

Assessing Acute Transcutaneous Carnosine Delivery as an Ergogenic  
Aid in Middle Distance Running

Stuart Hofmeyr

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AUT School of Sport, Exercise, and Health

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## Abstract

This study investigated the ergogenic effect of acute application of a topical carnosine gel on middle distance running performance. In a block-randomised, single-blind, crossover design, 16 trained middle-distance runners (9 males, 7 females; age  $25 \pm 5$  years; height,  $177 \pm 7$  cm; mass,  $67 \pm 6$  kg, training duration  $8.3 \pm 3.2$  h/wk) performed an 800m outdoor individual time-trial under three different conditions: no-gel trial (NG), informed carnosine – given placebo gel (PG), and informed carnosine – given carnosine gel trial (CG). Gel dose was 0.2ml/kg body mass ( $13.4 \pm 1.3$  mL) which was applied to the upper and lower legs 60 min prior to the time-trial. Blood lactate (BLa), heart rate (HR) and perceptual responses were determined pre and post time-trial. Linear mixed modelling revealed that there was no difference in 800m performance time ( $p = .276$ ), lap split difference ( $p = .419$ ), peak HR ( $p = .956$ ), perceived readiness ( $p = .644$ ), or differential RPE ( $p = .805$  to  $.891$ ), between conditions. There was an overall effect of trial condition on post-trial peak blood lactate ( $p = .029$ ), with a greater peak blood lactate in CG than NG trials (NG =  $15.0 \pm 4.2$ , PG =  $15.5 \pm 3.9$ , CG =  $16.5 \pm 3.7$  mmol/L,  $p = .017$ ,  $d = 0.45$ ), but not PG vs CG trials ( $p = .114$ ) or NG vs PG ( $p = .420$ ). In conclusion, despite some evidence for greater blood lactate concentration, the application of a topical carnosine gel has no ergogenic placebo or true ergogenic effect on middle-distance running performance.

**Keywords:** acid–base balance, ergogenic aids, lotion, sprint-endurance, high-intensity exercise, buffer

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## Attestation of Authorship

“I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor used artificial intelligence tools or generative artificial intelligence tools (unless it is clearly stated, and referenced, along with the purpose of use), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning.”

Signed:


## Co-Authored Works

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<b>Kilding</b>	Conception and design of the project or output; analysis or interpretation of research data; drafting the manuscript
<b>Maunder</b>	Conception and design of the project or output; interpretation of research data; drafting the manuscript
<b>Rothschild</b>	Conception and design of the project

Stuart Hofmeyr



Andrew Kilding



Ed Maunder



Jeff Rothschild



## List of Abbreviations

ATP	Adenosine Triphosphate
ATPase	Adenosine Triphosphatase
BLa	Blood Lactate
cAMP	Cyclic adenosine monophosphate
CV%	Coefficient of Variability
ES:	Effect Size
HCO <sub>3</sub> <sup>-</sup>	Bicarbonate
HR	Heart Rate
K	Rate Constant (in chemical equilibrium)
Ka	Acid Dissociation Constant
La <sup>-</sup>	Lactate
LDH	Lactate Dehydrogenase
LMM	Linear Mixed Modelling/Model
MCT	Monocarboxylate Transporters
MRS	Magnetic Resonance Spectroscopy
NAD <sup>+</sup>	Nicotinamide Adenine Dinucleotide
NADH	Nicotinamide Adenine Dinucleotide Hydride
NaHCO <sub>3</sub> <sup>-</sup>	Sodium Bicarbonate
PCr	Phosphocreatine
PDH	Pyruvate Dehydrogenase
PFK	Phosphofructokinase
Phos	Glycogen Phosphorylase
PKA	Acid dissociation constant
RPE	Rate of Perceived Exertion
SERCA	Sarco/endoplasmic Reticulum
CaATPase	Calcium ATPase
SR	Sarcoplasmic Reticulum
TnC	Troponin-C
TT	Time Trial
TTE	Time to Exhaustion
TWD	Total Work Done
VO <sub>2</sub>	Oxygen Uptake

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### *Artificial Intelligence*

Artificial intelligence was used in the production of this thesis to help structure, organise and sequence ideas within writing. It was also used to summarise previously written sections and improve written grammar and concision.

## Ethics Approval

All experimental procedures of this thesis were approved by the Auckland University of Technology Ethics Committee on 6<sup>th</sup> November (24/271)

## Chapter 1: Introduction

Ergogenic aids are an important tool commonly used within sporting contexts from recreational to elite athletes. They function to address specific limiting factors during exercise in a way that can improve performance measures and outcomes. It is important that research attempts to independently determine the effectiveness of the many different supplements that are available to athletes and that claim to enhance performance. The outcomes of such applied research can be used to shape athletes' and practitioners' decisions regarding supplementation in the context of their own physiology and sporting event. Indeed, the current thesis aims to add to the immature but growing body of literature concerning topically applied supplements, such as LactiGo™, under unique contexts and performance environments. Specifically, this thesis aims to determine the effect of acute, topical carnosine on middle-distance running performance.

The outline of this thesis is shown in Table 1. Following this short introduction, Chapter 2 is a literature review which describes physiological processes that underpin the exercise response, acidosis as a source of peripheral fatigue and buffer-based compounds as ergogenic aids. Chapter 3 is the main experimental study of this thesis, which addresses the following research questions: (i) does the acute topical application placebo or carnosine gel improve 800m time-trial performance? (ii) does the application of topical carnosine gel change peak lactate response in trained middle-distance runners? (iii) does the acute topical application placebo or carnosine gel alter perceived readiness to perform before, and perceived effort after an 800m time-trial. This chapter is written in a format suitable for future submission to a peer-reviewed journal. It is acknowledged that due to this thesis being presented in Format 2: manuscript structure, there is some repetition between the literature review in Chapter 2, and the introduction of the manuscript in Chapter 3. Finally, Chapter 4, will further discuss the results of Chapter 3, placing them in an applied context and offering directions for further research.

*Table 1. Thesis Outline*

Chapter	Title	Purpose
1	Introduction	General introduction to the thesis
2	Supplementation in the context of High Intensity Exercise	Narrative literature review on acidosis as a limiting factor during high intensity exercise, and the primary supplements used to mitigate its effects
3	The Effect of Acute Topical Carnosine Application in Middle Distance Running	A randomised, crossover study assessing the effect of acute topical carnosine application on 800 meter time-trial performance and peak lactate in trained runners.
4	Summary and future directions	Overall discussion in which the results of Chapter 3 are applied to practice, and future research directions are offered

## Chapter 2: Literature Review

### Introduction

Sporting performance at the highest level demands athletes push themselves to the limits of their physiological capacity. Many Olympic and competitive events, particularly those lasting from 1 to 10 minutes, such as the 400m, 800m, and 1500m run, rowing, and cycling pursuits lead to marked disturbances in muscle pH (Cairns & Lindinger, 2025) and metabolite accumulation (Cairns, 2013) that contribute to fatigue and limit performance (Hultman et al., 1985; Sprague & Mann, 1983). Given the central role of acidosis in these scenarios, there has been longstanding interest in strategies that might attenuate its effects (Dennig et al., 1931). Among the most promising of these is supplementation designed to enhance the body's capacity to tolerate these chemical changes either through oral ingestion of agents like sodium bicarbonate (Grgic, Grgic, et al., 2021) and  $\beta$ -alanine (Trexler et al., 2015), or more recently, through topical delivery methods (Prausnitz et al., 2004) that aim to bypass limitations associated with gastrointestinal tolerance or the need for chronic dosing.

The aim of this review is to synthesise the literature around buffering strategies for high-intensity exercise, with a particular focus on the emerging role of transcutaneous supplementation. Specifically, it will (1) examine the physiological mechanisms underpinning high-intensity exercise and the role of acidosis, (2) review the compounds and evidence supporting traditional oral buffering agents such as  $\beta$ -alanine and sodium bicarbonate, and (3) explore novel topical applications, particularly carnosine-based products, for their potential as ergogenic aids in sport.

### Exercise Metabolism

#### *Acute exercise Metabolism*

Exercise metabolism functions to maintain the supply of high-energy adenosine triphosphate (ATP) to skeletal muscle. ATP is required for many cellular processes within myocytes including membrane excitability ( $\text{Na}^+/\text{K}^+$  ATPase), sarcoplasmic reticulum (SR) calcium handling ( $\text{Ca}^{2+}$  ATPase) and myofilament cross-bridge cycling (myosin ATPase) (MacIntosh et al., 2012). However, ATP is not stored in muscle in large quantities and is only able to supply energy sufficient for a few seconds in an all-out effort (Hargreaves & Spriet, 2020). Accordingly, other metabolic pathways are utilised including both substrate-level (anaerobic) and oxidative (aerobic) phosphorylation. Here we will discuss the pathways that lead to the generation of ATP, and how the contribution of these pathways shapes the exercise response, particularly during high intensity exercise.

During anaerobic phosphorylation most ATP is derived from the breakdown of phosphocreatine (PCr) and carbohydrates (Medbo & Tabata, 1993; Parolin et al., 1999). Beyond ATP glycolysis produces a series of intermediary molecules, most notably pyruvate, nicotinamide adenine dinucleotide hydride (NADH) and hydrogen ions ( $H^+$ ). These pathways have a very high power (rate of ATP production) but are extremely limited in their capacity (Sahlin et al., 1998). During aerobic phosphorylation most ATP is derived from the oxidation of carbohydrates and free fatty acids (Hawley et al., 2014) which is reliant on the delivery of oxygen to tissue and is characterised by its utilisation of hydrogen ions and electron-transporters to drive the production of ATP along with carbon dioxide, and water. These pathways have a very large capacity, with comparatively less power (Sahlin et al., 1998). The relative contribution of each metabolic pathway during exercise is determined by many factors between-individuals such as training status, diet, sex, age and environment, however within an individual the two primary factors are the intensity and duration of exercise (Romijn et al., 1993).

### *Intensity Dependent Response*

Exercise intensities are commonly categorised into ‘intensity domains’ - moderate, heavy, severe and extreme - with each characterised by their distinct oxygen uptake kinetics and blood lactate response (Jammick et al., 2020; Mann et al., 2013; Roston et al., 1987). During moderate intensity exercise,  $VO_2$  reaches a plateau and blood lactate and  $H^+$  concentrations remain near baseline (Hollidge-Horvat et al., 1999, 2000). ATP production is met primarily by oxidative phosphorylation (Barstow et al., 1994; Jorfeldt et al., 1978; Robergs et al., 2004; Rossiter et al., 1999) in type I muscle fibres (Henneman et al., 1965), with low calcium flux (Howlett et al., 1998). During heavy intensity exercise cytoplasmic ATP turnover increases alongside the recruitment of type II muscle fibres (Gaesser & Poole, 1996; Jones et al., 2011; Katz & Sahlin, 1988, 1990; Robergs et al., 2004) accompanied by a moderate amount of calcium flux. Blood and muscle lactate concentrations rise above baseline while muscle pH decreases, but a steady-state is achieved (Jorfeldt et al., 1978; Vanhatalo et al., 2016). The severe and extreme domains represent high-intensity exercise, where there is further recruitment of fatigable type II muscle fibres (Gaesser & Poole, 1996; Jones et al., 2011) and substantial calcium flux (Howlett et al., 1998). Blood and muscle lactate continue to rise, muscle pH progressively declines (Poole et al., 1988; Vanhatalo et al., 2016) and physiological steady-state cannot be achieved. Each domain therefore elicits a unique response, meaning the limiting factors are not strictly uniform across intensities.

### *Acidosis During High-intensity Exercise*

Acid-base balance is crucial factor that exists within homeostasis and physiological function of the body. Characterised by the presence of compound that either donate or accept a proton ( $H^+$ ) (Brönsted,

1923; Lowry, 1923). At rest intracellular pH is 7.0 to 7.2 while plasma is 7.3-7.4, and as mentioned above shows a continual drop during high-intensity exercise (Hermansen & Osnes, 1972). pH declines toward values of 6.6 and lower at task failure (Cairns & Lindinger, 2025; Juel et al., 1990). The relationship between reduction in pH and performance is clear but the mechanism by which this occurs has been a subject of investigation for quite some time (Fitts, 1994). Proposed mechanisms include impacts of calcium regulation at the sarcoplasmic reticulum, myofilament function and finally metabolism (Cairns & Lindinger, 2025), all of which have the capacity to impact available energy or the translation of energy to mechanical outcomes.

While  $H^+$  does not appear to impair the release of  $Ca^{2+}$  from the sarcoplasmic reticulum (SR) when normal physiological processes are involved, it does however inhibit  $Ca^{2+}$  reuptake by Sarcoplasmic/Endoplasmic Reticulum Calcium ATPase (SERCA) leading to slower relaxation time across both maximal and submaximal workloads (Wolosker et al., 1997). Reductions of pH to 6.0-6.5 see declines in shortening velocity by 15-30% (Karatzaferi et al., 2008; Knuth et al., 2006; Nelson & Fitts, 2014), a process likely due to changes in myosin ATPase activity (Blanchard et al., 1984; Parkhouse, 1992; Woodward & Debold, 2018). The effect of inhibited  $Ca^{2+}$  reuptake has also been reinforced in vitro where unloaded filament velocities declined as a result of slowed detachment between contractile fibres (Debold et al., 2008; Greenberg et al., 2010; Jarvis et al., 2018; Longyear et al., 2014; Woodward & Debold, 2018). Another effect at the site of myofilament is a reduction of  $Ca^{2+}$  sensitivity characterised by a shift in the force -  $Ca^{2+}$  relationship (Nelson et al., 2014; Pate et al., 1995; Westerblad et al., 1997; Westerblad & Allen, 1993) particularly in type II fibres (Nelson & Fitts, 2014). This change is likely driven by actions on troponin-C (TnC) that actively inhibit the binding of free  $Ca^{2+}$  and reduce cross-bridge formation that underly the suppression of force and power (el-Saleh & Solaro, 1988; Meyer et al., 1991; Parsons et al., 1997; Unger & Debold, 2019).

Beyond the direct effects of acidity on contraction, intracellular acidosis may also impact muscle function through the availability and supply of ATP. Increases in  $[H^+]$  severely inhibit the activity of phosphofructokinase (PFK) (Dobson et al., 1986; Trivedi & Danforth, 1966) and glycogen phosphorylase (Phos) (Chasiotis et al., 1983; Hollidge-Horvat et al., 1999; Kasvinsky & Meyer, 1977; Parolin et al., 1999), two key enzymes that regulate the release of glycogen and commitment of metabolic fuel to the glycolytic pathway (Bloxham et al., 1973; Cori et al., 1939). Increased  $[H^+]$  also reduces adenylate cycles activity, which lowers cyclic adenosine monophosphate (cAMP) and subsequent activation of glycogen phosphorylase for glycolysis (Chasiotis et al., 1983). These processes combine to see a reduction in glycolytic flux, reducing not only the supply of ATP but the production of key measurable metabolites such as lactate (Hollidge-Horvat et al., 1999)

Many of the effects of acidosis were initially discovered through isolated fibre preparations where changes in force output appeared notably small (< 10 %) under physiological conditions. Investigations

however, in intact animals and humans have confirmed that this impact translates to exercising muscle (Hultman et al., 1985; Kowalchuk et al., 1984; Sutton et al., 1981). It is this foundational understanding that has shaped the hypothesis that acidosis, alongside other anaerobic metabolites, are a physiological limiting factor in performance (Noakes et al., 2005; Siegler et al., 2016). There are well understood mechanisms within human physiology that see compounds within the body buffer pH in what we understand as a means of maintaining homeostasis an subsequent function (Shaw & Gregory, 2022). This has led to the wider exploration and manipulation of these compounds with the goal of improving muscle and whole-body performance.

## **Acid Buffers in the Human Body**

Buffers function to mitigate changes in hydrogen ion concentration both in intracellular and extracellular environments (Shaw & Gregory, 2022). Acid buffers do this by accepting a proton ( $H^+$ ) allowing for the maintenance of cellular function in skeletal muscle, particularly throughout that of high-intensity exercise. Intracellular buffers act at the site of accumulation to effectively remove free hydrogen ions within the cell, this includes dipeptides like anserine and carnosine (Davey, 1960), and some do it through the catalytic reduction of metabolic intermediaries (pyruvate) (Kemp, 2005). Extracellular buffers such as bicarbonate ( $HCO_3^-$ ) act in extracellular fluid acting to improve the removal of hydrogen ions from skeletal muscle (Cairns & Lindinger, 2025). In the sub sections below, each key compound will be described, including where they are found and how they are formed.

### *Lactate as an Intracellular Buffer*

At lower intensities pyruvate forms during glycolysis and is destined for oxidation at the mitochondria. However, increases in energy demand mean that there comes a point where the this rate of oxidation is unable to match the rate of pyruvate and metabolite production (Noakes et al., 2005; Siegler et al., 2016). Many have commonly viewed pyruvate as the end product of glycolysis, however its presence is comparatively minimal compared to lactate (Medbo & Tabata, 1993; Parolin et al., 1999). The conversion between pyruvate and lactate is a reversible reaction catalysed by lactate dehydrogenase (LDH). In the response to high intensity exercise the accumulation of glycolytic products ( $H^+$  and NADH) in the cytosol. This shifts the reaction toward the production of lactate, consequently consuming  $H^+$  and regenerating  $NAD^+$ . This mechanism underpins the co-occurrence that is the increase in  $[H^+]$  and  $[La^-]$  during high-intensity exercise (G. C. Henderson et al., 2004; Robergs et al., 2004). At rest intramuscular lactate concentrations lie between 0.4 – 3.4 mM, and following high-intensity exercise generally increases up to 30 mM in an approximate 20-fold change (Cairns & Lindinger, 2025).

The primary regulators of lactate movement between intra and extra-cellular environments in skeletal muscle, are monocarboxylate transporters (Brooks, 2018). These are a class of passive membrane protein identified in skeletal muscle and utilise the  $H^+$  concentration gradient to co-transport lactate and  $H^+$ . The MCT4 isoform primarily functions to extrude lactate from the cell and is most prevalent in glycolytic, type II fibres that see high intracellular concentrations of metabolites during exercise (Cairns, 2013). The MCT1 isoform primarily functions to import lactate for oxidation, most prevalent in oxidative/type I fibres that are quiescent or inactive (Kowalchuk et al., 1988; Lindinger et al., 2013). These combined processes are defined by Brooks (Brooks, 2018) to explain the lactate shuttle theory, where by temporary intermediaries of metabolism can be transported and utilised elsewhere. Importantly this is a pathway by which  $H^+$  is removed from intracellular environments into circulation in a process that limits intracellular accumulation and attenuates fatigue (Bisetto et al., 2019; Kitaoka et al., 2022; Westerblad & Allen, 1992).

#### *Carnosine as an Intracellular Buffer*

Carnosine ( $\beta$ -alanyl-L-histidine) is a dipeptide molecule that is synthesised through the combination of  $\beta$ -Alanine and L-Histidine. It exists most prominently in skeletal muscle. (Davey, 1960; Hill et al., 2007; Smith, 1938). Biopsies from human *Vastus Lateralis* show concentrations ranging from 12-60 mmol/kg, making it one of the most abundant small compounds with comparable values to that of phosphocreatine, creatine and ATP (Harris et al., 1974). Early research conducted by Bate-Smith (1938) demonstrated that it had a imidazole side-chain with a pKa of 6.83 (Deutsch & Eggleton, 1938), placing it in apposition to buffer protons in a key pH range observed during increased energy demand as discussed above. This idea was reinforced by Davey and Mannion who made the case that carnosine contribution to buffering lay somewhere within the large range of 7-40% (Davey, 1960; Mannion et al., 1992). Following this, observations were made as the variance among individuals with power athletes having higher carnosine levels than both that of untrained and endurance trained individuals (Parkhouse et al., 1985). Discoveries such as this opened the door for investigation into other methods by which we might be able to manipulate intramuscular carnosine in an effort to delay fatigue during high-intensity exercise.

Several factors such as species, gender, age, fibre type, diet and exercise have all been considered as determinants of intramuscular carnosine (Harris et al., 2012), with diet and exercise now becoming a key focus for intervention. Carnosine is present within the diet primarily through the consumption of meat and fish (Abe, 2000) though the presence of carnosinase in the gut and plasma suggests that it is returned to its amino components in that of  $\beta$ -Alanine and L-Histidine before reaching the blood (Park et al., 2005). This leaves carnosine to be re-synthesised *in situ* by the enzyme carnosine synthase (Drozak et al., 2010a), with a magnitude dependant on the availability of  $\beta$ -Alanine (Harris, 2006). This is the

line of thought taken by many researchers in exercise performance, with many articles investigating the effect of supplemented carnosine on both exercise capacity and performance.

### *Bicarbonate as an Extracellular Buffer*

Bicarbonate is a weak base that exists in large concentrations in the human body and is understood to underpin one of the most important buffers systems in the body. Brönsted–Lowry define a base as a proton ( $H^+$ ) acceptor (Brönsted, 1923; Lowry, 1923), reducing  $[H^+]$  and pH of a given system as defined by:

$$pH = -\log [H^+]$$

In the context of bicarbonate, ( $HCO_3^-$ ) contribute to extracellular buffering **by** accepting protons to form carbonic acid ( $H_2CO_3$ ), which subsequently dissociates into water and carbon dioxide. This relationship forms a buffer system that it made up of a weak acid and its conjugate base, acting in a dynamic fashion to neutralise the effects of large changes in  $[H^+]$  and subsequent pH.



In this buffer there is an equilibrium established between the ionised and non-ionised forms, this value is defined as the rate constant  $K_a$ .

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

This can be re-arranged to form the Henderson equation (L. J. Henderson, 1908)

$$[H^+] = K_a \frac{[A^-]}{[HA]}$$

The logarithms can be taken to give the Henderson-Hasselbalch equation (Hasselbalch, 1916)

$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

The  $pK_a$  is characterised by an equal concentration of acid/conjugate base and determines the pH at which the buffer is most effective. At rest pH is approximately 7.4, and the ratio of  $HCO_3^-$  to  $H_2CO_3$  is 5000:1. A 1:1 ratio of these compounds occurs a pH 6.1 ( $pK_a$  value), telling us that this system possesses its greatest ability to resist changes in pH under conditions of metabolic acidosis. This mechanism plays a key role in maintaining acid–base homeostasis during metabolic disturbances much like that of high-intensity exercise.



## Supplementation Strategies to Improve Buffer Capacity

The discovery of these compounds, along with the proposed role of acidosis in fatigue lay the foundation for future investigation. Early works by Dennig et al. (1931) made the observations that alkalosis prior to exercise improve work capacity. Soon after this, came the understanding that compounds such as carnosine to buffer changes (Davey, 1960; Deutsch & Eggleton, 1938). These were the discoveries that drove exploration into the augmentation of specific compounds, now with the intention of improving exercise performance and capacity. In this section, current oral supplementation strategies will be described and linked to their respective changes in physiological status and performance.

### *Oral Supplementation of $\beta$ - Alanine*

$\beta$ -Alanine is a non-protogenic and nonessential amino acid that is a rate limiting factor in the synthesis of carnosine (Harris, 2006). The molecule itself can be synthesised in the liver in small quantities otherwise is obtained from carnosine containing food such as beef, pork, poultry and fish (Trexler et al., 2015). The use of oral  $\beta$ -Alanine supplementation has been shown to increase muscular carnosine through chronic dosing strategies of 4-6 g/day for 4+ weeks. This form of chronic, cumulative dosing has shown to induce large relative increases (42-66 %) in muscle carnosine (Harris et al., 2009; Stellingwerff et al., 2012). Supplementation with  $\beta$ -Alanine has shown to attenuate changes in pH during high intensity exercises (Baguet et al., 2010), supporting the theory that underlies the justification for supplementation. There does not, however, appear to be any consistent evidence that is responsible other metabolic markers such as blood lactate (Glenn et al., 2015).

The review of studies investigating the effect of dietary supplementation of  $\beta$ - Alanine on endurance performance (Table 2) suggests the evidence is promising, but by no means certain. The studies were presented in Table 2 were all blinded, utilising a randomised placebo-control design, testing maximal whole-body exercise performance trials of 1–4 minutes duration in trained athletes. Of these, only four of seven showed significant improvements in their chosen performance measure, and those that did reported relatively small (~2%) changes. It's for this reason that meta-research plays a key role, searching for small effect or marginal improvements, while often operating with small sample sizes.

Systematic reviews and meta-analyses have helped shape the consensus in regard to the supplementation of  $\beta$ -Alanine and performance, especially across a variety of study designs and assessment methods (Hobson et al., 2012; Saunders, Elliott-Sale, et al., 2017). To date, the literature has shown a small to moderate effect size that is moderated by a few key factors (Georgiou et al., 2024;

Huerta Ojeda et al., 2020). The most effective doses appear to be those that are higher (5.4-6.4 g daily) that extend over a more chronic period of 4+ weeks (Georgiou et al., 2024). Test structure is another key factor with clear effects only observed in maximal exercise from 1-10 minutes (Georgiou et al., 2024; Hobson et al., 2012; Saunders, Elliott-Sale, et al., 2017) aligning with the time domain that elicits the greatest pH (Cairns, 2006). This concept of test structure also extends toward open-ended capacity testing vs fixed distance or duration (performance) testing. Both appear to show differences over a placebo group; however, the effect sizes found in capacity tests are up to twice as large.

Table 2. Studies investigating  $\beta$ -Alanine supplementation and sport performance. Studies were limited to blinded and randomised control-trial design adopting maximal whole-body exercise performance trials of 1–4 minutes duration in trained athletes.

Study	Pop. Sample	Dose & Duration	Sport and Performance Test	Main Findings (Mean Change $\pm$ SD)
<b>Bellinger &amp; Minahan 2016(c)</b>	14 Cyclists 25 $\pm$ 7 years	6.4 g/day 4 weeks	1km Cycle TT	$\downarrow$ 0.1 $\pm$ 0.6 % in time ( $p = .770$ ) $\downarrow$ 0.2 $\pm$ 0.6 % power output ( $p = .520$ )
<b>Bellinger &amp; Minahan 2016(a)</b>	17 Cyclists 25 $\pm$ 6.years	6.4 g/day 4 weeks	Cycling TTE 120% VO <sub>2</sub> max	$\uparrow$ 7.3 $\pm$ 4.6 % in TTE ( $p = .041$ )
<b>Brisola et al. 2017</b>	22 Water-polo Players	4.8 g/d - 6.4 g/d 4 weeks	200m TT swim	$\downarrow$ 2.2 $\pm$ 2.6 % in 200m time ( $p > .05$ )
<b>Painelli et al. 2013</b>	7 Swimmers 21 $\pm$ 3 years	3.2 - 6.4 g/day 3 weeks	100 & 200m TT swim	$\downarrow$ 2.1 $\pm$ 2.1 % in 100m time ( $p = .07$ ) $\downarrow$ 2.0 $\pm$ 1.0 % in 200m time ( $p = .002$ )
<b>Ducker et al. 2013</b>	18 Runners 22 $\pm$ 6 years	6.4 g/day 4 weeks	800m TT	$\downarrow$ 2.5 $\pm$ 0.3 % in 800m time ( $p = .02$ )
<b>Howe et al. 2013</b>	16 Cyclists 24 $\pm$ 6 years	65 mg/kg/day 4 weeks	4 min cycling TWD	$\uparrow$ 1.6 $\pm$ 1.9% in average power ( $p = .25$ )
<b>Milioni et al. 2019</b>	17 Cyclists 25 $\pm$ 6 years	6.4 g/day 4 weeks	Running TTE 115% VO <sub>2</sub> max	No reported difference in TTE ( $p = .33$ ) NA

TTE = Time to Exhaustion , TWD = Total work done, TT = Time trial, NA = Not Available

### Oral Supplementation of Sodium-bicarbonate

Sodium bicarbonate (NaHCO<sub>3</sub><sup>-</sup>) is an alkaline bicarbonate salt that falls into the same category as compounds such as sodium citrate and calcium/sodium lactate. The acute oral consumption of these compounds has shown to be an effective method to induce acute alkalosis (Heibel et al., 2018). This is evident in rises in plasma [HCO<sub>3</sub><sup>-</sup>] from 25 to 30 mM (de Oliveira et al., 2022; Gough et al., 2018; Street et al., 2005) accompanied by an upward shift in resting/pre-exercise pH of  $\sim$ 0.06, an augmentation large enough to be considered an acute alkalosis (de Oliveira et al., 2022). This is thought to better maintain the trans-sarcolemma [H<sup>+</sup>]-gradient in a way that facilitates the extrusion of H<sup>+</sup> and lactate<sup>-</sup> via MCT4 in skeletal muscle. In support of this hypothesis, evidence has consistently shown the use of sodium

bicarbonate to attenuate the fall of pH observed during high intensity exercise (Correia-Oliveira et al., 2017; Costill et al., 1984; Mildenhall et al., 2023; Nielsen et al., 2002; Stephens et al., 2002), an observation not consistently reflected in other post-exercise measures such as blood lactate (Carr, Hopkins, et al., 2011). Gastrointestinal (GI) distress is a very commonly reported symptom associated with the consumption of alkalising agents (Carr, Slater, et al., 2011). This extends to bloating, abdominal pain, nausea and vomiting, all of which have the potential to negatively impact performance (Saunders et al., 2014).

Table 3 presents a series of studies assessing the effect of sodium bicarbonate supplementation on performance. All studies included were blinded, utilising a randomised cross-over design, testing maximal whole-body exercise performance trials of 1–4 minutes duration in trained athletes. The outcome of these, similar to  $\beta$ -alanine, saw a combination of results between results of no significance and those with a small improvement of 1-3 %. The nature of these results once again highlights the need for meta-research, to often overcome power limitations associated with both small sample sizes and marginal performance improvements. The accumulation of studies investigating the ergogenic oral sodium bicarbonate reveal very small to small effect sizes when compared to a placebo ( $ES_{0.5} = 0.17$ , 95% CrI 0.12 – 0.21) de Oliveira et al. (2022). There is general consensus that a 0.3 g/kg dose is optimal, with the largest effect size observed in events that last 0.5–10 minutes. The timing of the dose before exercise is variable between 90 and 225 minutes (de Oliveira et al., 2020), likely due to the variable nature of blood acid-base balance in response to a given dose (Boegman et al., 2020). de Olivera and Colleagues note that this effect is reliant on multiple potential moderating factors. This once again includes exercise type, favouring open ended capacity tests and any form of prior exercise and repeated bouts over that of a single one (de Oliveira et al., 2022).

Table 3. Studies investigating acute sodium bicarbonate supplementation and performance. Studies were limited to maximal whole-body exercise within 1–4 Minutes, within specifically trained athletes. All studies implemented a blinded and randomised cross-over design.

Study	Pop. Sample	Dose & Duration	Sport and Performance Test	Main Findings (Mean Change $\pm$ SD)
<b>Driller et al. 2012</b>	8 cyclists 8 $\pm$ 8 years	0.3 g/kg 60+30 min prior	4 min Cycle	$\uparrow$ 1.4 % in power output ( $p > .05$ )
<b>Lindh et al. 2008</b>	9 Swimmers 20 $\pm$ 2 years	0.3 g/kg 30+60 min prior	200m Swim	$\downarrow$ 3.2 $\pm$ 1.3 % in 200m time ( $p < .05$ )
<b>Painelli et al. 2013</b>	7 swimmers 21 $\pm$ 3 years	0.3 g/kg 90 min prior	100m Swim TT 200 Swim TT	$\downarrow$ 2.6 $\pm$ 3.2 % in 100m time ( $p = .02$ ) $\downarrow$ 1.4 $\pm$ 0.8 % in 200m time ( $p < .01$ )
<b>Pruscino et al. 2008</b>	6 swimmers ? years	0.3 g/kg 90+30 min prior	200m Swim TT	1.2 $\pm$ 1.4 % improvement ( $p = .06$ )
<b>Thomas et al. 2016</b>	11 Cyclists 25 $\pm$ 3 years	0.3 g/kg 90 min prior	70s Cycle	$\uparrow$ 2.7 $\pm$ NA % in average power ( $p < .05$ )
<b>Tiryaki &amp; Atterbom, 1995</b>	15 runners 22 $\pm$ 3 years	0.3 g/kg 5+150 min prior	600m Run TT	$\downarrow$ 1.9 $\pm$ 2 % in time ( $p > .05$ )
<b>Van Montfoort et al. 2004</b>	15 Runners 31 $\pm$ 3 years	0.3 g/kg 90 min prior	Supramaximal Running	$\uparrow$ 2.7 $\pm$ 2% in TTE ( $p < .05$ )
<b>Voskamp et al. 2020</b>	32 Cyclists 28 $\pm$ 7 years	0.3 g/kg 150 min prior	2km Cycle TT	$\downarrow$ 0.2 $\pm$ 0.5% in time ( $p > .05$ )
<b>Wilkes et al. 1983</b>	6 Runners Varsity	0.3 g/kg 120+30 min prior	800m Run TT	$\downarrow$ 1.8 $\pm$ 0.7% in time ( $p < 0.05$ )

TTE = Time to Exhaustion , TWD = Total work done, TT = Time trial, NA = Not Available

## Novel Concepts: Transcutaneous/Topical Delivery

While current best practice within high performance systems commonly leans on the use of oral  $\beta$ -Alanine and sodium bicarbonate as ergogenic tools to increase buffer capacity and performance, this does not mean the exploration of alternative avenues and pathways have been ignored. The oral pathway typically requires the repeated ingestion of a powder reliant on the adherence of an athlete, absorption capacity and tolerance of the gut along-side the associated effects of bloating, nausea and paraesthesia (Grgic, Grgic, et al., 2021) These practical challenges and potential side-effects has led to the exploration of other delivery methods. Recently, topical delivery, a method favoured for its convenience, lack of pain and gut discomfort through application to the skin has gained interest (Prausnitz et al., 2004).

### *Topical Sodium Bicarbonate: PR Lotion<sup>®</sup>*

In the past decade this exploration of alternative delivery systems led to the release of products such as PR Lotion<sup>®</sup> (Amp Human Performance, Park City, UT), one of the most commonly known products based upon the transcutaneous delivery of sodium bicarbonate to the blood. The main principle of this

being the ability to more frequently and effectively utilise its performance enhancing benefits, without the undue GI distress that could potentially ruin a performance.

To date, a small number of studies have investigated the effect of topical sodium bicarbonate on blood pH and performance outcomes (Table 4). For example, McKay et al. (2020) reported no change in pH when compared to a placebo, and significantly less than the change observed after oral bicarbonate supplementation. This apparent no effect of topical bicarbonate on pH was a consistent finding among most studies. Two studies by Gurton and colleagues (Gurton et al., 2023; Gurton, Gough, et al., 2024) found no difference between that of the lotion and placebo, all while oral delivery proved to drive measurable change. Gibson et al. (2023) appears to be the only study where a change in both intramuscular (~0.13) and serum (~0.04) pH, using intramuscular dialysate, was observed. However, the structure of these analyses relied on within group comparisons with no between group comparisons and a notably small sample size (n = 9, n = 4).

Performance measures were taken in three of the four studies described. McKay et al. (2020) saw the 2 unique comparisons made. The first of which revealed no difference in performance capacity test between an oral vs topical delivery and the second of which saw no difference in repeated Wingate effort power between bicarbonate and placebo gels. Gurton et al. (2023) saw a small improvement in average sprint time during short (25m) sprint intervals with limited recovery (25s), however this improvement was not maintained in a subsequent Yo-Yo IR2 test of which there was no difference improvement over the placebo group. Gurton et al. (2024) took a slightly difference approach investigating a range of performance measures across a soccer-specific match simulation. This once again supported similar findings in that oral sodium bicarbonate was able to generate differences while the topical lotion was not.

Table 4. Studies investigating topical sodium bicarbonate supplementation and performance. All studies implemented a blinded and randomised cross-over design. \*Significant difference over placebo group.

Study	Pop. Sample	Dose & Duration	Sport and Performance Test	Main Findings
McKay et al. 2020	10 cyclists or triathletes <i>No age given</i>	0.9036 g/kg 30 min prior	3 × 30-s maximal sprints with 90-s recovery	= pH pre-exercise = mean power ( $p = .108$ ) = peak power ( $p = .448$ ) = peak BL <sub>a</sub> (NR)
Gurton et al. 2023	14 rec. trained men 27 ± 6 years	0.9036 g/kg 120 min prior	Yo-Yo IR2 Test 8 × 25 m sprint Test	= pH pre-exercise ↑ 17% distance for Yo-Yo ( $p = .084$ ) ↓ 2% sprint time ( $p = .36, d = 0.34$ ) Lower RPE after some sprints*
Gurton et al. 2024	10 male soccer players 24 ± 3 years	0.9036 g/kg 120 min prior	8 × 25 m sprints Throughout a soccer-specific (SAFT90) test	= pH pre-exercise = fastest sprint time ( $p = .206$ ) = average sprint times ( $p = .123$ ) Lower RPE's after first block

NR = not reported, BL<sub>a</sub> = Blood lactate, RPE = rate of perceived exertion

### *Topical Carnosine*

The topical application of L-carnosine in a commercially available product called LactiGo™ has recently sparked interest as an alternative way of delivery carnosine to muscle with the goal of improved performance. Since entering the market in 2017 it has existed as the only commercially available product that promises to make use of this potential pathway. In short, it is a glycerine-based carrier gel that consists of a patented carnosine-magnesium complex that is reportedly designed to deliver a 150 mg dose of carnosine per 10 mL of gel. This complex was tested in-house by Dissette and colleagues who used a reconstructed 3D model of the human epidermis (MatTek In Vitro Life Science Laboratories, Bratislava, Slovak Republic). Here they demonstrated that free carnosine was able to traverse the epidermal model, and that the proprietary carnosine-magnesium complex was able to improve this delivery capacity by up to 60% (Dissette et al., 2018). It is important to note however that this was in a model and theoretical absorption was taken over a period of 24 and 48 hours. Subsequently, Dieter et al. (2021) assessed the ability of this product to alter carnosine concentrations in equine skeletal muscle showing that a 60mL dose delivered to a notably small 25 cm<sup>2</sup> section of the gluteal muscle induced significant changes in muscle carnosine concentration 30 and 60 minutes post application at 35 and 46% respectively. This observation was made in tissue that has skin properties similar to human such as thickness and innervation however, it should be noted that equine muscle often has a different fibre type distribution, which may skew the ability to observe comparable change.

To date, there appear to have been only 3 published papers (Beaven et al., 2025; Harnish & Miller, 2023; Sharpe & Macias, 2016) that have reported on the use of LactiGo™ within a human performance context. The first study by Sharpe & Macias (2016), written in-house, investigated the effect of LactiGo™ (10 mL) on Yo-Yo test performance and all-out 3 x 1000m run performance in footballers. An ~4% improvement in distance covered in the Yo-Yo test ( $p = .069$ ) and average 1000m time ( $p = .036$ ,  $d = 0.812$ ) was observed. There are some obvious limitations to the study with an ordered and unblinded experimental design adopted which could have implications on participant perception and order-effects. Also, interestingly, Sharpe & Macias (2016) reported these comparisons between NC (no cream) and WC+LG (warm-up cream + LactiGo™) rather than comparing WC+LG to WC (warm-up cream) alone for a more valid comparison of effects. More recently, Harnish & Miller (2023) took a similar approach, though with a more robust, randomised and blinded, placebo design. They investigated the effect of the same absolute dose on Wingate power across 5 sprints in trained cyclists. However, in contrast to the positive outcomes reported by Sharpe & Macias (2016) showed no significant difference in 15 s power, 30 s power, peak lactate and total work done was observed following topical application. Finally, work by Beaven et al. (2025) took a combined approach investigating the effect of LactiGo™ on Olympic-level rugby seven's players. Athletes completed a set

of intervals each at a set workload (3 W/kg) before completing a 6 s max effort, repeated 12 times on 30 s rest. The topical carnosine condition produced a higher average peak power compared to placebo; however, the difference was only deemed significant ( $p < .05$ ) for 3 of the 12 repetitions and no effect of condition on heart rate and rating of perceived exertion was observed, suggesting effects were minimal. These studies have begun to shape our understanding of the impact that topical application of carnosine might have however there is certainly room for further studies with alternative approaches. No studies have investigated its effect in a single race-like continuous, maximal bout where metabolic acidosis is significant (Cairns & Lindinger, 2025), nor have any investigated the belief effect associated with the topical application of such a product. This establishes a need for further research to help better understand the effect of such a product on performance.

Table 5. Studies investigating topical carnosine gel (LactiGo™) supplementation and performance. All studies implemented a blinded and randomised cross-over design *except* that of Sharpe & Macias as noted. \*Significant difference over placebo group.

Study	Pop. Sample	Dose & Duration	Sport and Performance Test	Main Findings
<b>Sharpe &amp; Macias 2016</b>	11 Soccer players 22 ± 2 years	10ml arms, legs, torso 45 min prior	Yo-Yo IR1 (~ 7-8 min)  3 x 1000m run (~ 12 min)	↑ 1% distance for Yo-Yo ( $p = .066$ , no e.s.) ↓ 4% time for 3x1 km ( $p = .036$ , no e.s.)  <i>Note: control reference trial was no-product, unblinded and subject to order effect.</i>
<b>Harnish &amp; Miller 2023</b>	15 Cyclists 18-50 years	10ml thigh, calves, glutes 60m prior	Cycle ergometer: 5 x 30s Wingate / 5m active recovery	↓ 2% mean power ( $p = .81$ , $\omega^2 < 0.01$ ) = mean power ( $p = .56$ , $\omega^2 = 0.01$ ) ↑ 6% peak lactate ( $p = .41$ , $\omega^2 = 0.02$ )  <i>Note: tested menthol effect too</i>
<b>Beaven et al. 2025</b>	8 Rugby players 30 ± 4 years	10mL thighs, calves 45 min prior	Cycle ergometer: 12 x 24s (3 W/kg) + 6s max / 30s rest	↑ 8.5% peak power ( $p < .01$ , $d = 0.78$ )* = average 6s power ( $p > .05$ )  No effect on HR or RPE ( $p > .05$ )

## Belief Theory and its Relevance to Sport Supplement Research

The placebo or nocebo effect is a psychobiological response to a purported treatment, and has been shown to influence outcomes in a sport performance context (Beedie et al., 2018; Hurst et al., 2017). A placebo treatment is traditionally administered within randomised controlled trial to control for the "real" or "true" effects of the treatment that is under investigation. Despite this intentional choice of design, many studies follow common ethical practice that reveals this trial structure to participants before engaging in the research. This leaves the participant "unknown" to which treatment they are receiving, however leaves the opportunity for them to guess and introduce a belief effect. This belief in what one thinks has been received has proven to modulate outcome measures such as power output during cycling, from approximately -2 to 10 % with large effect sizes up to  $d = 0.8$  (Hurst et al., 2020), predominantly in studies that used caffeine supplementation - one of the most known researched

ergogenic aids in sport. Another moderator of effects exists in the administration route or mode of delivery, with comparisons being made among clinical interventions (Buerger et al., 2023), however this is yet to be demonstrated clearly among sporting populations in the context of athletic performance.

When investigated in the context of buffer based ergogenic aids such as  $\beta$ -Alanine and sodium bicarbonate, the placebo effect appears to be much smaller at -1 to 3 % with effect closer to  $d = 0.14$  (Bellinger & Minahan, 2016b; McClung & Collins, 2007). It appears that one of the largest modulators when it comes to this observable effect is what an individual has been told. In a paper by De La Vega et al. (2017), three different groups all received a placebo, while being told that they received a supplement that either (1) “would improve performance”, (2) “may or may not improve performance” or (3) “would not affect performance”. The outcomes of this study showed a clear improvement in group one ( 5.9%,  $d = 0.28$  ) with no clear difference across the other two groups. Given that effect sizes larger than  $d = 0.2$  are suggested to be beneficial for athletes (Hopkins et al., 1999), there is certainly an argument to be made for the continued investigation of the placebo effect in sports supplementation for performance. It also highlights the potential need to manipulate participant belief in order to remove potential biases and gain a more accurate understanding of both the placebo and “true” effects. There appears to be no published research on the belief effects relating to topical carnosine in sport contexts.

## Summary

The evidence presented throughout this review highlights the potential role of hydrogen ion accumulation during high intensity exercise and the importance of endogenous short-term buffering systems in maintaining function in skeletal muscle. Compounds like  $\beta$ -alanine and sodium bicarbonate, delivered orally, have demonstrated small benefits that justify their use, particularly in exercise lasting between 1 and 10 minutes. However, challenges such as gastrointestinal distress (bicarbonate) or dosing adherence ( $\beta$ -alanine) limit their practical utility in some populations.

Emerging interest in transcutaneous or topical delivery offers a novel approach, potentially circumventing some limitations of oral routes. Products like PR Lotion<sup>®</sup> (topical bicarbonate) and LactiGo<sup>™</sup> (topical carnosine) have gained traction as accessible alternatives. However, current human performance trials provide limited and inconsistent evidence for meaningful ergogenic effects. Furthermore, many such studies are plagued by small sample sizes, something that isn't new in sport supplementation research, however it means that meaningful conclusions will likely be reliant on the cumulative outcomes and meta-research.

A critical and often underappreciated aspect of sports supplementation research is the influence of belief. The placebo effect can modulate outcomes meaningfully, though it appears smaller in buffering agents compared to stimulants like caffeine. Importantly, the way information is framed to participants

(i.e., expectancy manipulation) may be as influential as the intervention itself. This raises the need for more placebo-oriented study designs that aim measure both physiological and psychological (belief-based) effects while also mitigating the effect of participant bias on outcomes.

Given the small number of studies on topical carnosine in humans, especially under blinded and controlled conditions, there is a clear gap in the literature. This gap is particularly relevant to middle-distance race events that place athletes squarely within the severe exercise domain, where buffering capacity is critical to performance. Thus, the present thesis seeks to address this gap by investigating the effects of topically applied carnosine on 800m running performance, contributing novel insights into both the physiological and perceptual domains of ergogenic supplementation.

# Chapter 3: The Effects of Topical Carnosine Application on Running Performance in Trained Middle-Distance Athletes

## Introduction

### *The Challenge of High Intensity Exercise*

Understanding the determinants of middle-distance running events is complex given the role of physiological, biomechanical, and tactical factors, all of which can contribute in a variety of manners to produce a given performance (Bellinger et al., 2021; Sandford & Stellingwerff, 2019). Middle-distance events are performed in the severe to extreme intensity domain, characterised by large metabolic disturbances that negatively impact muscle function and subsequent performance capacity (Cairns & Lindinger, 2025). These disturbances include the increased accumulation of reactive oxygen species (ROS) and lactate along with the progressive reduction in pH (Cairns & Lindinger, 2025; Hermansen & Osnes, 1972; Juel et al., 1990). The accumulation of hydrogen ions negatively impacts muscle contractile function through the reduction of contraction velocity, relaxation time, and calcium sensitivity (Nelson et al., 2014; Nelson & Fitts, 2014; Unger & Debold, 2019; Wolosker et al., 1997), and metabolic function through the inhibition of key glycolytic enzymes such as glycogen phosphorylase and PFK (Dobson et al., 1986; Hollidge-Horvat et al., 1999; Parolin et al., 1999). These changes may appear small (<10%) however are still large enough to limit whole body performance and alter outcomes in high-level sporting competition (Hultman et al., 1985; Kowalchuk et al., 1984; Sprague & Mann, 1983; Sutton et al., 1981). Given the potential role of metabolic acidosis in muscle fatigue during severe to extreme-intensity exercise, such as middle-distance running, researchers have explored the augmentation and manipulation of proton accepting compounds such as bicarbonate and carnosine in an attempt to mitigate reductions in pH and improve physical performance.

### *The Role of Carnosine in Muscle Physiology*

Carnosine ( $\beta$ -alanyl-L-histidine) is a dipeptide molecule found in relatively high concentrations in excitable tissues such as the brain and skeletal muscle (Davey, 1960; Drozak et al., 2010b; Hill et al., 2007; Smith, 1938). In skeletal muscle, carnosine is one of the most abundant small compounds alongside phosphocreatine, creatine and ATP (Harris et al., 1974), with greater concentrations found in glycolytic (type II) over oxidative (type I) fibres (Harris et al., 1998; Hill et al., 2007). Carnosine is synthesised through the combination of  $\beta$ -Alanine and L-Histidine and is notably dependant on the availability of the former through dietary intake (Harris et al., 2006). Carnosine buffers the accumulation of  $H^+$  to maintain cellular pH (Dunnett & Harris, 1997; Harris et al., 1990), acts as an

antioxidant (Boldyrev et al., 1987; Klebanov et al., 1998), and regulates of myosin ATPase/Ca<sup>2+</sup> sensitivity (Dutka & Lamb, 2004; Lamont & Miller, 1992; Parker & Ring, 1970). These are cellular functions relied upon to maintain homeostatic function, highlighting the important implications of carnosine during large metabolic disturbances such as those observed during exercise in the severe/extreme domain.

### *β-Alanine Supplementation and Performance*

As β-Alanine is a limiting factor in carnosine synthesis, oral β-Alanine ingestion has been a key focus in sports supplementation research since the early 2000s. Oral β-Alanine ingestion can increase skeletal muscle carnosine content by ~55%, with responses ranging from 15- 80% over 8-9 weeks (Baguet et al., 2009; Hill et al., 2007). The impact of oral β-Alanine on performance has been investigated across a variety of dosing strategies and performance measures revealing small to moderate effect sizes during maximal exercise from 1-10 minutes (Georgiou et al., 2024; Saunders, Elliott-Sale, et al., 2017). The largest effects have been observed over dosing protocols that deliver 4-6 g over 4+ weeks (Trexler et al., 2015). While β-alanine supplementation remains an established method for elevating intramuscular carnosine concentrations, emerging approaches such as transdermal delivery aim to bypass limitations of oral dosing and paraesthesia to provide more targeted, rapid ergogenic effects.

### *Topical Carnosine*

Topical L-carnosine application is an alternative strategy used to increase skeletal muscle carnosine content evident in the emergence of commercially available products such as LactiGo™ (LactiGo Inc., Las Vegas Nevada). The delivery of carnosine via topical application to skeletal muscle has been demonstrated in small sections of gluteal, equine muscle (Dieter et al., 2021) with increases in muscular carnosine of up to 46 % over a period of 40 – 60 minutes. While no human data exists, the impact of this product has been investigated in a small handful of papers in humans each with a unique application of high-intensity exercise. For example, Sharpe & Macias (2016) investigated Yo-Yo IR and a 3 x 1000m run performance in footballers, reporting a 4 % difference in average 1000m run time. More recently, Harnish & Miller (2023) investigated repeated Wingate performance and reported only small effects of topical carnosine in mean sprint interval power and peak blood lactate in trained cyclists. Similarly, Beaven et al. (2025) reported 8.5 % improvements in peak power ( $p < .01$ ,  $d = 0.78$ ) but not mean (6 s) sprint power during high-intensity cycle-ergometer trial designed to match the demands of a rugby 7s match. However, no studies have investigated its effect in a single race-like continuous, maximal bout where metabolic acidosis is significant (Cairns & Lindinger, 2025), nor have any investigated the belief effect associated with the topical application of such a product, and finally no

studies have investigated the effect of such as product on differential RPE, discriminating between muscular and respiratory fatigue.

Therefore, the aim of this study was to investigate the effects of application of a topical carnosine gel on 800m time-trial performance and peak lactate response in trained middle-distance runners. The secondary aim was to assess the belief effect of topical carnosine, while investigating the effect of both placebo and carnosine containing gels on differential RPE. It was hypothesised that topical carnosine would improve 800m time trial performance, reducing overall 800m time and increase the peak lactate response due to improved buffering capacity.

## **Methods**

### *Participants*

Sixteen trained runners were recruited to take part in this investigation (9 males, 7 females; age  $25 \pm 5$  years; height,  $177 \pm 7$  cm; mass,  $67 \pm 6$  kg; BMI  $21 \pm 1.2$  kg/m<sup>2</sup>). All participants were free of illness and musculoskeletal injury (>3 months) and had a self-reported time that met one of the three middle-distance performance standards listed in Table 6.. The study was conducted in the late-competitive and early-off season. In the 12 weeks preceding the study, self-reported training duration was  $8.3 \pm 3.2$  h/week, and training volume  $59 \pm 33$  km/week. Individuals were excluded if they had supplemented with  $\beta$ -alanine in the previous four weeks (Baguet et al., 2009). All participants completed a general health screening and provided written informed consent. This study was performed in accordance with the standards of the Declaration of Helsinki, 2013, and the Auckland University of Technology Ethics Committee approved all procedures (24/27).

### *Sample Size*

Our *a priori* sample size calculation conducted on G\*Power (version 3.1, University Kiel, Germany) revealed that a sample size of 18 participants was needed to provide adequate power to detect a small effect size of 0.25 (Sullivan & Feinn, 2012). This calculation was based on the use of a repeated measures ANOVA ( $\alpha = .05$ ,  $1 - \beta = 0.8$ ,  $1 \times 3$ , correlation among repeated measures = 0.7,  $\epsilon = 1$ ). 17 participants completed all three trials, while one participant had one of their trials discarded due to not meeting the pre-trial conditions, the data from their remaining two trials were included in analysis. The ability to recruit and complete data collection with more participants was limited by timelines established for the degree in which the thesis was submitted.

Table 6. Performance standard. The minimum (self-reported) performance standards required within the past 24 months to qualify for participation. World Athletics Standard (WAS) was taken from standard released for World Athletics Championships, Tokyo 2025.

Event	Male			Female		
	Standard	WAS	%	Standard	WAS	%
800m	02:15.0	01:44.50	70.8	02:30.0	1:59.00	73.9
1500m	04:30.0	03:33.00	73.2	05:00.0	4:01.00	75.4
3000m	10:00.0	-	-	11:00.0	-	-

### Study Design

The study adopted a block-randomised, single-blind, crossover design with three experimental trials: a no-gel trial (NG), an informed carnosine, given placebo gel trial (PG) and an informed carnosine, given carnosine gel trial (CG). Participants performed three outdoor running performance trials each trial was  $7 \pm 5$  days apart, having refrained from high-intensity exercise in the previous 24 hours. Participants were instructed to maintain a similar diet 24h prior to each performance trial and abstain from caffeine ingestion 12 hours prior.

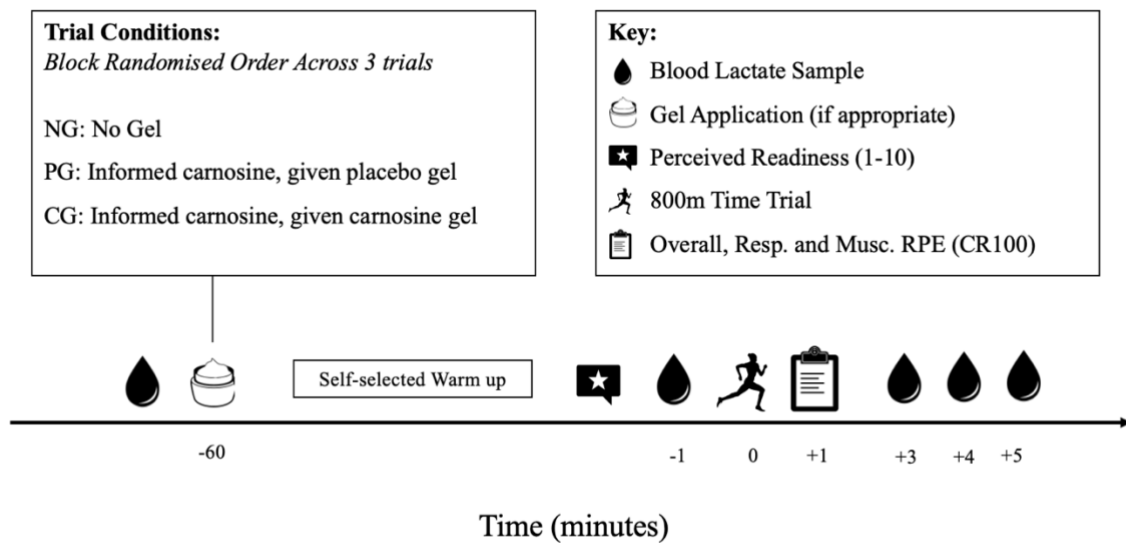


Figure 1. Experimental design. The experimental design and data collection timeline, including product application timing and key measurements relative to the 800m time-trial. Negative time values indicate time pre-trial, positive indicates time post-trial.

### *Supplement Delivery*

On two of the three trials (PG and CG), one hour prior to the performance trial and under supervision, participants applied 0.2 mL/kg (bw) of unlabelled gel to their own upper and lower legs. The PG and CG gel were indistinguishable having been produced by the same manufacturer (LactiGo™), with PG containing the same as CG except no carnosine. No gels used contained menthol to avoid any analgesic or interactive effects (Barwood et al., 2020). Participants were intentionally informed that both trials using gel contained the active carnosine ingredient. This was to minimise the effect of subconscious bias on the belief/psychological effect of the supplement (Saunders, De Oliveira, et al., 2017). Participants were informed of the deception and structure of the trials after completion and were given the opportunity to withdraw their data.

### *Running Performance*

Participants completed an 800m individual running performance time trial in each of the three trial conditions. All trials were performed on an outdoor all-weather track. Environmental conditions were sampled for the duration of each trial using a portable weather station (*Kestrel 5400 WBGT Heat Stress Tracker*) on a rotating vane mount. Mean wind, temperature, humidity and barometric pressure values were recorded for each trial. Participants were instructed to wear the same footwear across all trials. Prior to each trial, a self-selected warm-up was completed which was repeated during each subsequent trial for consistency. Time and split data were collected using a single set of Vald Smart Speed Plus Photocell lights placed at the start/finish line at a set (torso) height. Trials were self-started from a static position directly behind the lights. A camera (Sony A6100, 24fps) was also used at the finish line as an alternative measure of time to completion in-case of technical malfunction in the photocell unit. Times were defined using manual frame selection of the moment at which the participants torso crossed the physical tripod holding the photocell unit. Values were recorded as  $t_{400}$  and  $t_{800}$  (s). For pacing insights, the split difference between first and second lap times was calculated as: *second lap - first lap* (s). Within-participant averages and standard deviations were determined for calculation of coefficient of variability (CV%) between trials.

### *Physiological Measures*

Capillary blood lactate concentration was measured from the fingertip prior to product application, prior to time trial initiation (post-warm up), and then 3-, 4- and 5-min post-trial (Gupta et al., 2021) using a handheld analyser (Arkray Lactate Pro 2 (LT-1730)). The peak blood lactate concentration ( $BLa_{peak}$ ) was defined as the maximum value obtained post-test. Heart rate was captured for the duration of the trial (Polar H10), and peak HR was recorded.

### *Perceptual Measures*

Perceived readiness was assessed prior to the initiation of the 800m trial using a 1-10 scale where: 1 (*not ready at all to deliver a max effort*) to 10 (*extremely ready to deliver a max effort*) (Ingham et al., 2013). Differential RPE was recorded 1 min-post trial (CR100) to assess overall, respiratory and muscular effort (McLaren et al., 2017).

### *Statistical Analysis*

Data are expressed mean  $\pm$  standard deviation unless otherwise stated. Data analysis was conducted in JASP (Version 0.19.3). Visual inspection of the Q-Q plot indicated that residuals were approximately normally distributed, supporting the assumption of normality. Mauchly's test indicated that the assumption of sphericity was not violated. Therefore, uncorrected values are reported. Variables were entered into a linear mixed model on JASP and differences between groups (conditions) were analysed according to each outcome measure (*800m time, split difference, peak heart rate, peak lactate and RPE*). Trial condition (*NG, PG, CG*) and trial order (*1-3*) were included as fixed effects variables and participant as a random effects grouping factors. Overall, fixed effects were analysed and when appropriate, contrasts were used to make comparison between two groups at a time. The belief or placebo effect is referenced in comparisons between NG and PG trials. The true or physiological effect is referenced in comparisons between PG and CG trials. The combined effect is referenced in comparisons made between NG and CG trials. Statistical significance was inferred when  $p \leq .05$ . Cohen's d effect sizes were calculated using outputs from the linear mixed models. All variability statistics were calculated and reported as within-participant values.

## **Results**

Environmental conditions were recorded during each outdoor time trial to account for potential performance influences. Values are expressed as a total range (*within-participant mean  $\pm$  SD*). Temperature ranged from 10.4 - 22.8°C ( $16.5 \pm 2.35$ ), with wind speeds between 0 - 2.37 ms<sup>-1</sup> ( $0.8 \pm 0.47$ ). Humidity ranged from 67.3 to 100 % ( $91.83 \pm 6.67$ ) with barometric pressure between 1007.4 and 1034.00 mmHg ( $1021.63 \pm 5.52$ ). No trials were conducted under heavy rain however the track surface was often wet from overnight rain.

### Performance and Pacing

There was no overall effect of condition ( $F(2, 27.03) = 1.349, p = .276$ ) or order ( $F(2, 27.03) = 0.307, p = .738$ ) on 800m time, all contrasts made between conditions revealed no significant differences ( $p > .05$ ). There was also no overall effect of condition on split difference ( $F(2, 25.18) = 0.902, p = .419$ ). There was an overall effect of trial order on split difference  $F(2, 25.15) = 4.307, p = .025$ .

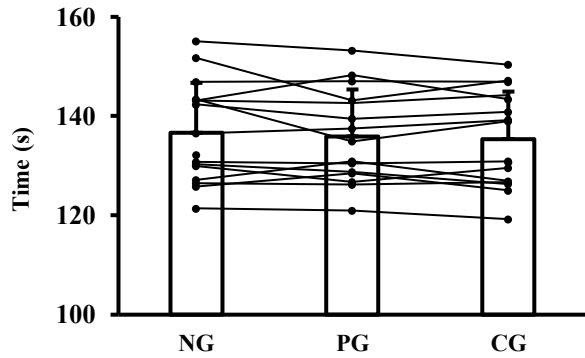


Figure 2. 800m Time. Mean ( $\pm$  standard deviation) 800m running performance time following application of a No gel (NG), Placebo gel (PG) and Carnosine containing gel (CG). There was no effect of condition or order ( $p > .05$ ), indicating no difference in performance across trials.

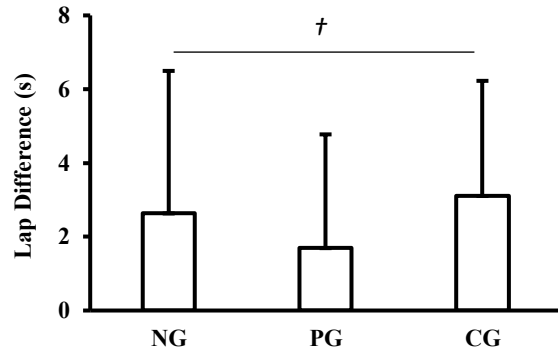


Figure 3. Pace Split. Mean ( $\pm$  standard deviation) lap split difference following application of a No gel (NG), Placebo gel (PG) and Carnosine containing gel (CG) prior to a 800m running performance time-trial. Calculated as: second lap – first (s). There was no effect of condition ( $p > .05$ ), there was an effect of order † ( $p < .05$ ).

### Physiological Measures

There was no overall effect of condition ( $F(2, 27.26) = 0.894, p = .421$ ) or order ( $F(2, 27.26) = 0.045, p = .956$ ) on the peak heart rate recorded during trials, all contrasts made between conditions revealed no significant differences ( $p > .05$ ). There was an overall effect of condition on peak blood lactate ( $F(2, 27.15) = 4.038, p = .029$ ) with contrasts between groups revealing a significant difference between NG and CG trials ( $p = .017$ ) with a moderate effect size ( $d = 0.45$ ). The comparison between NG and PG trials was insignificant ( $p = .420, d = 0.13$ ), so to was that between PG and CG ( $p = .114, d = 0.31$ ). There was also no effect of order ( $F(2, 27.15) = 0.498, p = .613$ ) on peak blood lactate.

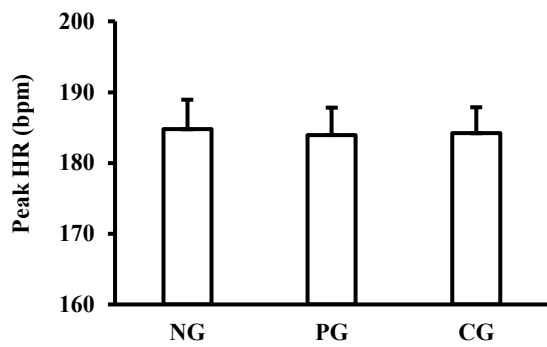


Figure 4. Peak heart rate (bpm). Mean ( $\pm$  standard deviation) Peak HR during an 800m time trial following topical application of No gel (NG) Placebo gel (PG) and Carnosine gel (CG) trial. There was no effect of condition or order ( $p > .05$ ), indicating no difference in performance across trials.

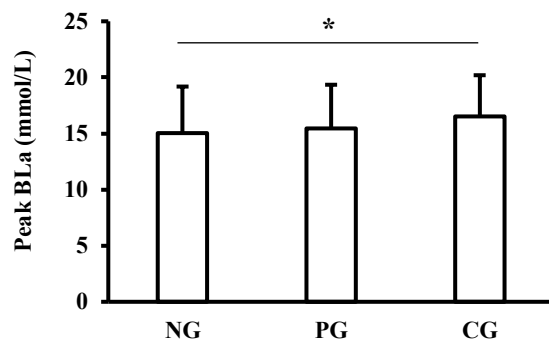


Figure 5. Peak blood lactate concentration (mmol/L). Mean ( $\pm$  standard deviation) Peak BLA post 800m time trial following topical application of No gel (NG) Placebo gel (PG) and Carnosine gel (CG) trial. There was no effect of order ( $p > .05$ ). There was an overall effect of condition ( $p < .05$ )\*

### Perceptual Measures

There was no overall effect of condition ( $F(2, 26.83) = 0.218, p = .644$ ) or order ( $F(2, 26.83) = 0.218, p = .805$ ) on perceived readiness, all contrasts made between conditions revealed no difference(s) of significance ( $p > .05$ ). There was also no overall effect of condition on overall ( $F(2, 27.16) = 0.116, p = .891$ ), respiratory ( $F(2, 27.22) = 0.215, p = .808$ ) or muscular ( $F(2, 27.59) = 0.921, p = .410$ ) RPE recorded post time-trial. There was no overall effect of order on any of these measures ( $p > .05$ ).

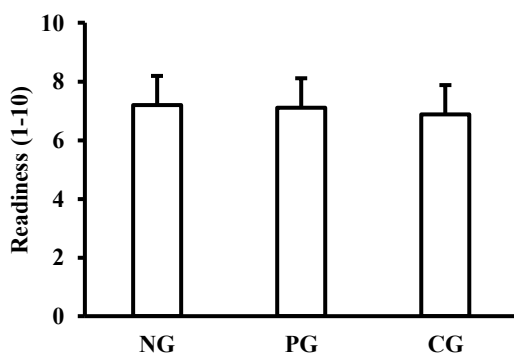


Figure 6. Perceived Readiness. Mean ( $\pm$  standard deviation) readiness rated pre time-trial using a 1-10 scale under No gel (NG), Placebo gel (PG) and Carnosine gel (CG) conditions. There was no effect of condition or order ( $p > .05$ ), indicating no difference in perceived readiness across trials.

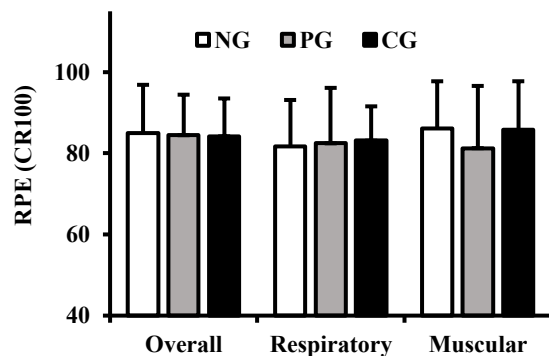


Figure 7. Differential RPE. Mean ( $\pm$  standard deviation) readiness rated post 800m time-trial using a CR100 scale under No gel (NG), Placebo gel (PG) and Carnosine gel (CG) conditions. There was no effect of condition or order ( $p > .05$ ), indicating no difference in overall, respiratory and muscular RPE across trials.

## Discussion

The primary aim of this study was to determine the ergogenic effect of a single dose of topical carnosine gel on 800m running performance. We hypothesised that the application of topical carnosine would improve 800m run time and cause a greater peak lactate post time-trial than that of a placebo due to improved buffering. Our primary observations were that the topical application of carnosine gel did not improve 800m time-trial performance when compared to a placebo gel but increased post-trial blood lactate in some trials. Our secondary observations were that the application of a placebo gel did not improve performance when compared to that of no gel. These data suggest that despite an altered physiological response in some, the belief and true physiological effects of topical carnosine were insufficient to alter 800m performance outcomes in this study.

### *Performance*

Similar to previous findings involving topical applications of carnosine (Beaven et al., 2025; Harnish & Miller, 2023; Sharpe & Macias, 2016) the current study did not observe a true physiological or placebo effect on performance enhancement (Figure 2). Differences presented between conditions were very small presenting a difference in marginal means of 0.21 s, 0.15 % (PG-CG), 0.95s, 0.70 % (NG-CG) and 1.16s (0.85 %). These observations of insignificant differences are in line with the current, observations bar a few specific outcomes noted by Sharpe et al. (2016) and Beaven et al. (2025). The first of these by Sharpe et al. (2016) saw a 4 % improvement in distance covered over a 3×1000 m run however failed to compare randomised trials and make a comparison to a blinded placebo group. The second by Beaven et al. (2025) saw 8.5 % average improvement in peak power across 12x6 s sprint efforts within high-intensity intervals. With that said, the mean 6s power by Beaven et al. (2025), and the Wingate performance (both peak and mean power) by Harnish & Miller (2023) all fail to drive changes greater than that of their placebo controls. Comparisons to other studies investigating the effect of  $\beta$ -alanine and sodium bicarbonate on 800m performance see a rather large discrepancy, with Ducker et al. (2013) and Wilkes et al. (1983) both seeing an approximate 2 % improvement in time in with statistical significance ( $p < 0.05$ )

As mentioned, the placebo effect as measured by the difference between NG and PG trials, although insignificant, was actually larger than the true, physiological effect. At a 0.70% improvement this presented as a very small effect size of  $d = 0.1$ , in line with magnitudes and observations of De La Vega et al. (2017) and Hurst et al. (2017). Beyond the potential placebo effect, it is also important to consider the influence of test structure on measures of performance. Currell & Jeukendrup (2008) found that performance tests such as those used in this study, typically exhibit greater variability than exercise capacity tests ( $CV = 1.2\%$  and  $0.6\%$  respectively). This aligns with observations made as the estimated

effect sizes consistently appear larger when capacity tests are used for both oral  $\beta$ -alanine and sodium bicarbonate (de Oliveira et al., 2022; Georgiou et al., 2024; Saunders, Elliott-Sale, et al., 2017). In the search for likely very small to small effect sizes, this design choice may have played a role in increasing variability such that the presence of a significant difference was masked and it is almost certain that more studies would be needed to detect an effect if present, whether it is due to the belief or true effect of the supplement.

In the present study, an outdoor performance trial was performed rather than attempting to simulate performance using laboratory-based time trials due to better ecological validity (Peserico & Machado, 2014). It is acknowledged that testing on an indoor track where conditions are more stable, particularly that of wind, would be preferable. However, our monitoring of daily environmental conditions to ensure that weather remained within acceptable ranges meant that it is unlikely that the environmental conditions played significant role in influencing any outcome measures.

### *Lactate*

Severe-to-extreme intensity ‘middle-distance’ events are synonymous with a high glycolytic energy production (REF) and reduction in pH (REF). In support, blood lactate concentration peaked at  $15.7 \pm 3.3$  mmol indicative of significant use of the glycolytic pathway. The peak blood lactate was observed  $3.9 \pm 0.9$  minutes post-time trial, which reinforces the selection of our multiple post-trial measurement points, which is in line with observations made previously (Watanabe et al., 2024). In the present study, there was an overall effect of trial condition on peak lactate ( $p = .029$ ) with the only difference observed between NG and CG ( $p = .017$ ,  $d = 0.451$ ) conditions (Figure 5). This observation means that there was no statistical difference between carnosine (CG) and placebo groups ( $p = .114$ ,  $d = 0.31$ ). This is consistent with the study by Harnish & Miller (2023) who similarly saw no significant change ( $p > .05$ ) in peak lactate after repeated Wingate efforts with LactiGo™ application. Insignificance aside, the overall effect observed in this study alongside the moderate effect sizes of 1-1.5 mmol/L observed between placebo and carnosine groups in this study ( $d = 0.31$ ) and Harnish & Miller ( $\omega^2 = 0.02$ ) suggest a possible interaction.

A possible explanation for the increase in peak lactate is that as the accumulation of  $H^+$  ions is attenuated, the inhibitory stimulus for glycolysis is reduced leading to greater glycolytic flux and production of lactate (Sahlin, 1978). Changes in peak lactate after maximal exercise is an observation that has been made during specific studies investigating sodium bicarbonate (Hobson et al., 2014) however the majority of work that has investigated supplements such as  $\beta$ -alanine and sodium bicarbonate have observed changes in performance without observable changes in post-test blood lactate (Carr, Hopkins, et al., 2011), bringing its relevance into question. Regardless of this, 1 – 1.5

mmol/L increases are likely indicative of underlying change, highlighting the need to further investigate more direct measures of metabolism such as blood gases pH or  $\text{HCO}_3^-$ , to understand how this compound takes effect during exercise.

### *Pacing*

Pacing is an important attribute for success in middle-distance running. At the elite level, world records have been shown to be run with a characteristic positive split i.e. a second lap slower than the first (Casado et al., 2021). Indeed, this is a strategy often naturally adopted during maximum efforts and has been confirmed to be advantageous in achieving a faster time over 800m (Bellinger et al. 2021). In the present study, it was clear that participants (blinded to pace and time), on average, gave preference to this strategy with participants running the first lap  $2.5 \pm 3.3$  s quicker than the second. Notably, there was a large amount of variation in this value ( $CV = 57\%$ ), much more than that of the 800m time itself ( $CV = 1.3\%$ ). This questions the idea that pacing plays such a critical role in 800m time and supports the notion of a fixed anaerobic work capacity described within critical speed/power models (Poole et al., 2016).

While there was no effect of trial condition on pacing ( $p = .276$ , Figure 3. Pace Split. Mean ( $\pm$  standard deviation) lap split difference following application of a No gel (NG), Placebo gel (PG) and Carnosine containing gel (CG) prior to a 800m running performance time-trial. Calculated as: second lap – first (s). There was no effect of condition ( $p > .05$ ), there was an effect of order  $\dagger$  ( $p < .05$ ), there was an effect of trial order on pacing ( $p = .025$ ). The change in split difference through trials (1-3) was not unidirectional, moving from +4.0 to +1.5 and then back to +2.3 s, in what may represent some type of overadjustment and correction. Regardless of this potential interaction, the block randomised structure and use of an LMM made sure that that each effect (condition and order) was examined on its own, reinforcing the point that the supplementation did not impact pacing strategy.

### *Perceptual Measures*

Another important aspect related to enhancing performance is how an ergogenic aid can alter how an athlete feels, in particular their perceived readiness to perform. Historically, oral buffer approaches such as sodium bicarbonate and sodium citrate have been associated with distinct gastrointestinal response (Grgic, Pedisic, et al., 2021), topical delivery offers a way to potentially address this short-coming and enhance athletes perceived readiness to perform. However, in this regard, there was no significant differences in perceived readiness across trial conditions (Figure 6), a finding that indicates that there was no placebo or true-physiological effect on the athletes perceived readiness to perform. Likewise, the post-trial differential RPE data indicated no difference between trials, a finding in agreement with

the that made by Beaven et al. (2025) as the only carnosine-gel study to present RPE data between groups. The use of differential RPE and discrimination of muscular and respiratory RPE appeared to be of no additional value compared to overall RPE, maintaining no significant effect of any trial condition or order. Future analyses may choose to further investigate the differences nuances of differential RPE and it's practical capacity to discriminate between central and peripheral sources of fatigue through using more objective measures such as gas analyses and EMG,

### *The Placebo Effect*

Finally, it is well accepted that there is a powerful influence of what an athlete believes is performance-enhancing - an influence that can lead to measurable improvements even in the absence of any physiological mechanism. Supplement studies are a case of this phenomenon with clearly demonstrated, performance effects, driven entirely by a participants belief (De La Vega et al., 2017). Belief also has demonstrated the ability to modulate performance outcomes within traditional placebo-control trial designs, with differences in outcome driven by what the individual thinks they have received. The experimental design adopted in the present study, which involved deception, allowed for examination of belief effects while also minimising the modulation of belief on true, physiological effect. No belief effects were observed with an insignificant 0.85% improvement in 800m time between no gel and placebo gel trials ( $p = .429$ ,  $d = 0.10$ ). This is somewhat in line with observations made by Bellinger & Minahan (2016b) who saw an insignificant improvement 1.5% improvement ( $p = .40$ ,  $d = 0.17$ ) after perceived  $\beta$ -alanine ingestion. It stands in contrast, however, with a similar 1.5% improvement seen by McClung & Collins (2007) 1.5% ( $p < .05$ ,  $\eta^2 = .355$ ). A key difference between these studies appears to be the presence (McClung & Collins, 2007), or absence (Bellinger & Minahan, 2016b) of specific or intentional education and information.

### *Limitations*

While this study provides limited insights into the ergogenic effect, several limitations should be considered when interpreting the findings. The sample size was limited by participant availability, with only a fraction of the available population meeting the criteria set while also willing to disrupt their own training. This limitation may have reduced the power of the study to detect smaller effects (Serdar et al., 2021). There was also considerable spacing between trials (up to 28 days), which was far beyond the original 10 planned, however it was often the case that weather forced less favourable rescheduling, which may have introduced variability in training status or recovery (Hughes et al., 2018). Another limitation was the absence of muscle carnosine or blood acid-balance measures. This meant no new exploration of LactiGo's ability to drive changes in carnosine in human muscle while forcing the

inference of buffer effects from blood lactate. Lastly, while participants were informed that the gel contained an active ingredient, the study did not employ specific expectancy manipulation (e.g., explicitly stating it would enhance performance), which may have limited the magnitude of any potential belief effect often seen in placebo research (De La Vega et al., 2017).

### *Conclusion*

In conclusion, the perceived or real effect of applying topical carnosine was unable to drive performance improvement over an 800m time-trial performance in trained runners. In the absence of any changes in perceived effects prior or during performance trials, it appears there is no negative effects associated with the use of topical carnosine. The increased post-test peak lactate concentration between NG and CG trials shows some promise that topical carnosine has some buffering properties but there is still little known about the capacity of a topical gel such as LactiGo™ to change intramuscular carnosine levels and influence glycolytic and buffering processes in muscle. Further trials should look to investigate this delivery method and capacity and use alternative testing approaches such as exercise capacity trials (both continuous/interval) to reduce variability within performance outcome measures. This will hopefully add to the current knowledge base of whether such products can influence physiology and performance in middle distance events.

## Chapter 4: Summary and Future Directions

The primary aim of this study was to determine the ergogenic effect of a single dose of topical carnosine gel on 800m running performance. It was hypothesised that the application of topical carnosine would result in a reduced 800m run time and a greater post time-trial peak lactate concentration than that of a placebo and control trial. Our primary observations were that (i) the topical application of carnosine gels did not improve 800m performance over a placebo trial, (ii) the application of a carnosine gels and placebo gels did increase post-test blood lactate and (iii) the application of a placebo gel did not improve 800m performance over a trial without gel. This data suggests that topical carnosine gel may be related to an altered physiological response however cannot be linked to changes in stated performance outcomes. This chapter will discuss the primary practical applications of this thesis and then future recommendations for future research.

### **Application to Practice**

It has been reported that up to 85 % of athletes routinely use dietary (oral) supplements, 46 % of which state is with the intention to enhance their performance (Maughan et al., 2007), either by attempting to augment training responses and adaptations, improve recovery from training, and/or improve competition-day performance by altering specific physiological pathways related to performance. Scientific support of the efficacy of many nutritional supplements is variable, and this can be due to study design, supplement dosing regimens, participant characteristics and assessment methods. A classification system for performance supplements has been developed by AIS to signal the strength of the evidence-base and to guide athletes, coaches and scientists working with athletes (*Australian Sports Commission*). When considering the application, relevance and contribution of the present study's findings to the evidence-base, the wider literature exploring topical carnosine use for performance enhancement is also considered. To summarise, there are 2 studies reporting no effect (Harnish & Miller, 2023, present study) and 2 studies reporting beneficial performance outcomes of topical carnosine in athletes (Beaven et al., 2025; Sharpe & Macias, 2016) making it difficult to provide clear recommendations for practice. The findings from the present study align with recent work by, Harnish & Miller (2023) reinforcing the notion that topical carnosine does not produce a consistent ergogenic effect across different performance measures. Notably, this study extends those findings by demonstrating that the absence of a meaningful effect also applies to a single bout of continuous high-intensity exercise, not just repeated-effort protocols (Beaven et al., 2025; Harnish & Miller, 2023; Sharpe & Macias, 2016). Given the current limited and inconsistent evidence, topical carnosine gel would currently be classified as a Group C (supplements with some evidence of benefit in specific

situations, but further research required) or Group D (supplements with limited or no evidence of benefit) substance according to the AIS classification system. Further work is required to elaborate on the limitations of the current and previous studies approaches to advance practical guidance. Until then the choice lies with athletes and coaches to weigh up the potential benefits and risks associated with the addition of such a supplement into their event-specific strategies.

### **Future research directions**

To further advance our understanding of topical carnosine and its potential impact on performance and physiology, it is recommended that future studies aim to investigate the effect of specific dosing strategies on human muscle invitro while also using alternative assessment methods.

To date, the only study that has attempted to quantify the effects of topical application on intramuscular carnosine was Dieter et al. (2021) in equine muscle. While promising outcomes were reported (up to 76% increase in carnosine 60 min following application, compared to placebo), a fairly large discrepancy between the context in which this was demonstrated (equine model) and the context in which it is sold and primarily promoted for us (human athletes). For this reason, future research should look to quantify changes in intramuscular carnosine levels following topical application of varying doses, using similar methods to that reported by Dieter and colleagues. This may be an opportunity to investigate the magnitude and time course of carnosine changes (appearance and disappearance rates) in human muscle. It would also be interesting to compare carnosine levels to those observed following chronic  $\beta$ -alanine oral supplementation, and whether there is any true impact of magnesium-salt adjacent delivery, as purported by the manufacturer. Future research may also investigate the possibility of repeated applications, or possible combined effects along-side oral  $\beta$ -alanine, or other buffers. While intramuscular carnosine has been measured previously through biopsy followed by chromatography or mass spectrometry ((Carvalho et al., 2018; De Salles Painelli et al., 2018; Harris et al., 2006), it may be useful to explore less-invasive techniques such as magnetic resonance spectroscopy (MRS) which may provide an more feasible alternative, particularly among trained athletes (Baguet et al., 2009; da Eira Silva et al., 2020; Derave et al., 2007).

Future testing should consider to better design procedures that prioritise the reduction of variability in performance outcomes measures. Given our current understanding of this space in regard to supplements, such as  $\beta$ -alanine and sodium bicarbonate, we know that the effect sizes are likely to be small. Given this, future works might benefit from making specific design choices, such as choosing a time to exhaustion test over that of a fixed work/duration task, and powering studies accordingly. Design choices such as this may play a key role in reducing variability allowing for a greater opportunity to quantify the true performance effects of topical carnosine application in athletes.

## **Conclusion**

In conclusion, the topical application of carnosine and placebo gels did not improve 800m time-trial performance over that of no gel, suggesting no placebo or true - physiological effect despite small changes in post-test blood lactate. The primary recommendations for future research are that: (i) the scale at which intramuscular carnosine can be increased via topical application are investigated, using either invasive (biopsy) or non-invasive methods, and (ii) the performance enhancing effect are investigated in the context of a performance capacity test. Further knowledge of these will help shape and mould the scientific consensus and allow us to gain a more nuanced and detailed understanding of whether this supplement can contribute to enhancing performance in high-intensity sporting events.

## Reference List

- Abe, H. (2000). Role of Histidine-Related Compounds as Intracellular Proton Buffering Constituents in Vertebrate Muscle. *65*(7).
- Alkilani, A., McCrudden, M. T., & Donnelly, R. (2015). Transdermal Drug Delivery: Innovative Pharmaceutical Developments Based on Disruption of the Barrier Properties of the Stratum Corneum. *Pharmaceutics*, *7*(4), 438–470. <https://doi.org/10.3390/pharmaceutics7040438>
- Australian Sports Commission | Supplements. (2022, July). <https://www.ausport.gov.au/ais/nutrition/supplements>
- Baguet, A., Koppo, K., Pottier, A., & Derave, W. (2010).  $\beta$ -Alanine supplementation reduces acidosis but not oxygen uptake response during high-intensity cycling exercise. *European Journal of Applied Physiology*, *108*(3), 495–503. <https://doi.org/10.1007/s00421-009-1225-0>
- Baguet, A., Reyngoudt, H., Pottier, A., Everaert, I., Callens, S., Achten, E., & Derave, W. (2009). Carnosine loading and washout in human skeletal muscles. *Journal of Applied Physiology*, *106*(3), 837–842. <https://doi.org/10.1152/jappphysiol.91357.2008>
- Barstow, T. J., Buchthal, S., Zanconato, S., & Cooper, D. M. (1994). Muscle energetics and pulmonary oxygen uptake kinetics during moderate exercise. *Journal of Applied Physiology*, *77*(4), 1742–1749. <https://doi.org/10.1152/jappl.1994.77.4.1742>
- Barwood, M. J., Gibson, O. R., Gillis, D. J., Jeffries, O., Morris, N. B., Pearce, J., Ross, M. L., Stevens, C., Rinaldi, K., Kounalakis, S. N., Riera, F., Mündel, T., Waldron, M., & Best, R. (2020). Menthol as an Ergogenic Aid for the Tokyo 2021 Olympic Games: An Expert-Led Consensus Statement Using the Modified Delphi Method. *Sports Medicine*, *50*(10), 1709–1727. <https://doi.org/10.1007/s40279-020-01313-9>
- Beaven, C. M., James, C., McMaster, D. T., & Brockelbank, N. (2025). Topical carnosine gel improves intermittent high-intensity exercise performance in world-class rugby sevens players. *Journal of the International Society of Sports Nutrition*, *22*(1), 2550311. <https://doi.org/10.1080/15502783.2025.2550311>
- Beedie, C., Benedetti, F., Barbiani, D., Camerone, E., Cohen, E., Coleman, D., Davis, A., Elsworth-Edelsten, C., Flowers, E., Foad, A., Harvey, S., Hettinga, F., Hurst, P., Lane, A., Lindheimer, J., Raglin, J., Roelands, B., Schiphof-Godart, L., & Szabo, A. (2018). Consensus statement on placebo effects in sports and exercise: The need for conceptual clarity, methodological rigour, and the elucidation of neurobiological mechanisms. *European Journal of Sport Science*, *18*(10), 1383–1389. <https://doi.org/10.1080/17461391.2018.1496144>

- Bellinger, P. M., Derave, W., Lievens, E., Kennedy, B., Arnold, B., Rice, H., & Minahan, C. (2021). Determinants of Performance in Paced and Maximal 800-m Running Time Trials. *Medicine & Science in Sports & Exercise*, 53(12), 2635. <https://doi.org/10.1249/MSS.0000000000002755>
- Bellinger, P. M., & Minahan, C. L. (2016a). Metabolic consequences of  $\beta$ -alanine supplementation during exhaustive supramaximal cycling and 4000-m time-trial performance. *Applied Physiology, Nutrition, and Metabolism*, 41(8), 864–871. <https://doi.org/10.1139/apnm-2016-0095>
- Bellinger, P. M., & Minahan, C. L. (2016b). Performance effects of acute  $\beta$ -alanine induced paresthesia in competitive cyclists. *European Journal of Sport Science*, 16(1), 88–95. <https://doi.org/10.1080/17461391.2015.1005696>
- Bellinger, P. M., & Minahan, C. L. (2016c). The effect of  $\beta$ -alanine supplementation on cycling time trials of different length. *European Journal of Sport Science*, 16(7), 829–836. <https://doi.org/10.1080/17461391.2015.1120782>
- Bisetto, S., Wright, M. C., Nowak, R. A., Lepore, A. C., Khurana, T. S., Loro, E., & Philp, N. J. (2019). New Insights into the Lactate Shuttle: Role of MCT4 in the Modulation of the Exercise Capacity. *iScience*, 22, 507–518. <https://doi.org/10.1016/j.isci.2019.11.041>
- Blanchard, E. M., Pan, B. S., & Solaro, R. J. (1984). The effect of acidic pH on the ATPase activity and troponin Ca<sup>2+</sup> binding of rabbit skeletal myofilaments. *The Journal of Biological Chemistry*, 259(5), 3181–3186.
- Bloxham, D. P., Clark, M. G., Holland, P. C., & Lardy, H. A. (1973). A model study of the fructose diphosphatase–phosphofructokinase substrate cycle. *Biochemical Journal*, 134(2), 581–586. <https://doi.org/10.1042/bj1340581>
- Boegman, S., Stellingwerff, T., Shaw, G., Clarke, N., Graham, K., Cross, R., & Siegler, J. C. (2020). The Impact of Individualizing Sodium Bicarbonate Supplementation Strategies on World-Class Rowing Performance. *Frontiers in Nutrition*, 7. <https://doi.org/10.3389/fnut.2020.00138>
- Boldyrev, A. A., Dupin, A. M., Bunin AYa, Babizhaev, M. A., & Severin, S. E. (1987). The antioxidative properties of carnosine, a natural histidine containing dipeptide. *Biochemistry International*, 15(6), 1105–1113.
- Brisola, G. M. P., Milioni, F., Papoti, M., & Zagatto, A. M. (2017). Effects of 4 Weeks of  $\beta$ -Alanine Supplementation on Swim-Performance Parameters in Water Polo Players. *International Journal of Sports Physiology and Performance*, 12(7), 943–950. <https://doi.org/10.1123/ijsp.2016-0133>

- Brönsted, J. N. (1923). Einige Bemerkungen über den Begriff der Säuren und Basen. *Recueil Des Travaux Chimiques Des Pays-Bas*, 42(8), 718–728. <https://doi.org/10.1002/recl.19230420815>
- Brooks, G. A. (2018). The Science and Translation of Lactate Shuttle Theory. *Cell Metabolism*, 27(4), 757–785. <https://doi.org/10.1016/j.cmet.2018.03.008>
- Buergler, S., Sezer, D., Gaab, J., & Locher, C. (2023). The roles of expectation, comparator, administration route, and population in open-label placebo effects: A network meta-analysis. *Scientific Reports*, 13(1), 11827. <https://doi.org/10.1038/s41598-023-39123-4>
- Cairns, S. P. (2013). Holistic approaches to understanding mechanisms of fatigue in high-intensity sport. *Fatigue: Biomedicine, Health & Behavior*, 1(3), 148–167. <https://doi.org/10.1080/21641846.2013.765086>
- Cairns, S. P., & Lindinger, M. I. (2025). Lactic acidosis: Implications for human exercise performance. *European Journal of Applied Physiology*. <https://doi.org/10.1007/s00421-025-05750-0>
- 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>
- Carr, A. J., Slater, G. J., Gore, C. J., Dawson, B., & Burke, L. M. (2011). Effect of sodium bicarbonate on [HCO<sub>3</sub><sup>-</sup>], pH, and gastrointestinal symptoms. *International Journal of Sport Nutrition and Exercise Metabolism*, 21(3), 189–194. <https://doi.org/10.1123/ijsnem.21.3.189>
- Carvalho, V. H., Oliveira, A. H. S., de Oliveira, L. F., da Silva, R. P., Di Mascio, P., Gualano, B., Artioli, G. G., & Medeiros, M. H. G. (2018). Exercise and β-alanine supplementation on carnosine-acrolein adduct in skeletal muscle. *Redox Biology*, 18, 222–228. <https://doi.org/10.1016/j.redox.2018.07.009>
- Casado, A., González-Mohino, F., González-Ravé, J. M., & Boullosa, D. (2021). Pacing Profiles of Middle-Distance Running World Records in Men and Women. *International Journal of Environmental Research and Public Health*, 18(23), 12589. <https://doi.org/10.3390/ijerph182312589>
- Chasiotis, D., Hultman, E., & Sahlin, K. (1983). Acidotic depression of cyclic AMP accumulation and phosphorylase b to a transformation in skeletal muscle of man. *The Journal of Physiology*, 335, 197–204. <https://doi.org/10.1113/jphysiol.1983.sp014528>
- Cori, C. F., Schmidt, G., & Cori, G. T. (1939). The Synthesis of a Polysaccharide from Glucose-1-Phosphate in Muscle Extract. *Science*, 89(2316), 464–465. <https://doi.org/10.1126/science.89.2316.464>

- Correia-Oliveira, C. R., Lopes-Silva, J. P., Bertuzzi, R., McConell, G. K., Bishop, D. J., Lima-Silva, A. E., & Kiss, M. A. P. D. (2017). Acidosis, but Not Alkalosis, Affects Anaerobic Metabolism and Performance in a 4-km Time Trial. *Medicine and Science in Sports and Exercise*, 49(9), 1899–1910. <https://doi.org/10.1249/MSS.0000000000001295>
- Costill, D. L., Verstappen, F., Kuipers, H., Janssen, E., & Fink, W. (1984). Acid-base balance during repeated bouts of exercise: Influence of HCO<sub>3</sub>. *International Journal of Sports Medicine*, 5(5), 228–231. <https://doi.org/10.1055/s-2008-1025910>
- Currell, K., & Jeukendrup, A. E. (2008). Validity, Reliability and Sensitivity of Measures of Sporting Performance. *Sports Medicine*, 38(4), 297–316. <https://doi.org/10.2165/00007256-200838040-00003>
- da Eira Silva, V., Painelli, V. de S., Shinjo, S. K., Ribeiro Pereira, W., Cilli, E. M., Sale, C., Gualano, B., Otaduy, M. C., & Artioli, G. G. (2020). Magnetic Resonance Spectroscopy as a Non-invasive Method to Quantify Muscle Carnosine in Humans: A Comprehensive Validity Assessment. *Scientific Reports*, 10(1), 4908. <https://doi.org/10.1038/s41598-020-61587-x>
- Davey, C. L. (1960). The significance of carnosine and anserine in striated skeletal muscle. *Archives of Biochemistry and Biophysics*, 89(2), 303–308. [https://doi.org/10.1016/0003-9861\(60\)90059-X](https://doi.org/10.1016/0003-9861(60)90059-X)
- De La Vega, R., Alberti, S., Ruíz-Barquín, R., Soós, I., & Szabo, A. (2017). Induced beliefs about a fictive energy drink influences 200-m sprint performance<sup>†</sup>. *European Journal of Sport Science*, 17(8), 1084–1089. <https://doi.org/10.1080/17461391.2017.1339735>
- de Oliveira, L. F., Dolan, E., Swinton, P. A., Durkalec-Michalski, K., Artioli, G. G., McNaughton, L. R., & Saunders, B. (2022). Extracellular Buffering Supplements to Improve Exercise Capacity and Performance: A Comprehensive Systematic Review and Meta-analysis. *Sports Medicine*, 52(3), 505–526. <https://doi.org/10.1007/s40279-021-01575-x>
- de Oliveira, L. F., Saunders, B., Yamaguchi, G., Swinton, P., & Giannini Artioli, G. (2020). Is Individualization of Sodium Bicarbonate Ingestion Based on Time to Peak Necessary? *Medicine and Science in Sports and Exercise*, 52(8), 1801–1808. <https://doi.org/10.1249/MSS.0000000000002313>
- De Salles Painelli, V., Nemezio, K. M., Pinto, A. J., Franchi, M., Andrade, I., Riani, L. A., Saunders, B., Sale, C., Harris, R. C., Gualano, B., & Artioli, G. G. (2018). High-Intensity Interval Training Augments Muscle Carnosine in the Absence of Dietary Beta-alanine Intake. *Medicine & Science in Sports & Exercise*, 50(11), 2242. <https://doi.org/10.1249/MSS.0000000000001697>

- Debold, E. P., Beck, S. E., & Warshaw, D. M. (2008). Effect of low pH on single skeletal muscle myosin mechanics and kinetics. *American Journal of Physiology-Cell Physiology*, 295(1), C173–C179. <https://doi.org/10.1152/ajpcell.00172.2008>
- Dennig, H., Talbott, J. H., Edwards, H. T., & Dill, D. B. (1931). Effect of Acidosis and Alkalosis upon Capacity for Work. *The Journal of Clinical Investigation*, 9(4), 601–613. <https://doi.org/10.1172/JCI100324>
- Derave, W., Özdemir, M. S., Harris, R. C., Pottier, A., Reyngoudt, H., Koppo, K., Wise, J. A., & Achten, E. (2007).  $\beta$ -Alanine supplementation augments muscle carnosine content and attenuates fatigue during repeated isokinetic contraction bouts in trained sprinters. *Journal of Applied Physiology*, 103(5), 1736–1743. <https://doi.org/10.1152/jappphysiol.00397.2007>
- Deutsch, A., & Eggleton, P. (1938). The titration constants of anserine, carnosine and some related compounds. *Biochemical Journal*, 32(2), 209–211. <https://doi.org/10.1042/bj0320209>
- Dieter, B. P., Macias, C. J., Sharpe, T. J., Roberts, B., Wille, M., Young, A., Reisenauer, C., Cantrell, B., & Bayly, W. M. (2021). Transdermal delivery of carnosine into equine skeletal muscle. *Comparative Exercise Physiology*, 17(5), 429–434. <https://doi.org/10.3920/CEP200077>
- Dissette, V., Bignozzi, C. A., Valacchi, G., Pecorelli, A., Manfredini, S., & Vertuani, S. (2018). Evaluation of the Transepidermal Penetration of a Carnosine Complex in Gel Formulation by 3D Skin Models. *Cosmetics*, 5(4), 67. <https://doi.org/10.3390/cosmetics5040067>
- Dobson, G. P., Yamamoto, E., & Hochachka, P. W. (1986). Phosphofructokinase control in muscle: Nature and reversal of pH-dependent ATP inhibition. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 250(1), R71–R76. <https://doi.org/10.1152/ajpregu.1986.250.1.R71>
- Driller, M. W., Gregory, J. R., Williams, A. D., & Fell, J. W. (2012). The Effects of Serial and Acute NaHCO<sub>3</sub> Loading in Well-Trained Cyclists. *Journal of Strength and Conditioning Research*, 26(10), 2791–2797. <https://doi.org/10.1519/jsc.0b013e318241e18a>
- Drozak, J., Veiga-da-Cunha, M., Vertommen, D., Stroobant, V., & Van Schaftingen, E. (2010a). Molecular Identification of Carnosine Synthase as ATP-grasp Domain-containing Protein 1 (ATPGD1). *Journal of Biological Chemistry*, 285(13), 9346–9356. <https://doi.org/10.1074/jbc.M109.095505>
- Drozak, J., Veiga-da-Cunha, M., Vertommen, D., Stroobant, V., & Van Schaftingen, E. (2010b). Molecular Identification of Carnosine Synthase as ATP-grasp Domain-containing Protein 1 (ATPGD1). *Journal of Biological Chemistry*, 285(13), 9346–9356. <https://doi.org/10.1074/jbc.M109.095505>

- Ducker, K. J., Dawson, B., & Wallman, K. E. (2013). Effect of Beta-Alanine Supplementation on 800-m Running Performance. *International Journal of Sport Nutrition and Exercise Metabolism*, 23(6), 554–561. <https://doi.org/10.1123/ijsnem.23.6.554>
- Dunnett, M., & Harris, R. C. (1997). High-performance liquid chromatographic determination of imidazole dipeptides, histidine, 1-methylhistidine and 3-methylhistidine in equine and camel muscle and individual muscle fibres. *Journal of Chromatography B: Biomedical Sciences and Applications*, 688(1), 47–55. [https://doi.org/10.1016/S0378-4347\(97\)88054-1](https://doi.org/10.1016/S0378-4347(97)88054-1)
- Dutka, T. L., & Lamb, G. D. (2004). Effect of Carnosine on Excitation–Contraction Coupling in Mechanically-Skinned Rat Skeletal Muscle. *Journal of Muscle Research and Cell Motility*, 25(3), 203–213. <https://doi.org/10.1023/B:JURE.0000038265.37022.c5>
- el-Saleh, S. C., & Solaro, R. J. (1988). Troponin I enhances acidic pH-induced depression of Ca<sup>2+</sup> binding to the regulatory sites in skeletal troponin C. *The Journal of Biological Chemistry*, 263(7), 3274–3278.
- Fitts, R. H. (1994). Cellular mechanisms of muscle fatigue. *Physiological Reviews*, 74(1), 49–94. <https://doi.org/10.1152/physrev.1994.74.1.49>
- Gaesser, G. A., & Poole, D. C. (1996). The slow component of oxygen uptake kinetics in humans. *Exercise and Sport Sciences Reviews*, 24, 35–71.
- Georgiou, G. D., Antoniou, K., Antoniou, S., Michelekaki, E. A., Zare, R., Ali Redha, A., Prokopidis, K., Christodoulides, E., & Clifford, T. (2024). Effect of Beta-Alanine Supplementation on Maximal Intensity Exercise in Trained Young Male Individuals: A Systematic Review and Meta-Analysis. *International Journal of Sport Nutrition and Exercise Metabolism*, 34(6), 397–412. <https://doi.org/10.1123/ijsnem.2024-0027>
- Gibson, B. M., Needham, K. W., Kaiser, B. W., Wilkins, B. W., Minson, C. T., & Halliwill, J. R. (2023). Transcutaneous delivery of sodium bicarbonate increases intramuscular pH. *Frontiers in Physiology*, 14. <https://doi.org/10.3389/fphys.2023.1142567>
- Glenn, J. M., Gray, M., Stewart, R., Moyon, N. E., Kavouras, S. A., DiBrezza, R., Turner, R., & Baum, J. (2015). Incremental effects of 28 days of beta-alanine supplementation on high-intensity cycling performance and blood lactate in masters female cyclists. *Amino Acids*, 47(12), 2593–2600. <https://doi.org/10.1007/s00726-015-2050-x>
- Gough, L. A., Deb, S. K., Sparks, S. A., & McNaughton, L. R. (2018). Sodium bicarbonate improves 4 km time trial cycling performance when individualised to time to peak blood bicarbonate in trained male cyclists. *Journal of Sports Sciences*, 36(15), 1705–1712. <https://doi.org/10.1080/02640414.2017.1410875>

- Greenberg, M. J., Mealy, T. R., Jones, M., Szczesna-Cordary, D., & Moore, J. R. (2010). The direct molecular effects of fatigue and myosin regulatory light chain phosphorylation on the actomyosin contractile apparatus. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 298(4), R989–R996. <https://doi.org/10.1152/ajpregu.00566.2009>
- Grgic, J., Grgic, I., Del Coso, J., Schoenfeld, B. J., & Pedisic, Z. (2021). Effects of sodium bicarbonate supplementation on exercise performance: An umbrella review. *Journal of the International Society of Sports Nutrition*, 18, 71. <https://doi.org/10.1186/s12970-021-00469-7>
- Grgic, J., Pedisic, Z., Saunders, B., Artioli, G. G., Schoenfeld, B. J., McKenna, M. J., Bishop, D. J., Kreider, R. B., Stout, J. R., Kalman, D. S., Arent, S. M., VanDusseldorp, T. A., Lopez, H. L., Ziegenfuss, T. N., Burke, L. M., Antonio, J., & Campbell, B. I. (2021). International Society of Sports Nutrition position stand: Sodium bicarbonate and exercise performance. *Journal of the International Society of Sports Nutrition*, 18(1), 61. <https://doi.org/10.1186/s12970-021-00458-w>
- Gupta, S., Stanula, A., & Goswami, A. (2021). Peak Blood Lactate Concentration and Its Arrival Time Following Different Track Running Events in Under-20 Male Track Athletes. *International Journal of Sports Physiology and Performance*, 16(11), 1625–1633. <https://doi.org/10.1123/ijsp.2020-0685>
- Gurton, W. H., Gough, L. A., Siegler, J. C., Lynn, A., & Ranchordas, M. K. (2024). Oral but Not Topical Sodium Bicarbonate Improves Repeated Sprint Performance During Simulated Soccer Match Play Exercise in Collegiate Athletes. *International Journal of Sport Nutrition and Exercise Metabolism*, 34(6), 362–371. <https://doi.org/10.1123/ijsnem.2024-0059>
- Gurton, W. H., Greally, J., Chudzikiewicz, K., Gough, L. A., Lynn, A., & Ranchordas, M. K. (2023). Beneficial effects of oral and topical sodium bicarbonate during a battery of team sport-specific exercise tests in recreationally trained male athletes. *Journal of the International Society of Sports Nutrition*, 20(1), 2216678. <https://doi.org/10.1080/15502783.2023.2216678>
- Gurton, W. H., King, D. G., Ranchordas, M. K., Siegler, J. C., & Gough, L. A. (2024). Enhancing exercise performance and recovery through sodium bicarbonate supplementation: Introducing the ingestion recovery framework. *European Journal of Applied Physiology*, 124(11), 3175. <https://doi.org/10.1007/s00421-024-05578-0>
- Hargreaves, M., & Spriet, L. L. (2020). Skeletal muscle energy metabolism during exercise. *Nature Metabolism*, 2(9), 817–828. <https://doi.org/10.1038/s42255-020-0251-4>
- Harnish, C. R., & Miller, B. (2023). Transdermal carnosine gel fails to improve repeated Wingate performance in trained male cyclists: A randomized controlled cross-over trial. *Journal of*

Sports Science and Nutrition, 4(2), 106–111.  
<https://doi.org/10.33545/27077012.2023.v4.i2b.193>

- Harris, R. C., Dunnett, M., & Greenhaff, P. L. (1998). Carnosine and taurine contents in individual fibres of human vastus lateralis muscle. *Journal of Sports Sciences*, 16(7), 639–643.  
<https://doi.org/10.1080/026404198366443>
- Harris, R. C., Hultman, E., & Nordesjö, L. O. (1974). Glycogen, glycolytic intermediates and high-energy phosphates determined in biopsy samples of musculus quadriceps femoris of man at rest. Methods and variance of values. *Scandinavian Journal of Clinical and Laboratory Investigation*, 33(2), 109–120.
- Harris, R. C., Jones, G. A., Kim, H. J., Kim, C. K., Price, K. A., & Wise, J. A. (2009). Changes in muscle carnosine of subjects with 4 weeks supplementation with a controlled release formulation of beta-alanine (Carnosyn™), and for 6 weeks post. *The FASEB Journal*, 23(S1).  
[https://doi.org/10.1096/fasebj.23.1\\_supplement.599.4](https://doi.org/10.1096/fasebj.23.1_supplement.599.4)
- Harris, R. C., Marlin, D. J., Dunnett, M., Snow, D. H., & Hultman, E. (1990). Muscle buffering capacity and dipeptide content in the Thoroughbred horse, Greyhound dog and man. *Comparative Biochemistry and Physiology Part A: Physiology*, 97(2), 249–251.  
[https://doi.org/10.1016/0300-9629\(90\)90180-Z](https://doi.org/10.1016/0300-9629(90)90180-Z)
- Harris, R. C., Tallon, M. J., Dunnett, M., Boobis, L., Coakley, J., Kim, H. J., Fallowfield, J. L., Hill, C. A., Sale, C., & Wise, J. A. (2006). The absorption of orally supplied β-alanine and its effect on muscle carnosine synthesis in human vastus lateralis. *Amino Acids*, 30(3), 279–289.  
<https://doi.org/10.1007/s00726-006-0299-9>
- Harris, R. C., Wise, J. A., Price, K. A., Kim, H. J., Kim, C. K., & Sale, C. (2012). Determinants of muscle carnosine content. *Amino Acids*, 43(1), 5–12. <https://doi.org/10.1007/s00726-012-1233-y>
- Hasselbalch, K. A. (1916). Die Berechnung der Wasserstoffzahl des Blutes aus der freien und gebundenen Kohlensäure desselben, und die Sauerstoffbindung des Blutes als Funktion der Wasserstoffzahl. Julius Springer.
- Hawley, J. A., Hargreaves, M., Joyner, M. J., & Zierath, J. R. (2014). Integrative Biology of Exercise. *Cell*, 159(4), 738–749. <https://doi.org/10.1016/j.cell.2014.10.029>
- Heibel, A. B., Perim, P. H. L., Oliveira, L. F., McNaughton, L. R., & Saunders, B. (2018). Time to Optimize Supplementation: Modifying Factors Influencing the Individual Responses to Extracellular Buffering Agents. *Frontiers in Nutrition*, 5, 35.  
<https://doi.org/10.3389/fnut.2018.00035>

- Henderson, G. C., Horning, M. A., Lehman, S. L., Wolfel, E. E., Bergman, B. C., & Brooks, G. A. (2004). Pyruvate shuttling during rest and exercise before and after endurance training in men. *Journal of Applied Physiology*, 97(1), 317–325. <https://doi.org/10.1152/jappphysiol.01367.2003>
- Henderson, L. J. (1908). The theory of neutrality regulation in the animal organism. *American Journal of Physiology-Legacy Content*, 21(4), 427–448. <https://doi.org/10.1152/ajplegacy.1908.21.4.427>
- Henneman, E., Somjen, G., & Carpenter, D. O. (1965). Functional Significance of Cell Size in Spinal Motoneurons. *Journal of Neurophysiology*, 28(3), 560–580. <https://doi.org/10.1152/jn.1965.28.3.560>
- Hermansen, L., & Osnes, J. B. (1972). Blood and muscle pH after maximal exercise in man. *Journal of Applied Physiology*, 32(3), 304–308. <https://doi.org/10.1152/jappl.1972.32.3.304>
- Hill, C. A., Harris, R. C., Kim, H. J., Harris, B. D., Sale, C., Boobis, L. H., Kim, C. K., & Wise, J. A. (2007). Influence of  $\beta$ -alanine supplementation on skeletal muscle carnosine concentrations and high intensity cycling capacity. *Amino Acids*, 32(2), 225–233. <https://doi.org/10.1007/s00726-006-0364-4>
- Hobson, R. M., Harris, R. C., Martin, D., Smith, P., Macklin, B., Elliott-Sale, K. J., & Sale, C. (2014). Effect of Sodium Bicarbonate Supplementation on 2000-m Rowing Performance. <https://doi.org/10.1123/ijssp.2013-0086>
- Hobson, R. M., Saunders, B., Ball, G., Harris, R. C., & Sale, C. (2012). Effects of  $\beta$ -alanine supplementation on exercise performance: A meta-analysis. *Amino Acids*, 43(1), 25–37. <https://doi.org/10.1007/s00726-011-1200-z>
- Hollidge-Horvat, M. G., Parolin, M. L., Wong, D., Jones, N. L., & Heigenhauser, G. J. (1999). Effect of induced metabolic acidosis on human skeletal muscle metabolism during exercise. *The American Journal of Physiology*, 277(4), E647–658. <https://doi.org/10.1152/ajpendo.1999.277.4.E647>
- Hollidge-Horvat, M. G., Parolin, M. L., Wong, D., Jones, N. L., & Heigenhauser, G. J. F. (2000). Effect of induced metabolic alkalosis on human skeletal muscle metabolism during exercise. *American Journal of Physiology-Endocrinology and Metabolism*, 278(2), E316–E329. <https://doi.org/10.1152/ajpendo.2000.278.2.E316>
- Hopkins, W. G., Hawley, J. A., & Burke, L. M. (1999). Design and analysis of research on sport performance enhancement. *Medicine and Science in Sports and Exercise*, 31(3), 472–485. <https://doi.org/10.1097/00005768-199903000-00018>

- Howe, S. T., Bellinger, P. M., Driller, M. W., Shing, C. M., & Fell, J. W. (2013). The Effect of Beta-Alanine Supplementation on Isokinetic Force and Cycling Performance in Highly Trained Cyclists. *International Journal of Sport Nutrition and Exercise Metabolism*, 23(6), 562–570. <https://doi.org/10.1123/ijsnem.23.6.562>
- Howlett, R. A., Parolin, M. L., Dyck, D. J., Hultman, E., Jones, N. L., Heigenhauser, G. J. F., & Spriet, L. L. (1998). Regulation of skeletal muscle glycogen phosphorylase and PDH at varying exercise power outputs. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 275(2), R418–R425. <https://doi.org/10.1152/ajpregu.1998.275.2.R418>
- Huerta Ojeda, Á., Tapia Cerda, C., Poblete Salvatierra, M. F., Barahona-Fuentes, G., & Jorquera Aguilera, C. (2020). Effects of Beta-Alanine Supplementation on Physical Performance in Aerobic–Anaerobic Transition Zones: A Systematic Review and Meta-Analysis. *Nutrients*, 12(9), 2490. <https://doi.org/10.3390/nu12092490>
- Hughes, D. C., Ellefsen, S., & Baar, K. (2018). Adaptations to Endurance and Strength Training. *Cold Spring Harbor Perspectives in Medicine*, 8(6), a029769. <https://doi.org/10.1101/cshperspect.a029769>
- Hultman, E., Del Canale, S., & Sjöholm, H. (1985). Effect of induced metabolic acidosis on intracellular pH, buffer capacity and contraction force of human skeletal muscle. *Clinical Science*, 69(5), 505–510. <https://doi.org/10.1042/cs0690505>
- Hurst, P., Foad, A., Coleman, D., & Beedie, C. (2017). Athletes Intending to Use Sports Supplements Are More Likely to Respond to a Placebo. *Medicine & Science in Sports & Exercise*, 49(9), 1877–1883. <https://doi.org/10.1249/mss.0000000000001297>
- Hurst, P., Schipof-Godart, L., Szabo, A., Raglin, J., Hettinga, F., Roelands, B., Lane, A., Foad, A., Coleman, D., & Beedie, C. (2020). The Placebo and Nocebo effect on sports performance: A systematic review. *European Journal of Sport Science*, 20(3), 279–292. <https://doi.org/10.1080/17461391.2019.1655098>
- Ingham, S. A., Fudge, B. W., Pringle, J. S., & Jones, A. M. (2013). Improvement of 800-m Running Performance With Prior High-Intensity Exercise. *International Journal of Sports Physiology and Performance*, 8(1), 77–83. <https://doi.org/10.1123/ijsp.8.1.77>
- Jamnick, N. A., Pettitt, R. W., Granata, C., David B. Pyne, & Bishop, D. J. (2020). An Examination and Critique of Current Methods to Determine Exercise Intensity. *Sports Medicine*, 50(10), 1729–1756. <https://doi.org/10.1007/s40279-020-01322-8>

- Jarvis, K., Woodward, M., Debold, E. P., & Walcott, S. (2018). Acidosis affects muscle contraction by slowing the rates myosin attaches to and detaches from actin. *Journal of Muscle Research and Cell Motility*, 39(3–4), 135–147. <https://doi.org/10.1007/s10974-018-9499-7>
- Jones, A. M., Grassi, B., Christensen, P. M., Krstrup, P., Bangsbo, J., & Poole, D. C. (2011). Slow Component of V̇O<sub>2</sub> Kinetics: Mechanistic Bases and Practical Applications. *Medicine & Science in Sports & Exercise*, 43(11), 2046–2062. <https://doi.org/10.1249/MSS.0b013e31821fcfc1>
- Jorfeldt, L., Juhlin-Dannfelt, A., & Karlsson, J. (1978). Lactate release in relation to tissue lactate in human skeletal muscle during exercise. *Journal of Applied Physiology*, 44(3), 350–352. <https://doi.org/10.1152/jappl.1978.44.3.350>
- Juel, C., Bangsbo, J., Graham, T., & Saltin, B. (1990). Lactate and potassium fluxes from human skeletal muscle during and after intense, dynamic, knee extensor exercise. *Acta Physiologica Scandinavica*, 140(2), 147–159. <https://doi.org/10.1111/j.1748-1716.1990.tb08986.x>
- Karatzafiri, C., Franks-Skiba, K., & Cooke, R. (2008). Inhibition of shortening velocity of skinned skeletal muscle fibers in conditions that mimic fatigue. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 294(3), R948–R955. <https://doi.org/10.1152/ajpregu.00541.2007>
- Kasvinsky, P. J., & Meyer, W. L. (1977). The effect of pH and temperature on the kinetics of native and altered glycogen phosphorylase. *Archives of Biochemistry and Biophysics*, 181(2), 616–631. [https://doi.org/10.1016/0003-9861\(77\)90268-5](https://doi.org/10.1016/0003-9861(77)90268-5)
- Katz, A., & Sahlin, K. (1988). Regulation of lactic acid production during exercise. *Journal of Applied Physiology*, 65(2), 509–518. <https://doi.org/10.1152/jappl.1988.65.2.509>
- Katz, A., & Sahlin, K. (1990). Role of oxygen in regulation of glycolysis and lactate production in human skeletal muscle. *Exercise and Sport Sciences Reviews*, 18, 1–28.
- Kemp, G. (2005). Lactate accumulation, proton buffering, and pH change in ischemically exercising muscle. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 289(3), R895–R901. <https://doi.org/10.1152/ajpregu.00641.2004>
- Kitaoka, Y., Takahashi, K., & Hatta, H. (2022). Inhibition of monocarboxylate transporters (MCT) 1 and 4 reduces exercise capacity in mice. *Physiological Reports*, 10(17), e15457. <https://doi.org/10.14814/phy2.15457>

- Klebanov, G. I., Teselkin YuO, Babenkova, I. V., Lyubitsky, O. B., Rebrova OYu, Boldyrev, A. A., & Vladimirov YuA. (1998). Effect of carnosine and its components on free-radical reactions. *Membrane & Cell Biology*, 12(1), 89–99.
- Knuth, S. T., Dave, H., Peters, J. R., & Fitts, R. H. (2006). Low cell pH depresses peak power in rat skeletal muscle fibres at both 30°C and 15°C: Implications for muscle fatigue. *The Journal of Physiology*, 575(3), 887–899. <https://doi.org/10.1113/jphysiol.2006.106732>
- Kowalchuk, J. M., Heigenhauser, G. J., & Jones, N. L. (1984). Effect of pH on metabolic and cardiorespiratory responses during progressive exercise. *Journal of Applied Physiology*, 57(5), 1558–1563. <https://doi.org/10.1152/jappl.1984.57.5.1558>
- Kowalchuk, J. M., Heigenhauser, G. J., Lindinger, M. I., Obminski, G., Sutton, J. R., & Jones, N. L. (1988). Role of lungs and inactive muscle in acid-base control after maximal exercise. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 65(5), 2090–2096. <https://doi.org/10.1152/jappl.1988.65.5.2090>
- Lamont, C., & Miller, D. J. (1992). Calcium sensitizing action of carnosine and other endogenous imidazoles in chemically skinned striated muscle. *The Journal of Physiology*, 454(1), 421–434. <https://doi.org/10.1113/jphysiol.1992.sp019271>
- Lindh, A., Peyrebrune, M., Ingham, S., Bailey, D., & Folland, J. (2008). Sodium Bicarbonate Improves Swimming Performance. *International Journal of Sports Medicine*, 29(6), 519–523. <https://doi.org/10.1055/s-2007-989228>
- Lindinger, M. I., Leung, M. J., & Hawke, T. J. (2013). Inward flux of lactate<sup>-</sup> through monocarboxylate transporters contributes to regulatory volume increase in mouse muscle fibres. *PloS One*, 8(12), e84451. <https://doi.org/10.1371/journal.pone.0084451>
- Longyear, T. J., Turner, M. A., Davis, J. P., Lopez, J., Biesiadecki, B., & Debold, E. P. (2014). Ca<sup>++</sup>-sensitizing mutations in troponin, P(i), and 2-deoxyATP alter the depressive effect of acidosis on regulated thin-filament velocity. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 116(9), 1165–1174. <https://doi.org/10.1152/japplphysiol.01161.2013>
- Lowry, T. M. (1923). The uniqueness of hydrogen. *Journal of the Society of Chemical Industry*, 42(3), 43–47. <https://doi.org/10.1002/jctb.5000420302>
- MacIntosh, B. R., Holash, R. J., & Renaud, J.-M. (2012). Skeletal muscle fatigue—Regulation of excitation-contraction coupling to avoid metabolic catastrophe. *Journal of Cell Science*, 125(Pt 9), 2105–2114. <https://doi.org/10.1242/jcs.093674>

- Mann, T., Lamberts, R. P., & Lambert, M. I. (2013). Methods of Prescribing Relative Exercise Intensity: Physiological and Practical Considerations. *Sports Medicine*, 43(7), 613–625. <https://doi.org/10.1007/s40279-013-0045-x>
- Mannion, A. F., Jakeman, P. M., Dunnett, M., Harris, R. C., & Willan, P. L. T. (1992). Carnosine and anserine concentrations in the quadriceps femoris muscle of healthy humans. *European Journal of Applied Physiology and Occupational Physiology*, 64(1), 47–50. <https://doi.org/10.1007/BF00376439>
- Maughan, R. J., Depiesse, F., & Geyer, H. (2007). The use of dietary supplements by athletes. *Journal of Sports Sciences*, 25(sup1), S103–S113. <https://doi.org/10.1080/02640410701607395>
- McClung, M., & Collins, D. (2007). “Because I know It will!”: Placebo Effects of an Ergogenic Aid on Athletic Performance. *Journal of Sport and Exercise Psychology*, 29(3), 382–394. <https://doi.org/10.1123/jsep.29.3.382>
- McKay, A. K. A., Peeling, P., Binnie, M. J., Goods, P. S. R., Sim, M., Cross, R., & Siegler, J. (2020). Topical sodium bicarbonate: No improvement in blood buffering capacity or exercise performance. *International Journal of Sports Physiology and Performance*, 15(7), 1005–1011. <https://doi.org/10.1123/ijsp.2019-0345>
- McLaren, S. J., Smith, A., Spears, I. R., & Weston, M. (2017). A detailed quantification of differential ratings of perceived exertion during team-sport training. *Journal of Science and Medicine in Sport*, 20(3), 290–295. <https://doi.org/10.1016/j.jsams.2016.06.011>
- Medbo, J. I., & Tabata, I. (1993). Anaerobic energy release in working muscle during 30 s to 3 min of exhausting bicycling. *Journal of Applied Physiology*, 75(4), 1654–1660. <https://doi.org/10.1152/jappl.1993.75.4.1654>
- Meyer, R. A., Adams, G. R., Fisher, M. J., Dillon, P. F., Krisanda, J. M., Brown, T. R., & Kushmerick, M. J. (1991). Effect of decreased pH on force and phosphocreatine in mammalian skeletal muscle. *Canadian Journal of Physiology and Pharmacology*, 69(2), 305–310. <https://doi.org/10.1139/y91-047>
- Mildenhall, M. J., Maunder, E. D., Plews, D. J., Lindinger, M. I., & Cairns, S. P. (2023). Plasma Acidosis and Peak Power after a Supramaximal Trial in Elite Sprint and Endurance Cyclists: Effect of Bicarbonate. *Medicine and Science in Sports and Exercise*, 55(5), 932–944. <https://doi.org/10.1249/MSS.0000000000003104>
- Milioni, F., de Poli, R. A. B., Saunders, B., Gualano, B., da Rocha, A. L., Sanchez Ramos da Silva, A., Muller, P. de T. G., & Zagatto, A. M. (2019). Effect of  $\beta$ -alanine supplementation during high-intensity interval training on repeated sprint ability performance and neuromuscular fatigue.

- Journal of Applied Physiology, 127(6), 1599–1610.  
<https://doi.org/10.1152/jappphysiol.00321.2019>
- Nelson, C. R., Debold, E. P., & Fitts, R. H. (2014). Phosphate and acidosis act synergistically to depress peak power in rat muscle fibers. *American Journal of Physiology-Cell Physiology*, 307(10), C939–C950. <https://doi.org/10.1152/ajpccell.00206.2014>
- Nelson, C. R., & Fitts, R. H. (2014). Effects of low cell pH and elevated inorganic phosphate on the pCa-force relationship in single muscle fibers at near-physiological temperatures. *American Journal of Physiology. Cell Physiology*, 306(7), C670-678. <https://doi.org/10.1152/ajpccell.00347.2013>
- Nielsen, H. B., Bredmose, P. P., Strømstad, M., Volianitis, S., Quistorff, B., & Secher, N. H. (2002). Bicarbonate attenuates arterial desaturation during maximal exercise in humans. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 93(2), 724–731. <https://doi.org/10.1152/jappphysiol.00398.2000>
- Noakes, T., St, C., & Lambert, E. (2005). From catastrophe to complexity: A novel model of integrative central neural regulation of effort and fatigue during exercise in humans: summary and conclusions. *British Journal of Sports Medicine*, 39(2), 120–124. <https://doi.org/10.1136/bjism.2003.010330>
- Painelli, V. de S., Roschel, H., Jesus, F. de, Sale, C., Harris, R. C., Solis, M. Y., Benatti, F. B., Gualano, B., Lancha, A. H., & Artioli, G. G. (2013). The ergogenic effect of beta-alanine combined with sodium bicarbonate on high-intensity swimming performance. *Applied Physiology, Nutrition, and Metabolism = Physiologie Appliquee, Nutrition Et Metabolisme*, 38(5), 525–532. <https://doi.org/10.1139/apnm-2012-0286>
- Park, Y. J., Volpe, S. L., & Decker, E. A. (2005). Quantitation of Carnosine in Humans Plasma after Dietary Consumption of Beef. *Journal of Agricultural and Food Chemistry*, 53(12), 4736–4739. <https://doi.org/10.1021/jf047934h>
- Parker, C. J., & Ring, E. (1970). A comparative study of the effect of carnosine on myofibrillar-ATPase activity of vertebrate and invertebrate muscle. *Comparative Biochemistry and Physiology*, 37(3), 413–419. [https://doi.org/10.1016/0010-406X\(70\)90569-4](https://doi.org/10.1016/0010-406X(70)90569-4)
- Parkhouse, W. S. (1992). The effects of ATP, inorganic phosphate, protons, and lactate on isolated myofibrillar ATPase activity. *Canadian Journal of Physiology and Pharmacology*, 70(8), 1175–1181. <https://doi.org/10.1139/y92-163>

- Parkhouse, W. S., McKenzie, D. C., Hochachka, P. W., & Ovalle, W. K. (1985). Buffering capacity of deproteinized human vastus lateralis muscle. *Journal of Applied Physiology*, 58(1), 14–17. <https://doi.org/10.1152/jappl.1985.58.1.14>
- Parolin, M. L., Chesley, A., Matsos, M. P., Spriet, L. L., Jones, N. L., & Heigenhauser, G. J. F. (1999). Regulation of skeletal muscle glycogen phosphorylase and PDH during maximal intermittent exercise. *American Journal of Physiology-Endocrinology and Metabolism*, 277(5), E890–E900. <https://doi.org/10.1152/ajpendo.1999.277.5.E890>
- Parsons, B., Szczesna, D., Zhao, J., Slooten, G. V., Kerrick, W. G. L., Putkey, J. A., & Potter, J. D. (1997). The effect of pH on the Ca<sup>2+</sup> affinity of the Ca<sup>2+</sup> regulatory sites of skeletal and cardiac troponin C in skinned muscle fibres. *Journal of Muscle Research and Cell Motility*, 18(5), 599–609. <https://doi.org/10.1023/A:1018623604365>
- Pate, E., Bhimani, M., Franks-Skiba, K., & Cooke, R. (1995). Reduced effect of pH on skinned rabbit psoas muscle mechanics at high temperatures: Implications for fatigue. *The Journal of Physiology*, 486(3), 689–694. <https://doi.org/10.1113/jphysiol.1995.sp020844>
- Peserico, C. S., & Machado, F. A. (2014). Comparison between running performance in time trials on track and treadmill. *Revista Brasileira de Cineantropometria & Desempenho Humano*, 16, 456–464. <https://doi.org/10.5007/1980-0037.2014v16n4p456>
- Poole, D. C., Burnley, M., Vanhatalo, A., Rossiter, H. B., & Jones, A. M. (2016). Critical Power: An Important Fatigue Threshold in Exercise Physiology. *Medicine and Science in Sports and Exercise*, 48(11), 2320–2334. <https://doi.org/10.1249/MSS.0000000000000939>
- Poole, D. C., Ward, S. A., Gardner, G. W., & Whipp, B. J. (1988). Metabolic and respiratory profile of the upper limit for prolonged exercise in man. *Ergonomics*, 31(9), 1265–1279. <https://doi.org/10.1080/00140138808966766>
- Prausnitz, M. R., & Langer, R. (2008). Transdermal drug delivery. *Nature Biotechnology*, 26(11), 1261–1268. <https://doi.org/10.1038/nbt.1504>
- Prausnitz, M. R., Mitragotri, S., & Langer, R. (2004). Current status and future potential of transdermal drug delivery. *Nature Reviews. Drug Discovery*, 3(2), 115–124. <https://doi.org/10.1038/nrd1304>
- Pruscino, C. L., Ross, M. L. R., Gregory, J. R., Savage, B., & Flanagan, T. R. (2008). Effects of sodium bicarbonate, caffeine, and their combination on repeated 200-m freestyle performance. *International Journal of Sport Nutrition and Exercise Metabolism*, 18(2), 116–130. <https://doi.org/10.1123/ijsnem.18.2.116>

- Robergs, R. A., Ghiasvand, F., & Parker, D. (2004). Biochemistry of exercise-induced metabolic acidosis. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 287(3), R502–R516. <https://doi.org/10.1152/ajpregu.00114.2004>
- Romijn, J. A., Coyle, E. F., Sidossis, L. S., Gastaldelli, A., Horowitz, J. F., Endert, E., & Wolfe, R. R. (1993). Regulation of endogenous fat and carbohydrate metabolism in relation to exercise intensity and duration. *American Journal of Physiology-Endocrinology and Metabolism*, 265(3), E380–E391. <https://doi.org/10.1152/ajpendo.1993.265.3.E380>
- Rossiter, H. B., Ward, S. A., Doyle, V. L., Howe, F. A., Griffiths, J. R., & Whipp, B. J. (1999). Inferences from pulmonary O<sub>2</sub> uptake with respect to intramuscular [phosphocreatine] kinetics during moderate exercise in humans. *The Journal of Physiology*, 518(3), 921–932. <https://doi.org/10.1111/j.1469-7793.1999.0921p.x>
- Roston, W. L., Whipp, B. J., Davis, J. A., Cunningham, D. A., Effros, R. M., & Wasserman, K. (1987). Oxygen uptake kinetics and lactate concentration during exercise in humans. *The American Review of Respiratory Disease*, 135(5), 1080–1084. <https://doi.org/10.1164/arrd.1987.135.5.1080>
- Sahlin, K. (1978). Intracellular pH and energy metabolism in skeletal muscle of man. With special reference to exercise. *Acta Physiologica Scandinavica. Supplementum*, 455, 1–56.
- Sahlin, K., Tonkonogi, M., & Söderlund, K. (1998). Energy supply and muscle fatigue in humans. *Acta Physiologica Scandinavica*, 162(3), 261–266. <https://doi.org/10.1046/j.1365-201X.1998.0298f.x>
- Sandford, G. N., & Stellingwerff, T. (2019). “Question Your Categories”: The Misunderstood Complexity of Middle-Distance Running Profiles With Implications for Research Methods and Application. *Frontiers in Sports and Active Living*, 1. <https://doi.org/10.3389/fspor.2019.00028>
- Saunders, B., De Oliveira, L. F., Da Silva, R. P., De Salles Painelli, V., Gonçalves, L. S., Yamaguchi, G., Mutti, T., Maciel, E., Roschel, H., Artioli, G. G., & Gualano, B. (2017). Placebo in sports nutrition: A proof-of-principle study involving caffeine supplementation. *Scandinavian Journal of Medicine & Science in Sports*, 27(11), 1240–1247. <https://doi.org/10.1111/sms.12793>
- Saunders, B., Elliott-Sale, K., Artioli, G. G., Swinton, P. A., Dolan, E., Roschel, H., Sale, C., & Gualano, B. (2017).  $\beta$ -alanine supplementation to improve exercise capacity and performance: A systematic review and meta-analysis. *British Journal of Sports Medicine*, 51(8), 658–669. <https://doi.org/10.1136/bjsports-2016-096396>

- Saunders, B., Sale, C., Harris, R. C., & Sunderland, C. (2014). Sodium bicarbonate and high-intensity-cycling capacity: Variability in responses. *International Journal of Sports Physiology and Performance*, 9(4), 627–632. <https://doi.org/10.1123/ijsp.2013-0295>
- Serdar, C. C., Cihan, M., Yücel, D., & Serdar, M. A. (2021). Sample size, power and effect size revisited: Simplified and practical approaches in pre-clinical, clinical and laboratory studies. *Biochemia Medica*, 31(1), 010502. <https://doi.org/10.11613/BM.2021.010502>
- Sharpe, T. M., & Macias, C. J. (2016). Evaluation of the Efficacy of Lactigo™ Topical Gel as an Ergogenic Aid. *Journal of Exercise Physiology Online*, 19(3), 15–23.
- Shaw, I., & Gregory, K. (2022). Acid–base balance: A review of normal physiology. *BJA Education*, 22(10), 396–401. <https://doi.org/10.1016/j.bjae.2022.06.003>
- Siegler, J. C., Marshall, P. W. M., Bishop, D., Shaw, G., & Green, S. (2016). Mechanistic Insights into the Efficacy of Sodium Bicarbonate Supplementation to Improve Athletic Performance. *Sports Medicine - Open*, 2(1), 41. <https://doi.org/10.1186/s40798-016-0065-9>
- Smith, E. C. B. (1938). The buffering of muscle in rigor; protein, phosphate and carnosine. *The Journal of Physiology*, 92(3), 336–343. <https://doi.org/10.1113/jphysiol.1938.sp003605>
- Sprague, P., & Mann, R. V. (1983). The Effects of Muscular Fatigue on the Kinetics of Sprint Running. *Research Quarterly for Exercise and Sport*, 54(1), 60–66. <https://doi.org/10.1080/02701367.1983.10605273>
- Stellingwerff, T., Decombaz, J., Harris, R. C., & Boesch, C. (2012). Optimizing human in vivo dosing and delivery of  $\beta$ -alanine supplements for muscle carnosine synthesis. *Amino Acids*, 43(1), 57–65. <https://doi.org/10.1007/s00726-012-1245-7>
- Stephens, T. J., McKenna, M. J., Canny, B. J., Snow, R. J., & McConell, G. K. (2002). Effect of sodium bicarbonate on muscle metabolism during intense endurance cycling. *Medicine and Science in Sports and Exercise*, 34(4), 614–621. <https://doi.org/10.1097/00005768-200204000-00009>
- Street, D., Nielsen, J.-J., Bangsbo, J., & Juel, C. (2005). Metabolic alkalosis reduces exercise-induced acidosis and potassium accumulation in human skeletal muscle interstitium. *The Journal of Physiology*, 566(Pt 2), 481–489. <https://doi.org/10.1113/jphysiol.2005.086801>
- Sutton, J. R., Jones, N. L., & Toews, C. J. (1981). Effect of pH on Muscle Glycolysis during Exercise. *Clinical Science*, 61(3), 331–338. <https://doi.org/10.1042/cs0610331>
- Thomas, C., Delfour-Peyrethon, R., Bishop, D. J., Perrey, S., Leprêtre, P.-M., Dorel, S., & Hanon, C. (2016). Effects of pre-exercise alkalosis on the decrease in  $\dot{V}O_2$  at the end of all-

- out exercise. *European Journal of Applied Physiology*, 116(1), 85–95.  
<https://doi.org/10.1007/s00421-015-3239-0>
- Tiryaki, G. R., & Atterbom, H. A. (1995). The effects of sodium bicarbonate and sodium citrate on 600 m running time of trained females. *The Journal of Sports Medicine and Physical Fitness*, 35(3), 194–198.
- Trexler, E. T., Smith-Ryan, A. E., Stout, J. R., Hoffman, J. R., Wilborn, C. D., Sale, C., Kreider, R. B., Jäger, R., Earnest, C. P., Bannock, L., Campbell, B., Kalman, D., Ziegenfuss, T. N., & Antonio, J. (2015). International society of sports nutrition position stand: Beta-Alanine. *Journal of the International Society of Sports Nutrition*, 12(1), 30. <https://doi.org/10.1186/s12970-015-0090-y>
- Trivedi, B., & Danforth, W. H. (1966). Effect of pH on the kinetics of frog muscle phosphofructokinase. *The Journal of Biological Chemistry*, 241(17), 4110–4112.
- Unger, M., & Debold, E. P. (2019). Acidosis decreases the Ca<sup>2+</sup> sensitivity of thin filaments by preventing the first actomyosin interaction. *American Journal of Physiology. Cell Physiology*, 317(4), C714–C718. <https://doi.org/10.1152/ajpcell.00196.2019>
- Van Montfoort, M. C. E., Van Dieren, L., Hopkins, W. G., & Shearman, J. P. (2004). Effects of ingestion of bicarbonate, citrate, lactate, and chloride on sprint running. *Medicine and Science in Sports and Exercise*, 36(7), 1239–1243. <https://doi.org/10.1249/01.mss.0000132378.73975.25>
- Vanhatalo, A., Black, M. I., DiMenna, F. J., Blackwell, J. R., Schmidt, J. F., Thompson, C., Wylie, L. J., Mohr, M., Bangsbo, J., Krstrup, P., & Jones, A. M. (2016). The mechanistic bases of the power–time relationship: Muscle metabolic responses and relationships to muscle fibre type. *The Journal of Physiology*, 594(15), 4407–4423. <https://doi.org/10.1113/JP271879>
- Voskamp, A. E., van den Bos, S., Foster, C., de Koning, J. J., & Noordhof, D. A. (2020). The Effect of Sodium Bicarbonate Supplementation on the Decline in Gross Efficiency During a 2000-m Cycling Time Trial. *International Journal of Sports Physiology and Performance*, 15(5), 741–747. <https://doi.org/10.1123/ijsp.2019-0177>
- Watanabe, T., Inaba, T., Van Rassel, C. R., MacInnis, M. J., Kakinoki, K., & Hatta, H. (2024). Identifying physiological determinants of 800 m running performance using post-exercise blood lactate kinetics. *European Journal of Applied Physiology*, 124(10), 2951–2964. <https://doi.org/10.1007/s00421-024-05504-4>
- Westerblad, H., & Allen, D. G. (1992). Changes of intracellular pH due to repetitive stimulation of single fibres from mouse skeletal muscle. *The Journal of Physiology*, 449(1), 49–71. <https://doi.org/10.1113/jphysiol.1992.sp019074>

- Westerblad, H., & Allen, D. G. (1993). The influence of intracellular pH on contraction, relaxation and  $[Ca^{2+}]_i$  in intact single fibres from mouse muscle. *The Journal of Physiology*, 466, 611–628.
- Westerblad, H., Bruton, J. D., & Lännergren, J. (1997). The effect of intracellular pH on contractile function of intact, single fibres of mouse muscle declines with increasing temperature. *The Journal of Physiology*, 500(1), 193–204. <https://doi.org/10.1113/jphysiol.1997.sp022009>
- Wilkes, D., Gledhill, N., & Smyth, R. (1983). Effect of acute induced metabolic alkalosis on 800-m racing time. *Medicine & Science in Sports & Exercise*, 15(4), 277. [https://journals.lww.com/acsm-msse/abstract/1983/15040/effect\\_of\\_acute\\_induced\\_metabolic\\_alkalosis\\_on.4.aspx](https://journals.lww.com/acsm-msse/abstract/1983/15040/effect_of_acute_induced_metabolic_alkalosis_on.4.aspx)
- Wolosker, H., Rocha, J. B. T., Engelender, S., Panizzutti, R., Miranda, J. D., & Meis, L. D. (1997). Sarco/endoplasmic reticulum  $Ca^{2+}$ -ATPase isoforms: Diverse responses to acidosis. *Biochemical Journal*, 321(2), 545–550. <https://doi.org/10.1042/bj3210545>
- Woodward, M., & Debold, E. P. (2018). Acidosis and Phosphate Directly Reduce Myosin's Force-Generating Capacity Through Distinct Molecular Mechanisms. *Frontiers in Physiology*, 9, 862. <https://doi.org/10.3389/fphys.2018.00862>

# Appendices

## Appendix A. Ethics Acceptance



6 November 2024

Andrew Kilding  
Faculty of Health and Environmental Sciences

Dear Andrew

Re Ethics Application: **24/271 Assessing transcutaneous carnosine as an ergogenic aid in middle distance running**

Thank you for your responses to AUTEC's conditions.

Your ethics application has been approved for three years until 6 November 2027.

### Standard Conditions of Approval

1. The research is to be undertaken in accordance with the [Auckland University of Technology Code of Conduct for Research](#) and as approved by AUTEC.
2. All public facing documents must have the AUTEC approval number and be of a high standard of spelling and grammar. Dates on the Information Sheet(s) and Consent Form(s) must be consistent.
3. Any amendments to the project must be approved by AUTEC prior to being implemented.
4. A progress report is due annually on the anniversary of the approval date.
5. A final report is due at the expiration of the approval period, or, upon completion of project.
6. Any serious or adverse events must be reported to AUTEC, this includes unforeseen issues that might affect continued ethical acceptability of the project.
7. AUTEC grants ethical approval only. You are responsible for obtaining management permission for access from any institution or organisation at which your research is being conducted and you need to meet all ethical, legal, public health, and locality obligations or requirements for the jurisdictions in which the research is being undertaken.

The application number and title need to be referenced on all correspondence related to this project.

All forms are available online <http://www.aut.ac.nz/research/researchethics>

For any enquiries, please contact the Secretariat at [ethics@aut.ac.nz](mailto:ethics@aut.ac.nz)  
(This is a computer-generated letter for which no signature is required)

The AUTEC Secretariat  
**Auckland University of Technology Ethics Committee**

Cc: [hfh1331@autuni.ac.nz](mailto:hfh1331@autuni.ac.nz); [ed.maunder@aut.ac.nz](mailto:ed.maunder@aut.ac.nz); [jeffrey.rothschild@aut.ac.nz](mailto:jeffrey.rothschild@aut.ac.nz)

## Appendix B. Deception Debrief



### Research Study Debriefing Form

Study Title: Assessing transcutaneous carnosine as an ergogenic aid in middle distance running  
AUTEC REF: 24/271

Thank you for your participation in our research project, which aimed to assess the ergogenic effects of applying topical carnosine (Lactigo Gel) prior to middle-distance running performance trials.

In sport, our prior beliefs about a supplement's effects can play a significant role in performance outcomes. This is referred to as the "belief effect". To measure the belief effect accurately requires a specific type of research design. In this regard, we wish to inform you that we provided you with some intentionally incomplete information about the study.

Specifically, you were informed at the beginning of the study that carnosine-containing Lactigo would be applied before both running performance trials. However, during one of these trials the application of a placebo product, with no active ingredient, was given to you. This allowed us to explore the "belief effect" under uniform conditions across both trials ie you thought both trials were the same when in reality they were different. This design element was essential to us understanding the psychological influence that believing in a supplement's efficacy might have on sport performance, apart from any direct physiological impact a product such as Lactigo might have. Such influences are known to shape motivation, strategy/behaviour, and ultimately, performance in sport.

We recognise that this study involved intentional deception, and we apologise for any discomfort it may have caused. However, we believe that this approach was essential to achieve the study's objectives while minimising potential risks or discomfort associated with the research.

Now that you have been informed of the true nature of the study, you may choose to withhold your data if you are uncomfortable with the deception used. If you would prefer not to contribute your data, please contact a member of our research team listed below and we will remove it from further analysis. If you are comfortable with your participation, no further action is required and we look forward to analysing the data and answering an important research question.

We appreciate your understanding and hope to gain insights into the complex interactions between psychology and physiology in sports supplementation research to better inform practitioners, coaches and athletes.

#### Researcher contact details

Mr Stuart Hofmeyr [hfh1331@autuni.ac.nz](mailto:hfh1331@autuni.ac.nz)  
Prof Andrew Kilding [andrew.kilding@aut.ac.nz](mailto:andrew.kilding@aut.ac.nz)  
Dr Ed Maunder [ed.maunder@aut.ac.nz](mailto:ed.maunder@aut.ac.nz)

If you have any questions regarding your treatment or your rights as a participant in this research project, please contact the Auckland University of Technology, Ethics Committee (AUTEC) at [ethics@aut.ac.nz](mailto:ethics@aut.ac.nz).

## Appendix C. Data Collection Sheet

<b>Subject</b>	
Date	
Height (cm)	
Weight	

\*Enter to polar and sync

Pre-Test		
Time	Task	
-60	Clock Time	
	Lactate	mmol
	Product Application	
-30	Warm Up	
space to record		
-5	Readiness	(1-10)
	Lactate	
	Stryd Foot	L/R
0	Clock time	
Rec.	Stopwatch	Kestrel Climate

Post-Test		
Time	Task	
0	Lap 1	
	Lap 2	
	TTC	
+1	RPE (CR100)	
	Overall	
	Respiratory	
	Muscular	
+3	Lactate	mmol
+4	Lactate	mmol
+5	Lactate	mmol

Climate	
Wind	
Temp	
Humidity	
HI	
WGBT	
Baro	



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