

19 **ABSTRACT**

20 To defend against hydrogen cation accumulation and muscle fatigue during exercise, sodium
21 bicarbonate (NaHCO_3) ingestion is commonplace. The individualised dose-response relationship
22 between NaHCO_3 ingestion and blood biochemistry is unclear. The present study investigated the
23 bicarbonate, pH, base excess and sodium responses to NaHCO_3 ingestion. Sixteen healthy males (23 ± 2
24 years; 78.6 ± 15.1 kg) attended three randomised order-balanced, non-blinded sessions, ingesting a single
25 dose of either 0.1, 0.2 or 0.3 $\text{g} \cdot \text{kg}^{-1} \text{BM}$ of NaHCO_3 (Intralabs, UK). Fingertip capillary blood was
26 obtained at baseline and every 10 min for 1 h, then every 15 min for a further 2 h. There was a significant
27 main effect of both time and condition for all assessed blood analytes ($P \leq 0.001$). Blood analyte
28 responses were significantly lower following 0.1 $\text{g} \cdot \text{kg}^{-1} \text{BM}$ compared with 0.2 $\text{g} \cdot \text{kg}^{-1} \text{BM}$; bicarbonate
29 concentrations and base excess were highest following ingestion of 0.3 $\text{g} \cdot \text{kg}^{-1} \text{BM}$ ($P \leq 0.01$). Bicarbonate
30 concentrations and pH significantly increased from baseline following all doses; the higher the dose the
31 greater the increase. Large inter-individual variability was shown in the magnitude of the increase in
32 bicarbonate concentrations following each dose ($+2.0$ - 5 ; $+5.1$ - 8.1 ; and $+6.0$ - 12.3 $\text{mmol} \cdot \text{L}^{-1}$ for 0.1, 0.2
33 and 0.3 $\text{g} \cdot \text{kg}^{-1} \text{BM}$) and in the range of time to peak concentrations (30-150; 40-165; and 75-180 min for
34 0.1, 0.2 and 0.3 $\text{g} \cdot \text{kg}^{-1} \text{BM}$). The variability in bicarbonate responses was not affected by normalisation
35 to body mass. These results challenge current practices relating to NaHCO_3 supplementation and clearly
36 show the need for athletes to individualise their ingestion protocol and trial varying dosages prior to
37 competition.

38

39 **Key words:** Extracellular buffering, pH, fatigue

40 INTRODUCTION

41 High-intensity exercise increases hydrogen cation (H^+) production in the working muscle (Hill and
42 Lupton, 1923). The majority of these H^+ are buffered, with only a small fraction being free in the
43 cytosol to cause a decline in intracellular pH (Sahlin, 2014). It has been proposed that the decreased
44 intracellular pH is a critical factor in the development of fatigue during high-intensity exercise, either
45 via a direct effect on the muscle contractile machinery or by disruption to muscle energetics (Fitts,
46 1996). The ability to deal with this proton production is an important determinant of exercise
47 performance and capacity. Two defence mechanisms against intramuscular acidosis are evident,
48 namely, intramuscular physicochemical buffers and dynamic buffering (*i.e.*, the ability to transport H^+
49 out of the muscle and into the blood). Whilst the first line of defence is intramuscular physicochemical
50 buffering, the main controller of pH during high-intensity exercise is dynamic buffering, this process
51 allows the bicarbonate buffering system to minimise disruption to intramuscular pH (McNaughton et
52 al. 2008; Carr et al. 2011)

53

54 Supplementation with sodium bicarbonate ($NaHCO_3$) increases the efflux of H^+ out of the muscle and
55 the extracellular buffering capacity, thus delaying the onset of muscle fatigue, and maintaining exercise
56 performance (Cairns, 2006; Thomas et al. 2005). It is unsurprising that $NaHCO_3$ ingestion has been a
57 focus of researchers and athletes for over 30 years (Matson & Tran, 1993; Linderman & Gaosselink,
58 1994), with mixed findings in regards to the ergogenic efficacy of $NaHCO_3$ (for review see Peart et al.
59 2012). Some of these differences might be explained by differences dosing strategies. Several dosing
60 strategies are employed within with the sporting field, with $NaHCO_3$ doses of 0.2-0.5 $g \cdot kg^{-1} BM$ being
61 consumed to enhance exercise performance (McNaughton et al. 1991). Nonetheless, ingestion of 0.3
62 $g \cdot kg^{-1} BM$ is most commonplace, consumed 60-90 min prior to exercise (Renfree, 2007; Price & Singh,
63 2008; Siegler et al. 2010) in flavoured water or capsules (Peart et al. 2012). Consumption of 0.3 $g \cdot kg^{-1}$
64 BM typically increases blood bicarbonate concentrations by $\sim 5-6 \text{ mmol} \cdot L^{-1}$ from baseline (Matson &
65 Tran, 1993; Price et al. 2003; Robergs et al. 2005; Saunders et al. 2014; Miller et al. *in press*), which

66 has been suggested to enhance the buffering process sufficiently to result in an ergogenic benefit (Carr
67 et al. 2011).

68

69 Ingestion strategies can result in significant alterations in blood parameters, with peak acid-base
70 disturbances occurring between 60 and 90 min post ingestion of $0.3 \text{ g}\cdot\text{kg}^{-1}\text{BM}$ of NaHCO_3 (Renfree,
71 2007; Price & Singh, 2008; Siegler et al. 2010). Although there remains uncertainty as to how different
72 doses affect the inter-individual variability in blood acid-base responses. Siegler et al. (2010) showed
73 that blood bicarbonate peaked 65 min post ingestion of $0.3 \text{ g}\cdot\text{kg}^{-1}\text{BM}$, although due to blood samples
74 assessed at 20 min intervals some important aspects of the temporal pattern in acid-base responses might
75 have been overlooked. It has been proposed that the blood buffering responses to NaHCO_3 ingestion
76 are highly individual (Peart et al. 2012; Saunders et al. 2014b) and in order to optimise ergogenic
77 potential, individualising the timing of exercise based on acid-base responses to NaHCO_3 ingestion
78 should be undertaken (Miller et al. *in press*). This highlights the need to examine how individuals
79 respond to varying NaHCO_3 doses.

80

81 NaHCO_3 ingestion can result in gastrointestinal (GI) distress (Carr et al. 2011; Siegler et al. 2012; Peart
82 et al. 2012), with 10% of participants not tolerating the doses needed to gain a beneficial performance
83 effect (McNaughton et al. 2008). As dose increases, GI discomfort is more commonplace, often without
84 additional performance improvements (McNaughton, 1991; Kahle et al. 2013). To combat GI
85 symptoms, stacking dose strategies has been implemented (Sale et al. 2011; Saunders et al. 2014a);
86 splitting larger doses ($0.3 \text{ g}\cdot\text{kg}^{-1}\text{BM}$) into smaller separate doses across a longer timeframe ($0.2 \text{ g}\cdot\text{kg}^{-1}$
87 BM followed by $0.1 \text{ g}\cdot\text{kg}^{-1}\text{BM}$). How blood bicarbonate concentrations are altered following different
88 dosages of NaHCO_3 requires further investigation.

89

90 Therefore, the present study investigated bicarbonate, pH, base excess and sodium (Na^+) responses to
91 three different doses of NaHCO_3 to determine the time course of changes and the inter-individual
92 variability in responses.

93 **METHODS**

94 **Participants**

95 Eighteen participants volunteered to participate in this non-blinded, order-balanced, crossover study.
96 Two participants withdrew due to GI distress, meaning that sixteen healthy males (age, 23 ± 2 years;
97 height, 1.80 ± 0.07 m; body mass, 78.6 ± 15.1 kg) completed all aspects of the study. Participants provided
98 written informed consent and completed a health screen questionnaire prior to taking part in the study,
99 which was first approved by the Nottingham Trent University Ethical Advisory Committee. Participants
100 had not ingested any nutritional supplement or suffered from any GI problems in the previous 6 months.

101

102 **Protocol and measurements**

103 Participants attended three supplementation sessions at the same time of day, in at least a 4 h post-
104 prandial state and having replicated 24 h dietary intake. Participants were instructed to abstain from
105 alcohol and strenuous/unaccustomed exercise for 24 h prior to each assessment, with caffeine prohibited
106 on test days. Compliance with these requests was verbally confirmed prior to each session. Participants
107 ingested a single dose of either 0.1, 0.2 or 0.3 g·kg⁻¹BM of NaHCO₃ (Intralabs, UK) in clear gelatine
108 capsules. Supplements were independently tested by HFL Sports Science, UK, ensuring no
109 contamination with steroids or stimulants according to ISO 17025 accredited tests.

110

111 Fingertip capillary blood was obtained before participants ingested NaHCO₃ with 500 ml of water.
112 Following ingestion, blood was obtained every 10 min for 1 h, and then every 15 min for a further 2 h,
113 during which time participants rested in a seated position. 80 μL of whole blood was collected in a
114 heparin-coated clinitube (Radiometer Ltd, UK), and immediately analysed for pH, bicarbonate and Na⁺
115 concentrations with base excess being calculated (Radiometer ABL 900, UK).

116

117 **Statistical Analysis**

118 Based on an *a priori* power calculation (using Ducker et al. 2013); a minimum of 12 participants were
119 required to achieve 95% power at $P < 0.01$, with 18 participants recruited to allow for dropouts. Statistical
120 analyses were completed using SPSS version 22 (SPSS Inc., Chicago, IL, USA) and Microsoft Excel
121 (Microsoft Inc., USA). Data were analysed using two-way (condition X time) repeated measures
122 ANOVA. Assessed variables were tested for normality using the Shapiro–Wilks test, and for
123 homogeneity using the Levene test. A Greenhouse-Geisser correction was applied when Mauchly’s test
124 indicated that sphericity assumptions were violated. Blood analytes at each time-point were compared
125 using a one-way ANOVA, with significance based on Bonferroni-corrected p-values. Net area under
126 the curve (AUC) was calculated (as per Gannon et al. 1989), and compared using a one-way ANOVA
127 with Bonferroni-corrected *post hoc* analysis. Linear regression analyses were performed to investigate
128 relationships between baseline and absolute changes in bicarbonate concentrations. Statistical
129 significance was accepted at $P \leq 0.05$, with data presented as mean \pm 1 standard deviation (SD).

130

131 **RESULTS**

132 The AUC was significantly greater for bicarbonate (0.1 g·kg⁻¹BM: 314.4±96.1 mmol·L⁻¹·180min⁻¹; 0.2
 133 g·kg⁻¹BM: 697.7±122.8 mmol·L⁻¹·180min⁻¹, 0.3 g·kg⁻¹BM: 915.7±182.2 mmol·L⁻¹·180min⁻¹), pH (0.1
 134 g·kg⁻¹BM: 5.05±2.60 pH units·180min⁻¹; 0.2 g·kg⁻¹BM: 9.03±2.93 pH units·180min⁻¹; 0.3 g·kg⁻¹BM:
 135 10.35±3.97 pH units·180min⁻¹), base excess (0.1 g·kg⁻¹BM: 379.6±122.0 mEq·L⁻¹·180min⁻¹; 0.2 g·kg⁻¹
 136 BM: 824.4±156.7 mEq·L⁻¹·180min⁻¹; 0.3 g·kg⁻¹BM: 1078.6±210.3 mEq·L⁻¹·180min⁻¹) and Na⁺ (0.1 g·kg⁻¹
 137 BM: -48.7±195.7 mmol·L⁻¹·180min⁻¹; 0.2 g·kg⁻¹BM: 111.4±223.5 mmol·L⁻¹·180min⁻¹; 0.3 g·kg⁻¹BM:
 138 358.6±292.5 mmol·L⁻¹·180min⁻¹) following 0.3 g·kg⁻¹BM compared to 0.2 g·kg⁻¹BM (with the exception
 139 of pH responses; P≤0.05) and 0.1 g·kg⁻¹BM doses (P≤0.05). Overall responses to 0.2 g·kg⁻¹BM were
 140 significantly greater than 0.1 g·kg⁻¹BM (P≤0.05).

141

142 Baseline bicarbonate (F_(2,30)=2.0; P=0.20), pH (F_(2,30)=0.7; P≤0.51), base excess (F_(2,30)=1.7; P≤0.20) and
 143 Na⁺ (F_(2,30)=0.3; P≤0.78) levels (Table 1) were not significantly different between doses. There was a
 144 significant main effect of time for bicarbonate (F_(14,210)=72.6; P≤0.001), pH (F_(14,210)=39.8; P≤0.001),
 145 base excess (F_(14,210)=70.5; P≤0.001) and Na⁺ (F_(14,210)=11.3; P≤0.001) levels, with increases following
 146 NaHCO₃ ingestion under all supplemental conditions (Table 1).

147

148 There was a significant main effect of NaHCO₃ dose on bicarbonate (F_(2,30)=53.0; P≤0.001), pH
 149 (F_(2,30)=18.4; P≤0.001), base excess (F_(2,30)=56.2; P≤0.001) and Na⁺ (F_(2,30)=27.0; P≤0.001) levels. *Post*
 150 *hoc* analysis showed that the responses of all blood analytes were significantly lower following 0.1 g·kg⁻¹
 151 BM than following 0.2 g·kg⁻¹BM (all P≤0.001 with the exception of pH [P>0.05]) and 0.3 g·kg⁻¹BM
 152 doses (P≤0.003; Table 1). Bicarbonate concentrations (P≤0.01) and base excess (P≤0.001) were
 153 significantly higher following 0.3 g·kg⁻¹BM compared to 0.2 g·kg⁻¹BM, although there were no
 154 significant differences in pH and Na⁺ concentrations between these doses. There were significant dose
 155 by time interactions for bicarbonate (F_(28,420)=17.2; P≤0.001), pH (F_(28,420)=5.4; P≤0.001), base excess

156 ($F_{(28,420)}=18.4$; $P\leq 0.001$), and Na^+ ($F_{(28,420)}=5.0$; $P\leq 0.001$) responses; time point comparisons for blood
157 analytes are displayed in Table 1.

158

159 Across each time interval there was large variability in the responses of blood analytes following each
160 NaHCO_3 dose (Table 1). From this point the results will focus solely on blood bicarbonate
161 concentrations in the interests of brevity and given that this is the primary outcome measure of interest.
162 With respect to bicarbonate concentrations, the greatest variability in responses occurred between ~20
163 and 75 min after ingestion (Table 1). Variability was not reduced when data were normalised for body
164 mass (data not shown). Individual blood bicarbonate responses are displayed in Figure 1.

165

166 The absolute increases in bicarbonate concentrations from baseline to peak values (Figure 2) were
167 significantly greater following the ingestion of $0.3 \text{ g}\cdot\text{kg}^{-1}\text{BM}$ ($8.2\pm 1.4 \text{ mmol}\cdot\text{L}^{-1}$) than ingestion of 0.1
168 $\text{g}\cdot\text{kg}^{-1}\text{BM}$ ($3.6\pm 0.8 \text{ mmol}\cdot\text{L}^{-1}$; $P\leq 0.001$) or $0.2 \text{ g}\cdot\text{kg}^{-1}\text{BM}$ ($6.1\pm 0.9 \text{ mmol}\cdot\text{L}^{-1}$; $P\leq 0.001$). The magnitude
169 of responses ranged from $2.0\text{-}5.0 \text{ mmol}\cdot\text{L}^{-1}$ for $0.1 \text{ g}\cdot\text{kg}^{-1}\text{BM}$, $5.1\text{-}8.1 \text{ mmol}\cdot\text{L}^{-1}$ for $0.2 \text{ g}\cdot\text{kg}^{-1}\text{BM}$ and
170 $6.0\text{-}12.3 \text{ mmol}\cdot\text{L}^{-1}$ for $0.3 \text{ g}\cdot\text{kg}^{-1}\text{BM}$ doses (Figure 2). One participant achieved an increase of $5 \text{ mmol}\cdot\text{L}^{-1}$
171 from baseline, with none achieving an increase of $6 \text{ mmol}\cdot\text{L}^{-1}$ from baseline following $0.1 \text{ g}\cdot\text{kg}^{-1}\text{BM}$
172 (Table 2). With the ingestion of $0.2 \text{ g}\cdot\text{kg}^{-1}\text{BM}$, all 16 participants achieved an increase of $5 \text{ mmol}\cdot\text{L}^{-1}$
173 from baseline and 9 participants achieved an increase of $6 \text{ mmol}\cdot\text{L}^{-1}$ from baseline (Table 2). All
174 participants achieved an increase of $6 \text{ mmol}\cdot\text{L}^{-1}$ from baseline following the ingestion of $0.3 \text{ g}\cdot\text{kg}^{-1}\text{BM}$
175 (Table 2).

176

177 Individual magnitudes of responses between baseline and peak values were ranked, with only three
178 participants (1, 7 and 10) consistently in the greatest 8 responders and three participants (4, 6 and 15)
179 consistently in the least 8 responders on each dose (Table 2). The magnitudes of the responses were
180 more consistent within participants when comparing 0.2 and $0.3 \text{ g}\cdot\text{kg}^{-1}\text{BM}$ doses (Table 2); 6
181 participants (1, 7, 9, 10, 12, 16) were in the greatest 8 responders and 6 participants (4, 6, 8, 13, 14, 15)

182 were in the least 8 responders. There was a significant difference in time-to-peak blood bicarbonate
183 concentrations ($F_{(2,30)}=15.7$, $P\leq 0.001$) between doses (Table 2). The time between ingestion and peak
184 responses of blood bicarbonate demonstrated high inter-individual variability, with times ranging from
185 30-150 min (mean: 78 min; CoV: 44%) following 0.1 g·kg⁻¹BM, 40-165 min (mean: 98; CoV: 32%)
186 following 0.2 g·kg⁻¹BM and 75-180 min (mean: 123 min; CoV: 29%) following 0.3 g·kg⁻¹BM. No
187 relationship between baseline bicarbonate concentrations and the subsequent increase in response to
188 NaHCO₃ supplementation was shown for any dose (0.1 g·kg⁻¹BM: $R^2=0.01$; 0.2 g·kg⁻¹BM: $R^2=0.19$; 0.3
189 g·kg⁻¹BM: $R^2=0.01$).

190 **DISCUSSION**

191 This is the first study to report blood analyte responses from 15 time points over 3 hrs, with a high
192 temporal frequency of sampling, following NaHCO₃ ingestion at three differing doses. Despite
193 individualising NaHCO₃ dosing (based on individual body mass) a high degree of inter-individual
194 variability existed with regards to the magnitude of change in blood analyte levels and the time to peak.
195 The magnitude of the increase in blood analytes was dose-dependent, with greater increases achieved
196 with larger doses of NaHCO₃, although the range in responses was also greater at these highest dose.
197 These data challenge the most commonly suggested supplementation protocol of 0.3 g·kg⁻¹BM
198 administered ~60 min prior to performance (McNaughton, 1991; Siegler et al. 2012; Duncan et al.
199 2014), which is unlikely to result in optimal blood biochemistry for all individuals. It is difficult to
200 compare the time-course relationship following ingestion due to existing data being focused on either
201 pre- to post-exercise comparisons, or due to infrequent sample collection (Renfree et al. 2007; Siegler
202 et al. 2010; Carr et al. 2011; Miller et al. *in press*). Here we extend previous work examining the effect
203 of NaHCO₃ ingestion on acid-base responses (Renfree et al. 2007; Siegler et al. 2010; Carr et al. 2011;
204 Miller et al. *in press*), by employing a much greater temporal resolution (every 10 min) in sampling.
205 The mean time-to-peak for bicarbonate and pH responses following ingestion of 0.3 g·kg⁻¹BM was
206 greater than the 60-90 min previously documented (Renfree, 2007; Price & Singh, 2008; Siegler et al.
207 2010); even when ingesting smaller doses (>60 min). Time-to-peak for all variables increased in a step-
208 wise manner relative to dose; blood pH peaked at 75 (0.1 g·kg⁻¹BM), 105 (0.2 g·kg⁻¹BM) and 120 min
209 (0.3 g·kg⁻¹BM) post-ingestion. Our data suggest that the time intervals used in previous studies might
210 lead to some misinterpretation of findings relating to optimal blood analyte responses. It remains
211 unclear as to why high variability exists in time-to-peak when ingestion of NaHCO₃ was conducted
212 within a small and structured time period (10 min). Numerous factors which could explain this
213 variability, thus providing an avenue for future investigation.

214

215 If we use the 6 mmol·L⁻¹ above baseline cut-off for blood bicarbonate responses, as suggested by Carr
216 et al. (2011) to provide an ergogenic effect, it is clear that a dose of 0.3 g·kg⁻¹BM remains the most

217 relevant to ensure that all individuals reach this zone (Figure 2). Following 0.3 g·kg⁻¹BM, absolute
218 changes in blood bicarbonate ranged between 6.0 and 12.3 mmol·L⁻¹, with time-to-peak varying
219 between 75 and 180 min. This demonstrates that the time taken for individuals to achieve peak
220 concentrations or even performance relevant blood bicarbonate changes (Carr et al. 2011) is highly
221 variable, suggesting a need to consider individual responses to NaHCO₃ supplementation (Figure 1).
222 Practically, an *a priori* knowledge of an individual's blood responses following ingestion is required to
223 optimise outcomes. What is not yet clear is whether or not individuals respond consistently to the same
224 dose of NaHCO₃ or what factors influence bicarbonate release (*e.g.*, nutritional impact of gastric
225 emptying), providing an avenue for further work.

226

227 The current investigation might also help to explain discrepancies previously shown in relation to the
228 ergogenic effect of NaHCO₃ ingestion (for review see Carr et al. 2011), where numerous
229 methodological differences relating dosing strategy were employed. In the current study, to provide
230 consistency, participants were instructed to consume all capsules within 10 min, as per Siegler et al.
231 (2010). The time taken to ingest NaHCO₃ is often unreported or is >30 min (Carr et al. 2011), which
232 would theoretically cause more variability in individual peak responses than those reported in the current
233 study, as such comparisons to previous blood analyte responses are confounded. Gastric emptying has
234 shown considerable inter-individual variation (Paintaud et al. 1998; Barbosa et al. 2005), although there
235 is some consistency in intra-individual responses (Paintaud et al. 1998; Barbosa et al. 2005). These
236 findings suggest that it might be important to replicate dietary intake prior to ingestion in order to
237 develop a more consistent response to NaHCO₃ ingestion. Participants in the current investigation
238 replicated their 24 h dietary intake and remained fasted for 4 hrs prior to supplementation, where 90%
239 of food would be emptied from the stomach (Tougas et al. 2000). Meal volume, composition and texture
240 would, however, influence gastric emptying rates (Donohoe et al. 2009). An overnight fast would not
241 be representative of athlete behaviour and so we decided to use a 4 h fast to provide a balance between
242 experimental control and ecological validity. It should, however, be noted that the results of future
243 studies might differ with alternative dietary intake patterns. During the current investigation non-

244 arterialised fingertip capillary blood samples have been used to assess blood analyte responses. The PO₂
245 values for the current investigation were 75.38 ± 2.14 for the 0.1 g·kg⁻¹BM condition, 74.14 ± 2.61 for
246 0.2 g·kg⁻¹BM and 73.18 ± 2.63 for the 0.3 g·kg⁻¹BM condition as an average across all time points. Non-
247 warmed capillary blood samples are a useful and practical tool, reporting a strong correlation with
248 arterial samples for pH, HCO₃ and base excess variables (Yildizdas et al. 2004). This method is also in-
249 line with a number of previous investigations (Price & Simons, 2010; Bellinger et al. 2012; Siegler et
250 al. 2013; Saunders et al. 2014). In a small independent study, we confirmed that blood arterialisation
251 via warming the hand in a water bath (42°C) for 10 minutes did not alter blood gas parameters.
252 Nonetheless, it is important to suggest caution when comparing non-arterialised with arterialised
253 samples.

254

255 Blood bicarbonate concentrations were similar over the first 30 min following ingestion of all NaHCO₃
256 doses; blood pH also followed a similar pattern for the first 60 min post-ingestion. These findings
257 questions the use of doses above 0.1 g·kg⁻¹BM when the time between ingestion and performance is
258 relatively short (*i.e.*, following a high-intensity warm-up or when an athlete has multiple events over a
259 short period of time), especially when the same level of bicarbonate manipulation is achievable. In these
260 situations it would also be advisable to consume 0.1 g·kg⁻¹BM of NaHCO₃, given that lower doses
261 reduce the intensity and/or frequency of negative GI symptoms (McNaughton, 1992; Kahle et al. 2013),
262 which would benefit athletes in the competitive setting. Some athletes require co-ingestion of NaHCO₃
263 with food and fluid in order to reduce GI symptoms, therefore lowering the dose could lead to a
264 reduction in the amount of food/fluid ingested, vital for athletes competing numerous times within a
265 short period.

266

267 Following large quantities of NaHCO₃, carbonic acid formation occurs in the stomach and Na⁺
268 absorption and Na⁺ plasma concentration both increase (Heigenhauser, 1991). As the physiochemical
269 equilibrium shifts, water and CO₂ increase in the blood, thereby increasing CO₂ partial pressure (as
270 described by the Henderson-Hasselbalch equation). This mechanism alters the already acidic

271 environment of the stomach, which can result in GI distress, including stomach bloating, nausea, and
272 diarrhoea (McNaughton, 1992; Siegler et al. 2012). In the present study following NaHCO₃ ingestion
273 we have shown increased plasma Na⁺ concentrations, with the mean change being two times greater
274 following 0.3 g·kg⁻¹BM (4 mmol·L⁻¹) compared to 0.1 g·kg⁻¹BM (2 mmol·L⁻¹). The peak change in Na⁺
275 concentrations following 0.2 and 0.3 g·kg⁻¹BM occurred ~105 minutes post-ingestion, which broadly
276 corresponds to the timeframe of the greatest incidence of GI distress (~90 min following ingestion; Carr
277 et al. 2011). The inter-individual variability in the magnitude of change in Na⁺ concentrations might
278 explain why some individuals report GI distress, whilst others do not, even at the same NaHCO₃ dose.

279

280 In conclusion, the present data challenges the most commonly implemented NaHCO₃ supplementation
281 protocol and its efficacy to enhance buffering capacity and exercise performance for all individuals.
282 Due to the large inter-individual responses shown, individual and mean responses should be included
283 in future research and knowledge of the individual responses to NaHCO₃ supplementation is essential
284 in the applied setting. For individuals needing to ingest NaHCO₃ ≤30 min prior to the onset of exercise,
285 smaller doses can be ingested with no negative consequences for the additional extracellular buffering
286 potential.

287

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290

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293

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295 TS, GGA, BS and CS; data were collected and analysed by RLS; data interpretation and manuscript

296 preparation were undertaken by RLS, TS, SC, GGA, BS and CS. All authors approved the final version
297 of the paper.

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407 **TABLES**

408 **Table 1:** Blood bicarbonate, pH, base excess and Na⁺ responses across the 3 h duration following
409 NaHCO₃ ingestion. Mean time point comparisons are displayed for each blood analyte; ^x denotes a
410 significant difference between 0.1 and 0.2 g·kg⁻¹BM. ^Δ denotes a significant difference between 0.2 and
411 0.3 g·kg⁻¹BM. All comparisons are based on Bonferroni-corrected p-values of ≤0.003.

			Time post ingestion (min)															
			0	10	20	30	40	50	60	75	90	105	120	135	150	165	180	
Bicarbonate (mmolL ⁻¹)	0.1 g·kg ⁻¹ BM	Mean	25.7	25.5	26.4	27.1	27.5*	27.9*	28.0* ^X	27.9* ^X	28.0* ^X	28.1* ^X	27.9* ^X	27.4* ^X	27.4* ^X	27.2* ^X	27.2* ^X	
		SD	1.0	1.2	1.7	1.8	1.9	1.9	1.6	1.3	1.0	1.2	1.1	1.1	1.1	0.8	0.7	
	0.2 g·kg ⁻¹ BM	Mean	25.1	25.3	25.9	27.3	28.4	28.9	29.5	30.1	30.5 ^Δ	30.5 ^Δ	30.1 ^Δ	29.9 ^Δ	29.6 ^Δ	29.3 ^Δ	29.1 ^Δ	
		SD	0.87	1.27	1.58	1.74	1.71	1.62	1.19	1.04	0.97	0.85	1.19	1.18	1.24	0.84	0.92	
	0.3 g·kg ⁻¹ BM	Mean	25.5	25.6	26.7	27.9	29.4	30.0	30.6	31.7	32.1	32.3	32.4	32.2	32.2	31.7	31.4	
		SD	1.34	1.40	1.65	1.80	1.90	1.96	2.06	1.94	1.98	1.87	2.14	1.89	2.26	1.53	1.40	
pH	0.1 g·kg ⁻¹ BM	Mean	7.42	7.43	7.44	7.44	7.45	7.46	7.46*	7.46*	7.46* ^X	7.46*	7.45* ^X	7.45* ^X	7.45*	7.45*	7.44	
		SD	0.01	0.02	0.03	0.02	0.03	0.02	0.02	0.02	0.02	0.01	0.02	0.02	0.02	0.03	0.02	0.02
	0.2 g·kg ⁻¹ BM	Mean	7.42	7.42	7.43	7.45	7.46	7.47	7.47	7.47	7.48	7.48	7.48	7.48	7.48	7.48	7.47	7.46
		SD	0.02	0.02	0.03	0.03	0.03	0.04	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.03	0.03	0.03
	0.3 g·kg ⁻¹ BM	Mean	7.42	7.42	7.44	7.45	7.47	7.48	7.48	7.49	7.50	7.50	7.50	7.50	7.49	7.49	7.49	
		SD	0.02	0.02	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.03	0.03	0.03	0.02	
Base Excess (mEq L ⁻¹)	0.1 g·kg ⁻¹ BM	Mean	1.59	1.32	2.51	3.37*	3.84*	4.28* ^X	4.35* ^X	4.23* ^X	4.45* ^X	4.48* ^X	4.23* ^X	3.73* ^X	3.63* ^X	3.51* ^X	3.47* ^X	
		SD	1.29	1.54	2.02	2.23	2.27	2.25	1.93	1.70	1.26	1.41	1.30	1.28	1.28	0.92	0.84	
	0.2 g·kg ⁻¹ BM	Mean	0.96	1.12	1.71	3.43	4.71	5.28	6.09 ^Δ	6.68 ^Δ	7.18 ^Δ	7.29 ^Δ	6.90 ^Δ	6.74 ^Δ	6.40 ^Δ	6.16 ^Δ	5.87 ^Δ	
		SD	1.10	1.55	1.86	2.10	2.11	2.00	1.57	1.30	1.24	1.04	1.32	1.40	1.49	1.08	1.11	
	0.3 g·kg ⁻¹ BM	Mean	1.44	1.53	2.89	4.34	6.01	6.76	7.54	8.66	9.07	9.34	9.58	9.22	9.29	8.75	8.43	
		SD	1.66	1.76	2.05	2.25	2.26	2.35	2.41	2.23	2.31	2.12	2.38	2.09	2.43	1.68	1.53	
NA ⁺ (mmolL ⁻¹)	0.1 g·kg ⁻¹ BM	Mean	143	142	142	142	143	143	142*	143* ^X	142* ^X	143*	142*	143* ^X	143* ^X	142*	142*	
		SD	1	1	2	2	1	1	1	1	1	1	2	1	1	1	1	
	0.2 g·kg ⁻¹ BM	Mean	142	141	142	142	143	143	143	143	144	144	144	144	143	143	143	
		SD	2	1	2	2	2	2	2	1	1	2	1	2	1	1	1	
	0.3 g·kg ⁻¹ BM	Mean	142	142	142	143	144	144	144	145	145	145	145	145	145	145	145	
		SD	2	3	2	2	2	2	2	2	1	1	1	1	2	1	2	

412 **Table 2:** Individual blood bicarbonate responses following NaHCO₃ ingestion across supplemental condition. Absolute and percentage change in
413 bicarbonate responses refer to the difference between baseline and peak concentrations; absolute changes of ≥ 5 mmol·L⁻¹ are highlighted in bold.
414 Position based on response ranks participants on absolute change in descending order, highest response equates to 1, whilst lowest absolute change
415 equates to 16. Significant differences between supplementation conditions for absolute change and time-to-peak are denoted by * (0.1 and 0.3 g·kg⁻¹
416 ¹BM) ^X (0.1 and 0.2 g·kg⁻¹BM) and ^Δ (0.2 and 0.3 g·kg⁻¹BM; P≤0.05).

Participant number	0.1 g·kg ⁻¹ BM					0.2 g·kg ⁻¹ BM					0.3 g·kg ⁻¹ BM				
	Baseline (mmol·L ⁻¹)	Absolute Change (mmol·L ⁻¹)	Percentage change (%)	Time-to-peak (min)	Position based on response	Baseline (mmol·L ⁻¹)	Absolute Change (mmol·L ⁻¹)	Percentage change (%)	Time-to-peak (min)	Position based on response	Baseline (mmol·L ⁻¹)	Absolute Change (mmol·L ⁻¹)	Percentage change (%)	Time-to-peak (min)	Position based on response
1	23.7	3.9	16.5	90	5	23.2	6.9	29.7	90	3	23.7	8.9	37.6	165	
2	25.1	4.4	17.5	50	3	25.7	6.0	23.3	90	8	24.8	8.9	35.9	90	
3	25.9	2.7	10.4	120	14	25.5	6.0	23.5	120	9	25.5	8.1	31.8	105	
4	24.6	2.0	8.1	90	16	23.9	5.5	23.0	105	12	25.4	7.0	27.6	90	
5	25.3	3.8	15.0	120	6	24.7	5.6	22.7	105	10	25.1	8.5	33.9	150	
6	25.9	3.1	12.0	90	12	25.2	5.3	21.0	120	13	25.2	6.9	27.4	150	
7	25.1	3.8	15.1	50	7	24.9	6.4	25.7	90	6	27.1	8.8	32.5	120	
8	26.6	4.9	18.4	105	2	25.7	5.1	19.8	105	15	28.5	7.7	27.0	120	
9	26.6	2.6	9.8	75	15	25.3	7.1	28.1	120	2	26.7	12.3	46.1	150	
10	24.9	4.3	17.3	150	4	24.9	6.6	26.5	135	5	23.1	8.6	37.2	180	
11	25.0	3.1	12.4	90	13	24.9	6.4	25.7	90	7	24.2	7.0	28.9	180	
12	26.4	3.3	12.5	50	10	24.5	8.1	33.1	90	1	25.9	8.6	33.2	105	
13	24.9	5.0	20.1	30	1	26.7	5.5	20.6	40	11	26.7	6.0	22.5	90	
14	27.6	3.7	13.4	50	8	26.6	5.2	19.5	165	14	26.1	8.3	31.8	120	
15	26.8	3.2	11.9	40	11	25.1	5.1	20.3	60	16	24.9	6.6	26.5	75	
16	26.2	3.4	13.0	50	9	25.2	6.7	26.6	50	4	25.4	8.4	33.1	75	
Mean	25.7	3.6 ^{*X}	14.0	78 [*]		25.1	6.1 ^Δ	24.3	98 ^Δ		25.5	8.2	32.0	123	
SD	1.0	0.8	3.3	34		0.9	0.9	3.9	32		1.3	1.4	5.6	36	
Min	23.7	2.0	8.1	30		23.2	5.1	19.5	40		23.1	6.0	22.5	75	
Max	27.6	5.0	20.1	150		26.7	8.1	33.1	165		28.5	12.3	46.1	180	

FIGURE LEGENDS

Figure 1: Individual blood bicarbonate responses across the 3 hr following NaHCO₃ ingestion at 0.1(A), 0.2 (B) and 0.3 g·kg⁻¹BM (C).

Figure 2: Mean absolute change in bicarbonate concentrations across 15 intervals (3 hr) following ingestion of 0.1 (open circles), 0.2 (solid square) and 0.3 g·kg⁻¹BM (open triangle) of NaHCO₃. Zone of ergogenic effect (+6 mmol·L⁻¹) is based on concentrations from Carr et al. (2011).

FIGURES

Figure 1

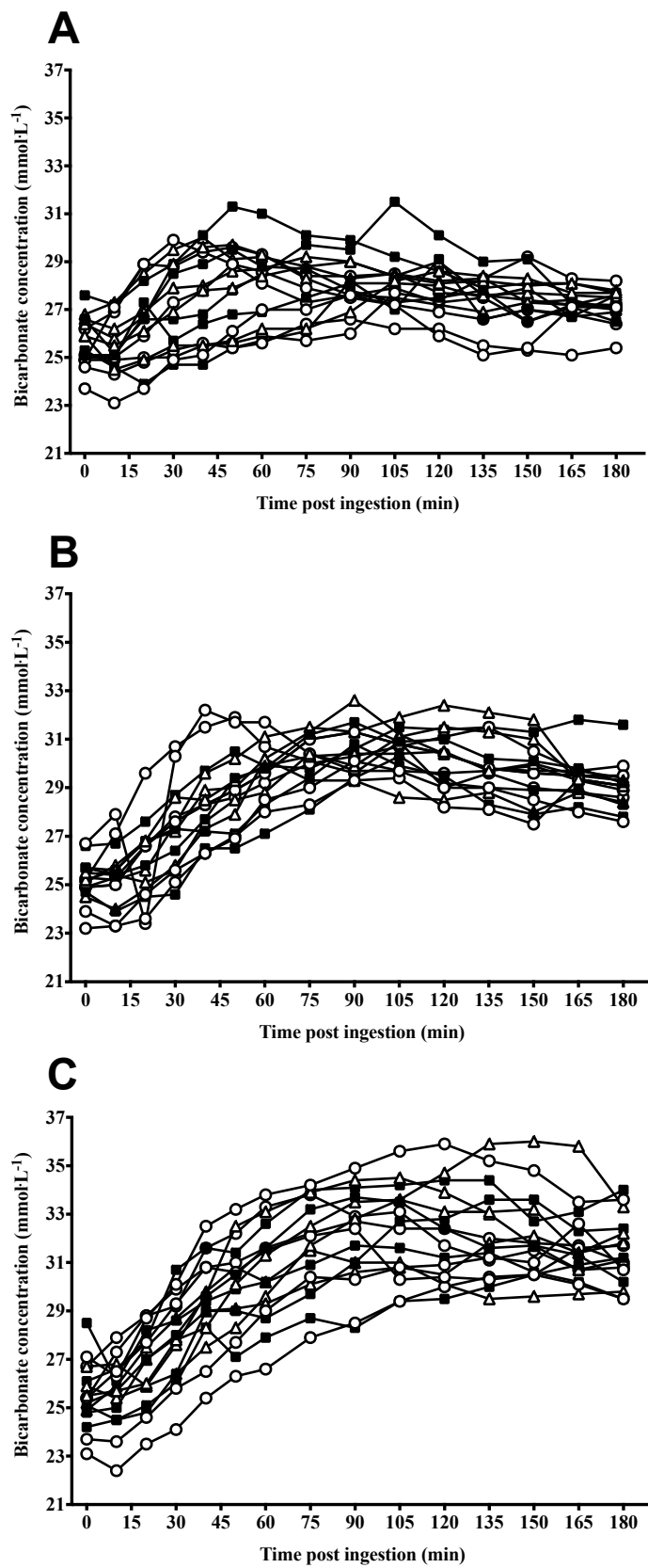


Figure 2

