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ORIGINAL ARTICLE

Curcumin supplementation likely attenuates delayed onset muscle soreness (DOMS)

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Abstract
Introduction Oral curcumin decreases inflammatory cytokines and increases muscle regeneration in mice.
Purpose To determine effects of curcumin on muscle damage, inflammation and delayed onset muscle soreness (DOMS) in humans.
Method Seventeen men completed a double-blind randomized-controlled crossover trial to estimate the effects of oral curcumin supplementation (2.5 g twice daily) versus placebo on single-leg jump performance and DOMS following unaccustomed heavy eccentric exercise. Curcumin or placebo was taken 2 d before to 3 d after eccentric single-leg press exercise, separated by 14-d washout. Measurements were made at baseline, and 0, 24 and 48-h post-exercise comprising: (a) limb pain (1–10 cm visual analogue scale; VAS), (b) muscle swelling, (c) single-leg jump height, and (d) serum markers of muscle damage and inflammation. Standardized magnitude-based inference was used to define outcomes.
Results At 24 and 48-h post-exercise, curcumin caused moderate-large reductions in pain during single-leg squat (VAS scale −1.4 to −1.7; 90 %CL: ±1.0), gluteal stretch (−1.0 to −1.9; ±0.9), squat jump (−1.5 to −1.1; ± 1.2) and small reductions in creatine kinase activity (−22–29 %; ±21–22 %). Associated with the pain reduction was a small increase in single-leg jump performance (15 %; 90 %CL ± 12 %). Curcumin increased interleukin-6 concentrations at 0-h (31 %; ±29 %) and 48-h (32 %; ±29 %) relative to baseline, but decreased IL-6 at 24-h relative to post-exercise (−20 %; ±18 %).
Conclusions Oral curcumin likely reduces pain associated with DOMS with some evidence for enhanced recovery of muscle performance. Further study is required on mechanisms and translational effects on sport or vocational performance.

Keywords Performance · Eccentric exercise · Inflammation · Recovery · Visual analogue scale

Abbreviations

AP-1	Activator protein 1
AIS	Australian Institute of Sport
CK	Creatine kinase
COX-2	Cyclooxygenase 2
DOMS	Delayed onset muscle soreness
DNA	Deoxyribonucleic acid
NF kappa B	Nuclear factor kappa beta
IL-6	Interleukin 6
1RM	One repetition maximum
TNF-alpha	Tumour necrosis factor alpha
VAS	Visual analogue scale

Introduction

DOMS is pain or discomfort that occurs after unaccustomed or high intensity eccentric exercise (Cheung et al.

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2003; Connolly et al. 2003; Lund et al. 1998; MacIntyre et al. 1995). DOMS is caused by muscle damage, which has associated symptoms of muscle shortening, increased passive stiffness, decreases in strength and power, localized soreness and disturbed proprioception (Proske and Morgan 2001). Symptoms can present from post-exercise and typically subside after 3–4 days (Clarkson and Sayers 1999). Reducing the negative effects of DOMS may maximise training and performance gains as well as prevent injury (Armstrong 1984; Eston and Peters 1999; Johansson et al. 1999; Sellwood et al. 2007).

Curcumin (diferuloylmethane) is an extract from the root of the curcuma plant, commonly known as turmeric root. Curcumin gives the spice turmeric its distinctive yellow colour. Previously used in Chinese (Itokawa et al. 2008) and Indian medicine, curcumin has documented anti-inflammatory, anticarcinogenic and antioxidant properties (Maheshwari et al. 2006; Menon and Sudheer 2007; Itokawa et al. 2008). It affects cytokine-mediated pathways by inhibiting NF kappa B, AP-1 binding to DNA and decreasing the production of the enzyme COX-2, all of which play a pivotal role in the inflammatory cascade (Thaloor et al. 1999; Davis et al. 2007).

Animal studies have shown that curcumin can increase muscle regeneration and improve behaviours associated with DOMS in mice (Davis et al. 2007). Systemic treatment with curcumin led to faster restoration of normal muscle architecture when given to mice after local tissue injury (Thaloor et al. 1999). In a study by Thaloor et al. (1999), mice masseter muscles were subjected to freeze injury, and those mice injected intraperitoneally with curcumin daily for 10 days, until sections were removed, showed large centrally nucleated recovering fibres in the site of damage; whereas the controls were devoid of regenerating fibres. Davis et al. (2007) treated mice with oral curcumin 3 days prior to downhill running and the curcumin-treated mice were able to run significantly longer before fatigue at 48 and 72 h and exhibited more spontaneous activity than the mice on placebo. Curcumin-treated mice also had statistically significant decreased IL-6, TNF-alpha concentrations at 24 and 72 h and CK activity at 24 h, compared to those treated with placebo.

To our knowledge, no studies have quantified the effect of curcumin on DOMS or measured muscle performance in humans using a robust, adequately powered double-blind placebo-controlled experimental design (Drobnic et al. 2014). The aim of this study was to evaluate the effect of oral curcumin compared to placebo on DOMS, using a double-blind randomized-controlled unilateral crossover trial. Functional and physical symptoms of DOMS and the recovery of performance were assessed in a cohort of healthy, active men. It was hypothesised that curcumin would lead to worthwhile effect size reductions in leg pain perception, swelling, systemic markers of muscle damage and inflammation and maintain the vertical jump performance after eccentric loading exercise designed to produce DOMS.

Methods

Participants

A total of 19 healthy men aged 18–39 y were recruited into the study. Participants were undertaking light to moderate regular physical activity including sports training e.g. social football and basketball, but not doing lower limb resisted exercise (mean ± SD endurance training 2.5 ± 2.2 h week^{-1}, team training 1.1 ± 1.6 h week^{-1}). Two withdrew from the study following acceptance due to the inability to attend testing commitments, and no replacements were added due to resource constraints. The remaining 17 subjects had an age 33.8 ± 5.4 year and weight 83.9 ± 10.0 kg (height not measured). Fifteen subjects had a dominant right leg and two a dominant left leg.

Design

Double-blind randomized-controlled unilateral-leg crossover trial was performed to compare the effects of taking oral curcumin versus placebo on single-leg jump performance and the levels of markers associated with DOMS after a bout of unaccustomed leg press exercise (Fig. 1). All subjects completed two experimental trials separated by at least 14 days. Randomization was applied to both the order of treatment or placebo and to the sequence of right or left leg use within the unilateral crossover. Exclusion criteria comprised regular leg weight training in the prior 3 months, current lower limb musculoskeletal injury, current use of non-steroidal anti-inflammatory drugs and neurological disease involving the lower limb. The AIS ethics committee approved the study and all participants provided written informed consent. All outcome assessments were carried out at the AIS Sports Medicine Department.

Randomization and masking

The randomization sequence was generated using a random numbers table (http://www.ramdomizer.org). Allocation was concealed using sequentially numbered medication. Investigators and participants were blinded by provision of the medications by AIS nursing staff according to the randomization protocol.

Eccentric exercise protocol

Participants performed a muscle damaging protocol consisting of seven sets of ten eccentric single-leg press

repetitions on a leg press machine (Vaile et al. 2008a). A single episode of eccentric exercise can have an effect on blood chemistry responses, muscle soreness and performance if the exercise is repeated within a few weeks (Brown et al. 1997; Byrnes and Clarkson 1986; Mair et al. 1995; Nosaka et al. 2001). Therefore, alternate legs were used for placebo and treatment.

The 1RM weight lifted concentrically was determined for each participant on protocol day 3 (Fig. 1). An eccentric loading protocol developed previously was used to induce DOMS (Vaile et al. 2007, 2008a). 120 % of the one repetition maximum was calculated on day one of the study and used for the weight lowered eccentrically. On protocol day 3 (Fig. 1), each participant performed 5 sets of 10 repetitions at 120 % 1RM and 2 sets of 10 repetitions at 100 % 1RM. 1RM was performed on each leg individually and each participant completed all 7 sets. The same protocol has been used to induce DOMS previously (Vaile et al. 2007, 2008a). During each eccentric contraction the load was resisted with the allocated leg from full knee extension to 90° angle of knee flexion with the eccentric contraction lasting for 3–5 s duration. After each eccentric contraction the load was raised by the subject, using both legs concentrically. Participants had a 3 min rest between sets.

Intervention

Participants swallowed with water 5 sealed identical opaque capsules containing either 2.5 g curcumin or placebo (2.5 g Avicel 105, an inert plant cellulose) twice daily for 2.5 days prior to exercise, then 5 capsules twice daily for 2.5 days after exercise. The capsules were prepared by a pharmacist using a specific protocol. The constituents of the curcumin used were bisdemethoxycurcumin 29 mg tablet^{-1}; demethoxycurcumin 62.7 mg tablet^{-1} and curcumin 964 mg tablet^{-1}, with total curcuminoids 1,060 mg tablet^{-1} (Eurofins Scientific Inc, Petaluma, CA). The dose was calculated from the previous mice experiments, taking human size and safety into account (Davis et al. 2007). There is no treatment related toxicity evident for daily doses of curcumin of 8 g for 3 months (Hsu and Cheng 2007). Subjects were advised not to carry out any leg weight training during the testing periods but were asked to continue their usual physical activity. Subjects were asked at the completion of the study whether they thought they could identify if they were taking curcumin or placebo. The participants reported that they could not distinguish between the treatment and placebo.

Outcome measures

All outcome measures were recorded during familiarisation and at baseline, immediately post the eccentric exercise, 24 and 48 h after the exercise (Fig. 1).

Muscle pain A VAS was used to measure quadriceps and gluteal skeletal muscle pain before and after the eccentric exercise. The VAS was a horizontal 10 cm line, marked with 1–10 with the terminal descriptors *no pain* and *severe pain* as used previously to monitor changes in perceived pain following muscle damaging protocols (Vaile et al. 2007, 2008a; Sellwood et al. 2007; Johansson et al. 1999; Cleak and Eston 1992; Harrison et al. 2001). Pain was rated for single-leg squat, walking downstairs, passive stretch of the quadriceps, passive stretch of the gluteals and single-leg vertical jump. Muscle pain was assessed before muscle tenderness.

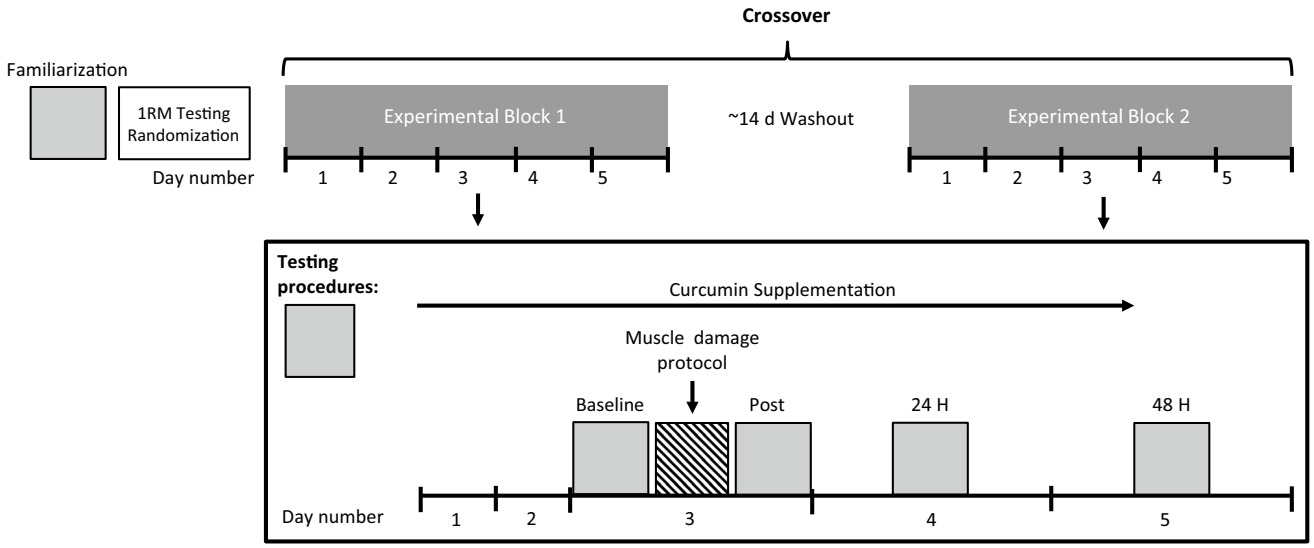

Fig. 1 Experimental design

Muscle tenderness Tenderness was assessed using a somedic pressure algometer (Somedic, Sollentuna, Sweden) at 4 standardized points. The quadriceps points were marked on the anterior thigh along a line drawn from the anterior superior iliac spine to the superior pole of the patella. One point was at the midpoint of this line (mid belly rectus femoris) and the other at 5 cm above the superior pole of the patella (musculotendinous junction). These Quadriceps points have been used previously in DOMS research (Sellwood et al. 2007). The first gluteal point was at the midpoint of a line drawn from the posterior superior iliac spine and greater trochanter and second at the midpoint of a line drawn from the PSIS to the ischial tuberosity. The points were marked at baseline with an indelible marker pen. Participants were asked to state when the pressure became unbearable and a force reading was made from the algometer. One measurement was made, due to the increasing pain associated with repeated measurements.

Swelling A non-stretch anthropometric measuring tape was used to measure swelling at three standardized points on the upper leg. The first point was 5 cm above the superior pole of the patella, the second at the midpoint of a line drawn between the proximal pole of the patella and anterior superior iliac spine (Sellwood et al. 2007) and the third at the sub gluteal line.

Jump performance Single-leg vertical squat jump was used to assess the effect of curcumin on quadriceps and gluteal function. The jump and reach method using Vertec (Vertec, Vertec Sports Imports, Hilliard, OH) was used to assess vertical jump performance. The maximum height obtained from three jumps was recorded. Vertical jump performance is an index of muscle power of the lower limbs.

Muscle damage and inflammation Serum samples were obtained for CK activity, as a marker of muscle damage (Vaile et al. 2007; Eston and Peters 1999), and for candidate curcumin-modulated inflammatory markers IL-6 and TNF-alpha (Davis et al. 2007; Thaloor et al. 1999; Maheshwari et al. 2006). Blood samples were collected in 9-ml serum separator tubes, left to clot, then spun at 4500 RPM for 5 min, with resulting serum aliquoted into four, 2 ml cryotubes and frozen immediately at −80 °C until analysis. TNF-alpha and IL-6 were analysed by chemiluminescent immunometric assay (Immulite 1, Siemens, Erlangen, Germany). CK activity was by wet chemistry (Hitachi 911, Roche, Boehringer, Germany).

Analysis

Sample size Sample size was calculated using magnitude-based clinical inference (Hopkins et al. 2009). In the absence of empirical data, the smallest effect size of 0.2 times mean sample variation ($SD_{between}$) in VAS of 16 on a 0–100 scale (Gaston-Johansson and Gustafsson 1990) was used as the value for the smallest meaningful change, with test–retest reliability calculated from Pearson $r = 0.88$ (Gaston-Johansson and Gustafsson 1990), where test–retest reliability equals the square root of $(1 - r)$ times $SD_{between}$. The calculations resulted in $n = 19$.

General method Estimates and uncertainty (90 % confidence interval) for the effect of treatment on outcomes were derived from a mixed model analysis of variance (Proc mixed, SAS 9.0, Cary, NC). Fixed effects were time and order of treatment within the crossover interacted with treatment to account for possible systemic repeated bout effect. The random effects were subject and the subject treatment interaction. All data except VAS were log-transformed prior to analysis to manage non-uniformity of error. Subject descriptive and VAS outcome data in line graphs are raw means and standard deviations. Unless otherwise noted, mean effects derived from the analysis of log-transformed variables are back log-transformed least-squares means or geometric adjusted means. All data are rounded to 2 significant figures.

Statistical inference The standardized effect sizes (curcumin-placebo/appropriate reference value for placebo) were interpreted using magnitude-based inference (Batterham and Hopkins 2006). Statements about the mixed model estimate of the true (large sample) value of effects were qualified using a modified Cohen's *d* effect size (trivial, 0.0–0.2; small, 0.2–0.6; moderate, 0.6–1.2; large, 1.2–2.0; very large, >2.0); in this scheme, the threshold for smallest substantial effect size was 0.2 (Hopkins et al. 2009). Uncertainly around the estimated standardized effect sizes was assigned a qualitative term for the following probability bins: <0.5 %, almost certainly not; <5 %, very unlikely; <25 %, unlikely; <75 %, possible; >75 %, likely; >95 %, very likely; >99.5 %, almost certain (Hopkins et al. 2009). An effect was unclear if the uncertainty (confidence interval) included both substantial increases and decreases (i.e. >5 %) (Hopkins et al. 2009). Readers are referred elsewhere for published descriptions, examples, and statistical rationale for magnitude-based inference (Rowlands et al. 2008a, 2014 ; Batterham and Hopkins 2006; Hopkins 2006).

Results

Muscle pain and swelling

All pain outcome measures showed an increase in VAS score from baseline at 24 and 48 h post indicating the exercise loading protocol was effective at producing DOMS (Fig. 2). Curcumin was associated with likely moderate to large effect size reductions in single-leg squat and gluteal stretch pain at 24 and 48 h, relative to baseline and/

or post-eccentric exercise; the effect size on gluteal stretch pain at 48 h was moderate, relative to the change at 24 h. Pain on walking down stairs was moderately reduced at 48 h (Table 1; Fig. 2). In contrast, pain upon stretching quadriceps muscle was not clearly affected by curcumin supplementation. At 24 and 48 h, curcumin generated moderate reductions in pain during the vertical jump, relative to post-eccentric exercise (Table 1; Fig. 2). The effect of curcumin on swelling and pain-pressure algometry outcomes were trivial or inconclusive (not shown for brevity).

Single-leg jump performance

Curcumin increased first jump height by a likely small magnitude from post-exercise to 24 h (15.4 %; 90 %CL ± 11.6 %) and 48 h (15.8 %; ±11.6 %), where the threshold for smallest important effect was 9.3 %. However, all other jump contrasts were trivial (contrasts not shown for brevity).

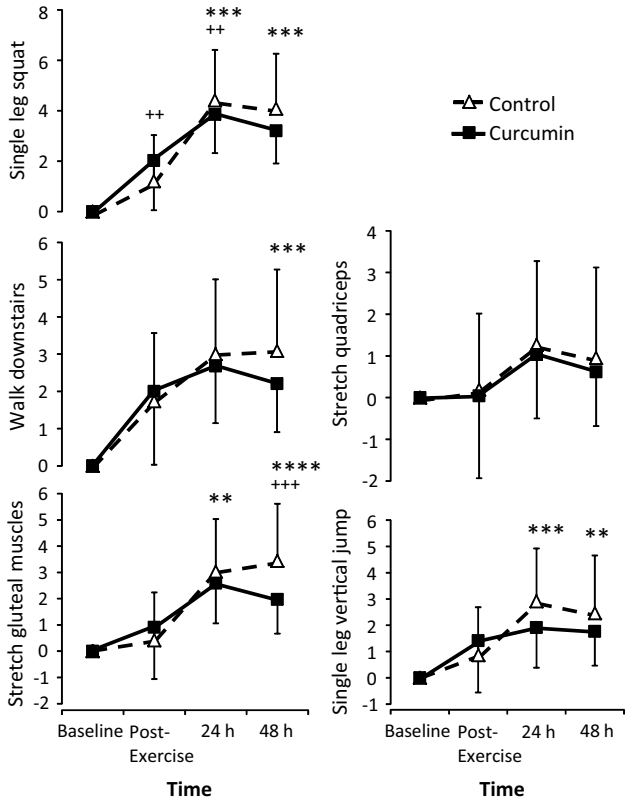

Fig. 2 Effect of curcumin supplementation on measures of leg pain in the 48 h period following recovery from eccentric exercise. All data are the mean change from *baseline* for VAS scale units with bars representing the SD. The qualified threshold for smallest substantial change in outcome in response to treatment is the 0.2 × baseline $SD_{between}$. A magnitude-based summary of statistical contrasts is in Table 1. To assist with identification of likely effects of treatment, the probability of substantial change is reproduced from Table 1 via inclusion above the time point for the respective contrast denoted by the unique symbol: relative to baseline +; relative to post-exercise, *. Accordingly, qualified likelihood was shown as increased number of symbols (*used for example): *possible, **likely, ***very likely, ****most likely

Muscle damage and inflammation

Curcumin had a likely small lowering impact on serum CK activity at 24 h (−22 %; 90 %CL ± 22 %) and 48 h (−29 %; ±21 %) post-exercise relative to baseline. Meanwhile, curcumin increased (likely small standardized differences) serum IL-6 immediately post-exercise (31 %; ±29 %) and again at 48-h post-exercise (32 %; ±29 %) relative to baseline, but decreased IL-6 at 24-h relative to post-exercise (−20 %; ±18 %). Curcumin had no impact on TNF-alpha concentrations (Fig. 3).

Discussion

The main finding from the current study was that curcumin supplementation caused moderate to large-sized reductions in DOMS-related leg–muscle pain symptoms at several sites, which was associated with lower blood CK and higher blood IL6. There was also some evidence for improved muscle performance (measured by increased first jump height) at 24–48 h post-eccentric exercise, but other jumps were trivial so more work is required to clarify the nature of the effect on performance. To the authors' knowledge, this is the first double-blind within-subject controlled randomized trial to evaluate the effect of practical quantities of oral curcumin on DOMS in human subjects and provides new information on possible utility of the nutrient in sports and rehabilitation.

The results suggest that curcumin has potential to be part of the nutritional intake of individuals wishing to lower post-exercise soreness, which may hasten return to effective training. In a recent single-blind pilot study on a novel delivery method of curcumin, human subjects had significantly less pain and less muscle damage on MRI than controls (Drobnic et al. 2014). Other nutritional supplements with antioxidant or anti-inflammatory properties have also been shown to lower post-exercise muscle soreness and damage markers. These supplements include: dairy protein (Rowlands et al. 2008b; Saunders 2007; Cockburn et al. 2008; Cooke et al. 2010) and tart cherries (Howatson et al. 2009; Kuehl et al. 2010). Other supplements with antioxidant or anti-inflammatory properties include exotic berries (acai, goji), quercetin, green tea and fish oils; however, there appears to be reduced translation in benefits from rodents to well-trained humans (Nieman et al. 2012). Comparably, variable results in reduction in DOMS have been shown with massage (Cheung et al. 2003). No effect has

Table 1 Effect of curcumin supplementation on leg-muscle pain during lower limb exercise

Mean effect comparisons (scale units)[a] with ±90 %CL[b] and Inference[d]						
Variable	Post-exercise baseline	24 h-baseline	48 h-baseline	24 h-post-exercise	48 h-post-exercise	Threshold[c]
Single-leg	0.9 ± 1.0	−0.5 ± 1.0	−0.8 ± 1.2	−1.4 ± 1.0	−1.7 ± 1.0	
Squat	Moderate[e]	Unclear	Moderate[e]	Large[f]	Large[f]	0.22
Walk	0.3 ± 0.9	−0.3 ± 0.6	−1.0 ± 1.2	−0.6 ± 1.2	−1.3 ± 1.2	
Downstairs	Unclear	Unclear	Unclear	Unclear	V. Large[f]	0.12
Gluteal	0.6 ± 0.9	−0.3 ± 0.9	−1.3 ± 0.8	−1.0 ± 0.9	−1.9 ± 0.9	
Stretch	Unclear	Unclear	Moderate[f]	Moderate[e]	Large[g]	0.25
Quadriceps	−0.1 ± 1.1	−0.2 ± 0.9	−0.3 ± 1.0	−0.1 ± 0.8	−0.2 ± 1.0	
Stretch	Unclear	Unclear	Unclear	Unclear	Unclear	0.41
Single-leg						
Vertical	0.7 ± 1.2	−0.8 ± 1.2	−0.3 ± 1.2	−1.5 ± 1.2	−1.1 ± 1.2	
Jump	Unclear	Unclear	Unclear	Moderate[f]	Moderate[e]	0.27

[a] Effect of curcumin vs control derived from the analysis of the raw VAS scale units

[b] ±90 %CL: add and subtract this number to the mean effect to obtain the 90 % confidence limits for the true difference

[c] Threshold for substantial is the smallest standardized difference =0.2 times baseline standard deviation

[d] Symbols for the probability of a substantial change follow the magnitude-based descriptor

[e] Likely (>75 %)

[f] Very likely (>95 %)

[g] Most likely (>99.5 %)

been shown with stretching, cryotherapy, electrical modalities, homoeopathy and ultrasound (Cheung et al. 2003).

Curcumin was hypothesised to lower DOMS through an anti-inflammatory mechanism. Unlike in the earlier animal studies referred to above, the effect of curcumin on TNF-alpha was inconclusive and IL6 variable. The small reduction in blood CK at 24 and 48 h post-exercise with curcumin, however, is in keeping with our hypothesis for lower muscle damage and suggests the effect of curcumin may support restoration of membrane integrity as a component of improved recovery from muscle damage. The small possible changes in CK, inconclusive effect of TNF and IL6 suggests that only minimal muscle damage was caused by the eccentric protocol. The peak median CK increase of 200 % from baseline, increase in CK at 24 and 48 h in both control and curcumin-treated subjects indicates that the eccentric protocol may have caused muscle trauma, often associated with DOMS (Vaile et al. 2008b); however, other studies have shown peak increases up to 600 % (Byrne and Eston 2002a, b). TNF-alpha was also selected for analysis in the current study because of its inhibitory effect on muscle tissue repair following injury (Moresi et al. 2008). The blunting of CK with curcumin treatment is in keeping with a prior animal study (Davis et al. 2007) and suggests the effect of curcumin is transient and related to improved membrane integrity due to an effect on inflammatory or other regeneration processes. Non-steroidal anti-inflammatory drugs have not been shown to alter DOMS or CK following ultramarathon competition (Nieman et al. 2006), suggesting curcumin might work via a mechanism separate from inflammatory-mediated responses.

The relative lowering of IL-6 at 24-h post-exercise support the proposed anti-inflammatory action of curcumin, however, the small increases IL-6 immediately post-exercise and 48 h post-exercise prevent firmer conclusions. Large increases in inflammatory cytokines in the working muscle, blood and possibly the brain were proposed by other researchers to trigger DOMS (Willoughby et al. 2003a, b). Curcumin has been reported to block the activity of transcription factor NF-kappaB, reduce AP-1 binding to DNA as well as decreasing the production of COX-2, all of which play a role in the inflammatory cascade (Singh and Aggarwal 1995); (Davis et al. 2007; Thaloor et al. 1999). Curcumin appears to target NF- kappaB as opposed to COX-2, indicating the potential for less serious side effects than NSAIDs. (Davis et al. 2007). NF-kappaB was not measured but should be included in future research. The analgesic effect of curcumin is related to the desensitisation or inhibition of transient receptor potential ion channels (Di Pierro et al. 2013a). This analgesic effect may have played a role in the reduction in pain in our subjects. All VAS measures showed a reduction in pain except quads stretch, which can be accounted for by the eccentric exercise preferentially targeting the gluteal muscles. The analgesic mechanism may also account for the likely small increase in first jump performance followed by trivial

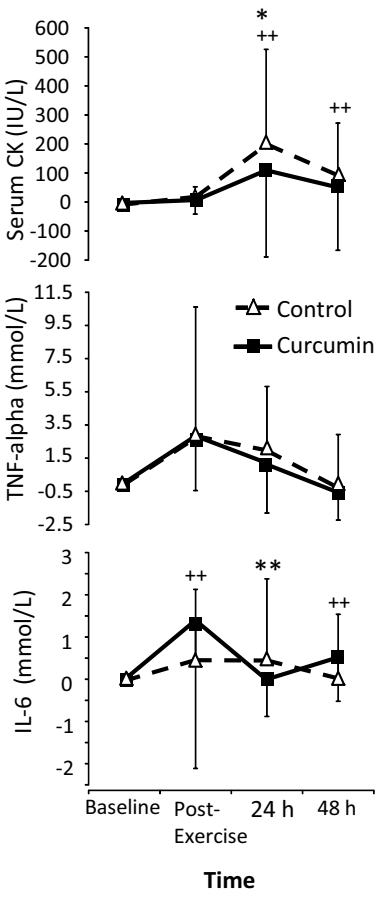

Fig. 3 Effect of curcumin supplementation on muscle damage and inflammatory cytokines. Data are the mean change from *baseline* with *bars* representing the SD. To assist with identification of likely effects of treatment, the probability of substantial change is reproduced from Table 1 via inclusion above the time point for the respective contrast denoted by the unique symbol: relative to baseline +; relative to post-exercise, *. Accordingly, qualified likelihood was shown as increased number of symbols (*used for example): *possible, **likely, ***very likely, ****most likely

second and third jump performance; or alternatively, curcumin could affect performance by an as yet-to-be-defined regulatory mechanism acting on phosphocreatine availability or metabolism.

Additionally, curcumin-lowered IL-1 beta content in the brain, and it has been hypothesised that curcumin is capable of enhancing a behavioural response due to CNS effect (Davis et al. 2007). This could account for the reduction in pain measured by VAS by reducing the perceived discomfort. An in vitro study of human tenocytes has shown curcumin-modulated NF- kappa B signalling via inhibition of IL-1 beta (Buhrmann et al. 2011).

Inflammatory processes, such as activation of IL-1 beta networks, are central to successful skeletal muscle regeneration response to injury (Tidball and Villalta 2010); regeneration is both pro-inflammatory and anti-inflammatory. Therefore, suppression of transient inflammation by nutritional supplementation might, in fact, be negative for recovery from exercise-induced muscle trauma. Chronic application of some other nutritional supplements with antioxidant and inflammatory properties (e.g. vitamin C and E) during a period of training attenuated performance gains (Braakhuis et al. 2014; Nikolaidis et al. 2012); however, negative effect on training adaptation may not be the case for all micronutrients (Braakhuis et al. 2013). Therefore, future work should examine not only the effect of reduced soreness relating to short-term restoration of training capacity, but also the long-term supplement-interaction effect on training adaptation mechanisms and phenotype. In contrast, beneficial effects of supporting exercise adherence in clinical populations (e.g. diabetes, peripheral arterial disease) who suffer muscle pain and soreness associated with exercise (Hirsch et al. 2001) may outweigh dampening of signalling for adaptive stimuli (Di Pierro et al. 2013b).

A strength of this study is that it is a rigorous double-blinded randomized design with a crossover of alternate legs between subjects, to counter carryover of the response to curcumin affecting the results in the subsequent experimental block. To gain further analytical power, the treatment effect on pain, power and algometry outcomes was compared within-subject between legs. Additionally, the within-block pre- and post-analysis cancel out the potential influence of dominant and non-dominant leg effects on outcomes. The current study also allowed for the evaluation of the utility of curcumin as a potential treatment and prevention for muscle soreness. Accordingly, we observed no side effects experienced by the subjects while taking curcumin and blinding was successful. Therefore, we conclude there were no negative or harmful effects evident by taking the current dose of curcumin.

A limitation of the current study was the use of an algometer which indicated levels to the subject, potentially influencing the outcome and could account for the trivial algometer results. Other limitations include sample time points and inference to exercise mode. Including a measurement at 72 h post-exercise would have added to the rigour of this research as muscle soreness following heavy eccentric exercise can last up to 4 days. Prior studies on treatment for DOMS have shown a drop-off in pain post-exercise levels by 72 h (Vaile et al. 2008a; Sellwood et al. 2007) and this was the rationale for the last measurement at 48 h. We chose a heavy eccentric exercise model shown to induce muscle trauma inflammation (Vaile et al. 2007, 2008a) because it provided a proof-of-principle model. However, we clearly acknowledge that not all sports or physical activities have heavy eccentric contraction components (e.g. cycling, swimming), and follow-up research is required to verify if any benefits to lower muscle soreness accrues in predominantly concentric-only exercise.

Furthermore, well-trained individuals are less susceptible to DOMS, warranting investigation in trained muscle to determine if the magnitude of the pain reduction is also of a worthwhile magnitude in the athlete cohort (Cheung et al. 2003). The effect of curcumin on DOMS in females should also be examined as oestrogen is thought to be muscle protective (Dieli-Conwright et al. 2009; Enns and Tiidus 2010). The effect on military performance may also be worthwhile, where soldiers are often exposed to heavy eccentric loading during day-long activity (Cleak and Eston 1992). Finally, the use of various additives, for example, biopirine and modified curcumin formulations to improve absorption warrant investigation. Limited bioavailability is seen in rats with a 2 g kg^{-1} dose. The dose in the current study is approximately 0.3 g kg^{-1} calculated from previous animal studies (Davis et al. 2007) and was shown to be well tolerated, and therefore, practical. Nevertheless, it is possible that a larger effect size on DOMS and performance recovery would be seen with a larger dose or using modified curcumin formulations to improve absorption.

In conclusion, 2.5 d of curcumin supplementation prior to and following heavy eccentric exercise in healthy men likely lowered subsequent pain associated with DOMS and lowered a blood marker for muscle damage, but with equivocal evidence for reduced systemic inflammation. These findings provide the first empirical evidence to support the possibility of using curcumin to prevent and combat DOMS associated with heavy exercise. Further research is required to determine the mechanisms of action, to quantify if the effect is great enough to provide short-term worthwhile benefit to performance sports, military and other activity causing skeletal muscle trauma, and to assess curcumin's effect on females and clinical populations. Other work should explore the effects of chronic supplementation on training adaptation, to investigate the possibility of attenuated exercise adaptation in sport and clinical populations.

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