Citrulline Malate fails to improve German volume training performance in healthy young men and women

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Title: Citrulline Malate fails to improve German Volume Training performance in healthy young men and women.

Short Running Head: Citrulline fails to improve exercise performance

1   **Abstract**

2   **Background:** Citrulline malate (CM) is purported to buffer lactic acid, enhance

3   oxygen delivery, and attenuate muscle soreness. Anaerobic exercise trials with CM

4   have produced conflicting results. **Objective:** The aim of the current investigation

5   was to test the efficacy of CM on resistance training (RT) with the hypothesis that CM

6   would improve performance. **Design**: A double-blind, counter-balanced, randomised

7   control trial was utilised to assess the effects of CM on RT. 19 subjects (8 female)

8   (25.7 ± 7.7 years), regularly engaged in RT consumed either 8 g of CM (1.1 : 1 ratio)

9   or a placebo (6 g citric acid). Subjects attempted to perform a German Volume

10   Training (GVT) protocol comprising 10 sets of 10 repetitions of barbell curls at 80 %

11   of their one repetition maximum. **Results:** Repeated ANOVA suggested no effect of

12   CM on RT performance (treatment × time × order p = 0.217). There was no

13   difference (p = 0.320) in the total number of reps over the ten sets (CM median = 57,

14   IQR 45 to 73; placebo median = 61, IQR 51 to 69). Blood lactate and creatine kinase

15   did not differ between CM and placebo (p > 0.05). Finally, total muscle soreness was

16   reduced significantly in CM compared to placebo (treatment × time × order p = 0.004).

17   **Conclusions:** These results require corroboration; an ergogenic benefit is yet to be

18   established and weight trainers should exercise caution when assessing the efficacy

19   of CM. Future research should focus on the potential effects of loading doses of CM.

20   **Keywords:** Resistance Training, Supplementation, Muscle Soreness, Arginine,

21   Creatine Kinase, NOS

22

Introduction

24   Citrulline (CIT) is a non-essential amino acid, which acts as a nitrogen ion acceptor

25   from carbamoyl-phosphate within the urea cycle. The dietary supplement citrulline

26   malate (CM) has been purported to improve aerobic and anaerobic exercise

27   performance via a variety of mechanisms including improved ammonia, arginine and

28   lactic acid metabolism, alongside an increase in ATP production (da Silva et al.,

29   2018). Increasing muscle CIT may attenuate ammonia accumulation resulting in a

30   lactic acid buffer effect, which might enhance subsequent recovery, attenuate fatigue

31   and reduce post exercise muscle soreness (Ochia et al., 2012; Cutufrello et al.,

32   2015). Ammonia influences fatigue by stimulating phosphofructokinase, leading to

33   an increased rate of glycolysis (Takeda et al., 2011). This may increase blood lactic

34   acid during exercise inhibiting pyruvate oxidation leading to hydrogen ion

35   accumulation, and a reduction in muscle pH, and contractile potential (Cutufrello et

36   al., 2015).

37   Citrulline is also adjacent to arginine succinate in the urea cycle, and can be directly

38   synthesised to arginine. Studies have demonstrated that supplementation with CIT

39   increases circulating levels of arginine, which may simultaneously acting as a lactic

40   acid buffer, and vasodilator via nitric oxide synthase (Takeda et al., 2011; Cutufrello

41   et al., 2015; Martinez-Sanchez et al., 2017). Trials have demonstrated that blood

42   arginine increases to a greater extent with oral CIT than arginine due to splanchnic

43   extraction (Moinard et al., 2008; Sureda et al., 2010; Takeda et al., 2011; Wijnands et

44   al., 2015). By way of comparison, a 0.75 g twice daily oral dose of CIT resulted in

45   similar increase in blood arginine compared to a 1.6 g twice daily dose of arginine

46   (Schwedhelm et al., 2007). Finally, malate acid is combined with CIT to form the salt

47   CM. Malate is an intermediate in the TCA cycle, and increasing the pool size of

48   intermediates may theoretically increase oxidative ATP (Thomas et al., 2004),

49   although to date, no trials have investigated the performance enhancing effects of

50   malate.

51   Citrulline malate as an ergogenic aid and has become of interest to exercise

52   scientists in recent years, with studies suggesting conflicting effects on exercise

53   performance (Bendehan et al., 2002; Perez-Guisda and Jakeman 2010; Wax et al.,

54   2015; Wax et al., 2016; Farney et al., 2017; Glenn et al., 2017; da Silva et al., 2018).

55   However, some evidence suggests an acute dose of 6-8 g of CM improves

56   resistance training (RT) performance (Perez-Guisda and Jakeman 2010; Wax et al.,

57   2015; Wax et al., 2016; Glenn et al., 2017) and aerobic energy production (Bendehan

58   et al., 2002). More recently however, studies using similar dosages and comparable

59   RT protocols have found no effect (Farney et al., 2017; da Silva et al., 2018). The

60   aim of the current investigation was to assess the effects of CM on German Volume

61   Training (GVT) performance to elucidate its efficacy of this potential ergogenic aid.

62   We hypothesised that supplementation with CM would increase the total amount of

63   work performed during repeated bouts of exercise.

64

65   **Subjects and Methods**

66   **Subjects**

67   Twenty one subjects volunteered to participate in this study. Two females dropped

68   out, without citing a reason for doing so, leaving 12 males and 7 females who

69   completed the study. Table 1 displays the subject characteristics. Subjects were

70   recruited from Sheffield Hallam University campus via posters, and word of mouth.

71   All subjects were healthy, non-smokers, free from injury and any underlying health

72 conditions, and not currently using medication or taking supplements containing CM.

73 Subjects were advised to follow their normal diet and supplement regime for the

74 duration of their involvement in the trial, to avoid strenuous exercise 48 h pre and

75 post laboratory visits and to maintain their regular exercise schedule post 48 h. All

76 subjects were at least "moderately resistance trained" defined as following a

77 structured RT programme at least twice per week, for the last 6 months. Written

78 consent was obtained from all subjects prior to taking part in the trial. The Sheffield

79 Hallam University Business School Food Research Ethics Committee approved the

80 trial.

81   *(Table one approx. here)*

82

83 **Experimental Design**

84 A randomised double-blind placebo cross-over design was implemented. Each

85 subject reported to the laboratory on three separate occasions 7 days apart. Subjects

86 were randomised to either CM or placebo using a random number generator and an

87 independent researcher (JG) performed concealment. The treatments were

88 counterbalanced and blinding was revealed on completion of the trial. On the first

89 visit subjects had, the GVT protocol and the muscle soreness visual analogue scale

90 (VAS) explained to them. Subjects then performed a bicep barbell curl one rep

91 maximum (1RM) test, used to calculate 80% 1RM used for the GVT.

92 On the second and third visits, subjects arrived fasted to the laboratory, provided a

93 blood sample and then consumed either 8 g of CM or a placebo which were both

94 provided as sports drinks. Subjects then completed a 24 h dietary recall and baseline

95 muscle soreness VAS was recorded. One hour after consuming the sports drink,

96 subjects performed the GVT barbell curl protocol (10 sets to failure with a maximum

97 of 10 repetitions per set, one-minute rest between sets). The total number of

98 repetitions was counted across each set, and failure was determined when a full

99 range of motion could no longer be completed. Following the GVT a second blood

100 sample was taken, subjects then completed the muscle soreness VAS and then

101 again at 24, 48 and 72 h. The following week subjects completed the trial under the

102 opposite treatment condition.

103

104 **Anthropometrics and Muscle Soreness Scale**

105 Height and weight were assessed using a stadiometer (Holtain, Crymych, United

106 Kingdom) and column scale (Seca, Birmingham, United Kingdom), body composition

107 via bioelectrical impedance (Bodystat 1500, Douglas, Isle of Man) and body mass

108 index (BMI) was calculated kg/m^2. Muscle soreness was scored using a 100 mm

109 VAS at four sites on the upper and lower arm (Biceps brachii: long and short head

110 and Brachioradialis and Flexor carpi radialis). On the VAS 0 indicated no pain, and

111 100 indicated the worst pain imaginable. The sum of the four sites was combined and

112 used to represent total soreness at each time point. Muscle soreness was recorded

113 immediately pre and post exercise under supervision and self-assessed at 24, 48

114 and 72 h following GVT. A demonstration of how to self-palpate and score the

115 muscle soreness was provided by the researchers along with an instruction sheet

116 with diagrams detailing the points of palpation. The research team reminded the

117 subjects to complete muscle soreness VAS at the same time of day using both text

118 message and email prompts.

119

Supplementation Protocol

Subjects were provided with either 8 g of CM (1.1:1 ratio, 4.2 g citrulline, 3.8 g malate, Bulk Powders, United Kingdom), or a placebo 6 g of citric acid (Sigma-Aldrich, Dorset, United Kingdom). Both placebo and supplement drinks were mixed in 70 ml of fruit cordial and 150 ml of water and consumed within 5 minutes. The dosages and timing of the CM were based on research showing that peak CIT levels occur 1 h after administration (Moinard et al., 2008). The CM and placebo drinks were both well tolerated, and subjects reported no side effects.

Assessment of Supplement Quality

Determination of the supplement quality was assessed using nuclear magnetic resonance (NMR) spectroscopy. The CM utilised in the present investigation had a purported ratio of 2:1 citrulline to malate (Bulk Powders, United Kingdom). Briefly, a standard NMR tube containing 100 mg of the CM supplement powder was added to 1 mL of D_2O (Fisher Scientific, UK). The sample was then warmed to 40 °C and agitated to ensure complete dissolution of the solid for analysis of the total organic fraction. Once the solid was dissolved, the solution was cooled to room temperature and analysed on a Bruker Avance DPX-400 NMR spectrometer operating at resonance frequencies of 400 MHz (1H) and 100 MHz (^{13}C). All 1H and 13C NMR chemical environments in both CIT and malic acid were unambiguously assigned using 1H, 1H‑COSY, 13C, DEPT‑135, HSQC and HMBC experiments. The 1H NMR signals were then integrated, with the signal resulting from H9 on malic acid (at ∂ = 4.37 ppm) being calibrated as 1. The integration values for the triplicate runs were then calculated. All possible comparisons of integral values between chemical

144 environments in CIT and those in malate were then performed and the mean nuclear

145 ratios for each individual replicate were then compiled into overall mean and

146 standard deviation values, which represent the citrulline:malate molar ratio calculated

147 from 8 individual data comparisons and three total experimental repeats.

148

German Volume Training and One Rep Max Testing

150 The 1RM testing protocol was carried out in accordance with the recommendations

151 of the National Strength and Conditioning Association (2015). 48 hours prior to and

152 48 h after each visit to the laboratory subjects were asked to refrain from all

153 strenuous exercise. Subjects fasted and avoided caffeine intake on the morning of

154 testing. Both GVT sessions were performed at the same time of day (± 1 h), 7 days

155 apart, and under the same laboratory environmental conditions (21ºC, 45 - 55%

156 Relative Humidity). One hour after consuming the sports drink subjects completed a

157 warm-up (5 min brisk walk followed by 3 sets of barbell curls with no weight on the

158 bar) before proceeding with the GVT consisting of 10 sets, of 10 repetitions of barbell

159 curls at 80 % of the subjects 1RM, with 60 s rest between sets. The numbers of

160 complete repetitions performed for each set were recorded with the set terminating

161 when the subject could no longer complete a full repetition, full repetitions were

162 determined by one of the investigators (TS).

163

Blood Sampling, Lactate and Creatine Kinase Analysis

165 Prior to the GVT exercise protocol, subjects reported to the laboratory and rested for

166 10 minutes in a seated position. Immediately after the GVT a second blood sample

167   was obtained. Blood samples were obtained via finger prick using a lancet (Accu-

168   chek, Safe-T-Pro). A 20 ɥl blood sample was taken with a capillary tube and added to

169   an Eppendorf containing heparin and saline lactate was then read immediately using

170   a Biosen C-line (EKF Diagnostics, Ebendorfer, Germany). Creatine kinase (CK) was

171   measured via a 30 µL capillary sample collected pre and post-exercise in Microsafe

172   Collection and dispensing tube (Inverness Medical, Cheshire, UK) and applied

173   immediately to a Reflotron Creatine kinase strip (Refletron Plus clinical chemistry

174   analyser; Woodley Laboratory Diagnostics, Bolton, United Kingdom).

175

176   **Dietary Intake and Analysis**

177   Subjects were instructed to consume similar foods the day before testing and refrain

178   from starting/stopping any new dietary/supplement regimes for the duration of their

179   involvement in the trial. Prior to taking part in the GVT subjects completed a 24 h

180   dietary recall. Nutritics (version 2017, Dublin, Ireland) dietary analysis software was

181   used to analyse the data (see Table 2). Nutrition data was adjusted for bodyweight

182   and expressed as grams and calories per kg of bodyweight.

183

184   **Statistics**

185   All data were analyzed using SPSS (IBM, version 24). The main outcome measure,

186   RT performance during GVT, was analysed using a 2 condition (CM and placebo)

187   repeated measures analysis of variance to determine any differences in performance

188   over the ten sets (treatment × time). Treatment order was added to the model as a

189   covariant (treatment × time × order). Muscle soreness was analysed in the same way,

190   using the sum of the 4-site muscle soreness VAS for each time point. Mauchly's test

191   of sphericity was applied to determine sphericity, where this was violated; the

192   Greenhouse-Geisser estimate was used. Data for blood lactate, CK, total reps (the

193   sum of all repetitions across all 10 GVT sets), and dietary intake were assessed for

194   normality using the Kolmogorov-Smirnov test. A paired sample t-test or Wilcoxon

195   Signed Rank test was used as appropriate, when data met the requirements for

196   parametric or non-parametric testing. Statistical significance was established at $p <$

197   0.05. Where data was normally distributed it is presented as means, standard

198   deviation and 95 % confidence interval (CI). For non-normally distributed data the

199   median and the inter-quartile range were presented.

200

Results

202   Analysis of dietary recall indicated no difference ($p > 0.05$) in macronutrient or energy

203   intake, between CM and placebo conditions (Table 2). Subjects confirmed that they

204   did not stop or start any new supplements over the duration of the trial. Determination

205   of the citrulline to malate ratio revealed the supplement contained a 1.1:1 ratio

206   citrulline to malate rather than the purported 2:1 ratio advertised on the back of the

207   packaging. Resistance training performance during the GVT is presented in Figure 1.

208   There was no significant difference, between the CM and placebo condition, on GVT

209   performance, measured by repetitions performed per set (treatment ✕ time $p = 0.174$).

210   Treatment order had no effect on GVT performance (treatment ✕ time ✕ order $p =$

211   0.217). There was a significant effect of time ($p < 0.001$) on GVT performance, *e.g.*

212   the number of repetitions performed declined as sets progressed (mean repetitions

213   set 1, placebo 9.8 ± 0.7 vs CM 9.5 ± 1.1; set 10, placebo 4.4 ± 2.9 vs CM 4.6 ± 2.4).

214 There was no statistically significant difference (Z = 0.995, p = 0.320) in the total

215 number of repetitions achieved over the ten sets of GVT between the CM (median =

216 57, IQR 45 - 73) and placebo conditions (median = 61, IQR 51 - 69).

217   *(Table 2, and Figure 1 approx. here)*

218 Blood lactate data is presented in Figure 2. Lactate increased significantly (p < 0.001)

219 post GVT in both the CM (mean lactate pre, 1.9 ± 0.6, post 4.7 ± 2.0 mM) and

220 placebo conditions (mean lactate pre, 1.8 ± 0.6, post 4.9 ± 1.7 mM). There was

221 however, no difference (t = 0.434 p = 0.670) in the magnitude of change in lactate

222 post GVT between CM and placebo with a mean increase of 3.01 mM (95 % CI 2.41

223 - 3.62). There was no difference in CK levels post GVT under the CM treatment (pre,

224 172 I/U IQR 48.5 - 222.9; post, 179.00 IQR 149.5 - 370.4, Z = 1.552, p = 0.121),

225 however there was a difference under the placebo condition (pre, 145 I/U IQR 52.9 -

226 333.0; post, 219 IQR 91.1 - 423.2, Z = 1.991, p = 0.046). The median difference of

227 the differences the subjects for CK pre to post exercise did not differ (Z = 0.052, p =

228 0.959) between CM (median = 66.1 I/U IQR 34.3 - 152.6) or the placebo condition

229 (median = 60.4 I/U IQR 19.3 - 150.0).

230   *(Figure two approx. here)*

231 The effect of CM on 72 h muscle soreness is detailed in Figure 3. Muscle soreness

232 was significantly higher in the placebo compared to the CM treatment over 72 h

233 (treatment × time p = 0.004). The statistical difference was maintained when

234 treatment order was included in the model (treatment × time × order p = 0.008).

235   *(Figure three and table two approx. here)*

236 **Discussion**

237   In the current investigation, we hypothesised that an acute dose of CM prior to an

238   exercise session would increase the total amount of work performed during GVT.

239   Citrulline malate had no effect on GVT performance, blood lactate or CK compared to

240   a placebo, although subjects did report an overall reduction in muscle soreness. The

241   results of the present investigation accept the null hypothesis and are in agreement

242   with recent findings showing no effect of CM on RT performance (Farney et al., 2017;

243   Chappell et al. 2018; da Silva et al., 2018,). Moreover, these findings are in contrast

244   to others who have identified an effect of CM with RT (Wax et al., 2015; Wax et al.,

245   2016; Glenn et al., 2017). Specifically, Perez-Guisda and Jakeman (2010) and Wax

246   et al., (2016) reported a 13 and 12.5 % respectively, increase in the number of

247   repetitions achieved after consecutive bouts of RT following CM supplementation.

248   By way of comparison, a similar increase would have amounted to an 8-repetition

249   difference in the total repetitions between the CM and placebo condition in the

250   present investigation.

251   The reduction in soreness identified with CM was accompanied by a lack of

252   difference in the total amount of work performed between treatment groups. This

253   could lead to the conclusion that less soreness was elicited from the same workload

254   when the subjects consumed CM. Although we note that subjects did not report high

255   values for muscle soreness pre or post exercise, which may reflect the nature of the

256   exercise i.e only small muscle groups were involved in our protocol. da Silva et al.

257   2017 and Chappell et al. 2018, both found a greater degree of soreness, this seems

258   to be commensurate with protocols involving larger muscle groups. We also note a

259   lack of any immediate difference in CK or lactate levels between conditions, which

260   might be expected to accompany any difference in soreness. The lack of change, in

261   these markers or muscle damage and exercise intensity is in agreement with recent

262 trials utilising CM during RT protocols (Wax et al., 2015; Wax et al., 2016; da Silva et

263 al., 2017; Farney et al., 2017). Effects of CM on muscle soreness and RT have so far

264 produced mixed results, with both reductions in soreness (Perez-Guisado & Jakeman

265 2010) and no difference when compared to placebo (da Silva et al., 2017; Chappell

266 et al., 2018). Curiously, trials of aerobic exercise have so far indicated a reduction in

267 soreness utilising CM (Tarozona-Diaz et al., 2013, Martinez-Sanchez et al., 2017).

268 Potential explanations for a reduction in soreness therefore may be attributed to

269 CIT's role in the urea cycle and the augmented clearance of ammonia (Callis et al.,

270 1991).

271 Finally, we sought to corroborate the level of the active ingredient used in the present

272 investigation with the manufacturer's labelling. The data suggests that the amounts of

273 active ingredient in the supplement varied, by almost half, from the manufacturers

274 labelling. The dosage consumed by subjects was 4.2 g CIT and 3.8 g malate (1.1:1

275 ratio) instead of the intended 6 g CIT and 2 g malate (2:1 ratio). A previous

276 investigation reported similar findings from five "over the counter" CM supplements

277 (Chappell et al., 2018).The disparity between the actual and intended dosage may

278 account for a lack of significant findings. Moinard et al., (2008) however, reported a

279 significant increase in plasma CIT using a similar dosage to the one used in the

280 present investigation. Moreover, the data highlights the need for researchers to

281 conduct analyses of supplement quality prior to publishing trials. Caution therefore

282 needs to be taken when assessing any dose-response study using commercial CM

283 supplements. Commercial supplements, however, are the products recreationally

284 active individuals and athletes alike use in an attempt to aid recovery and improve

285 performance.

286

Strengths and Limitations

A counterbalanced design was employed to account for a potential training effect, and statistical analysis identified that subjects did not perform better on their second GVT session compared to the first. There was also no difference in dietary intake for the 24 hours preceding testing, between the CM and placebo conditions, Therefore any lack of statistical finding may not be attributed to a disparity in diet (e.g. an increased carbohydrate or energy intake between conditions).

The investigation did not include a measure of ammonia to accompany the data gathered on lactate and CK to corroborate the difference in muscle soreness. Furthermore, although we advised subjects to rest 48 h prior to commencing the trial, several subjects had elevated CK suggesting engagement in prior exercise. Increases in CK levels in response to exercise are known to be highly variable and increase significantly in days following exercise (Ehlers et al. 2002). Creatine kinase was only measured immediately post exercise and a measurement taken alongside muscle soreness over 72 h would have elucidated the recovery process more clearly. Moreover, measurements of muscle soreness were self-reported between the 24-72 h measures potentially and supervised measures would have been preferable. The subjects involved in the present investigation were not a homogenous group. Training experience varied and no controls were put in place to account for the impact of menstrual cycling. Finally, we utilised citric acid as a placebo condition. We only found a single study focused on the effect of citric acid on exercise. Sugino et al. (2007) utilised an 8 day loading protocol combined with aerobic exercise, the authors found no effect on performance, blood citric acid or lactate levels. The placebo was effective at replicate the taste of CM and was well tolerated.

311 Subjects completed the trial fasted to eliminate the influence of feeding on

312 performance. We could alternatively have included a standardised breakfast in the

313 protocol to reflect the probability that exercise is often not carried out in a fasted state.

314 Finally, we asked the participants not to stop or start any other supplement intake for

315 the duration of the trial and a condition of participation was that they weren't taking

316 any supplements containing CM. Although we acknowledge the potential effects of

317 other supplements on performance the crossover design of this study to some extent

318 mitigates against this. Secondly we are reminded of the real-world nature of

319 supplement intake whereby in reality people will not postpone ongoing

320 supplementation regimes when they begin new ones.

321

322 **Conclusion**

323 An acute dose of 8 g CM (1.1:1 ratio) did not confer any benefits to the main outcome

324 measure of RT performance, in a moderately trained group. Total muscle soreness

325 was reduced over the 72 h following CM treatment however; both CK and lactate

326 were unaffected immediately following exercise. This is the first study to date to test

327 the effectiveness of CM using a GVT free weight exercise protocol. Further trials on

328 acute and chronic use of CM are warranted to confirm or deny its effectiveness as an

329 ergogenic aid. Athletes and coaches should proceed with caution when deciding

330 whether to utilise CM as part of a supplementation protocol; the present study and

331 current literature is mixed and recommendation of CM as an anaerobic ergogenic aid

332 is not warranted based on the present results, although we note with caution there

333 may be a positive effect on muscle soreness. Finally, in light of our findings, future

334   researchers should endeavour to carry out chemical analysis to ensure the validity of

335   treatment dose.

336

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Tables

Table 1 Participant Characteristics (n - 19, 12 male, 7 female)

Age (years)	Height (m)	Weight (kg)	BMI (kg/m^2)	Bodyfat (%)
25.7 ± 7.7	1.7 ± 0.1	75.3 ± 13.7	24.8 ± 2.9	18.3 ± 5.8

Abbreviations: m, metres; kg, kilogram; BMI, body mass index.

All values are mean ± SD

Table 2. 24 Hour Dietary Intakes Preceding the German Volume Training

	Placebo	Citrulline Malate	P value
Carbohydrate (g / kg BW)	3.8 ± 1.8	3.2 ± 1.7	0.285
Protein (g / kg BW)	2.2 ± 1.5	1.8 ± 0.9	0.575
Fat (g / kg BW)	1.0 ± 0.4	0.9 ± 0.4	0.223
Energy (Kcal / kg BW)	34.6 ± 10.7	28.8 ± 10.7	0.730

Abbreviations: g, grams; kg, kilograms, BW, bodyweight; Kcal, calories.

 (Paired t-test: Fat; Wilcoxon Signed Rank Carbohydrate, Protein and Energy). All values are means ± SD,

Legends for Figures

Figure 1 - The effect of citrulline malate on resistance training performance. Exercise performance with the placebo is represented by the solid black line (n = 19); citrulline malate is represented by the dashed line (n = 19). (repeated measures ANOVA time $p < 0.05$; treatment × time × order $p > 0.05$) The data presented is the mean ± SD.

Figure 2 - The effect of citrulline malate on blood lactate following resistance training. Pre-exercise lactate values are represented by the grey bars (n = 18); post-exercise values are represented by the black bars (n = 18); the white bars represent the magnitude of change between placebo and supplement (n = 18). Results analysed using a paired t-test, * indicates significant difference pre to post exercise. The data presented is the mean ± SD.

Figure 3 - The effect of citrulline malate on muscle soreness following resistance training. Muscle soreness with the placebo is represented by the solid black line (n = 19); citrulline malate is represented by the dashed line (n = 19). Over time muscle soreness was significantly higher in the placebo compared to citrulline malate treatment (repeated measures ANOVA: treatment × time × order p = 0.008). The data presented is the mean ± SD.