of the studies included in this review were categorized as being of poor quality.

Discussion

There is limited evidence that the combined ingestion of caffeine and sodium bicarbonate provides additive effects on exercise performance. Contrasting data have been reported in the included studies, with the findings suggesting that: only caffeine was ergogenic; isolated and combined ingestion of both supplements was comparably ergogenic; caffeine and caffeine plus sodium bicarbonate improved performance compared to sodium bicarbonate (but not when compared to placebo); none of the supplements provided an ergogenic effect. Possible reasons that might explain the discrepancies in findings are examined in the paragraphs below, coupled with several suggestions for future studies.

Exercise task and caffeine supplementation

When examining the studies included in this review, it is clear that they varied in the exercise tasks used for evaluating performance. Therefore, this could be a possible explanation for the discrepancies in findings. When aiming to explore the effects of combined caffeine and sodium bicarbonate intake on exercise performance, it is important to use exercise tasks for which it has already been established that both supplements are ergogenic when provided in isolation. Previous research found that isolated ingestion of caffeine and sodium bicarbonate may enhance performance in rowing and swimming tasks, SJFT, as well as cycling time trials and cycling to exhaustion (Durkalec-Michalski et al. 2019; Gough et al. 2018; Grgic, Diaz-Lara, et al. 2020; Lindh et al. 2008; MacIntosh and Wright, 1995; McNaughton sand Cedaro, 1991; Southward et al. 2018). Given that the ergogenic effects of caffeine and sodium bicarbonate on these exercise tasks have been previously established, it does not seem that the differences in the used exercise performance tests between the studies explain the discrepancies in the findings. In addition to the exercise tasks, it does not seem that factors related to caffeine supplementation would be responsible for the differences in study results, as the included studies used protocols of caffeine supplementation that are recommended in the literature and are considered to represent the "best practice" (McLellan et al. 2016). Specifically, all studies provided caffeine supplementation 30 to 60 minutes pre-exercise in doses from 3 to 6 mg/kg, and these protocols are highly effective (McLellan et al. 2016). Therefore, this review's main focus is on factors related to the protocols of sodium bicarbonate supplementation.

Increases in blood bicarbonate

As mentioned previously, the primary aim of sodium bicarbonate supplementation is to increase levels of blood bicarbonate (Heibel et al. 2018). Previous research has suggested that increases by 5 and 6 mmol/L (from baseline levels to levels recorded pre-exercise) are needed to experience a *potential* and *almost certain* ergogenic effect of sodium bicarbonate, respectively (Heibel et al. 2018). Four included studies did not measure blood parameters and, therefore, the increases in blood bicarbonate in these studies remain unclear (Christensen et al. 2014; Felippe et al. 2016; Ferguson, 2016; Rezaei et al. 2019). Out of the studies that reported these data, in two studies (Carr, Gore, et al. 2011; Kilding et al. 2012), acute increases in blood bicarbonate were below 5 mmol/L, and in two studies above 5 mmol/L (Higgins et al. 2016; Pruscino et al. 2008). Interestingly, in the only study (Kilding et al. 2012) out of these four that reported ergogenic effects of sodium bicarbonate ingestion (either alone or in combination with caffeine), the increase in blood bicarbonate was the smallest (+3.4 and +3.7 mmol/L). One study that explored several different parameters between groups of "responders" and "non-responders" to sodium bicarbonate ingestion found that both cohorts experienced similar acute increases in blood bicarbonate (Saunders et al. 2014). Furthermore, there was no significant correlation between acute increases in blood bicarbonate and increases in exercise performance (Saunders et al. 2014). Therefore, the changes in blood bicarbonate are not the sole factor determining the ergogenic potential of sodium bicarbonate. Other factors, such as the associated side-effects, also need to be considered.

Side-effects associated with sodium bicarbonate

As noted previously, due to CO_2 buildup in the gut following sodium bicarbonate ingestion, the use of this supplement can result in quite severe side-effects, such as stomach cramps, diarrhea, and vomiting (Saunders et al. 2014). Generally, studies report that negative side-effects of sodium bicarbonate supplementation are experienced by 10% to 45% of all included participants, even though the incidence and severity of side-effects can vary based on the supplementation protocol utilized (Carr, Slater, et al. 2011; Froio de Araujo Dias et al. 2015; Saunders et al. 2014). This should be considered given that some studies reported that side-effects might moderate the ergogenic effects of sodium bicarbonate. For example, Saunders et al. (2014) found that sodium bicarbonate ingestion was ergogenic for exercise performance only when the participants who experienced gastrointestinal distress were excluded from the analysis. A follow-up trial from the same research group also reported that the side-effects of sodium bicarbonate supplementation impacted the overall exercise responses in at least one out of the four performed trials (Froio de Araujo Dias et al. 2015). In other words, sodium bicarbonate may provide effects on performance that range from ergogenic to ergolytic, and this seems to be somewhat dependent on the experienced side-effects. Indeed, in one of the included studies, caffeine and caffeine plus sodium bicarbonate ingestion enhanced performance only when compared to the isolated ingestion of sodium bicarbonate, but not when compared to the placebo trial (Higgins et al. 2016). In the study by Higgins et al. (2016), the performance was actually the worst when sodium bicarbonate was ingested in isolation, possibly because the participants generally reported high abdominal discomfort pre-exercise in this trial. Similarly to these findings, in the study by Carr, Gore, et al. (2011), only caffeine was found to be ergogenic for rowing performance. Sodium bicarbonate did not increase performance, most likely due to the reports of side-effects (nausea, vomiting, diarrhea, and dizziness) associated with the ingestion of this supplement. In the only study that reported additive effects of combining caffeine and sodium bicarbonate, none of the included athletes reported significant gastrointestinal discomfort in any of the trials (Felippe et al. 2016). Therefore, even though it is not possible to directly determine if side-effects are responsible for the discrepancies in the findings, it seems that minimizing possible side-effects might help to optimize the ergogenic effects of sodium bicarbonate.

Optimizing the response to sodium bicarbonate

Future studies conducted on this topic should consider utilizing protocols of supplementation that lead to considerable acute increases in blood bicarbonate while minimizing the associated side-effects. There are several methods that researchers could consider to accomplish such effects. One aspect is related to the timing of supplementation. Siegler et al. (2012) demonstrated that providing sodium bicarbonate supplementation in the dose of 0.3 g/kg at either 180 minutes, 120 minutes, or 60 minutes before starting with the exercise trials resulted in similar acute increases in blood bicarbonate. However, the severity of the side-effects was the highest at 90 minutes post-ingestion, and then progressively decreased over time. Carr, Slater, et al. (2011) also reported that the incidence of gastrointestinal side-effects was the greatest at 90 minutes after sodium bicarbonate ingestion. In the included studies that reported ergogenic effects of sodium bicarbonate (either in isolation or in combination with caffeine), supplementation started at 120 minutes before exercise (Felippe et al. 2016; Kilding et al. 2012; Rezaei et al. 2019). In the studies were sodium bicarbonate did not improve performance, supplementation was provided from 60 to 90 minutes before the start of the exercise trial (Carr, Gore, et al. 2011; Christensen et al. 2014; Higgins et al. 2016; Pruscino et al. 2008). This might suggest that the participants were required to perform the exercise task at a moment when they experienced the most severe side-effects, which might have had a negative effect on their exercise performance.

Besides the timing of ingestion, another option that could be considered to minimize side-effects, while not compromising increases in blood bicarbonate is the use of delayed-release capsules. Hilton et al. (2019) recently compared the effects of sodium bicarbonate ingested as an aqueous solution or in delayed-release capsules. The incidence and severity of side-effects were significantly lower when sodium bicarbonate was ingested in delayed-release capsules. Additionally, as compared to the aqueous solution, bicarbonate concentrations were significantly higher with delayed-release capsules at 130 minutes, 140 minutes, and 160 minutes post-ingestion. Even though sodium bicarbonate supplementation is generally provided very close to the exercise session, one recent study used a protocol where the supplementation started three days before the exercise test (Delextrat et al. 2018). The participants ingested a daily dose of 0.4 g/kg, split into three equal amounts throughout the day. The last ingested dose was at 7 pm on the day before the test. None or very limited gastrointestinal adverse events were reported by the participants, with no significant difference in the incidence of side-effects between the sodium bicarbonate and placebo trial. This protocol of supplementation also resulted in ergogenic effects on performance of repeated sprints and jumps (Delextrat et al. 2018). Using some of these methods might help to minimize the side-effects associated with sodium bicarbonate supplementation and would help to maximize performance in the conditions where this supplement is ingested.

Finally, there is a possibility that even with optimal protocols of caffeine and sodium bicarbonate supplementation and with the use of exercise tests for which it is already established that both supplements may be ergogenic, there still might not be an additive effect of combining caffeine and sodium bicarbonate. Even though there is logical reasoning to believe that combined caffeine and sodium bicarbonate ingestion would provide additive effects, it needs to be considered that there might be a ceiling effect of acute increases in performance with sports supplements. A ceiling effect might be especially evident in high-level athletes whose performance is already, by definition, towards the upper end of human exercise performance capabilities and might be approaching absolute physical limits (Berthelot et al. 2015). Such ideas, however, remain to tested in future studies.

Statistical analysis and sample size

Some of the discrepancies in findings between the studies could also stem from their respective choices for statistical analysis. Even though a detailed discussion about statistical analyses is beyond the scope of this article, one aspect warrants a brief mention. Specifically, one included study (Carr, Gore, et al. 2011) analyzed data using the Magnitude Based Inferences (MBI) approach. However, MBI was recently criticized due to the inflated type I error rates, and should likely be avoided in future studies conducted on the topic (Sainani, 2018). One additional factor that should be considered is the overall sample sizes in the included studies. Sample sizes in the studies can be generally considered as small, given that they ranged from 6 to 16 participants (median: 10 participants). Using the G*Power software (version 3.1.9.2; Düsseldorf, Germany), and assuming ANOVA: repeated measures, within factors as the statistical test, alpha value of 0.05, the statistical power of 0.80, one group and four measurements (i.e., placebo, caffeine, sodium bicarbonate, and caffeine plus sodium bicarbonate), and a moderate-to-high correlation between repeated measures of 0.80, a total of

15 participants is needed if to goal is to find an effect size of *d* = 0.40. Twenty-six and 56 participants are needed if the goal is to find an effect size of *d* = 0.30 and *d* = 0.20, respectively. Even though it is not fully clear to what extent can the differences in findings between the studies be attributed to their respective sample size, future studies on this topic would certainly benefit from the inclusion of a larger number of study participants.

Practical applications

No conclusive recommendations can be provided for athletes interested in combining caffeine and sodium bicarbonate supplementation due to the contrasting findings among the included studies. However, even though research is generally focused on mean differences, the importance of individual responses in sports nutrition has been recently recognized (Swinton et al. 2018). While in one study, only caffeine ingestion was ergogenic, individual responses highlight that some individuals experienced the best responses after ingesting sodium bicarbonate or caffeine and sodium bicarbonate (Christensen et al. 2014). Until future research is performed, recommendations are to use current guidelines for isolated caffeine and sodium bicarbonate supplementation as a starting point and then further experiment with different protocols to optimize the individual response.

Conclusion

Only one study that explored the isolated and combined effects of caffeine and sodium bicarbonate on exercise performance reported that a combination of both supplements provides additive effects. In other studies, the following findings were observed: (a) only caffeine was ergogenic; (b) isolated and combined ingestion of both supplements was comparably ergogenic; (c) neither isolated nor combined ingestion of caffeine and sodium bicarbonate provided a performance-enhancing effect; and, (d) caffeine and caffeine plus sodium bicarbonate improved performance compared to sodium bicarbonate (but not when compared to placebo). Even though the studies used currently recommended protocols of caffeine supplementation and exercise tasks for which the isolated ergogenic effects of caffeine and sodium bicarbonate are already established, the response to sodium bicarbonate supplementation was variable, which could largely explain the discrepancies in the findings. The protocols of sodium bicarbonate ingestion generally resulted in high incidence and severity of side-effects, which might have harmed exercise performance. Future studies that optimize the protocols of supplementation are needed to fully explore if the combined and caffeine and sodium bicarbonate ingestion provide any additive effects.

Declaration of interest

No conflicts of interest.

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Figure 1. Flow diagram of the search and study selection process

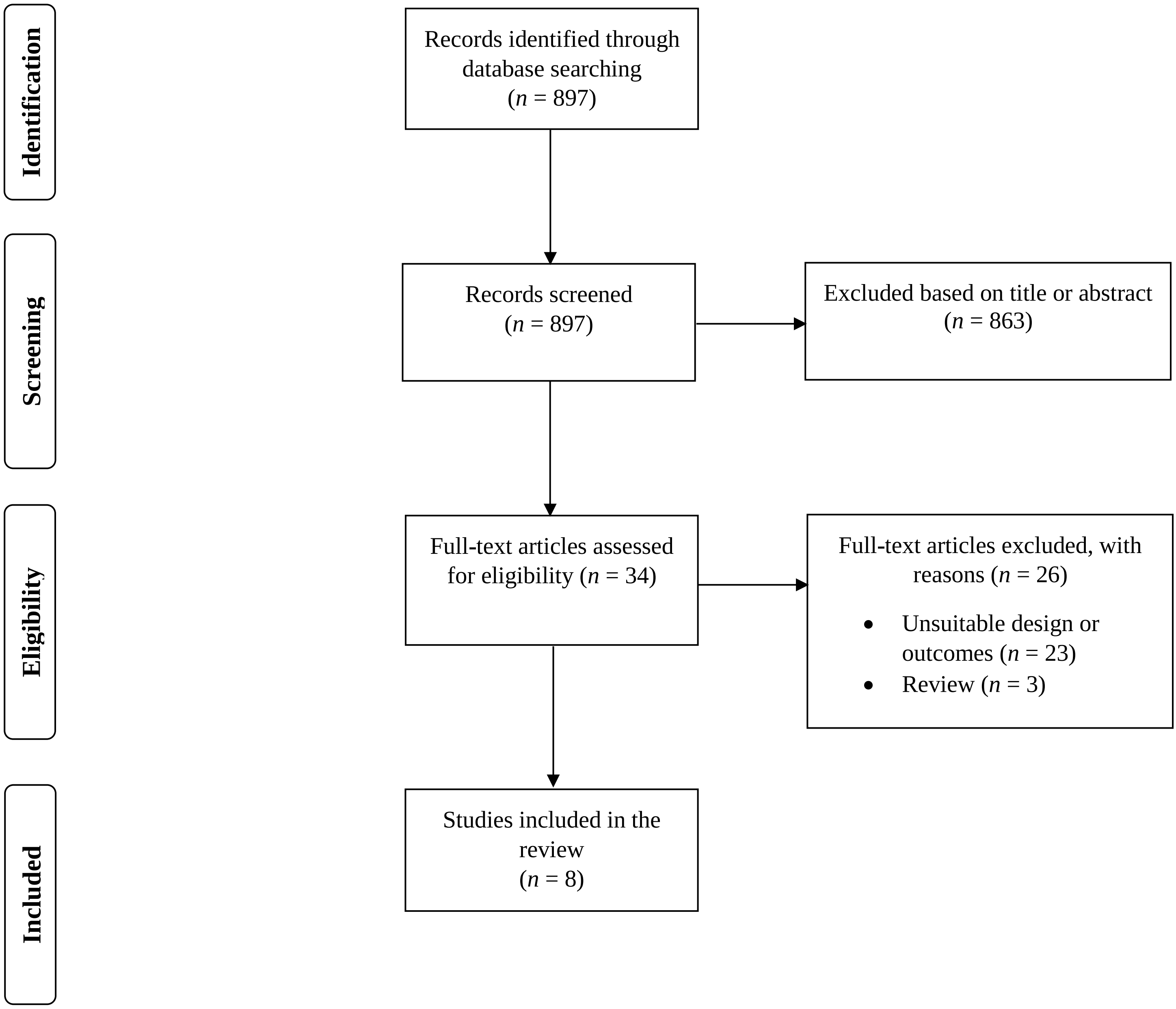

Table 1. Summary of studies included in the review

Study	Study participants	Exercise task	Supplementation protocols	Changes in pH and blood bicarbonate	Side effects	Main findings	Effect size*
Carr et al. (2011)	8 well-trained rowers (6 men and 2 women)	2000-m rowing	Caffeine: dose of 6 mg/kg ingested 30 min before exercise Sodium bicarbonate: an overall dose of 0.3 g/kg ingested in smaller doses 90 min and 30 min before exercise	**pH** *Pre-supplementation* Placebo: 7.40 ± 0.1 Caffeine: 7.40 ± 0.1 Sodium bicarbonate: 7.40 ± 0.05 Caffeine and sodium bicarbonate: 7.39 ± 0.2 *Pre-exercise* Placebo: 7.39 ± 0.3 Caffeine: 7.43 ± 0.3 Sodium bicarbonate: 7.46 ± 0.2 Caffeine and sodium bicarbonate: 7.48 ± 0.2 **Bicarbonate (mmol/L)** *Pre-supplementation* Placebo: 25.3 ± 1.1 Caffeine: 24.3 ± 1.1 Sodium bicarbonate: 24.6 ± 1.1 Caffeine and sodium bicarbonate: 24.7 ± 1.3 *Pre-exercise* Placebo: 24.4 ± 1.1 Caffeine: 24.3 ± 1.0 Sodium bicarbonate: 29.1 ± 1.9 Caffeine and sodium bicarbonate: 29.2 ± 2.9	With caffeine, participants reported irregular heartbeat, increased alertness, hand tremor, and feeling hyperactive and on edge. With sodium bicarbonate, participants reported nausea, vomiting, diarrhea, and dizziness.	As compared to placebo, only caffeine enhanced performance	*Power output* Caffeine: 0.13 Sodium bicarbonate: 0.03 Caffeine and sodium bicarbonate: 0.10 *Rowing time* Caffeine: 0.13 Sodium bicarbonate: -0.03 Caffeine and sodium bicarbonate: 0.05

Christensen et al. (2014)	12 elite rowers (11 men and 1 woman)	6 minutes of rowing	Caffeine: dose of 3 mg/kg ingested 45 min before exercise Sodium bicarbonate: an overall dose of 0.3 g/kg ingested 75 min before exercise	Not assessed	Even though stomach discomfort was the highest in the sodium bicarbonate and caffeine plus sodium bicarbonate trials, there was no significant difference (p = 0.10) between the conditions	As compared to placebo and sodium bicarbonate, only caffeine and caffeine plus sodium bicarbonate enhanced performance	*Rowing distance* Caffeine: 0.13 Sodium bicarbonate: -0.05 Caffeine and sodium bicarbonate: 0.12
Felippe et al. (2016)	10 judokas (all men)	SJFT	Caffeine: dose of 6 mg/kg ingested 60 min before exercise Sodium bicarbonate: an overall dose of 0.3 g/kg ingested in smaller doses 120 min, 90 min, and 60 min before exercise	Not assessed	No significant difference between the conditions in the gastrointestinal-discomfort questionnaire	When considering the results from all three SJFTs, only caffeine plus sodium bicarbonate improved performance as compared to placebo	*Number of throws* Caffeine: 0.67 Sodium bicarbonate: 0.57 Caffeine and sodium bicarbonate: 1.07
Ferguson (2010)	16 cyclists (all men)	3-km cycling time trial	Caffeine: dose of 6 mg/kg ingested 60 min before exercise Sodium bicarbonate: an overall dose of 0.3 g/kg ingested in smaller doses 20 h, 14 h, 8 h, and 2 h before exercise	Not assessed	Not assessed	No significant differences between trials	*Power output* Caffeine: 0.12 Sodium bicarbonate: 0.08 Caffeine and sodium bicarbonate: 0.30 *Cycling time* Caffeine: 0.31

							Sodium bicarbonate: 0.15 Caffeine and sodium bicarbonate: 0.48
Higgins et al. (2016)	13 non-cycling trained individuals (all men)	Cycling to volitional exhaustion	Caffeine: dose of 5 mg/kg ingested 60 min before exercise Sodium bicarbonate: an overall dose of 0.3 g/kg ingested 60 min before exercise	**pH** *Pre-supplementation* Placebo: ~7.42 Caffeine: ~7.42 Sodium bicarbonate: ~7.42 Caffeine and sodium bicarbonate: ~7.42 *Pre-exercise* Placebo: ~7.41 Caffeine: ~7.41 Sodium bicarbonate: ~7.46 Caffeine and sodium bicarbonate: ~7.46 **Bicarbonate (mmol/L)** *Pre-supplementation* Placebo: 24 ± 3 Caffeine: 25 ± 2 Sodium bicarbonate: 25 ± 2 Caffeine and sodium bicarbonate: 24 ± 2 *Pre-exercise* Placebo: 24 ± 2 Caffeine: 25 ± 2 Sodium bicarbonate: 33 ± 1 Caffeine and sodium bicarbonate: 31 ± 2	Pre-exercise and post-exercise, abdominal discomfort was greater in the sodium bicarbonate and caffeine plus sodium bicarbonate trials, as compared to placebo. No significant differences between conditions for gut fullness	Caffeine and caffeine plus sodium bicarbonate enhanced performance as compared to isolated ingestion of sodium bicarbonate, but not as compared to placebo	Not presented

Kilding et al. (2012)	10 well-trained cyclists (all men)	3-km cycling time trial	Caffeine: dose of 3 mg/kg ingested 60 min before exercise Sodium bicarbonate: an overall dose of 0.3 g/kg ingested in smaller doses 120 min and 90 min before exercise	**pH** *Pre-supplementation* Placebo: 7.49 ± 0.70 Caffeine: 7.47 ± 0.64 Sodium bicarbonate: 7.45 ± 0.71 Caffeine and sodium bicarbonate: 7.46 ± 0.67 *Pre-exercise* Placebo: 7.34 ± 0.90 Caffeine: 7.36 ± 0.87 Sodium bicarbonate: 7.43 ± 0.93 Caffeine and sodium bicarbonate: 7.43 ± 0.92 **Bicarbonate (mmol/L)** *Pre-supplementation* Placebo: 25.5 ± 1.4 Caffeine: 25.0 ± 1.1 Sodium bicarbonate: 25.5 ± 1.9 Caffeine and sodium bicarbonate: 25.1 ± 1.4 *Pre-exercise* Placebo: 20.5 ± 2.5 Caffeine: 20.1 ± 2.4 Sodium bicarbonate: 29.2 ± 4.1 Caffeine and sodium bicarbonate: 28.5 ± 3.8	No significant differences between conditions for gastric discomfort	Caffeine, sodium bicarbonate, and caffeine plus sodium bicarbonate ingestion enhanced performance as compared to placebo	*Power output* Caffeine: 0.21 Sodium bicarbonate: 0.24 Caffeine and sodium bicarbonate: 0.23 *Cycling time* Caffeine: 0.22 Sodium bicarbonate: 0.25 Caffeine and sodium bicarbonate: 0.25
Pruscino et al. (2008)	6 elite freestyle swimmers (all men)	2 x 200-m swimming	Caffeine: dose of 6 mg/kg ingested 45 min before exercise Sodium bicarbonate: an overall dose of 0.3 g/kg ingested in seven	**pH** *Pre-supplementation* Placebo: ~7.40 Caffeine: ~7.40 Sodium bicarbonate: ~7.40	With caffeine or sodium bicarbonate, the participants reported stomach cramps, diarrhea, or dizziness	No significant differences between trials	*Swimming time – bout 1* Caffeine: 0.42 Sodium bicarbonate: 0.22

			doses starting 90 min before exercise	Caffeine and sodium bicarbonate: ~7.40 *Pre-exercise* Placebo: ~7.40 Caffeine: ~7.40 Sodium bicarbonate: ~7.50 Caffeine and sodium bicarbonate: ~7.50 **Bicarbonate (mmol/L)** *Pre-supplementation* Placebo: ~25 Caffeine: ~25 Sodium bicarbonate: ~25 Caffeine and sodium bicarbonate: ~25 *Pre-exercise* Placebo: ~23 Caffeine: ~23 Sodium bicarbonate: ~32 Caffeine and sodium bicarbonate: ~32			Caffeine and sodium bicarbonate: 0.65 *Swimming time – bout 2* Caffeine: 0.09 Sodium bicarbonate: 0.40 Caffeine and sodium bicarbonate: 0.76
Rezaei et al. (2019)	8 karate athletes (sex was not specified)	Karate-specific aerobic test	Caffeine: dose of 6 mg/kg ingested 50 min before exercise Sodium bicarbonate: an overall dose of 0.3 g/kg ingested for 3 days before the exercise session; on the day of the testing, 0.1 g/kg was ingested	Not assessed	No participant reported severe abdominal discomfort, in any of the trials	Caffeine, sodium bicarbonate, and caffeine plus sodium bicarbonate ingestion enhanced performance as compared	*Time to exhaustion* Caffeine: 0.92 Sodium bicarbonate: 1.70 Caffeine and sodium bicarbonate: 1.26

			120 min, 90 min, and 60 min before exercise			to placebo and control	

All studies used a double-blind design; SJFT: Special Judo Fitness Tests; * calculated as the mean difference between the experimental trial and placebo divided by the pooled standard deviation

Table 2. Results of the methodological quality assessment

Reference	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Total score
Carr et al. (2011)	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Christensen et al. (2014)	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Felippe et al. (2016)	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Ferguson (2010)	No	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Higgins et al. (2016)	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Kilding et al. (2012)	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Pruscino et al. (2008)	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
Rezaei et al. (2019)	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	8
Yes: criterion is satisfied; No: criterion is not satisfied; Unclear: unable to rate												