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Curcumin attenuates delayed-onset muscle soreness and muscle function deficits following a soccer match in male professional soccer players

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30 Abstract

Purpose: To examine the effects of acute curcumin supplementation on recovery from a soccer 31 match in male professional players. Methods: In a randomised, placebo-controlled, crossover 32 design, 11 players from the under-23 team of an English Premier League club (age 19 ± 1 y, 33 body mass 79.4 ± 7.9 kg, height 180.8 ± 5.7 cm) consumed 500 mg of curcumin or a control 34 (Medium Chain Triglycerides) (CON) immediately, 12 and 36 h after a 90-min match. 35 Countermovement jump height (CMJ), reactive strength index (RSI), delayed onset of muscle 36 soreness (DOMS, 0-200 mm), and subjective wellbeing were measured before, 12, 36, and 60 37 h post-match. Global positioning systems (GPS) measured external load during matches and 38 dietary intake was recorded across the testing period. Results: GPS and dietary intake did not 39 differ between conditions (P \ge 0.246). Curcumin accelerated the recovery of CMJ (P \le 0.004), 40 and RSI ($P \le 0.001$), and reduced DOMS ($P \le 0.004$) at all post-match time-points (except 60 41 h-post for RSI). The greatest difference between control and curcumin was 12 h-post for CMJ 42 $(P < 0.001, 1.91 \pm 4.40 \text{ cm}, 95\%\text{CI}: 1.25 \text{ to } 2.57, g = 0.36)$ and RSI $(P = 0.003, 0.40 \pm 0.41)$ 43 AU, 95%CI: 0.17 to 0.63, g = 0.90), and 36 h-post for DOMS (P < 0.001, 47 ± 23 mm, 95%CI: 44 -67 to -27, g = 2.12). Conclusions: Curcumin intake <36 h after a soccer match attenuated 45 DOMS and muscle function deficits, suggesting curcumin may aid recovery in professional 46 male soccer players. 47

48 Key words: curcumin, polyphenols, team sports, muscle damage, recovery.

- 49 Introduction
- 50

Strenuous or unaccustomed exercise can damage skeletal muscle and the surrounding 51 extracellular matrix^{1,2}. This ultrastructural damage activates cell signalling pathways that 52 induce an inflammatory response to repair the tissues¹. Although necessary, the inflammatory 53 54 cascade that proceeds, largely driven through the cyclooxygenase and nuclear factor kappa beta (NF-κB) pathways^{1,3}, may precipitate symptoms of delayed onset of muscle soreness (DOMS) 55 and impair muscle force, at least in the short term^{1,2}. Indeed, deficits in muscle force and DOMS 56 can last >96 h following this type of exercise¹, impacting exercise performance in the 57 subsequent days. Several studies have shown that soccer, an intense intermittent sport, evokes 58 deficits in muscle function and DOMS that can last for 72 h following matches⁴. As soccer 59 players often have limited recovery time between matches (48–120 h) and even less between 60 training, their performance, wellbeing and even health could be compromised. One strategy to 61 alleviate these symptoms and accelerate recovery processes, is the use of pharmacological 62 drugs or nutritional dietary supplements⁴. 63

64

Non-steroidal anti-inflammatory drugs (NSAIDs) are often used to enhance muscle function 65 and reduce DOMS after exercise⁵. Although NSAIDs have attenuated DOMS in some studies, 66 findings in soccer players remain equivocal and there are concerns that NSAIDs could impair 67 muscle regeneration⁵. Despite medical departments and the International Federation of 68 Association Football (FIFA) warning against their use, NSAIDs are still commonly consumed 69 to support recovery in soccer⁴. As NSAIDs may have deleterious side effects, including 70 gastrointestinal stress, and impaired central nervous system function⁵, there is a growing 71 interest in the efficacy of nutritional supplements on DOMS and muscle force recovery in 72 73 soccer players.

74

Several nutritional supplements rich in (poly)phenols (chemical compounds especially abundant in plant foods⁶) have been examined for their potential benefits on markers of recovery following exercise. One (poly)phenol consistently shown to modulate exercise recovery is curcumin, a constituent of the spice turmeric⁷. The recovery enhancing effects of curcumin are believed to stem from its antioxidant and anti-inflammatory properties⁷. Indeed, curcumin can downregulate the pro-inflammatory cyclooxygenase-2 (COX-2)⁸ and NF- κ B pathways that are thought to propagate EIMD⁹. Curcumin has also been shown to decrease the 82 secretion of pro-inflammatory cytokines such as IL-8 and TNF- $\alpha^{8,10,11}$ that mediate DOMS 83 severity following exercise.

84

To date, studies showing that acute curcumin supplementation attenuates muscle force deficits 85 and DOMS following exercise are limited to sub-elite populations where exercise has been 86 experimentally induced in a laboratory environment⁷. As such, there is little evidence that the 87 beneficial effects observed in these studies translate to professional athletes after real-world 88 competitions^{7,12}. Thus, the aim of the present study was to examine the effects of acute 89 curcumin supplementation on the recovery of muscle function and DOMS following a soccer 90 match in professional male players. We hypothesised that acute curcumin supplementation 91 would accelerate the recovery of muscle function, as measured by our primary outcome, 92 countermovement jump (CMJ) height, a secondary outcome, reactive strength index (RSI), as 93 well as attenuate DOMS and positively influence subjective wellbeing (secondary outcomes) 94 following a match. 95

97 Method

98 Trail design

This study utilised a randomised, double-blind, placebo controlled, crossover design. After two 99 competitive league fixtures participants were supplemented with either curcumin (CURC) or a 100 placebo control (CON). Due to changes in team selection, 4 matches were required to collect 101 data for 11 players. Two days prior to matches, baseline measures of the dependent variables 102 (DOMS, countermovement jump height [CMJ], reactive strength index [RSI], and subjective 103 wellbeing) were recorded. These measures were repeated 12, 36 and 60 h following matches 104 and collected prior to training in a fasted state (~09:00-09:30). The trial was pre-registered 105 106 with the Open Science Framework (https://osf.io/9k72s/).

107 *Study population*

108 A convenience sample of eleven male professional soccer players from the under-23 squad of a Category 1 English Premier League football club (age 19 ± 1 y, body mass 79.4 ± 7.9 kg, 109 height 180.8 ± 5.7 cm) provided written informed consent for this study. All matches took place 110 at the squad's home venue (19:00 kick off) in the southeast of England between November 111 2021 and January 2022. The two matches for each participant were separated by >7 days, as 112 dictated by team selection, match location and injuries. Players completed a health history 113 questionnaire to evaluate contraindications to the study procedures (e.g., injury, recent 114 medication use, allergies to the supplements); none were excluded on this basis. The study 115 received ethical approval from Loughborough University (reference: 5842) and was conducted 116 according to the Declaration of Helsinki 7th revision, 2013 (Fortaleza, Brazil). 117

118 Study interventions

Players consumed 500 mg/day of a curcumin supplement (Elite Opti-Turmeric, Health Span, 119 UK) or 1000 mg/day of medium chain triglyceride (MCT) oil, which served as the control for 120 the study. As we could not procure a placebo supplement that was batch tested for prohibited 121 substances, we used a low dose (1000 mg/day; 1/6th of recommended) of MCT oil (Now, IL, 122 US) as a placebo. In addition to being batch tested, MCT was selected because; 1) it had a 123 similar appearance to the curcumin capsules; 2) there is no research or mechanistic rationale to 124 suggest MCT, especially at the low dose provided, would affect recovery processes after 125 126 exercise.

127 *Study outcomes*

Our primary outcome measure was CMJ height. Secondary outcomes were RSI, DOMS, and 128 subjective wellbeing. CMJ height and RSI were measured with an optoelectrical system 129 (Optojump, Bolzano, Italy), as in our previous work¹³. For CMJ, participants stood with their 130 feet shoulder width apart and jumped vertically with maximal force. For RSI, participants 131 performed a drop jump (DJ), stepping off a 30 cm high box, landing on both feet, and jumping 132 vertically. Players were instructed to jump with maximal effort and minimise ground contact 133 time. RSI was calculated as jump height (cm)/contact time (ms). For both sets of jumps (CMJ 134 and DJ), players were instructed to keep their hands fixed to their hips and had three attempts 135 136 separated by 60 s of recovery, with the mean used for data analysis. Participants routinely completed these measures as part of clubs monitoring processes and were thus familiarised to 137 such procedures. Inter-day coefficients of variation were 0.9% and 1.7% for CMJ and RSI, 138 respectively. 139

DOMS were assessed by visual analogue scale (VAS), during which players were asked to rate
the level of muscle soreness they felt in their legs during a squat to 90° knee flexion¹³.
Participants marked this on a 0-200 mm VAS from 0 mm "no soreness" to 200 mm "unbearably
painful", which was subsequently measured to the nearest mm, as previously administered by
the group¹³.

Subjective wellbeing was assessed using an in-house questionnaire that the players routinely complete as part of their monitoring programme. At each time-point (baseline, 12, 36 and 60 h), participants rated each of the following questions on a scale of 1 (positive) to 5 (negative): 1) How sore do your muscles feel today? 2) How fatigued do you feel today? 3) How well did you sleep last night? 4) How is your mood today? 5) How stressed do you feel today? The sum of the five responses per participant was used for data analysis; a higher score indicates worse wellbeing.

Participants wore Global Positioning Satellite (GPS) accelerometer units (OptimEye S5B, Version 7.18; Catapult Innovations, Melbourne, Australia) during matches to estimate physical load output (total distance, explosive distance and high-speed running, see Table 1 for further details) and were asked to record their dietary intake for the duration of each testing phase. Participants were told not to consume any other dietary supplements during the trials, but they could continue using other putative recovery practices (e.g., active recovery) if they were consistently used in both trials. These were monitored and recorded by the research team; two players consistently used a foam roller post-match; nine players employed no specific strategies. Participants also recorded their dietary intakes with online food diaries on match day (MD), match day +1 (MD+1; 12 h post) and match day + 2 (MD+2; 36 h post). Diaries were subsequently analysed for energy and macronutrient intake using online software (Nutritics, Dublin, IR); the average of the three days was used for data analysis.

164 Sample size

Our sample was size was determined by the time and resources available. The number of 165 participants we could recruit for this research was limited by number of players in the squad, 166 to those who are picked to play the matches, and various other extraneous variables such as 167 loans to other clubs and injuries. As our sample size was unavoidably limited, no formal sample 168 size calculation was performed. However, the research was deemed useful as, to our 169 knowledge, no other study had examined the effects of curcumin on recovery from a soccer 170 match in professional athletes and therefore the data and effect sizes will provide new insights 171 in to how its application in real-world sporting scenarios. 172

173 Randomization and blinding

The order of trials was determined by simple randomisation using a computer-generated list 174 (sealedenvelope.com) by an investigator not involved in data collection. Although the 175 supplements were not identical in taste and appearance, players were blinded to the aims of the 176 trials and only told that they were testing the effects of two different antioxidant supplements. 177 This was effective as according to a post-trial exit survey only two (18%) players correctly 178 179 guessed which supplement they received on each trial. The supplements were provided as two capsules in opaque envelopes and consumed immediately post-match (~21:00-21:30) and then 180 181 on MD+1 and MD+2 after the dependent variables were collected each morning (three days in total). 182

183 Statistical Analysis

184 Data were analysed using IBM SPSS Statistics for Windows, Version 27.0 (Armonk, NY: IBM 185 Corp) and are displayed as mean \pm standard deviation (SD). Normal distribution of data was 186 checked by inspecting histograms and the Shapiro-Wilk test (P > 0.05 = normal distribution). 187 CMJ, RSI, DOMS and wellbeing were analysed using a 2 (supplement) x 4 (time-point)

repeated measures ANOVA. As wellbeing data was not normally distributed according to the 188 Shapiro-Wilk test, the data was log-transformed and although this did not alter the result of the 189 Shapiro-Wilk test, visual inspection of histograms suggested the data now approximated a 190 normal distribution. The same ANOVAs were performed to examine for any trial order effects. 191 If the ANOVA indicated significant differences for main effects, post-hoc tests with Bonferroni 192 corrections were performed to identify the location of differences. Paired t-tests were used to 193 assess differences in dietary intake and GPS variables between intervention groups. TD, 194 duration and protein data were not normally distributed (Shapiro-Wilk: P > 0.05) and therefore 195 Wilcoxon signed-rank tests were used for analysis. For all tests, statistical significance was set 196 at P < 0.05. Hedge's g effect sizes were calculated for paired t-tests (g) (small, 0.2 -0.40; 197 medium, 0.5-0.79; large, ≥ 0.8)¹⁴. 198

- 200 **Results**
- 201

GPS data was not different between interventions across all parameters, indicating that matches
 resulted in similar external loads (Table 1). Average daily energy (kcal) and macronutrient (g)

- intake was also not different between interventions (Table 2). There were no trial order effects
- for CMJ, RSI, DOMS, or wellbeing (all group and interaction effects were $P \ge 0.244$).
- 206

Dependent variables are presented in Figure 1. CMJ, RSI, DOMS and subjective wellbeing all exhibited time effects following matches (P < 0.001). For each variable, the greatest difference from baseline occurred at 12 h-post (P ≤ 0.001). There were intervention effects for CMJ, RSI and DOMS (CMJ and DOMS: P ≤ 0.001 ; RSI: P = 0.024), but not for wellbeing (P = 0.052). All outcome variables displayed significant interaction effects: CMJ and RSI (P ≤ 0.001), DOMS (P = 0.003) and wellbeing (P = 0.006).

213

At all post-match time-points except 60 h-post for RSI, CMJ and RSI were significantly higher in the curcumin condition compared to control (CMJ: $P \le 0.003$, 95%CI: 0.53 - 1.25 to 2.13 - 2.57, g = 0.25-0.36; RSI: $P \le 0.004$, 95%CI: 0.13 - 0.17 to 0.35 - 0.63, g = 0.58-0.98; Figure 1). These differences between conditions peaked at 12 h-post, where CMJ and RSI were higher with curcumin than control (CMJ: P < 0.001, 1.91 ± 4.40 cm, 95%CI: 1.25 to 2.57, g = 0.36; RSI: P = 0.003, 0.40 ± 0.41 AU, 95%CI: 0.17 to 0.63, g = 0.90).

220

DOMS was greater than baseline at 12 h (P < 0.001, 70 ± 18 mm, 95%CI: 42 to 98, g = 3.57) and 36 h-post (P = 0.004, 53.55 ± 22.55, 95%CI: 17 to 89, g = 2.32) in the control condition, but not in the curcumin condition (P ≥ 0.175; Figure 1). At all post-match time-points DOMS was significantly lower in the curcumin condition compared to control (12 h- and 36 h-post: P <0.001, 95%CI: -68 to -24 and -67 to -27, g = 1.67 and 2.12, respectively; 60 h-post: P ≤ 0.004, 95%CI: -45 to -11, g = 1.40; Figure 1).

227

Following the matches, wellbeing was rated worse at 12 and 36 h-post in the control condition (P < 0.001, 95%CI: 2.96 to 6.86 and 1.47 to 4.71, g = 2.08 and 1.40, respectively; Fig. 1), but no changes were observed from baseline in the curcumin condition (P \ge 0.087). At 12 h and 60 h-post match, wellbeing was greater (lower score) with curcumin supplementation (P \le 0.034, 95%CI: -3.65 to -0.17 and -3.47 to -0.53, g = 0.76 and 1.17, respectively; Figure 1).

234 Discussion

The main finding of this study was that acute curcumin supplementation accelerated the recovery of muscle function attenuated DOMS in the 60h following a competitive soccer match in professional male players. This is the first study to examine the effects of curcumin supplementation on elite-level team-sport athletes using match-play as an ecologically valid model of exercise-induced muscle damage (EIMD).

240

In the present study, DOMS (and deficits in CMJ and RSI) were lower after curcumin 241 supplementation at all post-match time-points, except 60h-post for RSI. These findings are 242 consistent with studies that report expedited muscle function recovery after curcumin 243 supplementation in untrained/moderately trained cohorts^{11,15,16} and animals³. They also agree 244 with, to our knowledge, the only other study in well-trained athletes, where curcumin and 245 piperine supplementation attenuated deficits in 6-s sprint performance 12 h-post muscle 246 damage induced by single-leg downhill hopping in rugby players¹². In other studies, curcumin 247 supplementation has also mitigated DOMS after EIMD^{3,17} and in particular after resistance-248 exercise induced muscle damage⁷. Nonetheless, not all studies report analgesic effects with 249 curcumin^{12,15,16}. Although in Jager et al.¹⁶ eight-weeks of curcumin supplementation reduced 250 DOMS by 26% in the days after muscle damage, this was not statistically significant. Likewise, 251 Tanabe et al.¹⁵ did not observe any significant effects of curcumin on DOMS after a 150 mg 252 dose of curcumin immediately before and 12 h after exercise. These findings are perhaps a 253 consequence of the dosing strategies employed, which ceased before¹⁶ or 12 h¹⁵ after the EIMD 254 protocols. Like other (poly)phenols, plasma levels of curcumin metabolites peak within the 255 first few hours after intake, after which they are metabolised and eliminated from the body¹⁸. 256 Thus, for substantial analgesic effects, it may be essential to consume higher doses of curcumin 257 258 throughout the recovery process following EIMD.

259

The mechanisms by which curcumin may modify symptoms of EIMD remain unclear and examining these was beyond the scope of this trial. However, the effects in this study are likely associated with the bioactive effects of curcumin; curcumin interacts with multiple redox and inflammatory pathways¹⁶ and several human and animal studies demonstrate that curcumin downregulates NF- κ B^{9,19}. Down-regulating NF- κ B suppresses pro-inflammatory cytokines (such as IL-6, IL-8 and TNF- α) and modulates oxidative damage, which can impair muscle contractile function and sensitize pain receptors⁹. The suppression of pro-inflammatory 267 cytokines with curcumin supplementation has been demonstrated in both humans and animals 268 10,11 . Antagonising NF- κ B may also attenuate muscle function deficits post-EIMD by 269 supporting myoblast proliferation and differentiation²⁰. Specific to DOMS, curcumin may exert 270 its beneficial effects by supressing the production of algogenic substances such as 271 cyclooxygenase⁸ and prostaglandin E2²¹.

272

A further plausible mechanism by which curcumin may enhance recovery from EIMD is the 273 activation of nuclear factor erythroid 2-related factor 2 (Nrf2), a redox sensitive transcription 274 factor. Nrf2 upregulates cytoprotective redox enzymes such as catalase, glutathione peroxidase 275 and superoxide dismutase, which can modulate oxidative damage²² and, theoretically, DOMS 276 and impairments in muscle function associated with excess oxidant generation. Although 277 curcumin activates Nrf2²³, this effect has not been reported alongside markers of muscle 278 damage in humans. Animal data support this theoretical mechanism as curcumin ingestion 279 increased Nrf2 and antioxidant gene expression while concurrently decreasing markers of 280 muscle damage (creatine kinase, lactate dehydrogenase) and oxidative stress 281 (malondialdehyde) subsequent to exhaustive exercise in rats¹⁹. Moreover, a recent study with 282 (poly)phenol-rich cherry juice reported upregulation of antioxidant enzymes and gene 283 284 expression in human skeletal muscle coinciding with enhanced recovery of MIVC 48 h posteccentric exercise²⁴. We were unable to collect biological samples in this study and thus can 285 only postulate that supressing NF-kB and/or activating Nrf2 were mechanisms responsible for 286 curcumins effects in this study. 287

288

We have previously reported decreased subjective wellbeing in soccer players in the days after 289 a match²⁵, likely due to fatigue, muscle soreness and stressors related to elite performance and 290 sleep loss. In the current study, curcumin supplementation improved subjective wellbeing in 291 the days post-match compared to control, which contrasts to our previous work with tart-cherry 292 juice supplementation, which is also high in (poly)phenols¹³. Sciberas et al.²⁶ reported similar 293 findings; participants felt better with the causes and symptoms of psychological stress as 294 assessed by the Daily Analysis of Life Demands on Athletes (DALDA) after consuming 500 295 mg/day of curcumin 4-days prior to exercise. However, participants undertook this trial 296 glycogen depleted, and the DALDA is a retrospective means of measurements, increasing its 297 risk of recall bias. Whether the improved wellbeing in our study is a direct effect of curcumin 298 or an indirect effect of reduced DOMS and muscle function impairments is unclear. Lending 299 support to the former, several previous studies in older adults have suggested that curcumin's 300

anti-inflammatory and neuroprotective properties may enhance mood and improve cognitive function^{27,28}. However, these studies did not give an acute dose like ours, instead supplementing curcumin chronically (> 4 weeks^{27,28}).

304

Previously, curcumin supplementation ameliorated symptoms of EIMD with doses between 305 150 mg and 6 g/day⁷. We administered a dose of 500 mg/day on three consecutive days starting 306 307 immediately after exercise. The curcumin formulation contained 500 mg of NovaSOL® curcuminoids and 20mg Vitamin C delivered in a water-soluble and pH stable form, which 308 enhances its bioavailability²⁹. Although this formulation is shown as bioavailable²⁹, we were 309 unable to quantify circulatory curcumin concentrations in the present study. Interestingly, the 310 dose in the present study is lower than that used by Delecroix and colleagues¹² who gave elite 311 rugby players 6 g of curcumin and 60 mg of piperine/day from 48 h pre-exercise to 48 h post-312 exercise. Thus, our study suggests well-trained athletes may only require small acute doses of 313 curcumin to enhance recovery from EIMD and only up to MD+1 (36 h post-match). To our 314 knowledge, curcumin intake at these doses are safe, and no side effects were reported in our 315 study. However, further research is required to determine if regular doses of curcumin affect 316 exercise adaptations; indeed, some, but not all studies, suggest interfering with inflammatory 317 or antioxidant pathways may impede exercise adaptations³⁰. While the evidence for such 318 effects are weak³⁰, especially with (poly)phenols, further research should examine whether 319 longer-term or higher doses influence exercise adaptations. 320

321

A key limitation of this study was our inability to interrogate the mechanisms by which 322 curcumin could attenuate markers of EIMD; ideally, future studies would incorporate markers 323 324 of oxidative damage, redox status, and inflammation. Finally, our sample size is inherently constrained due to the limited number of players in a soccer squad. As such, our findings may 325 be more susceptible to type II errors and should be interpreted as such. Future studies could 326 increase statistical power by repeating the procedures with the same participants. Despite these 327 limitations, this study has many strengths, as it was the first to show that curcumin may alleviate 328 symptoms of muscle damage in professional soccer players after a competitive match. These 329 findings therefore have real-world practical application. Future research should seek to confirm 330 these findings in further applied studies with elite athletes and in lab-based studies that 331 concurrently investigate the underlying mechanisms. 332

333

334 **Practical Applications**

This study suggests that 500 mg/day of curcumin may enhance functional recovery in professional soccer players. As some studies suggest high doses of supplements with antioxidant features can impair exercise adaptations³⁰, until further research is conducted it may be prudent to supplement curcumin when recovery and not training adaptations are a priority (e.g. pre-season, tournaments). Indeed, curcumin could be taken when recovery time between competitive matches is limited to <72h, adaptations are not a priority, and/or players are still experiencing DOMS or impairments in muscle function.

342

343 Conclusion

344 Our findings are consistent with most studies in untrained populations using different models

of EIMD and suggest that curcumin might be an effective recovery aid in elite team-sport

346 players. Although these findings need to be confirmed with additional studies, they suggest

347 players recovery could be enhanced with curcumin supplementation, and therefore

348 supplementation should be considered during periods of fixture congestion

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Author contributions: TC, WA, EH, LJ and JS designed the study and sought ethical approval.

353 Data collection was undertaken by WA and AB. EH and TC completed data analysis and a

draft of the manuscript. All listed authors edited the manuscript draft and contributed to the

- 355 final manuscript submission.
- 356

357 Conflicts of Interest

- 358 The authors declare no conflicts of interest.
- 359

360

361 **Figure captions**

Figure 1 – (A) Countermovement-jump (CMJ) height, (B) reactive strength index (RSI), (C) delayed-onset muscle soreness (DOMS), and (D) subjective wellbeing before and 12, 36, and 60-hours post-match in the curcumin (solid dots) or control (open dots) trials. ¥ Signifies a difference between conditions at this time-point (P < 0.05); # Signifies a difference compared to baseline (pre-match) at this time-point (P < 0.05). Data are presented as % change from baseline for illustrative purposes only. Values are mean \pm SD. N = 11. AU indicates arbitrary units.

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