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Citrulline Malate Fails to Improve Repeated 300 m Swimming Times in Highly Trained Swimmers

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Abstract: Citrulline malate (CM) has been touted as a nutritional ergogenic aid for sports performance, with purported mechanisms of increased muscle blood flow, ammonia clearance, and adenosine triphosphate resynthesis. Combined, these physiological benefits may be best applied to whole-body endurance exercises, such as swimming, though this postulate has not yet been explored. In a double-blind, randomised, and crossover design, 11 national-level swimmers (age: 17 ± 3 years, height: 1.71 ± 0.05 m, body mass: 60.6 ± 8.3 kg) from a high-performance swimming club ingested either 15 g CM or a placebo (PLA) 60 min before six \times 300 m freestyle bouts (at 4.5 min intervals). Blood lactate, blood pressure, and ratings of perceived exertion were measured at baseline, 60 min post-ingestion, and immediately post-exercise. Neither mean 300 m swimming time (CM: 212.0 ± 9.6 vs. PLA: 212.8 ± 7.7 s, $p = 0.683$, $g = 0.09$) nor any individual swimming bouts ($p = 0.679$, $P\eta^2 = 0.02$) were improved with CM ingestion. Moreover, no differences in any physiological or subjective measures were identified between conditions (all $p > 0.05$). Whether the proposed CM mechanisms were active was unclear as more direct physiological measures (i.e., plasma NO, ammonia) may have been required. Resultantly, these observations do not support an ergogenic effect of acute CM ingestion in highly trained swimmers.

Keywords: sport nutrition; supplements; nutritional ergogenic aids; nitric oxide



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1. Introduction

Citrulline malate (CM) has recently garnered attention for its ergogenic potential [1]. The primary ingredient, L-citrulline, is a purported precursor to nitric oxide (NO) production, which is recognised to have multiple physiological benefits associated with enhanced exercise performance, including improvements in muscle blood flow, mitochondrial efficiency, glucose uptake, and type II muscle contractility [2–4]. Furthermore, L-citrulline is an intermediate in the urea cycle, such that supplementation could possibly enhance ammonia clearance, the production of which is increased during exercise [5]. Subsequently, reduced ammonia production could delay increases in blood lactate (La^-) during exercise, facilitating the oxidative metabolism of pyruvate and the potential for a higher rate of adenosine triphosphate (ATP) turnover [6]. Building on this, co-ingestion of malate with L-citrulline could elicit an additive and/or synergistic benefit on oxidative ATP turnover by aiding tricarboxylic acid (TCA) cycle flux [1]. Indeed, malate is involved in anaplerotic reactions within the TCA cycle [1], where its dehydrogenation into oxalacetate is critical for continued aerobic ATP turnover [7]. Whilst these purported ergogenic mechanisms are yet to be empirically confirmed, CM ingestion would appear to support whole-body exercise with a larger aerobic component [1], such that swimming training may be well placed to benefit from supplementation [8].

Equivocal results have been found when L-citrulline is supplemented prior to endurance exercise performance [9–11]; therefore, co-ingestion with malate could provide the missing link to a consistent ergogenic benefit. However, CM research to date has primarily focused on resistance training following early work by Pérez-Guisado and Jake-man [12]. The authors found that ingesting 8 g CM an hour before exercise increased bench press repetitions to failure when performed both before (+18%) and after (+53%) a chest-based workout; yet, subsequent similar research has since yielded equivocal findings [13,14]. Indeed, only two studies have measured performance in what could be regarded as whole-body endurance exercise, both of which failed to show a CM benefit towards time-to-exhaustion (T_{LIM}) cycling [15,16]. However, Gills et al. [16] administered an 8 g CM dose that has been associated with mixed performance outcomes [1], with a higher dose of 15 g potentially being required to elicit more consistent increases in plasma L-citrulline and NO [17], especially in trained athletes [18]. In contrast, Cunniffe et al. [15] measured performance following 10×15 m maximal cycling sprints, which could have (a) hindered aerobic work capacity by causing local muscle fatigue [19] and/or (b) allowed the window for ergogenic potential (~ 60 min post-ingestion) to pass before the endurance exercise had started [1]. Therefore, to explore whether CM could have practical benefits in sports, further research is needed to investigate whether 15 g CM has ergogenic potential during typical endurance training sets.

In swimming training, high-intensity intermittent efforts are commonly used to enhance endurance exercise performance [20]. The purpose of this study was therefore to investigate whether a CM dose of 15 g could be ergogenic for highly trained swimmers completing a typical endurance training set (six \times 300 m).

2. Materials and Methods

2.1. Participants

An a priori power calculation [repeated measures analysis of variance (ANOVA) for within-between interactions; two groups; six measures; $\alpha = 0.05$; $\beta = 0.80$; correspondence = 0.78 (based on repeatability data in Section 2.4)] suggested that 14 swimmers were required to identify a small effect size (0.20) in swimming performance (G*Power, v.3.1.9.4, Universität Düsseldorf, Düsseldorf, Germany). This study recruited 17 highly trained middle-distance swimmers (aged ≥ 16 years, nationally competitive at 200–400 m distances [21]); however, six swimmers withdrew from data collection before all data were collected (attrition \times 4, injury \times 1, withdrew consent \times 1). Based on the available participants and limited time to alter training schedules within a highly trained cohort, a final sample size of 11 highly trained swimmers (six males, five females; age: 17 ± 3 years; height: 1.71 ± 0.05 m; body mass: 60.6 ± 8.3 kg; 200 m freestyle World Aquatic points: 650 ± 99) was justified for the purpose of this study [22,23]. Throughout the investigation, all swimmers were engaged in an endurance training phase consisting of 6–8 pool (mean swimming volume: 52.1 ± 7.7 km \cdot week $^{-1}$) and 2–3 land-based (~ 60 min) training sessions \cdot week $^{-1}$. Written informed consent was provided prior to participation in this study by all swimmers and their primary caregivers if aged under 18 years. Institutional ethical approval was granted in accordance with the Declaration of Helsinki.

2.2. Preliminary Procedures

This study involved three trials as follows: one familiarisation and two experimental trials conducted in a double-blind, randomised, and crossover design. All swimmers were requested to limit their intake of nitrate-rich foods in the seven days before each trial, which was facilitated by sending a list of nitrate-rich foods to swimmers and caregivers prior to the familiarisation trial. Caffeine (12 h before exercise) and other acute ergogenic aids (7 days prior to exercise) were also asked to be avoided. Swimmers provided a written food diary before the familiarisation trial in order to replicate their diets for all subsequent trials. Adherence to controls was assessed via a verbal dietary recall before each trial, as per previous research [15,16]. Two swimmers reported the consistent use of chronic

ergogenic aids (i.e., beta-alanine, creatine) for more than 24 weeks, which was permitted given these supplements are typically co-ingested by highly trained swimmers [24], and because the largest physiological adaptations with these supplements would have already occurred [25,26]. All trials were conducted at the same time of day, separated by exactly 7 days to (a) reduce the effects of confounding variables, such as differences in sleep, training stress, nutrient timings, and circadian rhythms that may occur across the training week, and (b) allow ample washout time between experimental trials [1].

2.3. Experimental Procedures

On arrival at their training venue, swimmers engaged in 5 min of seated rest before completing baseline (BASE) physiological measures. Firstly, a 5 μ L capillary blood sample was drawn from the fingertip to assess blood La^- concentration (Lactate Pro 2, Akray, Kyoto, Japan), which was followed by three readings of blood pressure (systolic, SBP; diastolic, DBP) from the brachial artery using an automated sphygmomanometer (Boso-Medicus Uno, Bosch and Sohn, Jungingen, Germany). All three blood pressure measurements were taken on the poolside while the swimmer seated on a chair, with samples taken immediately after the other because of the time sensitivity of results. The mean of the three readings was used for data collection [27]. These physiological measures were taken on the premise that CM could reduce blood La^- and ammonia production [1], as well as enhance blood flow and reduce blood pressure during exercise [28], respectively. Following BASE measures, all swimmers were given an opaque sports bottle containing either 15 g CM or a placebo (PLA). The experimental solution consisted of 15 g CM (Myprotein, Manchester, UK), 100 mL orange cordial (Sainsburys, Leeds, UK), and 300 mL water. The PLA solution consisted of 400 mL orange cordial (Sainsburys, Leeds, UK), as per Cunniffe et al. [15]. Both solutions were ingested within a 5 min window, 60 min before the start of exercise. The CM dose and timings used in this study were thought to produce peak plasma L-citrulline and NO concentrations compared with other dosing strategies [17]. None of the swimmers had prior experience ingesting CM, and all solutions were created and randomised by an outside researcher.

All swimmers completed a 45 min warm-up prior to exercise, which first took place on the poolside with 15 min of self-selected, land-based activity. Though individual routines varied, land warm-ups typically involved skipping (3–5 min), full body mobility (5–10 min), and bodyweight strength exercises (3–5 min). Swimmers then entered a 25 m pool and completed a 30 min progressive intensity warm-up that was prepared by the head swimming coach. The remaining 15 min was spent in passive rest while swimming lanes were organised for the six \times 300 m swimming test. At this time, swimmers exited the pool and dried their arms with a towel, before being seated again on the poolside to give samples of pre-exercise (PRE-EX) blood La^- and blood pressure. All measures were taken from the same arm approximately 1–2 min after exercise. In addition, ratings of perceived exertion (RPE) were collected using a CR10 Borg scale [29] to rate the perceived intensity of the warm-up. All measurements (blood La^- , SBP, DBP, RPE) were collected one more time after the six \times 300 m swimming test (POST-EX), using the same methods as the PRE-EX samples. All warm-ups, swimming lanes, and timings were kept consistent for both experimental trials. At the end of each trial, swimmers were asked how confidently they could predict their supplement condition using a 1–5 Likert scale, with 1 representing ‘not confident at all’ and 5 representing ‘extremely confident’. If a score above three was given, then swimmers were asked to predict which supplement they had ingested.

2.4. Endurance Training Set

The six \times 300 m maximal freestyle swimming test was recommended by the head swimming coach based on prior use in this cohort. The test required maximal 300 m freestyle time trials at 4.5 min intervals for six bouts, with the time between 300 m completion and the following bout (~60 s) serving as passive rest, in line with previously reported endurance training sets [20]. In the three months prior to this study, four swim-

mers had completed the six × 300 m test on a frequent basis (3–6 attempts), demonstrating a high test-retest reliability for mean 300 m completion time [coefficient of variation (CV): 1.1–2.9%], as well as an ‘excellent’ reproducibility of results over their first three attempts [intraclass correlation coefficient (ICC): $r = 0.782$, $p = 0.005$] [30,31]. This exercise protocol was therefore considered as a suitable endurance swimming exercise test to measure performance in highly trained swimmers. Performance times were measured by two experienced swimming coaches, with the mean of the two times recorded for data analysis. Swimmers performed the six × 300 m test with a maximum of two per lane. Aggregated time-to-complete all 300 m time trials, mean 300 m time, and individual 300 m time-trial bouts were all analysed for possible CM versus PLA differences.

2.5. Statistical Analysis

All statistical tests were carried out using Statical Package for Social Sciences (v.25, IBM, Armonk, NY, USA), with statistical significance set at $p < 0.05$. All data were normally distributed, which was assessed using Shapiro–Wilk tests. Paired samples t -tests were used to compare mean performance outcomes (aggregated time-to-complete six × 300 m, mean 300 m time) following CM and PLA ingestion. Repeated measures ANOVAs were also used to compare CM and PLA differences within each exercise bout, as well as for physiological (La^- , SBP, DBP) and subjective (RPE) differences across the study timeframe. The data were screened for sphericity (Mauchly test) before each ANOVA, with either Huyn–Feldt (epsilon > 0.75) or Greenhouse–Geiser (epsilon < 0.75) corrections applied if violations occurred. For statistically significant results, pairwise comparisons were reported using the Bonferroni correction. Effect sizes were reported as partial eta squared (η^2) for ANOVA outcomes, which were interpreted as ‘small’ (0.01–0.05), ‘moderate’ (0.06–0.13), and ‘large’ (≥ 0.14) [32]. Additionally, effect sizes for pairwise comparisons were calculated and reported using Hedge’s g bias correction, which was selected based on this study’s sample size ($n < 20$) [33]. These effect sizes were interpreted as ‘small’ (0.20–0.49), ‘moderate’ (0.50–0.79), and ‘large’ ($g \geq 0.80$) [32]. The smallest worthwhile change (SWC) was calculated for mean 300 m time (± 2.9 s) by multiplying the standard deviation of 20 past attempts by 0.3 [34]. All data are reported as mean \pm standard deviation.

3. Results

3.1. Swimming Performance

There were no differences in the aggregated time-to-complete six × 300 m ($p = 0.679$, $g = 0.08$), mean 300 m time ($p = 0.683$, $g = 0.09$), or any individual 300 m swimming bout ($p = 0.679$, $\eta^2 = 0.02$) between CM and PLA conditions (Table 1). The results were also inconsistent at the individual level as nine swimmers exceeded the SWC (± 2.9 s) for mean 300 m performance time, with five swimming faster in the CM trial (mean change: -6.5 ± 2.5 s) and four swimming faster in the PLA trial (-5.4 ± 1.2 s), whereas only two swimmers maintained their performance times (Figure 1).

Table 1. Mean swimming times per bout during the 6 × 300 m freestyle test.

300 m Bout	Mean 300 m Time (s)		Effect Size (g)
	CM	PLA	
1	210.4 \pm 9.8	212.2 \pm 8.3	0.19
2	211.8 \pm 9.0	212.5 \pm 7.1	0.08
3	211.6 \pm 9.4	213.1 \pm 8.1	0.16
4	213.4 \pm 10.1	213.0 \pm 7.2	0.04
5	213.0 \pm 10.0	213.6 \pm 8.2	0.06
6	211.8 \pm 10.5	212.2 \pm 9.4	0.03
Mean	212.0 \pm 9.6	212.8 \pm 7.7	0.09
Aggregated	1272.0 \pm 57.8	1276.6 \pm 46.6	0.08

Mean \pm standard deviation.

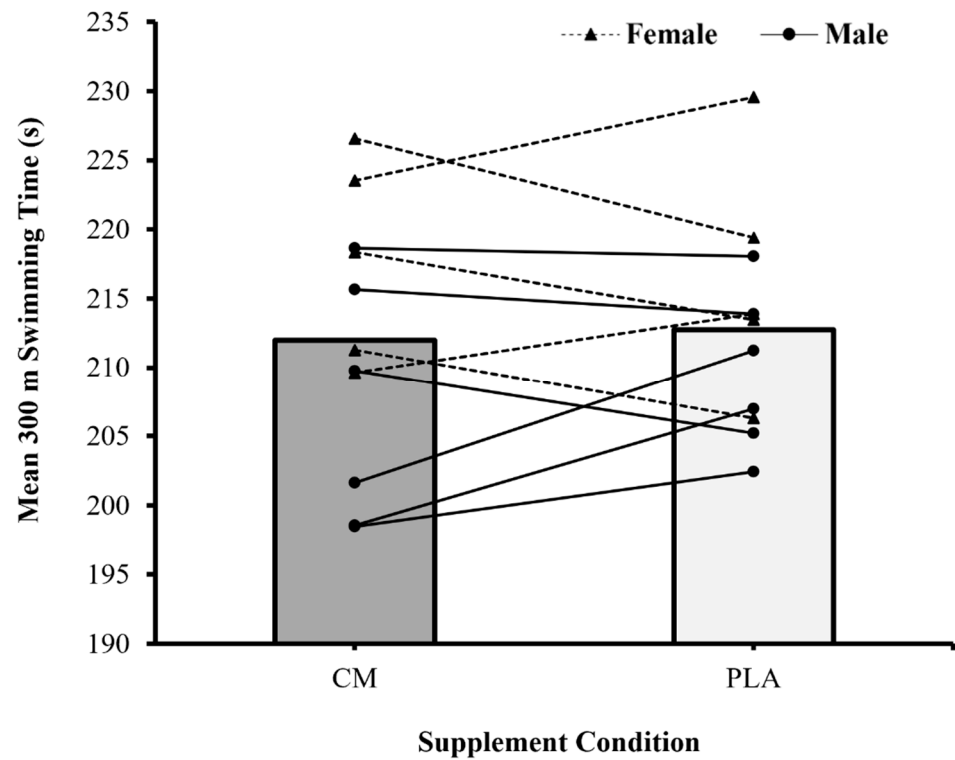


Figure 1. Mean 300 m swimming times during the six × 300 m freestyle test.

3.2. Physiological Variables

Blood La^- concentrations were similar between supplements across the study timeframe ($p = 0.126$, $\text{Pr}^2 = 0.19$; Figure 2). Although lacking statistical significance, a small effect size was calculated POST-EX at the group mean level (mean difference: $+1.4 \text{ mmol}\cdot\text{L}^{-1}$, $g = 0.46$).

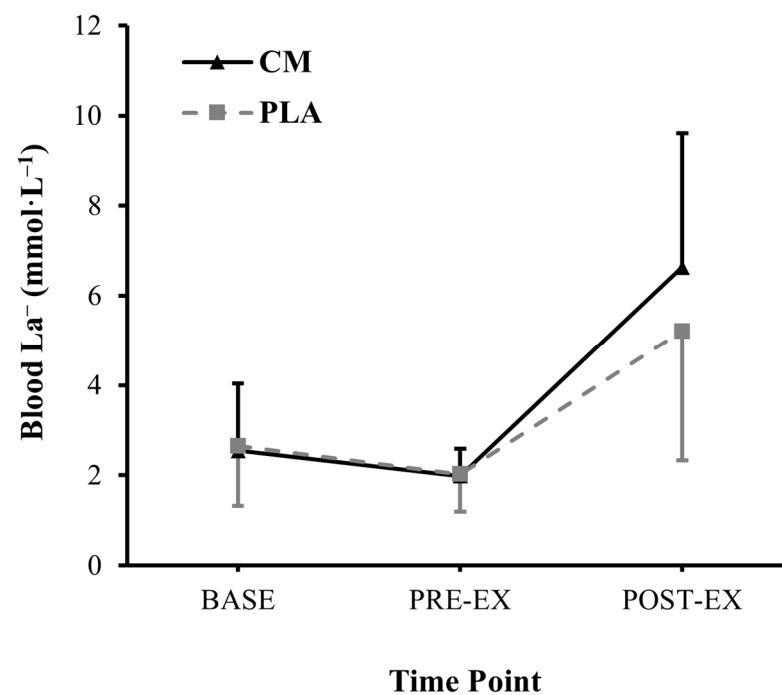


Figure 2. Mean changes in blood lactate (La^-) across the study timeframe.

There was no effect of CM on SBP ($p = 0.267$, $P\eta^2 = 0.12$) or DBP ($p = 0.311$, $P\eta^2 = 0.11$) across the study timeframe (Figure 3a,b). Despite this, a moderate effect size was calculated at the POST-EX time point between conditions for SBP (mean difference: +11 mmHg, $g = 0.64$).

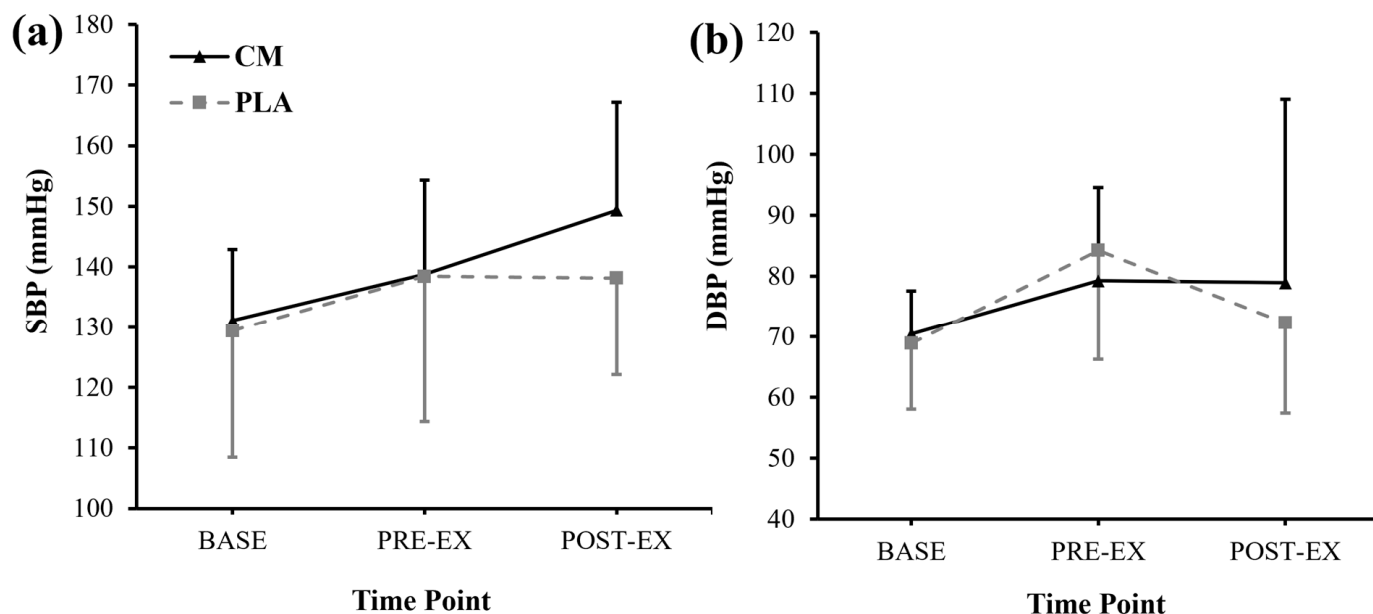


Figure 3. Mean changes in (a) systolic blood pressure (SBP) and (b) diastolic blood pressure (DBP) across the study timeframe.

3.3. Ratings of Perceived Exertion

There was no statistical significance between the group mean RPE scores ($p = 0.397$; $P\eta^2 = 0.07$) reported following the swimming test between the supplement conditions (CM: 9.0 ± 0.8 vs. PLA: 8.6 ± 1.1 units, $g = 0.40$). Warm-up RPE was consistent for both trials (CM: 5.5 ± 0.8 units vs. PLA: 5.5 ± 0.7 units, $g < 0.01$).

3.4. Order Effects and Supplement Predictions

There were no differences in the mean 300 m swimming times between the familiarisation and the two experimental trials ($p = 0.434$, $P\eta^2 = 0.08$). Swimmers predicted their supplement ingestion on 50% (11 of 22) of occasions.

4. Discussion

The aim of this study was to investigate the effect of 15 g CM on the high-intensity, intermittent swimming performance of highly trained swimmers. At the group mean level, CM did not have any influence during a six \times 300 m freestyle swimming test with inconsistent performance outcomes being observed. Moreover, while there were no statistically significant effects of CM on the physiological measures, there were small to moderate effect sizes that indicated an increased post-exercise blood pressure and blood La^- . These findings contrast the proposed ergogenic mechanisms, requiring further investigation when 15 g CM is ingested prior to exercise. Based on the current observations, the ingestion of CM does not appear to support high-intensity, endurance swimming training performance in highly trained cohorts.

Overall, this study failed to find a performance benefit when highly trained swimmers ingested 15 g CM an hour before swimming a typical endurance training test (six \times 300 m). This lack of ergogenic effect aligned with some previous research, with neither Cunniffe et al. [15] nor Gills et al. [16] reporting a performance benefit when male cyclists ingested 8–12 g CM prior to T_{LIM} cycling. One consistency among all three studies was the use of

trained participants, which could negate the CM effects on NO production since these systems may already be upregulated through training adaptations [35,36]. However, neither this study nor its predecessors directly measured NO bioavailability [15,16]; therefore, this speculation cannot be confirmed. Moreover, given that L-citrulline has previously been shown to have no effect on endurance exercise performance [9,11], further research may be needed to identify the optimal dosing strategy for CM supplementation. The current approach was thought to cause substantial increases in circulating L-citrulline concentrations [17]; however, this acute change may only benefit exercise efficiency, whereas more chronic loading (~15 days) may be needed to increase exercise tolerance in high-intensity, intermittent endurance training [18,37,38]. Resultantly, future research is required to investigate whether acute CM supplementation is more appropriate for continuous, submaximal swimming performances (i.e., 800–1500 m time trials) and whether longer supplement durations are needed to influence high-intensity, intermittent swimming performance.

It is also plausible that the lack of ergogenic effect in this study was because the CM supplement strategy did not stimulate the proposed mechanisms, with no statistical significance observed in measures of blood pressure, blood La^- accumulation, or RPE compared to PLA ingestion. Interestingly, an observation of effect sizes appeared to show that 15 g CM could have had an adverse effect on post-exercise SPB (+11 mmHg), indirectly supporting suggestions that blood flow regulation is not one of the primary acting mechanisms [38]. However, blood pressure changes should be interpreted cautiously since these measures were determined using a portable sphygmomanometer on the poolside, with noise (e.g., public swimming environment), postural changes (e.g., prone swimming to seated position), and/or machine accuracy all possibly affecting the sensitivity of results [39]. A small effect size also suggested that swimmers accumulated more blood La^- (+1.7 mmol·L⁻¹) post-exercise following CM ingestion. Nonetheless, variable blood La^- responses have been reported in CM and L-citrulline research [1,40]; therefore, it is unlikely that an increased blood La^- accumulation directly correlates to a reduction in ammonia buffering. As such, future studies are required using more direct measures of ammonia, blood flow, and muscle metabolic markers to establish whether the postulated ergogenic mechanisms are stimulated with acute CM supplementation. However, incorporating such measures can be invasive and produce logistical challenges that may not be appropriate in highly trained swimming cohorts.

A limitation of this research was that it was conducted within one swimming club, recruiting both male and female participants. Neither the menstrual cycle phase nor contraceptive use was considered based on suggestions that these factors do not cause significant disruption to exercise performance in highly trained females [41,42]. However, it is recognised that the current literature on menstrual cycle effects is limited and not specific to swimmers, and it is unknown whether sex affects the physiological responses to CM supplementation. Resultantly, further CM research focusing on one sex (particularly females) is warranted to elucidate its best use for athletes. Secondly, though this study used a supplemental approach thought to enhance plasma L-citrulline and NO concentrations [1,17], it is currently unclear whether this strategy gives a sufficient dose and timing to allow malate to have ergogenic actions. As such, further research may be needed to identify the dose-response relationships of L-citrulline, malate, and NO prior to use in order to optimise future supplement strategies.

5. Conclusions

Consuming 15 g CM an hour before a high-intensity, intermittent endurance swimming test (six × 300 m) did not produce any ergogenic benefits for highly trained swimmers. Moreover, no clear differences between CM and PLA occurred in measures of blood La^- , blood pressure, or RPE. These physiological measures were indirect, however, and it remains unclear as to whether the CM dose stimulated NO production, ammonia clearance, and/or muscle blood flow. Given that no clear benefits of the supplement were identified, this study cannot recommend CM as a nutritional ergogenic aid for endurance training

in highly trained swimmers. However, as the co-ingestion of L-citrulline and malate is a relatively new concept, future research is needed to elucidate optimal dosing practices for highly trained athletes (i.e., acute vs. chronic) and whether it can be more effective in different exercise modalities (i.e., continuous vs. intermittent).

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Informed Consent Statement: Informed consent was obtained from all participants and their caregivers (if aged under 18 years) prior to their involvement in the study.

Data Availability Statement: The raw data supporting the conclusions of this article will be made available by the authors on request.

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