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CAFFEINE AND SODIUM BICARBONATE SUPPLEMENTATION IN SPORT: MECHANISMS, PERFORMANCE EFFECTS, AND INTER-INDIVIDUAL VARIABILITY – A LITERATURE REVIEW

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ABSTRACT

Background: Caffeine and sodium bicarbonate are among the most extensively investigated ergogenic aids in sport. Although both supplements independently demonstrate performance-enhancing properties, uncertainty remains regarding their combined efficacy and the magnitude of inter-individual variability in response.
Aim: The purpose of this literature review was to critically synthesize contemporary evidence regarding (1) physiological mechanisms underlying caffeine and sodium bicarbonate supplementation, (2) independent performance outcomes across exercise modalities, (3) combined supplementation strategies, and (4) determinants of inter-individual responsiveness.
Material and methods: A structured narrative review was conducted using PubMed, Scopus, Web of Science, and SPORTDiscus. Twenty-three peer-reviewed human studies were included, comprising randomized controlled trials, systematic reviews, meta-analyses, and international position stands. Evidence was synthesized thematically.
Results: Caffeine consistently improves endurance, intermittent, and strength performance primarily via central adenosine receptor antagonism and reduced perception of effort. Sodium bicarbonate enhances high-intensity exercise capacity by increasing extracellular buffering capacity and facilitating proton efflux. However, additive ergogenic effects during combined supplementation are not consistently supported. Inter-individual variability is influenced by genetic polymorphisms (CYP1A2), habitual intake, gastrointestinal tolerance, training status, and nutritional context.
Conclusions: Caffeine and sodium bicarbonate independently demonstrate ergogenic potential under specific physiological conditions. Current evidence does not justify universal combined supplementation. Individualized protocols remain essential.

KEYWORDS

Caffeine, Sodium Bicarbonate, Ergogenic Aids, Buffering Capacity, Exercise Performance, Metabolic Acidosis

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1. Introduction

Optimizing exercise performance through nutritional and ergogenic strategies represents a central objective in contemporary sport science. In elite sport contexts, where performance margins are often minimal, small physiological or perceptual advantages may determine competitive outcomes. Consequently, evidence-based supplementation has become an integral component of applied sport nutrition practice. Among available ergogenic aids, caffeine and sodium bicarbonate remain two of the most extensively investigated and practically implemented supplements across both recreational and elite athletic populations (Kerksick et al., 2021; Grgic et al., 2021).

Caffeine is a naturally occurring methylxanthine widely consumed worldwide through coffee, tea, soft drinks, and concentrated supplemental formulations. Its ergogenic potential has been recognized for decades, and it is currently supported by international sport nutrition position stands as an effective performance-enhancing substance across multiple exercise modalities (Kerksick et al., 2021). The primary mechanism underlying caffeine's ergogenic action involves competitive antagonism of adenosine receptors (A1 and A2A) within the central nervous system, resulting in enhanced dopaminergic and noradrenergic neurotransmission (Spriet, 2014). By attenuating adenosine-mediated inhibition, caffeine reduces perception of effort, increases alertness, and may enhance voluntary motor unit recruitment during exercise (Lara et al., 2024).

In addition to its central effects, caffeine may influence peripheral physiological processes. Acute ingestion has been associated with increased catecholamine concentrations, altered substrate utilization, and enhanced carbohydrate oxidation during endurance exercise, particularly when co-ingested with carbohydrates (Yeo et al., 2005). Emerging evidence also suggests potential interactions with oxidative and inflammatory pathways (Barcelos et al., 2020), although the direct contribution of these mechanisms to acute ergogenic effects remains an area of ongoing investigation. Collectively, caffeine's multifaceted physiological profile

underscores its relevance across endurance, intermittent, and resistance-based performance contexts (Grgic et al., 2024).

Sodium bicarbonate supplementation, in contrast, targets extracellular acid–base regulation rather than central neural processes. High-intensity exercise characterized by substantial anaerobic glycolytic contribution results in hydrogen ion (H^+) accumulation and reductions in intramuscular pH. Although lactate was historically implicated as a primary cause of fatigue, contemporary biochemical analyses demonstrate that lactate itself is not directly responsible for performance decline; instead, proton accumulation and disturbances in excitation–contraction coupling contribute significantly to fatigue development (Robergs et al., 2004; Cairns & Lindinger, 2025). By increasing plasma bicarbonate concentration and extracellular pH, sodium bicarbonate enhances buffering capacity and facilitates hydrogen ion efflux from working skeletal muscle (Grgic et al., 2021; Deb et al., 2020). This mechanism is particularly relevant during high-intensity efforts lasting approximately one to ten minutes, where metabolic acidosis may meaningfully constrain performance.

Despite robust independent evidence supporting caffeine and sodium bicarbonate supplementation, investigations examining their combined ingestion have yielded inconsistent findings (Moesgaard et al., 2024; Smith et al., 2023; Roberts et al., 2023). The theoretical rationale for combined supplementation arises from targeting complementary fatigue pathways—central modulation via caffeine and peripheral buffering via sodium bicarbonate. However, empirical outcomes suggest that additive or synergistic effects are not universally observed. These discrepancies highlight the importance of contextualizing ergogenic efficacy within task-specific fatigue mechanisms and individual athlete characteristics.

Furthermore, substantial inter-individual variability complicates interpretation of supplementation research. Genetic polymorphisms within the CYP1A2 gene influence caffeine metabolism rate and may partially explain differences in ergogenic responsiveness (Guest et al., 2018; Womack et al., 2012; Wang et al., 2023). Habitual caffeine intake, expectancy effects, training status, sex-related hormonal modulation, and gastrointestinal tolerance may further modulate outcomes (Pickering & Kiely, 2020; Heibel et al., 2020). Variability in time-to-peak blood bicarbonate concentration similarly underscores the need for individualized timing strategies in sodium bicarbonate protocols.

Given these complexities, a purely descriptive comparison of ergogenic magnitudes is insufficient. A more integrative perspective that considers central–peripheral fatigue interactions, dose–response relationships, genotype-informed variability, and methodological heterogeneity is warranted. Accordingly, the purpose of this literature review is to critically synthesize contemporary evidence regarding (1) physiological mechanisms underlying caffeine and sodium bicarbonate supplementation, (2) independent and combined performance effects across exercise modalities, (3) determinants of inter-individual responsiveness, and (4) conceptual integration of these findings within a precision sport nutrition framework.

2. Research Materials and Methods

This study was conducted as a structured narrative literature review. Electronic databases including PubMed, Scopus, Web of Science, and SPORTDiscus were searched for relevant publications. Keywords included combinations of “caffeine”, “sodium bicarbonate”, “exercise performance”, “buffering capacity”, “metabolic acidosis”, and “CYP1A2”.

Inclusion criteria comprised: (1) peer-reviewed human studies; (2) randomized controlled trials, systematic reviews, meta-analyses, mechanistic investigations, or international position stands; (3) examination of caffeine and/or sodium bicarbonate supplementation in relation to exercise performance; and (4) publication in English.

Studies were excluded if conducted exclusively in animal models, lacking measurable performance outcomes, or focused on clinical populations without sport relevance. After screening and duplicate removal, twenty-three publications were included for thematic synthesis.

Data extraction focused on participant characteristics, supplementation protocols, exercise modality, performance outcomes, physiological mechanisms, and evidence of inter-individual variability. Due to methodological heterogeneity, a qualitative synthesis approach was adopted rather than meta-analytic aggregation.

3. Results

3.1 Physiological Basis of Fatigue and Acid–Base Regulation

High-intensity exercise requires rapid ATP resynthesis through anaerobic glycolysis. This metabolic demand is accompanied by hydrogen ion accumulation and reduced intramuscular pH (Robergs et al., 2004; Cairns & Lindinger, 2025). Elevated proton concentration may impair contractile protein function, calcium sensitivity, and enzymatic activity, contributing to fatigue development.

The bicarbonate buffering system represents the primary extracellular mechanism for regulating acid–base balance. Bicarbonate ions combine with hydrogen ions to form carbonic acid, which dissociates into carbon dioxide and water. Increased ventilation facilitates CO_2 removal, supporting pH regulation (Grgic et al., 2021; Robergs et al., 2004).

3.2 Mechanisms of Caffeine Action

Caffeine's ergogenic properties are primarily attributed to its role as a non-selective adenosine receptor antagonist. Adenosine functions as a neuromodulator that accumulates during prolonged wakefulness and sustained neural activity, exerting inhibitory effects on neuronal firing. By competitively binding to A1 and A2A receptors, caffeine reduces adenosine-mediated suppression of neurotransmitter release, resulting in enhanced dopaminergic, noradrenergic, and glutamatergic signaling (Kerksick et al., 2021; Spriet, 2014).

Increased dopaminergic activity within cortical and subcortical regions is particularly relevant to exercise performance. Dopamine plays a central role in motivation, reward processing, motor control, and perception of effort. By attenuating inhibitory signaling, caffeine may enhance willingness to sustain high workloads and delay voluntary cessation of exercise. Reductions in rating of perceived exertion are consistently reported across endurance and resistance exercise studies (Lara et al., 2024), supporting the hypothesis that central modulation of fatigue perception represents a primary ergogenic mechanism.

Caffeine may also influence corticospinal excitability and motor unit recruitment. Enhanced central drive can increase voluntary activation during maximal or near-maximal contractions, potentially contributing to improvements in maximal strength and power output (Grgic et al., 2024). While the precise neurophysiological pathways remain under investigation, evidence suggests that central facilitation may interact with peripheral contractile properties to augment force production.

At the muscular level, caffeine has been shown in vitro to enhance calcium release from the sarcoplasmic reticulum via modulation of ryanodine receptors. Although the concentrations required to produce substantial effects in isolated muscle preparations exceed typical ergogenic doses, smaller in vivo effects on excitation–contraction coupling cannot be entirely excluded (Spriet, 2014). Even modest alterations in calcium kinetics may influence contractile efficiency during high-intensity efforts.

Metabolically, caffeine ingestion is associated with increased circulating catecholamines, including epinephrine and norepinephrine. These hormonal responses may stimulate lipolysis and alter substrate utilization patterns during endurance exercise (Yeo et al., 2005). While early hypotheses emphasized glycogen sparing as a primary mechanism, contemporary evidence suggests that perceptual and central mechanisms likely play a more dominant role in acute ergogenic outcomes. Nevertheless, metabolic modulation may contribute to sustained performance in prolonged exercise contexts.

Caffeine may additionally interact with intracellular signaling pathways, including AMP-activated protein kinase (AMPK), potentially influencing metabolic efficiency and mitochondrial function. Although the relevance of these pathways to acute performance enhancement remains incompletely defined, they represent an area of emerging interest in exercise physiology research.

Importantly, caffeine's multifactorial physiological profile underscores that its ergogenic effects cannot be attributed to a single mechanism. Rather, performance enhancement likely arises from integrated central and peripheral influences, with relative contribution varying according to exercise modality, intensity, and duration.

3.3 Effects of Caffeine on Exercise Performance

Extensive experimental and meta-analytic evidence demonstrates that caffeine supplementation enhances exercise performance across a wide range of modalities, including endurance, intermittent, and resistance-based activities (Kerksick et al., 2021; Lara et al., 2024). Although the magnitude of improvement is typically described as small to moderate, such effects may hold substantial practical relevance in competitive sport, where marginal gains can influence outcomes.

In endurance exercise, caffeine has consistently been shown to improve time-trial performance, reduce time-to-completion, and extend time-to-exhaustion (Lara et al., 2024). The ergogenic benefits appear to be particularly robust in events lasting between 5 and 60 minutes, although improvements have also been observed in longer-duration tasks. Reduced perception of effort during sustained workloads likely represents a primary contributor to these improvements. Athletes may maintain a given power output at a lower perceived exertion or tolerate higher intensities before reaching volitional fatigue.

Importantly, caffeine may also influence pacing strategies. By attenuating central fatigue signals, caffeine may alter decision-making processes related to effort distribution during endurance tasks. Enhanced motivation and reduced perception of discomfort may allow athletes to adopt more aggressive pacing patterns without premature exhaustion. Such effects highlight the interaction between neurophysiological and behavioral determinants of performance.

In intermittent sports characterized by repeated high-intensity efforts interspersed with brief recovery periods—such as team sports—caffeine ingestion has been associated with improved repeated sprint ability, greater total work output, and maintenance of performance across successive bouts (Díaz-Lara et al., 2024). These benefits may stem from both central mechanisms and improved tolerance to metabolic stress. Enhanced alertness and reaction time may also confer tactical advantages in sport-specific contexts.

Resistance exercise performance similarly appears responsive to caffeine supplementation. Systematic reviews and meta-analyses report improvements in maximal strength, muscular endurance, and power output following acute ingestion (Grgic et al., 2024). Increased motor unit recruitment, enhanced voluntary activation, and reduced perception of effort likely contribute to these outcomes. Improvements in explosive performance, such as vertical jump height or sprint acceleration, have also been observed in some investigations, though results are not universally consistent.

Dose appears to influence performance outcomes, but not in a strictly linear manner. While early studies frequently employed doses of 5–9 $mgkg^{-1}$ body mass, contemporary evidence suggests that lower doses (approximately 2–3 $mgkg^{-1}$) may produce comparable ergogenic effects with fewer adverse reactions (Kerksick et al., 2021). Higher doses may increase the likelihood of side effects such as jitteriness, gastrointestinal discomfort, elevated heart rate, and sleep disruption, which may negate performance benefits in certain individuals.

Inter-individual variability remains a defining feature of caffeine research. Genetic polymorphisms in CYP1A2 influence caffeine metabolism rate and may partially explain differences in ergogenic responsiveness (Guest et al., 2018; Womack et al., 2012; Wang et al., 2023). Individuals classified as fast metabolizers may experience greater performance improvements in endurance contexts compared with slow metabolizers, although findings are not entirely consistent across studies.

Habitual caffeine intake may also modulate acute responsiveness. Some evidence suggests that regular caffeine consumers maintain ergogenic benefits despite potential tolerance to certain physiological effects (Pickering & Kiely, 2020). However, the necessity and duration of caffeine withdrawal prior to competition remain debated. Psychological expectancy effects further complicate interpretation, as belief in caffeine ingestion may independently enhance performance.

Collectively, the evidence supports caffeine as a broadly effective ergogenic aid across multiple exercise modalities. However, the magnitude of benefit depends on dose, timing, exercise type, individual phenotype, and contextual factors. Understanding these interacting determinants is essential for optimizing practical application.

3.4 Mechanisms of Sodium Bicarbonate Action

Sodium bicarbonate supplementation exerts its ergogenic effects primarily through modulation of extracellular acid–base balance. During high-intensity exercise, rapid ATP resynthesis via anaerobic glycolysis leads to increased production of hydrogen ions (H^+), contributing to reductions in intramuscular pH. Although lactate accumulation was historically considered the primary cause of fatigue, contemporary biochemical evidence indicates that proton accumulation and associated disturbances in excitation–contraction coupling represent more direct contributors to performance decline (Robergs et al., 2004; Cairns & Lindinger, 2025).

The bicarbonate buffering system constitutes the principal extracellular mechanism for regulating systemic pH. In this system, bicarbonate ions (HCO_3^-) combine with hydrogen ions to form carbonic acid (H_2CO_3), which subsequently dissociates into carbon dioxide (CO_2) and water (H_2O). Carbon dioxide is then removed via increased ventilation, facilitating maintenance of physiological pH during metabolically

demanding exercise. Oral ingestion of sodium bicarbonate increases plasma bicarbonate concentration and blood pH, thereby inducing a state of metabolic alkalosis (Grgic et al., 2021).

Elevated extracellular bicarbonate enhances the gradient for hydrogen ion efflux from skeletal muscle. This process is mediated in part by monocarboxylate transporters (MCT1 and MCT4), which facilitate the co-transport of lactate and hydrogen ions across the sarcolemma (Deb et al., 2020). By increasing the extracellular buffering capacity, sodium bicarbonate may accelerate proton removal from the intracellular environment, attenuating the decline in intramuscular pH and preserving contractile function during high-intensity efforts.

Impairments in contractile performance during acidosis are multifactorial. Reduced pH can interfere with calcium binding to troponin, decrease sensitivity of the contractile apparatus, and inhibit key glycolytic enzymes, thereby limiting ATP availability. By mitigating extracellular acidosis and facilitating proton efflux, sodium bicarbonate may delay these fatigue-related processes and prolong the capacity for high-intensity work.

Inter-individual variability in bicarbonate responsiveness may be influenced by several physiological factors. Baseline buffering capacity, muscle fiber composition, and glycolytic enzyme activity may affect the magnitude of benefit derived from extracellular alkalosis (Gough et al., 2024). Athletes with a higher proportion of type II muscle fibers or greater reliance on anaerobic metabolism may theoretically experience greater ergogenic effects, although direct empirical correlations remain limited.

Time to peak blood bicarbonate concentration exhibits considerable inter-individual variability, typically ranging between 60 and 180 minutes following ingestion (Heibel et al., 2020). This variability may reflect differences in gastric emptying rate, intestinal absorption, and renal regulation of acid–base balance. Consequently, standardized ingestion protocols may not align with peak alkalosis in all individuals, underscoring the importance of individualized timing strategies.

Gastrointestinal distress represents the most frequently reported adverse effect associated with sodium bicarbonate supplementation. Symptoms such as nausea, bloating, cramping, and diarrhea may compromise performance despite physiological alkalosis (Grgic et al., 2021). Strategies including split dosing, gradual loading protocols, and co-ingestion with meals have been proposed to mitigate these effects while preserving ergogenic potential.

Collectively, sodium bicarbonate operates primarily at the extracellular level to enhance buffering capacity and attenuate metabolic acidosis during high-intensity exercise. Its ergogenic efficacy is therefore most pronounced in exercise modalities characterized by substantial glycolytic contribution and rapid proton accumulation.

3.5 Effects of Sodium Bicarbonate on Exercise Performance

Systematic reviews demonstrate that sodium bicarbonate supplementation produces small but significant performance improvements in exercise tasks lasting approximately one to ten minutes, including rowing, cycling time trials, and middle-distance running (Deb et al., 2020; Gough et al., 2024).

However, performance benefits appear context-specific. Continuous endurance running performance demonstrates limited responsiveness to acute sodium bicarbonate ingestion (Miller et al., 2025). Such findings suggest that extracellular buffering is most relevant when anaerobic glycolysis substantially contributes to energy production.

Gastrointestinal discomfort remains the most frequently reported adverse effect and may limit practical application (Grgic et al., 2021). Individualized testing during training is therefore recommended prior to competitive use.

3.6 Combined Supplementation: Caffeine and Sodium Bicarbonate

The theoretical rationale for combined caffeine and sodium bicarbonate supplementation is grounded in the premise that these agents target complementary fatigue mechanisms. Caffeine primarily modulates central nervous system function, reducing perceived exertion and enhancing neural drive, whereas sodium bicarbonate improves extracellular buffering capacity, attenuating metabolically induced acidosis during high-intensity exercise (Kerksick et al., 2021; Grgic et al., 2021). From a mechanistic perspective, simultaneous targeting of central and peripheral fatigue pathways could be expected to produce additive or even synergistic performance effects.

However, empirical findings have not consistently supported this hypothesis. Several randomized controlled trials examining combined supplementation report no significant additive benefit beyond caffeine alone (Moesgaard et al., 2024; Smith et al., 2023; Roberts et al., 2023). In these studies, performance

improvements observed with caffeine were not further enhanced by co-ingestion of sodium bicarbonate, despite confirmed increases in blood bicarbonate concentration.

Multiple explanations may account for these findings. First, ergogenic efficacy likely depends on the dominant fatigue mechanism in a given exercise context. In endurance-based or intermittent tasks where perceptual regulation and central drive strongly influence performance, caffeine's central effects may represent the primary determinant of improvement. Under such conditions, additional enhancement of extracellular buffering may not meaningfully alter performance outcomes.

Second, ceiling effects may limit additive potential. If caffeine already maximizes central tolerance to effort and voluntary activation, performance may approach physiological or biomechanical limits that cannot be substantially extended through peripheral buffering alone. Similarly, in exercise modalities where metabolic acidosis is not the primary limiting factor, sodium bicarbonate may contribute minimally beyond central stimulation.

Third, methodological heterogeneity across studies complicates interpretation. Variations in dosing strategies, ingestion timing, gastrointestinal management protocols, participant training status, and exercise modality may influence combined supplementation outcomes (Moesgaard et al., 2024). In some trials, bicarbonate ingestion may not have coincided with peak alkalosis at the time of performance testing, potentially attenuating observable benefits.

Another important consideration is the interaction between perceptual and physiological fatigue. Caffeine-induced reductions in perceived exertion may alter pacing behavior and effort distribution, potentially overshadowing smaller physiological benefits conferred by extracellular buffering. If central perception of effort remains the dominant constraint, improvements in acid–base balance may not translate into measurable performance gains.

Conversely, it is plausible that combined supplementation may be more effective in specific contexts characterized by both high perceptual demand and substantial glycolytic contribution, such as repeated high-intensity intervals with limited recovery. However, empirical data supporting consistent synergy in such scenarios remain limited.

Gastrointestinal tolerance also represents a practical limiting factor. Sodium bicarbonate supplementation is frequently associated with gastrointestinal discomfort, which may counteract any physiological benefit. When co-ingested with caffeine—particularly at moderate to high doses—the risk of adverse symptoms may increase, potentially influencing performance negatively.

Importantly, absence of consistent additive effects does not imply lack of mechanistic complementarity. Rather, it suggests that fatigue during exercise is multidimensional and context-dependent. The relative contribution of central and peripheral factors may shift according to exercise duration, intensity, and individual phenotype. Consequently, combined supplementation may benefit certain individuals or tasks more than others.

Overall, current evidence indicates that while caffeine reliably enhances performance across multiple modalities, the addition of sodium bicarbonate does not uniformly produce further improvement. Future research incorporating individualized timing strategies, genotype stratification, and ecologically valid performance protocols may clarify conditions under which combined supplementation yields meaningful additive effects.

3.7 Inter-Individual Variability and Contextual Factors

Inter-individual variability represents one of the most significant challenges in interpreting ergogenic supplementation research. Although caffeine and sodium bicarbonate demonstrate consistent average performance benefits at the group level, substantial heterogeneity in responsiveness is observed across individuals. This variability likely reflects complex interactions among genetic, physiological, behavioral, and contextual factors.

With respect to caffeine, genetic polymorphisms within the CYP1A2 gene have received considerable attention. CYP1A2 encodes a hepatic cytochrome P450 enzyme responsible for approximately 95% of caffeine metabolism. Single nucleotide polymorphisms within this gene influence enzyme activity, leading to classification of individuals as relatively "fast" or "slow" metabolizers (Womack et al., 2012; Guest et al., 2018). Fast metabolizers may experience greater ergogenic benefits in endurance exercise, potentially due to more rapid conversion of caffeine to paraxanthine and other active metabolites. Conversely, slow metabolizers may exhibit attenuated performance improvements or greater susceptibility to adverse effects such as anxiety and sleep disturbance.

However, genotype alone does not fully explain observed variability. Environmental and behavioral factors interact dynamically with genetic predisposition. Habitual caffeine intake may modify acute responsiveness through tolerance development, although evidence suggests that performance benefits are often preserved despite regular consumption (Pickering & Kiely, 2020). The necessity of caffeine withdrawal prior to competition remains debated, with some studies indicating minimal difference between habitual and abstinent conditions.

Psychological expectancy also contributes to inter-individual variation. Belief in caffeine ingestion may independently influence performance outcomes via placebo mechanisms, particularly in tasks heavily influenced by perceived exertion and motivation (Kerksick et al., 2021). Distinguishing pharmacological from expectancy-driven effects requires rigorous blinding procedures and assessment of participant belief.

Sex-related hormonal influences further complicate interpretation. Estrogen has been shown to modulate CYP1A2 activity, potentially altering caffeine metabolism rate across menstrual cycle phases or in individuals using oral contraceptives (Womack et al., 2012). Consequently, pharmacokinetic variability may differ between male and female athletes, although sex-stratified analyses remain underrepresented in the literature.

In the context of sodium bicarbonate supplementation, inter-individual variability is influenced by both physiological and practical factors. Baseline buffering capacity, muscle fiber composition, and glycolytic enzyme activity may affect responsiveness to extracellular alkalosis (Gough et al., 2024). Athletes with greater reliance on anaerobic metabolism may derive proportionally larger benefit from enhanced buffering capacity.

Timing variability also plays a critical role. Peak blood bicarbonate concentration following ingestion can vary widely between individuals, typically ranging from 60 to 180 minutes (Heibel et al., 2020). Fixed ingestion protocols may therefore fail to coincide with peak alkalosis in some athletes, attenuating observable performance effects. Individualized timing strategies based on measured bicarbonate responses during training may improve efficacy.

Gastrointestinal tolerance represents an additional determinant of variability. Sodium bicarbonate frequently induces symptoms such as nausea, bloating, and diarrhea, which may negate physiological benefits (Grgic et al., 2021). Individual differences in gastric emptying rate, intestinal sensitivity, and co-ingestion practices influence symptom severity and, consequently, practical effectiveness.

Training status and exercise modality further modulate ergogenic responsiveness. Well-trained athletes may exhibit smaller absolute improvements due to already optimized physiological systems, yet even marginal gains may hold competitive relevance. Conversely, less-trained individuals may demonstrate larger relative improvements but with greater variability.

Collectively, inter-individual variability underscores the limitations of universal supplementation recommendations. Ergogenic responses should be conceptualized as probabilistic rather than deterministic. A precision-oriented approach integrating genetic profiling, habitual intake assessment, individualized timing, sex-specific considerations, and tolerance testing may provide a more effective framework for optimizing supplementation strategies in applied sport settings.

3.8 Dose–Response Relationships and Practical Optimization Strategies

Understanding dose–response relationships is essential for translating ergogenic supplementation research into applied sport settings. Although caffeine and sodium bicarbonate have demonstrated performance-enhancing properties across multiple exercise modalities, optimal dosing strategies remain dependent on individual phenotype, exercise characteristics, and contextual factors.

Historically, caffeine supplementation studies frequently employed doses ranging from 5 to 9 $mgkg^{-1}$ body mass. However, contemporary evidence indicates that lower doses, typically between 2 and 3 $mgkg^{-1}$, may produce comparable ergogenic benefits with reduced incidence of adverse effects (Kerksick et al., 2021; Lara et al., 2024). The dose–response curve for caffeine appears non-linear, suggesting a potential ceiling effect beyond moderate intake levels. Higher doses do not consistently produce proportionally greater performance improvements and may increase the likelihood of side effects such as anxiety, gastrointestinal discomfort, elevated heart rate, and sleep disruption.

The existence of a ceiling effect may partially explain inconsistencies observed in combined supplementation research. If moderate caffeine doses already maximize central stimulation and perception-related performance enhancements, additional pharmacological stimulation may not yield further benefit. This underscores the importance of individualized dose optimization rather than assuming “more is better.”

Timing represents another critical variable in caffeine supplementation. Peak plasma caffeine concentrations typically occur within 30–90 minutes following ingestion; however, inter-individual variability

is substantial (Guest et al., 2018). Factors such as gastric emptying rate, habitual caffeine intake, liver enzyme activity, and genetic polymorphisms within CYP1A2 influence pharmacokinetics (Womack et al., 2012; Wang et al., 2023). Consequently, fixed ingestion windows may not coincide with peak ergogenic effect in all athletes. Individualized timing trials during training sessions may therefore optimize competition-day strategies.

Chronic versus acute caffeine use also warrants consideration. While acute ingestion reliably enhances performance, chronic high intake may alter sleep architecture and recovery quality, indirectly affecting performance capacity. Strategic periodization of caffeine use—prioritizing key training sessions or competitions—may help preserve responsiveness while minimizing tolerance development.

Sodium bicarbonate supplementation similarly demonstrates dose-dependent effects. The commonly recommended acute dose of approximately 0.3 gkg^{-1} body mass has been shown to effectively increase plasma bicarbonate concentration and enhance high-intensity exercise performance (Grgic et al., 2021; Deb et al., 2020). However, doses exceeding this threshold may exacerbate gastrointestinal symptoms without conferring additional ergogenic benefit.

Inter-individual variability in time to peak alkalosis further complicates standardized dosing protocols. Peak blood bicarbonate concentration may occur anywhere between 60 and 180 minutes following ingestion (Heibel et al., 2020). Fixed ingestion guidelines (e.g., 60–90 minutes pre-exercise) may not align with peak buffering capacity for all athletes. Recent methodological approaches advocate individualized timing based on measured bicarbonate responses during familiarization trials, thereby aligning peak alkalosis with performance onset.

Alternative dosing strategies have also been explored. Split-dose protocols, in which sodium bicarbonate is consumed in smaller increments over a defined period, may reduce gastrointestinal distress while maintaining elevated blood bicarbonate levels (Gough et al., 2024). Gradual loading protocols across several days have been proposed as a strategy to attenuate acute gastrointestinal symptoms, though their comparative efficacy requires further investigation.

Nutritional context represents an additional determinant of ergogenic effectiveness. Carbohydrate availability influences endurance performance and may interact with caffeine's metabolic effects (Burke et al., 2021). Co-ingestion with meals may reduce gastrointestinal distress associated with sodium bicarbonate but may also delay absorption kinetics. Thus, optimization requires balancing physiological efficacy with practical tolerance.

When considering combined supplementation, synchronizing peak central stimulation from caffeine with peak extracellular alkalosis from sodium bicarbonate presents logistical challenges. Variability in pharmacokinetics for both substances suggests that individualized experimentation during training may represent the most effective strategy for identifying optimal timing combinations.

Collectively, dose–response relationships underscore the importance of precision in ergogenic supplementation. Standardized protocols derived from group-level averages may not produce optimal outcomes for all individuals. Instead, iterative, athlete-specific optimization—guided by physiological monitoring, tolerance assessment, and task-specific demands—may maximize performance benefits while minimizing adverse effects

4. Discussion

The present literature review critically synthesized current evidence regarding caffeine and sodium bicarbonate supplementation in sport. The findings confirm that both supplements independently demonstrate ergogenic potential; however, their effectiveness is highly context-dependent and influenced by exercise modality, dosing strategy, and inter-individual variability.

Caffeine remains one of the most consistently supported ergogenic aids in sport nutrition (Kerksick et al., 2021; Lara et al., 2024; Grgic et al., 2024). Its primary mechanism—adenosine receptor antagonism—reduces perception of effort and enhances central motor drive (Kerksick et al., 2021; Spriet, 2014). These central adaptations translate into improvements across endurance, intermittent, and resistance exercise contexts (Lara et al., 2024; Díaz-Lara et al., 2024). Additionally, peripheral mechanisms such as enhanced carbohydrate oxidation may contribute in prolonged endurance tasks (Yeo et al., 2005; Barcelos et al., 2020).

Sodium bicarbonate supplementation exerts its ergogenic effect primarily through increased extracellular buffering capacity (Grgic et al., 2021; Deb et al., 2020). This mechanism is particularly relevant in high-intensity exercise lasting approximately one to ten minutes, where anaerobic glycolysis contributes substantially to ATP resynthesis (Deb et al., 2020; Gough et al., 2024). While effect sizes are generally small, they may be meaningful in competitive sport where marginal differences determine performance outcomes.

Despite a strong theoretical rationale for combined supplementation, current evidence does not consistently demonstrate additive or synergistic effects when caffeine and sodium bicarbonate are co-ingested (Moesgaard et al., 2024; Smith et al., 2023; Roberts et al., 2023). Potential explanations include ceiling effects, exercise-specific dominance of central versus peripheral fatigue mechanisms, and increased gastrointestinal discomfort when multi-supplement protocols are implemented.

Inter-individual variability remains a critical determinant of supplementation outcomes. Genetic polymorphisms within CYP1A2 influence caffeine metabolism rate and may partly explain variability in ergogenic response (Guest et al., 2018; Womack et al., 2012; Wang et al., 2023). However, genotype alone does not determine performance enhancement, as habitual intake, psychological responsiveness, training status, and nutritional context also contribute (Pickering & Kiely, 2020; Burke et al., 2021).

In the context of sodium bicarbonate, variability in time-to-peak blood bicarbonate concentration underscores the importance of individualized timing strategies (Heibel et al., 2020). Emerging methodological refinements, including split dosing and modified-release formulations, may improve tolerability and practical application (Gough et al., 2024).

Limitations of the current literature include heterogeneous methodologies, relatively small sample sizes in combined supplementation studies, and underrepresentation of female athletes in some investigations. Future research should prioritize genotype-stratified randomized trials, individualized bicarbonate timing protocols, and sport-specific performance models to clarify potential synergistic effects.

5. Conclusions

Caffeine and sodium bicarbonate independently enhance exercise performance under specific physiological conditions. Caffeine demonstrates broad ergogenic applicability across endurance, intermittent, and strength-based modalities (Kerksick et al., 2021; Lara et al., 2024; Grgic et al., 2024), whereas sodium bicarbonate is most effective in high-intensity anaerobic exercise (Deb et al., 2020; Gough et al., 2024).

Current evidence does not support universal combined supplementation with caffeine and sodium bicarbonate (Moesgaard et al., 2024; Smith et al., 2023; Roberts et al., 2023). Instead, supplementation strategies should be individualized based on genetic profile, habitual intake, exercise demands, tolerance, and nutritional context.

Future investigations should focus on personalized supplementation frameworks, integrating genetic, physiological, and sport-specific factors to optimize performance outcomes.

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