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Ketone Bodies as Ergogenic Aids in Endurance Sports: Biochemical Mechanisms, Supplementation Protocols, and Performance Outcomes — A Literature Review

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Abstract

Ketone bodies — principally β-hydroxybutyrate (β-HB) and acetoacetate (AcAc) — are endogenous metabolites that serve as alternative fuel substrates during states of reduced carbohydrate availability. Advances in the synthesis of ketone esters (KE) and ketone salts (KS) have enabled the acute elevation of circulating ketones independent of dietary restriction, creating promising ergogenic opportunities. Ketone esters acutely raise blood β-HB to one-digit millimolar concentrations within 30–60 minutes and can shift substrate utilization toward ketone and fat oxidation, sparing muscle glycogen and lowering blood lactate during submaximal exercise; ketone salts produce substantially lower ketosis and weaker effects. The evidence on acute endurance performance is inconsistent: a single influential trial reported a small benefit when a ketone monoester was co-ingested with carbohydrate, but this has not been reliably reproduced, and other controlled trials report neutral or impaired performance, particularly with the less palatable acetoacetate diester and with ketone salts at higher intensities. A more consistent signal has emerged in the recovery and adaptation domain, where ketone ester ingestion has been associated with enhanced post-

exercise muscle glycogen synthesis and attenuated overreaching during intensified training. Overall, exogenous ketones are a biochemically plausible but unproven ergogenic strategy for acute endurance performance, with their most defensible current application lying in recovery; the heterogeneity of findings reflects differences in supplementation form, dose, timing, co-ingested macronutrients, training status, and exercise modality. Controlled trials with individualized protocols are needed before definitive recommendations may be established. This literature review evaluates the current evidence on the biochemical mechanisms, supplementation protocols, and effects of exogenous ketone body administration on endurance sport performance.

Keywords: ketone bodies, ergogenic aids, endurance performance, β-hydroxybutyrate, ketone esters, supplementation, sports nutrition

1. Introduction

Endurance sports — including marathon running, road cycling, triathlon, cross-country skiing, and open-water swimming — place extraordinary demands on the human metabolic system. Performance in these disciplines is fundamentally limited by the capacity to sustain high rates of aerobic energy production over extended durations, a process that relies on the efficient oxidation of both carbohydrate and lipid substrates. The concept of an ergogenic aid — any nutritional, mechanical, pharmacological, or psychological intervention capable of enhancing sport performance — has been a focus point in exercise science research.

Carbohydrate feeding strategies, including pre-exercise loading, in-competition ingestion, and high-carbohydrate dietary periodization, remain the cornerstone of endurance nutrition. However, the finite capacity of muscle and hepatic glycogen stores, combined with the metabolic perturbations associated with glycogen depletion ("bonking" or "hitting the wall"), has motivated decades of research into alternative fuel substrates. Fat oxidation, while theoretically unlimited in capacity, is restricted by the relatively slow rate at which fatty acids can supply adenosine triphosphate (ATP) during high-intensity exercise.

Ketone bodies — comprising β-hydroxybutyrate (β-HB), acetoacetate (AcAc), and acetone — represent a third metabolic fuel class, endogenously synthesized in hepatic mitochondria from acetyl-CoA derived principally from fatty acid β-oxidation. Under physiological conditions including prolonged fasting, starvation, or adherence to very-low-carbohydrate (ketogenic) diets, circulating ketone concentrations rise from baseline levels of approximately 0.1–0.5 mM to 1–6 mM, enabling substantial extra-hepatic oxidation, especially in cardiac and skeletal muscle and the central nervous system (Cahill, 2006). The ergogenic potential of ketone bodies gained significant scientific and commercial attention following the publication of Clarke et al. (2012) and subsequent work from other researchers (see table 2), which demonstrated that D-β-hydroxybutyrate-R-1,3-butanediol monoester (KE) could acutely elevate circulating β-HB without requiring dietary restriction. The pivotal study by Cox et al., reported that acute KE ingestion

combined with carbohydrate increased cycling time-trial performance by approximately 2% in trained athletes, a finding that led to considerable commercial development and subsequent research examination.

Despite considerable scientific interest, the body of evidence remains notably heterogeneous. Subsequent randomized controlled trials have produced conflicting results(see table 2), and mechanistic understanding — while advancing — is incomplete. Critical unresolved questions concern the optimal supplementation form, dosing, timing, and interaction with co-ingested macronutrients and diet, as well as the extent to which the ergogenic signal varies with training status, exercise intensity, and individual metabolic flexibility.

This literature review aims to synthesize the available evidence on three interconnected domains: (1) the biochemical mechanisms by which exogenous ketone bodies may enhance endurance performance, (2) the pharmacokinetics and supplementation protocols of principal ketone delivery forms, and (3) the performance outcomes observed in controlled experimental trials. By integrating these perspectives, we seek to provide a critical, evidence-based framework for researchers, practitioners, and endurance athletes considering ketone supplementation.

2. Methods

2.1 Search Strategy

This review was conducted as a narrative review. The literature search described below was intended to assemble a representative and current body of evidence guided by expert appraisal. This review draws on a structured literature search to assemble a representative and current picture of how exogenous ketone bodies affect endurance performance, and to place that picture in its mechanistic and practical context. The literature was identified through searches of PubMed, Web of Science, Scopus, and SPORTDiscus, covering work published up to 31 May 2026. Search terms combined the principal ketone-related concepts (ketone bodies, ketone esters, ketone salts, β-hydroxybutyrate, exogenous ketones) with terms for endurance exercise (endurance, aerobic, cycling, running, triathlon) and for performance outcomes (ergogenic effect, time trial, time-to-exhaustion, VO_2max, exercise capacity). These database searches were supplemented by hand-searching the reference lists of retrieved articles and relevant reviews.

2.2 Study Selection Criteria

In selecting which studies to foreground, priority was given to controlled human trials — randomized or crossover in design — in healthy, endurance-trained or recreationally active adults, in which an exogenous ketone supplement (ester, salt, or mixed precursor) was given either acutely or over a sustained period, and at least one quantitative endurance-relevant outcome was reported. Work falling outside this scope was treated as contextual rather than primary: studies using ketogenic diets alone, clinical or animal models, and uncontrolled single-arm reports informed the broader discussion but were not relied upon for performance conclusions.

3. Biochemistry of Ketone Bodies

3.1 Ketogenesis: Hepatic Synthesis Pathways

Ketone body synthesis (ketogenesis) occurs primarily in hepatic mitochondria and is fundamentally regulated by the intramitochondrial concentration of acetyl-CoA and the activity of 3-hydroxy-3-methylglutaryl-CoA synthase 2 (HMGCS2), the rate-limiting enzyme of the ketogenic pathway. Under conditions of increased fatty acid flux — characteristic of fasting, prolonged exercise, or carbohydrate restriction — hepatic β-oxidation generates acetyl-CoA at rates that exceed the oxidative capacity of the tricarboxylic acid (TCA) cycle. This excess acetyl-CoA undergoes condensation reactions to yield acetoacetate, the primary ketone body. (Suresh et al., 2025)

The biochemical pathway proceeds as follows: two molecules of acetyl-CoA are condensed by acetoacetyl-CoA thiolase to form acetoacetyl-CoA. HMGCS2 then catalyzes the addition of a third acetyl-CoA to yield 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA), which is subsequently cleaved by HMG-CoA lyase to produce acetoacetate and acetyl-CoA. Acetoacetate can be reversibly reduced to β-HB by the NAD^+-linked mitochondrial enzyme β-hydroxybutyrate dehydrogenase (BDH1), a reaction driven by the prevailing mitochondrial NADH/NAD^+ ratio. Acetone is formed non-enzymatically from the spontaneous decarboxylation of acetoacetate and represents a metabolically minor by-product. (Tsuruta et al., 2024)

Table 1. Biochemical Properties of the Three Ketone Bodies

Compound	Molecular Formula	Normal Blood Concentration	Elimination Half-life	Primary Metabolic Role
Acetoacetate (AcAc)	$CH_3COCH_2COO^-$	0.1–0.3 mM (fasted: up to 4 mM)	8-14 h	Direct fuel; precursor to β-HB and acetone
β-Hydroxybutyrate (β-HB)	$CH_3CH(OH)CH_2COO^-$	0.1–0.5 mM (fasted: up to 6 mM)	0,8-3,1 h	Primary circulating ketone; HDAC inhibitor
Acetone	CH_3COCH_3	Trace	Volatile – largely exhaled/ renally excreted	Minor metabolic by-product of spontaneous decarboxylation; exhaled

Note. β-HB = β-hydroxybutyrate; AcAc = acetoacetate; HDAC = histone deacetylase; mM = millimolar. Blood concentrations represent approximate fasted-state ranges in healthy adults. Data compiled from Laffel (1999), Clarke et al. (2012)

3.2 Peripheral Ketone Body Oxidation

In peripheral tissues — including cardiac muscle, skeletal muscle, renal cortex, and brain — ketone bodies are extracted from the circulation and oxidized via a pathway distinct from hepatic ketogenesis. β-HB is first oxidized back to acetoacetate by BDH1. Acetoacetate then undergoes succinyl-CoA:3-oxoacid CoA-transferase (SCOT/OXCT1)-mediated CoA transfer to yield acetoacetyl-CoA, which is transformed by acetoacetyl-CoA thiolase into two molecules of acetyl-CoA for entry into the TCA cycle.

The thermodynamic efficiency of ketone oxidation is frequently invoked in support of ergogenic claims, but the underlying data require careful interpretation. Expressed as the P/O ratio (ATP molecules produced per oxygen atom consumed), β-HB yields approximately 2.50, compared to 2.58 for glucose and 2.33 for palmitate (Harvey et al., 2019). Notably, relative to glucose — the substrate of principal interest in endurance exercise, given its finite glycogen reserves — ketone bodies offer no P/O advantage and are in fact marginally lower (2.50 vs. 2.58). The original proposition that ketone bodies are a more energetically efficient fuel, advanced by Veech et al. , rested not on the P/O ratio but on a distinct thermodynamic argument: an increased redox potential difference between the NAD and coenzyme Q couples and an elevated free energy of ATP hydrolysis observed in perfused heart preparations (Veech et al., 2001; Veech, 2004). These two arguments should not be conflated. Furthermore, such calculations are derived largely from in vitro and isolated-organ analyses, and their translation to intact exercising skeletal muscle in vivo remains debated.

3.3 Ketone Bodies as Signaling Molecules: Beyond Fuel

A paradigm shift in ketone body biology has emerged from the recognition that β-HB functions not only as a fuel substrate but as a bioactive signaling molecule with pleiotropic effects on cellular metabolism, gene expression, and inflammation (Newman & Verdin, 2014). Several mechanistic pathways are particularly relevant to exercise physiology.

3.3.1 HDAC Inhibition and Epigenetic Regulation

β-HB acts as a relatively selective inhibitor of class I histone deacetylases (HDACs), with HDAC inhibition and increased histone acetylation reported even at concentrations of 1–2 mM (Shimazu et al., 2013) — a range comfortably within the single-digit millimolar β-HB concentrations achieved after ketone monoester ingestion. HDAC inhibition promotes histone acetylation, increasing transcriptional accessibility at genes regulating oxidative stress resistance, including the FOXO3a-associated antioxidant targets manganese superoxide dismutase (MnSOD/SOD2) and catalase, as well as metallothionein-2 (MT2). This epigenetic mechanism, first characterized by Shimazu et al. (2013), may confer adaptive benefits in the context of exercise-induced oxidative stress, potentially reducing exercise-associated cellular damage and accelerating recovery. However, these effects were characterized largely in non-muscle tissue and cell culture, and intracellular β-HB exposure in exercising skeletal muscle may differ from circulating concentrations.

3.3.2 GPR109A and Sympathoadrenal Attenuation

β-HB is an endogenous agonist of the G-protein-coupled receptor GPR109A (also known as HCA2, or nicotinic acid receptor), expressed on adipocytes and immune cells. Activation of GPR109A inhibits adenylyl cyclase, reducing intracellular cAMP and attenuating sympathetically-mediated lipolysis and catecholamine release (Taggart et al., 2005). In the context of exercise, reduced adrenergic activation may modulate heart rate, blood lactate production, and perceived exertion, though the net effect on performance is complex and context-dependent.

3.3.3 NLRP3 Inflammasome Inhibition

β-HB has been demonstrated to inhibit the NLRP3 inflammasome — a multiprotein complex mediating the inflammatory response to metabolic danger signals — at concentrations of 1–5 mM (Youm et al., 2015). This inhibitory effect suppresses caspase-1 activation and the subsequent processing and release of pro-inflammatory cytokines including interleukin-1β (IL-1β) and interleukin-18 (IL-18). Given that exercise-induced inflammation contributes to post-exercise fatigue and delayed onset muscle soreness (DOMS), ketone-mediated inflammasome inhibition may represent a promising mechanism for accelerating exercise recovery.

4. Exogenous Ketone Supplementation Forms and Pharmacokinetics

4.1 Ketone Esters

Ketone esters represent the most potent commercially available form of exogenous ketone supplementation. The most extensively studied compound in the performance literature is the ketone monoester (R)-3-hydroxybutyl (R)-3-hydroxybutyrate [(R)-3-HB ester], commonly known as the Veech/Clarke monoester, developed through research at the US National Institutes of Health with funding from the Defense Advanced Research Projects Agency (DARPA). Upon oral ingestion, the ester bond is hydrolyzed by ubiquitous intestinal esterases, releasing R-1,3-butanediol (a chiral alcohol) and R-β-hydroxybutyrate directly. The liberated R-1,3-butanediol is subsequently metabolized hepatically to additional β-HB via alcohol dehydrogenase-mediated oxidation, such that each mole of monoester yields two moles of physiological D-β-HB (Stubbs et al., On the metabolism of exogenous ketones in humans 2017) Other chemically distinct ketone esters — including the bis-hexanoyl (R)-1,3-butanediol diester (a newer "C6" food-ingredient ester yielding lower peak ketosis of ~0.8–1.7 mM) and the R,S-1,3-butanediol acetoacetate diester — have also been described but are less prominent in endurance-performance research (Stubbs et al., 2021; Desrochers et al., 1995; Leckey et al., 2017)

4.2 Ketone Salts

Ketone salts consist of β-HB molecularly paired with sodium, potassium, calcium, or magnesium cations, in racemic (DL-β-HB) or enantiopure (D-β-HB) forms. Following oral ingestion, the salt dissociates, releasing free β-HB and the paired mineral cation. While ketone salts are generally better tolerated organoleptically than ketone esters, their pharmacokinetic profile is substantially less potent: typical doses of 10–30 g produce peak blood β-HB of only 0.5–1.5 mM, a level insufficient to substantially alter substrate oxidation patterns during high-intensity exercise (Fischer et al., 2018).

An additional pharmacokinetic consideration is that commercially available ketone salt products typically contain the racemic DL-β-HB mixture; only the D-isomer (R-β-HB) is the physiologically active stereoisomer; the L-isomer (S-β-HB) is poorly metabolized by human tissue, meaning racemic products must be dosed at roughly twice the quantity to deliver an equivalent amount of active D-β-HB. The mineral load of ketone salt products is a practical constraint: a 25 g racemic dose may deliver on the order of 1,000–2,700 mg of sodium (alongside calcium, magnesium, or potassium, depending on formulation), raising concerns regarding hypertension and fluid balance in chronic users, though acute ergogenic testing does not typically observe clinically significant hemodynamic effects.

4.3 Medium-Chain Triglycerides as Indirect Ketogenic Agents

Medium-chain triglycerides (MCTs), comprising primarily caprylic acid (C8:0) and capric acid (C10:0), represent an indirect ketogenic supplement that promotes endogenous hepatic ketogenesis following rapid intestinal absorption and portal delivery to the liver. Unlike long-chain fatty acids, MCTs bypass mitochondrial carnitine-dependent transport and undergo rapid β-oxidation; the resulting surplus acetyl-CoA that exceeds tricarboxylic acid cycle capacity is redirected toward ketone synthesis. Caprylic acid

(C8:0) is the most ketogenic of the medium-chain fatty acids. While MCT supplementation reliably elevates blood ketone concentrations above baseline, the magnitude of ketosis achieved (typically 0.5–1.5 mM at doses of 10–20 g) is modest relative to ketone esters, and higher doses (>20–30 g) frequently cause gastrointestinal distress, limiting practical utility in competitive settings (St-Pierre et al., 2019).

4.4 Supplementation Protocols for Athletic Application

Table 2. Summary of Randomized Controlled Trials Examining Exogenous Ketone Supplementation and Endurance Performance

Author(s), Year	n / Design	Supplementation Protocol	Exercise / Outcome Measure	Effect on Performance
Cox et al. (2016),	39 high-performance cyclists; RCT crossover (5 sub-studies)	Ketone monoester (R-3-hydroxybutyl R-3-hydroxybutyrate), ~573 mg/kg + carbohydrate	60-min submaximal preload + 30-min TT (distance covered)	Positive: ~2% greater distance vs CHO alone; reduced blood lactate and muscle glycogen use
Leckey et al. (2017),	10 highly trained male cyclists; RCT crossover	1,3-butanediol acetoacetate diester, 2 × 250 mg/kg, pre-race	~31-km simulated road TT	Negative: ~2% slower ($p<0.05$); frequent GI distress, likely contributing to impairment
Holdsworth et al. (2017)	12 trained men; RCT crossover (recovery study)	Ketone monoester + glucose, post-exercise	Post-exercise muscle glycogen synthesis (not a performance test)	Recovery: +~50% muscle glycogen synthesis vs glucose alone; no performance TT measured
Rodger et al. (2017)	12 trained cyclists; RCT crossover	β-HB ketone salt, before/during submaximal exercise	4-min maximal cycling test after submaximal exercise	Neutral: no improvement in 4-min cycling performance
O'Malley et al. (2017)	10 healthy active men; RCT crossover	Ketone salts (~0.3 g/kg), pre-exercise	Cycling TT (high-intensity)	Negative: impaired high-intensity TT performance; increased fat oxidation
Evans et al. (2019)	8 trained runners; RCT crossover	Ketone monoester, pre-exercise	10-km running TT	Neutral: no benefit on 10-km running performance
Poffé et al. (2019)	18 male cyclists; 3-week RCT (overload block)	Ketone monoester (KE), 3×/day during intensified training	Overreaching markers, recovery, endurance performance	Recovery/positive: blunted overreaching symptoms; improved recovery biomarkers & post-overload performance

Author(s), Year	n / Design	Supplementation Protocol	Exercise / Outcome Measure	Effect on Performance
Poffé et al. (2023)	18 healthy active men; 3-week RCT, parallel (overload block)	Ketone monoester (R-3-HB R-3-HB), 25 g post-exercise + pre-sleep, daily	Pro-angiogenic factors, EPO, muscle capillarization during endurance overload	Recovery/positive: increase in circulating EPO and muscular angiogenesis; not an acute TT test
Robberechts et al. (2023)	10 well trained male cyclists; RCT crossover (3 conditions)	Ketone monoester, post-exercise + pre-sleep	Polysomnographic sleep architecture after strenuous evening exercise	Recovery: increased sleep efficiency; counteracted exercise-induced decline in REM sleep; no TT measured
Evans et al. (2023)	9 healthy men; RCT crossover	Ketone monoester (R-3-HB R-3-HB), 0.29 g/kg ×4 post-exercise, + sucrose/protein	Post-exercise serum erythropoietin (EPO); not a performance test	Recovery/adaptation: increased post-exercise serum EPO vs nutrition alone
Quinones et al. (2024)	9 recreationally active men; RCT crossover, double-blind	Ketone monoester (25 g) + CHO (1.2 g/kg/h), during recovery	20-km + 5-km cycling TT after glycogen-lowering exercise and 4-h recovery	Neutral: no improvement in subsequent TT despite lower glycemia; dissociates glycogen/recovery effects from performance
Waldman et al. (2024)	12 trained **women**; RCT crossover, double-blind	Ketone monoester + CHO	Submaximal cycling + 10-km TT; cognitive battery post-exercise	Neutral (performance): no TT benefit; improved some post-exercise cognitive measures.

Note: RCT = randomized controlled trial; TT = time trial; GI = gastrointestinal; β-HB = β-hydroxybutyrate; CHO = carbohydrate; EPO = erythropoietin. Effects are classified as positive, negative, neutral, or recovery-related based on the primary publication. Holdsworth (2017), Poffé (2019, 2023), Evans (2023), and Robberechts (2023) assessed recovery/adaptation rather than acute time-trial performance.

Table 3. Comparison of Exogenous Ketone Supplementation Modalities: Pharmacokinetic and Practical Considerations

Supplement Type	Typical Dose	Timing	β-HB Peak (mM)	GI Tolerability	Evidence Level	Key Sources
Ketone monoester (KME) — (R)-3-hydroxybutyl (R)-3-hydroxybutyrate (Veech/Clarke ester)	0.4–0.6 g/kg BW	30–45 min pre-exercise	3–6 mM	Moderate (bitter taste; nausea, GI distress at higher doses)	Moderate–High (multiple RCTs)	Clarke et al. 2012; Cox et al. 2016;

Ketone diester (KDE) — 1,3-butanediol acetoacetate diester	~0.25–0.5 g/kg BW	~30 min pre-exercise	~1.5–3 mM	Poor (notably unpalatable; frequent GI distress)	Low–Moderate (few RCTs; ergolytic in Leckey 2017)	Leckey et al. 2017
Ketone salt (KS) — β-HB + $Na^+/K^+/Ca^{2+}/Mg^{2+}$	10–30 g (variable; racemic needs ~2× dose)	30–60 min pre-exercise	0.5–1.5 mM	Good–moderate (mineral/electrolyte load)	Low–Moderate (RCTs mostly neutral/negative)	Fischer et al. 2018; O'Malley et al. 2017
MCT oil (indirect ketogenic)	10–20 g (C8/C10)	30–90 min pre-exercise	0.5–1.5 mM	Poor (cramps, diarrhea at >20–30 g)	Low (variable results)	St-Pierre et al.2019
Ketogenic diet (endogenous)	<50 g CHO/day, ≥4 weeks	Chronic (dietary intervention)	1–3 mM (resting)	Good (once adapted)	Moderate (observational + RCTs)	Harvey et al. 2019

Note. β-HB = β-hydroxybutyrate; BW = body weight; CHO = carbohydrate; MCT = medium-chain triglyceride; GI = gastrointestinal; mM = millimolar. The ketone monoester (Veech/Clarke ester) reaches substantially higher β-HB than the 1,3-butanediol acetoacetate diester or ketone salts. Racemic (DL) salts require roughly twice the dose to deliver an equivalent amount of physiologically active D-β-HB.

5. Results: Performance Outcomes

5.1 Scope and Approach

This review draws on the body of peer-reviewed trials identified through the search strategy described in Section 2 that have examined exogenous ketone supplementation in the context of endurance and recovery. The relevant primary literature remains relatively small: as of the late 2010s, commentators noted that only a handful of controlled athlete studies of exogenous ketones had been published (Evans et al., 2017), and the field has expanded only modestly since. The studies included here were selected because they employ controlled designs (randomized crossover or parallel-group trials) in trained or recreationally active adults, use defined supplementation protocols (ketone esters, ketone salts, or related ketogenic agents), and report endurance-relevant outcomes such as time-trial performance, time-to-exhaustion, submaximal efficiency, or recovery markers.

Across this literature, findings are notably heterogeneous. A single influential trial reported an acute performance benefit when a ketone monoester was co-ingested with carbohydrate (Cox et al., 2016), whereas several subsequent trials found neutral effects (e.g., Evans et al., 2019; Rodger et al., 2017) and others reported impaired performance, particularly with the less palatable acetoacetate diester or with ketone salts at high-intensity workloads (Leckey et al., 2017; O'Malley et al., 2017). A separate and more consistent signal has emerged in the recovery and adaptation domain, where ketone ester ingestion has been associated with enhanced post-exercise muscle glycogen synthesis (Holdsworth et al., 2017) and attenuated overreaching during intensified training (Poffé et al., 2019). This divergence — acute

performance findings that conflict, alongside more promising recovery findings — frames the synthesis that follows.

5.2 Effects on Endurance Time-Trial Performance

Time-trial performance is the most ecologically valid measure of competitive endurance capacity, and it is here that the literature is most conflicting. The most frequently cited positive finding comes from Cox et al. (2016), in which co-ingestion of a ketone monoester with carbohydrate increased distance covered in a 30-minute cycling time-trial by approximately 2% relative to carbohydrate alone, accompanied by lower blood lactate and reduced muscle glycogen utilization. This result, however, has not been consistently reproduced. Using a different compound (the acetoacetate diester) in highly trained cyclists, Leckey et al. (2017) observed a roughly 2% impairment of ~31-km time-trial performance, an effect the authors linked to frequent gastrointestinal distress. Other controlled trials have reported neutral outcomes, including Evans et al. (2019) for 10-km running and Rodger et al. (2017) for short maximal cycling. In a subsequent trial from the same group, exogenous ketosis affected neither time-trial performance nor muscle glycogen breakdown during prolonged endurance exercise (Poffé et al., 2020). Taken together, the acute time-trial evidence does not support a robust, generalizable ergogenic effect; where benefit appears, it seems most plausible at moderate-to-high submaximal intensities and in combination with carbohydrate, whereas higher-intensity efforts and less palatable formulations are more often neutral or detrimental.

Ketone salts, which produce substantially lower blood ketone concentrations than esters, show a correspondingly weaker and less consistent performance signal. Salt-based trials have reported impaired high-intensity performance alongside increased fat oxidation, and the limited ketosis achieved with these formulations is the most likely explanation for their attenuated effect relative to esters (O'Malley et al.2017).

5.3 Effects on VO_2max and Submaximal Exercise Efficiency

There is no convincing evidence that acute or short-term exogenous ketone supplementation improves maximal oxygen uptake (VO_2max). This is biochemically unsurprising, since VO_2max is principally constrained by central cardiovascular oxygen-delivery capacity rather than by mitochondrial substrate availability, which exogenous ketones modify (Basset et al., 2000). The more plausible locus of any efficiency effect is submaximal exercise: several investigators have proposed, on the basis of the thermodynamic properties of ketone oxidation, that economy at moderate intensities might improve. The empirical support for a measurable improvement in submaximal economy is mixed and modest, and should be regarded as a hypothesis under investigation rather than an established finding. (Evans et al., 2017; Evans et al., 2022)

5.4 Effects on Substrate Oxidation and Metabolic Flexibility

Exogenous ketones do reliably alter substrate utilization, and this is the most mechanistically consistent part of the literature. Ketone ester ingestion typically lowers the respiratory exchange ratio during the early phase of exercise, reflecting a shift away from carbohydrate combustion toward ketone and fat oxidation. The clearest demonstration remains Cox et al. (2016), in which muscle biopsy data indicated attenuated glycogenolysis and lower intramuscular lactate during submaximal exercise, while skeletal muscle ATP turnover was maintained — consistent with ketone bodies acting as a supplementary fuel rather than simply suppressing total metabolic flux. Lower blood lactate at matched workloads has been observed in

several ketone ester trials, attributable both to reduced glycolytic pyruvate generation and possibly to ketone-related effects on pyruvate-to-lactate conversion. Whether this glycogen-sparing and lactate-lowering effect translates into a performance advantage is precisely the question on which the time-trial literature disagrees.

5.5 Recovery and Overreaching Studies

A more consistent and arguably more promising signal has emerged in the domain of recovery and training adaptation. Holdsworth et al. (2017) reported that co-ingestion of a ketone ester with glucose after exercise substantially increased post-exercise muscle glycogen synthesis relative to glucose alone, a mechanism the authors linked to ketone-induced elevation of insulin. Building on this, Poffé et al. (2019) conducted a three-week trial in which trained participants undertook an intensified (overload) training block while supplementing with a ketone ester or placebo. The ketone group showed blunted symptoms of overreaching, more favourable recovery and endocrine biomarkers, and better preservation of endurance performance across the overload period. These findings suggest that the most defensible application of exogenous ketones may lie in buffering the catabolic and inflammatory consequences of heavy training, rather than in acute within-session performance enhancement. It should be noted that this recovery literature remains small and warrants replication before firm recommendations are made.

5.6 Adverse Events and Safety Considerations

Gastrointestinal symptoms are the most commonly reported adverse effects of exogenous ketone supplementation, and their frequency and severity vary considerably with the compound, the dose, and co-ingested food. The acetoacetate diester has been associated with particularly poor palatability and frequent gastrointestinal distress at performance-relevant doses, and this distress has itself been implicated as a probable contributor to impaired performance in at least one trial (Leckey et al., 2017). Ketone monoesters are generally better tolerated than the diester but can still cause nausea and gastrointestinal discomfort, especially at higher boluses, whereas ketone salts tend to be better tolerated organoleptically, with the principal concern shifting to their high mineral-cation load rather than direct gastrointestinal irritation (Fischer et al., 2018). Serious adverse events have not been a prominent feature of the controlled trials conducted to date; for example, sustained ingestion of a ketone monoester three times daily for 28 days produced no clinically meaningful changes in vital signs, blood chemistry, or kidney function in healthy adults, with only mild, infrequent nausea reported (Soto-Mota et al., 2019). Importantly, exogenous ketosis is physiologically distinct from diabetic ketoacidosis: supplementation typically raises blood β-HB to the single-digit millimolar range, far below the concentrations seen in pathological ketoacidosis, and does so without the insulin deficiency and uncontrolled lipolysis that characterize that state (Harvey et al., 2019). Long-term safety data for sustained supplementation in athletic populations remain limited, and this gap should temper any move toward routine or prolonged use.

6. Discussion

6.1 Mechanistic Integration: Why Ketone Bodies May (or May Not) Be Ergogenic

The mechanistic case for ketone bodies as ergogenic aids rests on several interconnected biochemical propositions: (1) that elevated circulating β-HB can serve as an additional oxidative fuel substrate, sparing muscle glycogen for deployment at higher exercise intensities; (2) that ketone oxidation

may carry a thermodynamic efficiency advantage per unit oxygen, although — as discussed in Section 3.2 — this claim is contested and the relevant comparison with glucose does not clearly favor ketones; (3) that β-HB-mediated signaling effects, including class I HDAC inhibition, GPR109A activation, and NLRP3 inflammasome suppression, may confer metabolic and adaptive benefits during and after exercise; and (4) that reduced glycolytic flux attenuates lactate and hydrogen ion accumulation, potentially delaying peripheral fatigue.

Of these, the glycogen-sparing proposition has the firmest experimental footing. Muscle biopsy data, most notably from Cox et al. (2016), indicate reduced glycogenolysis during submaximal exercise following ketone ester ingestion, while ATP turnover is maintained — consistent with ketone oxidation substituting for glycolytic energy delivery rather than simply lowering total metabolic flux. The logical inference is that if this glycogen economy could be converted into sustained higher power output late in an event, a performance benefit should follow. The difficulty is that this inference is not reliably borne out: the time-trial literature does not consistently show such a benefit, which suggests that glycogen sparing, while real, is not by itself sufficient to guarantee improved performance.

Counterarguments reinforce this caution. It has been argued that the thermodynamic efficiency advantage of ketone oxidation, even where demonstrable in isolated preparations, may not translate to intact exercising human muscle, where substrate competition and enzyme kinetics operate under very different conditions. Moreover, the lower respiratory exchange ratio observed after ketone ingestion may reflect not superior efficiency but simply a shift toward ketone and fat utilization that could become disadvantageous at intensities demanding rapid glycolytic ATP production above the lactate threshold.

6.2 Reconciling Positive and Negative Trial Results

The central interpretive challenge is the heterogeneity between positive and negative trials. Several factors appear to be important. First, exercise intensity and duration appear important: the positive Cox et al. (2016) result was obtained during prolonged submaximal cycling, a context in which glycogen sparing would be expected to matter, whereas trials emphasizing shorter or higher-intensity efforts — where the glycolytic pathway cannot easily be replaced — have more often been neutral or negative. Second, the interaction with carbohydrate availability appears central; the clearest benefit was observed when the ketone ester was co-ingested with carbohydrate, and the relationship between exogenous ketones and carbohydrate-insulin dynamics is not fully resolved. Third, compound and formulation matter substantially: the acetoacetate diester used by Leckey et al. (2017) was both less palatable and associated with impaired performance, whereas ketone salts produce too little ketosis to alter substrate use meaningfully.

A further, largely untested possibility is that individual variability in metabolic flexibility — the capacity to adjust fuel oxidation to substrate availability — shapes the response to exogenous ketones. Athletes with already high fat-oxidative capacity might show blunted responses, while others could benefit proportionally more. This remains a hypothesis rather than an established finding and would require pre-supplementation metabolic phenotyping to test directly.

6.3 Comparison with Established Ergogenic Strategies

It is useful to situate exogenous ketones among better-established nutritional ergogenic aids, while being explicit that no reliable pooled effect size for ketones can be derived from the current heterogeneous

and conflicting literature. By contrast, caffeine is among the most robustly supported endurance ergogenics, with consistent benefits across many time-trial studies at doses of roughly 3–6 mg/kg (Guest et al., 2021); dietary nitrate (beetroot juice) shows smaller and more context-dependent benefits, particularly in less-trained individuals (Jones, 2014); and sodium bicarbonate can benefit shorter, high-intensity efforts through extracellular buffering (Carr et al., 2012). Against this backdrop, exogenous ketones currently sit below these agents in evidentiary strength: where any acute benefit appears, it is small and inconsistent, and unlike caffeine it has not been reliably reproduced. Their more distinctive potential may lie less in acute time-trial enhancement than in recovery and training-adaptation contexts.

Ketones may also interact with other nutritional strategies. The apparent dependence of the ergogenic signal on carbohydrate co-ingestion is consistent with the glycogen-sparing rationale operating against a background of adequate carbohydrate availability. Whether ketones combine usefully with caffeine, β-alanine, creatine, or bicarbonate — each acting through distinct mechanisms — has not been systematically established, although one trial reported that co-ingesting bicarbonate to offset ketone-induced acidosis unlocked an ergogenic effect of the ketone monoester during endurance exercise (Poffé et al., 2021).

6.4 Practical Limitations and Future Directions

Several practical barriers limit the adoption of ketone supplementation in competitive endurance sport. Ketone esters, particularly the diester, are unpalatable, which both reduces compliance and can complicate blinding in trials relying on subjective effort or performance outcomes (Leckey et al., 2017). Commercial ketone ester products remain expensive relative to most sports-nutrition products, limiting accessibility. Gastrointestinal intolerance at performance-relevant doses is common enough that individual tolerance testing well before competition is essential (Stubbs et al., 2019).

A further limitation concerns the external validity of the current evidence base with respect to sex. Almost all controlled trials of exogenous ketones in endurance and recovery contexts — including the recent recovery-domain studies — have been conducted exclusively in male participants. The principal exception is Waldman et al. (2024), one of the very few trials in trained women, which found no time-trial benefit from a ketone monoester co-ingested with carbohydrate but did report improvements in some post-exercise cognitive measures. A single such study is insufficient to establish whether the metabolic or performance response to exogenous ketones differs by sex, and this gap limits the generalizability of present conclusions rather than merely defining a direction for future work.

Priorities for future research include: (1) dose-optimization studies examining lower, potentially better-tolerated ester doses co-ingested with carbohydrate; (2) longer-term supplementation trials assessing adaptation-mediated effects on training quality, recovery, and competitive performance, given that the most consistent signal to date is in the recovery domain; (3) further trials in female athletes, who remain markedly underrepresented despite isolated exceptions, to determine whether ketone responses are sex-dependent; (4) mechanistic work on inter-individual variability in ketone pharmacokinetics and metabolic response, including any role of the gut microbiome; and (5) development and testing of more palatable, better-tolerated delivery formats.

7. Conclusions

This review has evaluated the biochemical mechanisms, supplementation protocols, and performance effects of exogenous ketone bodies in endurance sport. At the level of physiology, the case for exogenous ketones is real: ketone esters acutely raise circulating β-HB into the single-digit millimolar range — typically up to about 6 mM for the monoester — and this is sufficient to shift exercise substrate utilization, sparing muscle glycogen and lowering blood lactate during submaximal exercise. The difficulty lies in translating that metabolic shift into a competitive result.

On acute time-trial performance, the evidence is inconsistent. A single influential trial reported a small benefit when a ketone monoester was co-ingested with carbohydrate, but this finding has not been reliably reproduced, and other controlled trials have returned neutral or even impaired outcomes. Where a benefit does appear, it seems most plausible during prolonged submaximal exercise undertaken with concurrent carbohydrate, rather than during shorter or higher-intensity efforts where the glycolytic pathway cannot easily be replaced. By contrast, a more consistent signal has emerged away from acute performance — in recovery and training adaptation, including enhanced post-exercise muscle glycogen synthesis and attenuated overreaching during intensified training. The supporting mechanisms, among them class I HDAC inhibition, NLRP3 inflammasome suppression, and modulation of inflammatory and oxidative-stress pathways, are well established at the cellular level, even if their direct translation to athlete recovery still requires confirmation. This recovery application may ultimately prove more defensible than acute ergogenesis.

Two practical qualifications temper any recommendation. First, the heterogeneity of compounds, doses, timing, and study designs — compounded by gastrointestinal tolerability concerns — currently precludes generalized performance guidance, making individual tolerance testing and protocol optimization prerequisites for any use in competition. Second, the supplementation form matters: ketone salts reach substantially lower ketosis than esters, are generally insufficient to drive substrate-level ergogenic effects, and on present evidence are better regarded as electrolyte or potential recovery adjuncts than as acute performance aids.

In conclusion, exogenous ketone bodies occupy a distinctive position in the sports-nutrition landscape — mechanistically plausible and genuinely interesting, yet still unproven as a reliable route to a competitive performance advantage. As formulation technology improves and larger, better-controlled trials accumulate, particularly in the recovery domain and in underrepresented populations such as female athletes, the role of ketone supplementation in high-performance endurance sport should come into clearer focus.

References

Bassett, D. R., Jr, & Howley, E. T. (2000). Limiting factors for maximum oxygen uptake and determinants of endurance performance. Medicine and science in sports and exercise, 32(1), 70–84. https://doi.org/10.1097/00005768-200001000-00012

Cahill G. F., Jr (2006). Fuel metabolism in starvation. Annual review of nutrition, 26, 1–22. https://doi.org/10.1146/annurev.nutr.26.061505.111258

Carr, A. J., Hopkins, W. G., & Gore, C. J. (2011). Effects of acute alkalosis and acidosis on performance: a meta-analysis. Sports medicine (Auckland, N.Z.), 41(10), 801–814. https://doi.org/10.2165/11591440-000000000-00000

Clarke, K., Tchabanenko, K., Pawlosky, R., Carter, E., Todd King, M., Musa-Veloso, K., Ho, M., Roberts, A., Robertson, J., Vanitallie, T. B., & Veech, R. L. (2012). Kinetics, safety and tolerability of (R)-3-hydroxybutyl (R)-3-hydroxybutyrate in healthy adult subjects. Regulatory toxicology and pharmacology : RTP, 63(3), 401–408. https://doi.org/10.1016/j.yrtph.2012.04.008

Cox, P. J., Kirk, T., Ashmore, T., Willerton, K., Evans, R., Smith, A., Murray, A. J., Stubbs, B., West, J., McLure, S. W., King, M. T., Dodd, M. S., Holloway, C., Neubauer, S., Drawer, S., Veech, R. L., Griffin, J. L., & Clarke, K. (2016). Nutritional Ketosis Alters Fuel Preference and Thereby Endurance Performance in Athletes. Cell metabolism, 24(2), 256–268. https://doi.org/10.1016/j.cmet.2016.07.010

Desrochers, S., Dubreuil, P., Brunet, J., Jetté, M., David, F., Landau, B. R., & Brunengraber, H. (1995). Metabolism of (R,S)-1,3-butanediol acetoacetate esters, potential parenteral and enteral nutrients in conscious pigs. The American journal of physiology, 268(4 Pt 1), E660–E667. https://doi.org/10.1152/ajpendo.1995.268.4.E660

Evans, M., Cogan, K. E., & Egan, B. (2017). Metabolism of ketone bodies during exercise and training: physiological basis for exogenous supplementation. The Journal of physiology, 595(9), 2857–2871. https://doi.org/10.1113/JP273185

Evans, M., McSwiney, F. T., Brady, A. J., & Egan, B. (2019). No Benefit of Ingestion of a Ketone Monoester Supplement on 10-km Running Performance. Medicine and science in sports and exercise, 51(12), 2506–2515. https://doi.org/10.1249/MSS.0000000000002065

Evans, M., McClure, T. S., Koutnik, A. P., & Egan, B. (2022). Exogenous Ketone Supplements in Athletic Contexts: Past, Present, and Future. Sports medicine (Auckland, N.Z.), 52(Suppl 1), 25–67. https://doi.org/10.1007/s40279-022-01756-2

Evans, E., Walhin, J. P., Hengist, A., Betts, J. A., Dearlove, D. J., & Gonzalez, J. T. (2023). Ketone monoester ingestion increases postexercise serum erythropoietin concentrations in healthy men. American journal of physiology. Endocrinology and metabolism, 324(1), E56–E61. https://doi.org/10.1152/ajpendo.00264.2022

Fischer, T., Och, U., Klawon, I., Och, T., Grüneberg, M., Fobker, M., Bordewick-Dell, U., & Marquardt, T. (2018). Effect of a Sodium and Calcium DL-β-Hydroxybutyrate Salt in Healthy Adults. Journal of nutrition and metabolism, 2018, 9812806. https://doi.org/10.1155/2018/9812806

Guest, N. S., VanDusseldorp, T. A., Nelson, M. T., Grgic, J., Schoenfeld, B. J., Jenkins, N. D. M., … Campbell, B. I. (2021). International society of sports nutrition position stand: caffeine and exercise performance. Journal of the International Society of Sports Nutrition, 18(1). https://doi.org/10.1186/s12970-020-00383-4

Harvey, K. L., Holcomb, L. E., & Kolwicz, S. C., Jr (2019). Ketogenic Diets and Exercise Performance. Nutrients, 11(10), 2296. https://doi.org/10.3390/nu11102296

Holdsworth, D. A., Cox, P. J., Kirk, T., Stradling, H., Impey, S. G., & Clarke, K. (2017). A Ketone Ester Drink Increases Postexercise Muscle Glycogen Synthesis in Humans. Medicine and science in sports and exercise, 49(9), 1789–1795. https://doi.org/10.1249/MSS.0000000000001292

Jones A. M. (2014). Dietary nitrate supplementation and exercise performance. Sports medicine (Auckland, N.Z.), 44 Suppl 1(Suppl 1), S35–S45. https://doi.org/10.1007/s40279-014-0149-y

Laffel L. (1999). Ketone bodies: a review of physiology, pathophysiology and application of monitoring to diabetes. Diabetes/metabolism research and reviews, 15(6), 412–426. https://doi.org/10.1002/(sici)1520-7560(199911/12)15:6<412::aid-dmrr72>3.0.co;2-8

Leckey, J. J., Ross, M. L., Quod, M., Hawley, J. A., & Burke, L. M. (2017). Ketone Diester Ingestion Impairs Time-Trial Performance in Professional Cyclists. Frontiers in physiology, 8, 806. https://doi.org/10.3389/fphys.2017.00806

Newman, J. C., & Verdin, E. (2014). Ketone bodies as signaling metabolites. Trends in endocrinology and metabolism: TEM, 25(1), 42–52. https://doi.org/10.1016/j.tem.2013.09.002

O'Malley, T., Myette-Cote, E., Durrer, C., & Little, J. P. (2017). Nutritional ketone salts increase fat oxidation but impair high-intensity exercise performance in healthy adult males. Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme, 42(10), 1031–1035. https://doi.org/10.1139/apnm-2016-0641

Poffé, C., Ramaekers, M., Van Thienen, R., & Hespel, P. (2019). Ketone ester supplementation blunts overreaching symptoms during endurance training overload. The Journal of physiology, 597(12), 3009–3027. https://doi.org/10.1113/JP277831

Poffé, C., Ramaekers, M., Bogaerts, S., & Hespel, P. (2020). Exogenous ketosis impacts neither performance nor muscle glycogen breakdown in prolonged endurance exercise. Journal of applied physiology (Bethesda, Md. : 1985), 128(6), 1643–1653. https://doi.org/10.1152/japplphysiol.00092.2020

Poffé, C., Ramaekers, M., Bogaerts, S., & Hespel, P. (2021). Bicarbonate Unlocks the Ergogenic Action of Ketone Monoester Intake in Endurance Exercise. Medicine and science in sports and exercise, 53(2), 431–441. https://doi.org/10.1249/MSS.0000000000002467

Poffé, C., Robberechts, R., Van Thienen, R., & Hespel, P. (2023). Exogenous ketosis elevates circulating erythropoietin and stimulates muscular angiogenesis during endurance training overload. The Journal of physiology, 601(12), 2345–2358. https://doi.org/10.1113/JP284346

Quinones, M. D., Weiman, K., & Lemon, P. W. R. (2024). Ketone Monoester Followed by Carbohydrate Ingestion after Glycogen-Lowering Exercise Does Not Improve Subsequent Endurance Cycle Time Trial Performance. Nutrients, 16(7), 932. https://doi.org/10.3390/nu16070932

Robberechts, R., Albouy, G., Hespel, P., & Poffé, C. (2023). Exogenous Ketosis Improves Sleep Efficiency and Counteracts the Decline in REM Sleep after Strenuous Exercise. Medicine and science in sports and exercise, 55(11), 2064–2074. https://doi.org/10.1249/MSS.0000000000003231

Rodger, S., Plews, D., Laursen, P., & Driller, M. (2017). The effects of an oral β-hydroxybutyrate supplement on exercise metabolism and cycling performance. Journal of Science and Cycling, 6(1), 26-31. Retrieved from https://www.jsc-journal.com/index.php/JSC/article/view/304

Shimazu, T., Hirschey, M. D., Newman, J., He, W., Shirakawa, K., Le Moan, N., Grueter, C. A., Lim, H., Saunders, L. R., Stevens, R. D., Newgard, C. B., Farese, R. V., Jr, de Cabo, R., Ulrich, S., Akassoglou, K., & Verdin, E. (2013). Suppression of oxidative stress by β-hydroxybutyrate, an endogenous histone deacetylase inhibitor. Science (New York, N.Y.), 339(6116), 211–214. https://doi.org/10.1126/science.1227166

Soto-Mota, A., Vansant, H., Evans, R. D., & Clarke, K. (2019). Safety and tolerability of sustained exogenous ketosis using ketone monoester drinks for 28 days in healthy adults. Regulatory toxicology and pharmacology : RTP, 109, 104506. https://doi.org/10.1016/j.yrtph.2019.104506

St-Pierre, V., Vandenberghe, C., Lowry, C. M., Fortier, M., Castellano, C. A., Wagner, R., & Cunnane, S. C. (2019). Plasma Ketone and Medium Chain Fatty Acid Response in Humans Consuming Different Medium Chain Triglycerides During a Metabolic Study Day. Frontiers in nutrition, 6, 46. https://doi.org/10.3389/fnut.2019.00046

Stubbs, B. J., Cox, P. J., Evans, R. D., Santer, P., Miller, J. J., Faull, O. K., Magor-Elliott, S., Hiyama, S., Stirling, M., & Clarke, K. (2017). On the Metabolism of Exogenous Ketones in Humans. Frontiers in physiology, 8, 848. https://doi.org/10.3389/fphys.2017.00848

Stubbs, B. J., Cox, P. J., Kirk, T., Evans, R. D., & Clarke, K. (2019). Gastrointestinal Effects of Exogenous Ketone Drinks are Infrequent, Mild, and Vary According to Ketone Compound and Dose. International journal of sport nutrition and exercise metabolism, 29(6), 596–603. https://doi.org/10.1123/ijsnem.2019-0014

Stubbs, B. J., Blade, T., Mills, S., Thomas, J., Yufei, X., Nelson, F. R., Higley, N., Nikiforov, A. I., Rhiner, M. O., Verdin, E., & Newman, J. C. (2021). In vitro stability and in vivo pharmacokinetics of the novel ketogenic ester, bis hexanoyl (R)-1,3-butanediol. Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, 147, 111859. https://doi.org/10.1016/j.fct.2020.111859

Suresh, V. V., Sivaprakasam, S., Bhutia, Y. D., Prasad, P. D., Thangaraju, M., & Ganapathy, V. (2025). Not Just an Alternative Energy Source: Diverse Biological Functions of Ketone Bodies and Relevance of HMGCS2 to Health and Disease. Biomolecules, 15(4), 580. https://doi.org/10.3390/biom15040580

Taggart, A. K., Kero, J., Gan, X., Cai, T. Q., Cheng, K., Ippolito, M., Ren, N., Kaplan, R., Wu, K., Wu, T. J., Jin, L., Liaw, C., Chen, R., Richman, J., Connolly, D., Offermanns, S., Wright, S. D., & Waters, M. G. (2005). (D)-beta-Hydroxybutyrate inhibits adipocyte lipolysis via the nicotinic acid receptor PUMA-G. The Journal of biological chemistry, 280(29), 26649–26652. https://doi.org/10.1074/jbc.C500213200

Tsuruta, H., Yamahara, K., Yasuda-Yamahara, M., & Kume, S. (2024). Emerging Pathophysiological Roles of Ketone Bodies. Physiology (Bethesda, Md.), 39(3), 0. https://doi.org/10.1152/physiol.00031.2023

Veech, R. L., Chance, B., Kashiwaya, Y., Lardy, H. A., & Cahill, G. F., Jr (2001). Ketone bodies, potential therapeutic uses. IUBMB life, 51(4), 241–247. https://doi.org/10.1080/152165401753311780

Veech R. L. (2004). The therapeutic implications of ketone bodies: the effects of ketone bodies in pathological conditions: ketosis, ketogenic diet, redox states, insulin resistance, and mitochondrial metabolism. Prostaglandins, leukotrienes, and essential fatty acids, 70(3), 309–319. https://doi.org/10.1016/j.plefa.2003.09.007

Waldman, H. S., O'Neal, E. K., Barker, G. A., Witt, C. R., Lara, D. A., Huber, A. K., Forsythe, V. N., Koutnik, A. P., D'Agostino, D. P., Staiano, W., & Egan, B. (2024). A Ketone Monoester with Carbohydrate Improves Cognitive Measures Postexercise, but Not Performance in Trained Females. Medicine and science in sports and exercise, 56(4), 725–736. https://doi.org/10.1249/MSS.0000000000003352

Youm, Y. H., Nguyen, K. Y., Grant, R. W., Goldberg, E. L., Bodogai, M., Kim, D., D'Agostino, D., Planavsky, N., Lupfer, C., Kanneganti, T. D., Kang, S., Horvath, T. L., Fahmy, T. M., Crawford, P. A., Biragyn, A., Alnemri, E., & Dixit, V. D. (2015). The ketone metabolite β-hydroxybutyrate blocks NLRP3

inflammasome-mediated inflammatory disease. Nature medicine, 21(3), 263–269. https://doi.org/10.1038/nm.3804