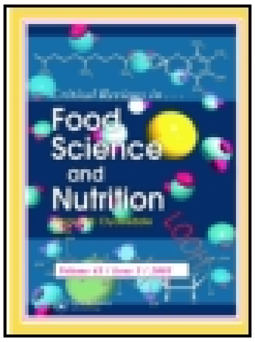

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REVIEW

Effects of curcumin supplementation on sport and physical exercise: a systematic review

Lara Gomes Suhett[a], Rodrigo de Miranda Monteiro Santos[b], Brenda Kelly Souza Silveira[a], Arieta Carla Gualandi Leal[a], Alice Divina Melo de Brito[a], Juliana Farias de Novaes[a], and Ceres Mattos Della Lucia[a]

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ABSTRACT

Curcumin is the main phenolic compound in turmeric. It has been investigated recently due to its numerous medicinal properties and health benefits. However, few studies assessed the effects of curcumin supplementation on physical activity practice. Therefore, the purpose of this review is to assess the available evidences with human beings about the potential effects of curcumin supplementation on sport and physical exercise. This systematic review was conducted within the period from January to February, 2019, following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) guidelines. The LILACS, Medline, SciELO and PubMed databases were used for the search, with no publication date limit. The following terms, with the respective Boolean operators, were searched: "curcumin" AND sports; "curcumin" AND exercise; curcumin AND "aerobic exercise"; "curcumin" AND "resistance exercise"; "curcumin" AND "endurance exercise"; "curcumin" AND "strength exercise". Eleven papers were selected for this review. Most of the studies displayed positive effects of the curcumin supplementation for athletes and physical exercise practitioners, and no side effects were reported. Participants supplemented with curcumin displayed reduced inflammation and oxidative stress, decreased pain and muscle damage, superior recovery and muscle performance, better psychological and physiological responses (thermal and cardiovascular) during training and improved gastrointestinal function. Curcumin supplementation appears to be safe and beneficial for sport and physical exercise in human beings. PROSPERO (CRD42019126763).

KEYWORDS
Turmeric; antioxidant; exercise; nutritional supplements; sports

Introduction

The turmeric (*Curcuma longa L.*) is an oriental spice of yellowish color from the ginger (*Zingiberaceae*) family (Ammon and Wahl 1991; Hewlings et al. 2017; Priyadarsini 2014). This spice is widely grown in tropical regions, with India being its main producer (Ammon and Wahl 1991). In Asian countries, turmeric is frequently used as a medicinal herb as well as in cooking due to its pleasant odor and slightly spicy and bitter taste (Ammon and Wahl 1991; Hewlings et al. 2017; Salehi et al. 2019). Its composition includes three curcuminoids: curcumin (60–70%), demetoxicurcumin (20–27%) and bisdemetoxicurcumin (10–15%), besides other components such as volatile oils (turmerone, atlantone and zingiberene), proteins, sugars and resins (Jurenka 2009; Nelson et al. 2017).

Curcumin (1.7-bis (4-hidroxi-3 methoxyphenol)-1.6 heptadiene-3.5-diona), also known as diferuloylmethane, is the main phenolic compound from the turmeric. This compound was isolated from the rhizomes of the turmeric in 1865 by Vogel and Pelletier (1815) and had its structure characterized by Miłobędzka, Kostanecki, and Lampe (1910). Curcumin has recently drawn worldwide attention of researchers (Salehi et al. 2019), who conducted studies that indicated that its medicinal properties are associated with the reduction of pain (Karlapudi et al. 2018; Sun et al. 2018), anti-inflammatory effects (Ghandadi and Sahebkar 2017; Mollazadeh et al. 2019), besides prevention and treatment of cardiovascular (Li et al. 2020; Momtazi-Borojeni et al. 2019) and gastrointestinal (GI) diseases (Ghosh et al. 2018; Mazieiro et al. 2018), cancer (Kunnumakkara et al. 2017; Mizumoto et al. 2019; Talib et al. 2018) and other chronic diseases (Kunwar and Priyadarsini 2016; Prasad et al. 2014; Salehi et al. 2019; Sharan Patel et al. 2019).

Also, studies that employed animal models reported positive results of curcumin supplementation for physical activity and sport performance (Huang et al. 2015), thus supporting muscle recovery and reduction of inflammation (Davis et al. 2007), improvement of mitochondrial biogenesis (Ray Hamidie et al. 2015), reduction of oxidative stress (Kawanishi et al. 2013), prevention of fatigue and muscle damage (Huang et al. 2015; Sahin et al. 2016). However, there is lack of studies conducted with humans that assessed

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the effects of curcumin supplementation on physical exercise. There is still no consensus in literature about the minimal dose for obtention of benefits for sports and exercise. Therefore, this review aimed to assess the currently available evidence about the potential effects of curcumin supplementation on humans in sports and physical exercise.

Materials and methods

Identification and selection of studies

This systematic review focused on the following research question: "Is curcumin supplementation advantageous for sports practice in humans?" The present paper was designed within the period from January to February 2019, based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyzes) guidelines and registered in PROSPERO (CRD42019126763).

The following databases were searched: dados Latin-American and Caribbean System on Health Sciences Information (LILACS), Medical Literature Analysis and Retrieval System Online (Medline), Scientific Electronic Library Online (SciELO) e National Library of Medicine, Bethesda, MD (PubMed), with no publication date limit.The following search strategy was carried out using the combination of important words related to curcumin and exercise, as well as the descriptors from the Medical Subject Headings (MeSH) index with the respective Boolean operators: "curcumin" AND "sports"; "curcumin" AND "exercise"; "curcumin" AND "aerobic exercise"; "curcumin" AND "resistance exercise"; "curcumin" AND "endurance exercise"; "curcumin" AND "strength exercise". The search was restricted to papers written in English language.

A protocol for identification and selection of original studies was defined by the authors (Figure 1). The papers were analyzed and selected manually, independently and simultaneously by two authors (L.G.S. and B.K.S.S). As for the cases that raised doubt, the reviewers jointly assessed the paper, in order to achieve an agreement. Initially, 346 papers were identified, and subsequently screened by their title and abstract. After the assessment of the eligibility criteria, 11 papers were selected for the present review.

Eligibility criteria

1. Inclusion: Published intervention studies with human beings, which assessed the effects of curcumin supplementation on sports and exercise performance.
2. Exclusion: Studies conducted with animals or in vitro; review papers; book chapters; books; abstracts; studies unrelated to curcumin supplementation; studies involving factors other than sports and physical exercise (e.g., osteoarthritis, depression, cardiovascular diseases, fibrosis, cancer); unpublished paper; monographs; thesis; dissertation; duplicated papers; studies whose authors have stated conflicts of interest.

Data extraction

Data gathered about the selected papers were: author; year of publication; country; study design; sample (n); sample age; dosage used; duration of the intervention; kind of physical exercise; outcome variables; main findings related to the effects of curcumin; presence of significant result and side effects.

Risk of bias

To assess the risk of bias of the studies included in this review, the Cochrane Collaboration tool was used (Higgins and Green 2008). The studies were assessed according to 3 levels of bias: high risk, low risk and unclear (insufficient information for an appropriate judgment). The following kinds of bias were considered: random sequence generation (selection bias); allocation concealment (selection bias); blinding of participants and personnel (performance bias); blinding of outcome assessment (detection bias); incomplete outcomes (friction bias); selective outcome reporting (reporting bias); and finally, other sources of bias (Higgins and Green 2008).

Results

Selection and description of the studies

A total of 346 papers were identified through the combined descriptors. From these, 11 original papers were eligible and were included in this review (Figure 1). All the selected studies are mostly randomized (n = 8) and crossover (n = 8) clinical trials, conducted with adult participants, whereas samples were comprised of male individuals (n = 8). Sample size and time of intervention varied from 8 to 47 participants and from 1 day to 3 months, respectively. The used curcumin dosages varied from 0.01 g to 6 g/day, and curcumin was administered either in isolation, or associated to other compounds (piperine; *Boswellia* extract). The kinds of exercises performed varied between aerobic (n = 7) and resistance (n = 4) (Table 1).

Other characteristics of the studies, such as author and year of publication, study location, are describe in Table 1. Table 2, in turn, displays the information about the outcome variables (curcumin's serum concentration, inflammation, muscle soreness and damage, recovery and muscle performance, oxidative stress markers, psychological and physiological parameters (thermal and cardiovascular) and GI function), besides the description of the main results and the presence of side effects reported in the studies.

Curcumin's serum concentration

Curcumin's serum concentration was assessed in less than half of the papers (n = 3) (Takahashi et al. 2013; Tanabe, Chino, Ohnishi, et al. 2019; Tanabe, Chino, Sagayama, et al. 2019). Significant differences were observed in curcumin's serum concentration, whereas in baseline the group supplemented before the resistance exercise (180 mg/day – 7 days) displayed higher values in comparison to the placebo and the group supplemented with curcumin after the exercise (180 mg/day – 4 days). Between 1 and 4 days after the

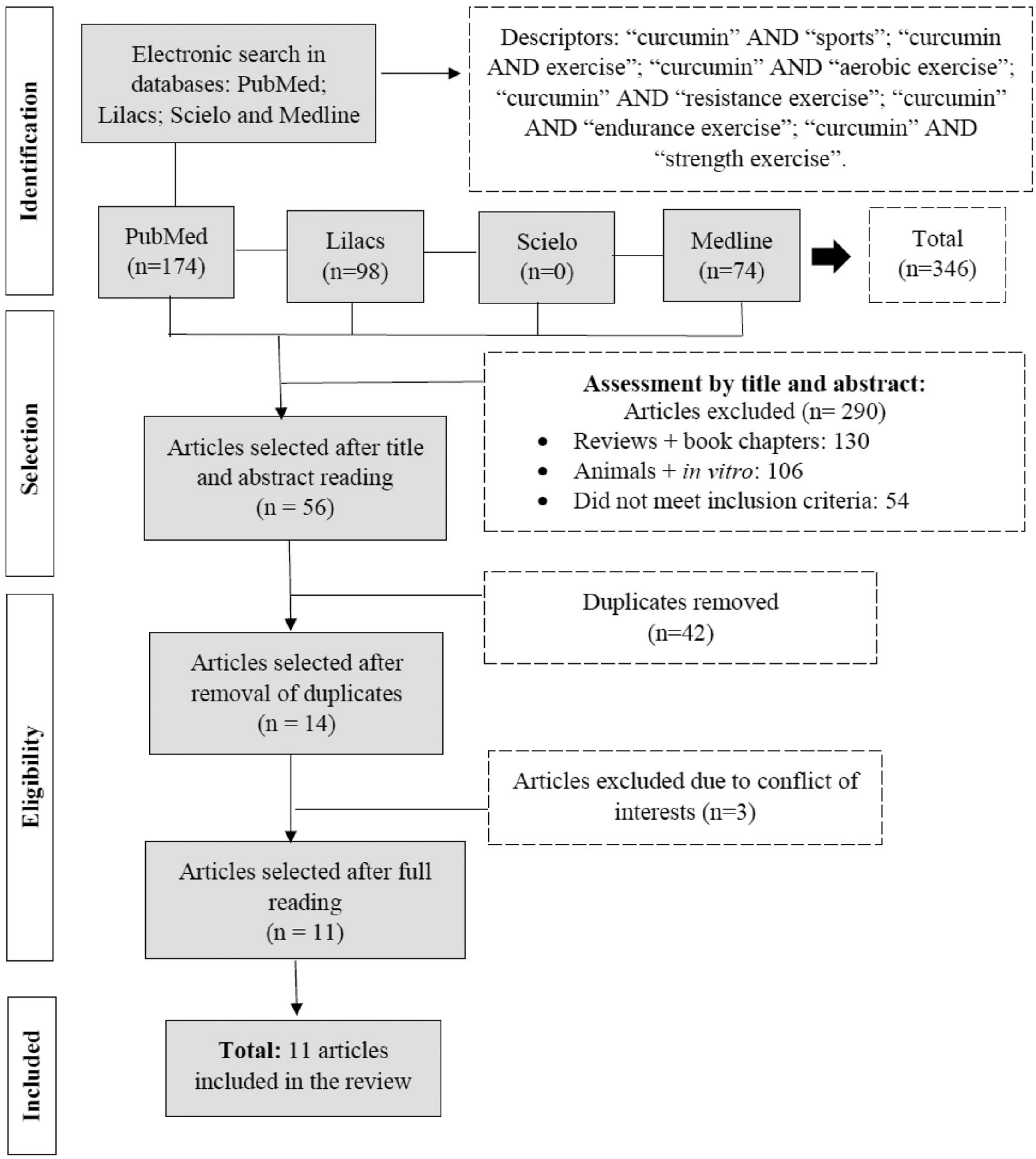

Figure 1. Protocol for identification and selection of eligible studies for the systematic review on the effects of curcumin supplementation on exercise.

exercise, the curcumin's serum concentration was higher in the group supplemented after the exercise (Tanabe, Chino, Sagayama, et al. 2019). Another study also assessed the effects of the curcumin supplementation (180 mg/day – 7 days) through two experiments, which analyzed the curcumin's serum concentration after performing resistance exercise. In experiment 1, curcumin supplementation was performed 7 days prior to the exercise, and a significant reduction in plasmatic concentration was observed, in comparison to the baseline. However, in experiment 2, curcumin supplementation was carried out during 7 days after the exercise, and a significant increase was observed for the curcumin's serum concentration 1 day after the exercise, compared to the baseline, and has remained as such in the 3, 5 and 7 subsequent days (Tanabe, Chino, Ohnishi, et al. 2019).

In turn, Sciberras et al. (2015) carried out curcumin supplementation before the aerobic exercise in the cycle ergometer (500 mg/day for 3 days + 500 mg pre-exercise) and assessed the curcumin's plasmatic concentration after the exercise and reported an average of 79.7 ± 26.3 mg/ml in the supplemented group, whilst no curcumin concentration was observed in the control group's plasma. Takahashi et al. (2013) supplemented curcumin 2 h prior to the aerobic exercise in the treadmill (group 1: 90 mg and group 2: 90 mg + 90 mg pre-exercise) and observed a significant increase of their serum concentrations in the baseline, immediately after, and 2 h after the exercise, in both supplemented groups, when compared to the placebo group.

Inflammation

Curcumin supplementation displayed significant reduction of inflammation derived from the physical exercise (Table 2). Szymanski et al. (2018), in their study with 8

Table 1. Characteristics of the studies included.

Author/year	Country	Study design	Sample (n)	Age	Intervention	Duration	Exercise test
Tanabe, Chino, Sagayama, et al. (2019)	Japan	Randomized single-blind parallel clinical trial	24 Healthy young individuals (20 M)	Group 1: 28.8 ± 3.6 years Group 2: 29.8 ± 3.4 years Group 3: 28 ± 3.2 years	Group 1: 180 mg/day of curcumin Theracurmin. Group 2: 180 mg/day of curcumin Theracurmin. Group 3: Placebo.	Group 1: 7 days before the exercise. Group 2: 4 days after the exercise. Group 3: 4 days after the exercise	Resistance exercise: 30 maximal eccentric isokinetic (120°/s) contractions of elbow flexors.
Tanabe, Chino, Ohnishi, et al. (2019)	Japan	Double-blind crossover clinical trial	20 Healthy individuals (20 M)	Experiment 1: 28.5 ± 3.4 years	Experiment 1: Group 1: 180 mg/day of Theracurmin curcumin. Group 2: Placebo (starch).	Experiment 1: 7 days before the exercise.	Resistance exercise: 30 maximal eccentric isokinetic (120°/s) contractions of elbow flexors.
Tanabe, Chino, Ohnishi, et al. (2019)	Japan	Double-blind crossover clinical trial	20 Healthy individuals (20 M)	Experiment 2: 29 ± 3.9 years	Experiment 2: Group 1: 180 mg/day of Theracurmin curcumin. Group 2: Placebo (starch).	Experiment 2: 7 days after the exercise.	Resistance exercise: 30 maximal eccentric isokinetic (120°/s) contractions of elbow flexors.
Szymanski et al. (2018)	USA	Double-blind crossover clinical trial	8 Healthy and physically active individuals (6 M and 2 W)	19 ± 1 years	Group 1: 500 mg/day of Meriva® curcumin. Group 2: Placebo.	3 days before the exercise.	1h of aerobic exercise (treadmill running) at 65% VO2 max.
Falgiano et al. (2018)	USA	Double-blind crossover clinical trial	8 Healthy and physically active individuals (6 M and 2 W)	19 ± 1 years	Group 1: 500 mg/day of Meriva® curcumin. Group 2: Placebo.	3 days before the exercise.	1 h of aerobic exercise (treadmill running) at 65% VO2 max.
McAllister et al. (2018)	USA	Randomized double-blind crossover clinical trial	14 Apparently healthy and physically active individuals (14 M)	21–30 years	Group 1: 1.5 g/day of curcumin. Group 2: Placebo (cellulose).	3 days before the exercise.	35 min of steady-state aerobic exercise (cycling) at 60% VO2 max with mental stress challenges.
Delecroix et al. (2017)	France	Randomized single-blind crossover clinical trial	10 Elite rugby players (10 M)	20.7 ± 1.4 years	Group 1: 6 g of curcumin + 60 mg of piperine/day. Group 2: Placebo (glucose).	4 days (2 days before and 2 days post-exercise)	25 repetitions over 25 m of one leg jumps on a 8% downhill slope with 90-second interval between them, covering 25m as fast as possible and stopping in a pre-defined zone of 3.5m at the end of the 25 m slope.
McFarlin et al. (2016)	USA	Randomized double-blind clinical trial	28 Individuals (10 M and 18 W)	Group 1: 20 ± 1 yearsGroup 2: 19 ± 2 years	Group 1: 400 mg/day of Longvida® curcumin. Group 2: Placebo (rice flour).	7 days (2 days before, on the day and 4 days after the exercise)	Resistance exercise: 6 series of 10 repetitions of eccentric exercise (leg press) with initial load set at 110% of the estimated 1RM
Chilelli et al. 2016	Italy	Controlled randomized parallel clinical trial	47 Cyclists (47 M)	Group 1: 45 ± 9 yearsGroup 2: 46 ± 8 years	Group 1: Mediterranean diet + 50 mg Phytome® turmeric (10 mg of curcumin) + 140 mg of *Boswellia* extract (105 mg of *boswellic acid.*) Group 2: Control (Mediterranean diet).	3 months.	Aerobic exercise (cycling), around 200 km weekly.

Nicol et al. (2015)	New Zealand	Controlled Randomized double-blind crossover clinical trial	17 Physically active individuals (17 M)	33.8 ± 5.4 years	Group 1: 5 g/day of curcumin Group 2: Placebo (Avicel 105).	5 days (2.5 days before and 2.5 days after the exercise)	Resistance exercise: 5 sets of 10 repetitions at 120% 1RM + 2 sets of 10 repetitions at 100% 1RM of eccentric exercise (single-leg press).
Sciberras et al. (2015)	United Kingdom	Randomized double-blind crossover clinical trial	11 Aerobic exercise athletes (11 M)	35.5 ± 5.7 years	Group 1: 500 mg/day of Meriva® curcumin. Group 2: Placebo. Group 3: No supplementation.	4 days (3 days before + 500 mg prior to exercise).	2 h of aerobic exercise (cycle ergometer – 70 rpm) at 95% power from lactate threshold.
Takahashi et al. (2013)	Japan	Randomized double-blind placebo-controlled crossover clinical trial	10 Healthy individuals (10 M)	26.8 ± 2 years	Group 1: 90 mg of curcumin 2 h before the exercise. Group 2: (180 mg/day) 90 mg of curcumin 2h before + 90 mg immediately after the exercise. Group 3: Placebo.	1 day.	2 h of aerobic exercise (treadmill walking or running) at 65% VO2 max.

g, grams; M, men; mg, milligrams; mg/day, milligrams per day; RM, repetition maximum; VO2 max, maximum rate of oxygen consumption; W, women.

physically active individuals, reported that the serum concentration of the interleukin receptor antagonist (IL1-RA) displayed higher elevation for the placebo group than for the curcumin group (CG) (500 mg/day – 3 days) after aerobic exercise (1 h of treadmill running), when compared to pre-exercise moment. After the exercise, the alpha tumor necrosis factor (TNF-α) increased in the placebo group (immediately after: 19% and 1 h after: 24%; $p = 0.01$), as well as interleukin-10 (IL-10) (immediately after: 61% and 1 h after: 42%; $p < 0.01$). However, such an increase was not observed for the CG ($p > 0.05$). Another study, carried out in Japan with 20 healthy males (Tanabe, Chino, Ohnishi, et al. 2019), reported that interleukin-8 serum concentration (IL-8) 12 h after the resistance exercise was lower for the CG in experiment 1 (180 mg/day – 7 days prior the exercise), compared to the placebo group. In a clinical trial performed in the USA with 28 individuals (McFarlin et al. 2016), the magnitude of the increases was significantly lower in the CG (400 mg/day – 7 days) for TNF-α (−25%; $p = 0.028$) and IL-8 (−21%; $p = 0.030$) after resistance exercise-induced muscle damage, in comparison to the placebo. Likewise, in a study carried out in New Zealand with 17 physically active males (Nicol et al. 2015), the authors observed that the CG (5 g/day – 5 days) displayed lower interleukin-6 (IL-6) concentration 24 h after the exercise (−20%; ±18%), compared to the moment immediately after the performance of resistance exercise. However, other studies did not report significant differences between the groups with respect to the inflammatory markers assessed (Chilelli et al. 2016; Falgiano et al. 2018; Sciberras et al. 2015).

Pain and muscle damage

Despite some inconclusive findings, in general, curcumin supplementation appears to be benefic for decreased pain and also muscle damage by decreasing serum CK (Table 2). Reduced muscle pain was observed on the 3rd day post-resistance exercise for the post-exercise CG (180 mg/day – 4 days) compared to the placebo group and the group supplemented 7 days prior to the exercise. However, there were no differences in relation to creatine kinase's (CK) serum concentration between groups (Tanabe, Chino, Sagayama, et al. 2019). Another study observed that the score for muscle pain was lower for the CG (180 mg/day – 7 days after the exercise) 3–6 days after the exercise when compared to the placebo group. In addition, CK serum concentrations were lower for the CG 5–7 days after the exercise in comparison to the placebo group (Tanabe, Chino, Ohnishi, et al. 2019). Similar findings were reported by Nicol et al. (2015), in which individuals supplemented with curcumin (5 g/day – 5 days) displayed reduced muscle pain and lower CK serum concentration CK (−22–29%; ± 21–22%) 24- and 48-hours post-resistance exercise.

Despite having observed significantly lower CK increases (−48%; $p = 0.035$) for the CG, McFarlin et al. did not report significant differences in quadriceps muscle pain between the groups after 6 series of 10 leg press repetitions with approximate load of 110% 1RM (repetition maximum).

Table 2. Outcome variables, main results and side effects.

Author/year	Outcome variables	Main results	Side effects? (yes/no)
Tanabe, Chino, Sagayama, et al. (2019)	Before, immediately after, and 1–4 d after: Curcumin's plasmatic concentration; MVC of elbow flexors; ROM of elbow joint; Muscle pain; CK.	Following resistance exercise, ROM was higher 3–4 days after the exercise for group 2 (curcumin supplementation after the exercise) compared to placebo. The score for muscle pain was lower for group 2–3 days after the exercise ($p < 0.05$).	–
Tanabe, Chino, Ohnishi, et al. (2019)	Before, immediately after, and 1–7 d after: Curcumin's plasmatic concentration; MVC of elbow flexors; ROM of elbow joint; Muscle pain; CK; IL-8; TNF-α; d-ROMs; BAP.	In experiment 1, IL-8 was lower 12h after the exercise for the CG, compared to placebo.	–
Tanabe, Chino, Ohnishi, et al. (2019)	Before, immediately after, and 1–7 d after: Curcumin's plasmatic concentration; MVC of elbow flexors; ROM of elbow joint; Muscle pain; CK; IL-8; TNF-α; d-ROMs; BAP.	In experiment 2, MVC and ROM were improved 3–7 days and 2–7 days after the exercise, respectively. Muscle soreness and CK were lower 3–6 days and 5–7 days after the exercise, respectively, for the CG compared to placebo.	–
Szymanski et al. (2018)	Before, immediately after, 1hr and 4hrs after: Physiological parameters (VE, VO2, VCO2, RER, PSI, Hydration, Heart rate, skin temperature, body temperature and internal temperature); I-FABP; Inflammation markers (MCP-1, IL-6, IL1-RA, IL-10, TNF-α).	I-FABP (after exercise: 87% vs. 58%; 1h after exercise: 33% vs. 18%), IL1-RA (1h after exercise: 153% vs. 77%) increased more after the exercise for the placebo group than the CG. TNF-α (after exercise: 19% and 1h after exercise: 24%; $p = 0.01$) and IL-10 (after exercise: 61% e 1h after exercise: 42%; $p < 0.01$) increased for the placebo group, but not for the CG ($p > 0.05$) after the exercise. The absolute increase of internal temperature ($2.42 \pm 0.26\,^{\circ}C$ vs. $2.13 \pm 0.30\,^{\circ}C$; $p = 0.019$), average body temperature ($2.38 \pm 0.24\,^{\circ}C$ vs. $2.12 \pm 0.28\,^{\circ}C$; $p = 0.049$), heart rate (39 ± 5 bpm vs. 30 ± 7 bpm; $p = 0.012$) and PSI (9.76 ± 0.57 vs. 8.73 ± 0.76; $p = 0.047$) were higher for the placebo compared to the CG over the 60min exercise. The risk of insolation was lower for the CG after 40-60 min of exercise ($p < 0.01$).	No
Falgiano et al. (2018)	Before, immediately after, 1hr and 4hrs after: TLR4; MyD88; pNF-κB; NF-κB; SIRT1; p-AMPK; pHSF-1; HSP70,	Compared to placebo, CG did not change protein expression in PBMC ($p > 0.05$) after exercise-induced exertional heat stress. However, reductions in the placebo and CGs were observed 1h after the exercise, in TLR4 (− 22.8 and -19.8%; $p= 0.03$), HSP70 (− 15.7% and -6.3%; $p= 0.04$), pAMPK (− 52.7% and -44.3%; $p< 0.01$) and SIRT1 (−49.5% and -46.1%; $p< 0.01$). The pNF-κB - NF-κB ratio increased in both conditions (+57.4% and +93.4%; $p= 0.02$).	No
McAllister et al. (2018)	Before, immediately after, 30 min and 1 hr after: Heart rate; GSH; SOD; H2O2; AOPP.	Curcumin ingestion did not result in significant impact on oxidative stress markers after exposure to double stress (mental and physical) for trained males.	–
Delecroix et al. (2017)	Immediately after, 24 hrs, 48 hrs and 72 hrs after: Concentric and isometric torque peak for knee extensor; 6-second one-leg sprint performance; Jumping performance; CK; Muscle soreness.	Effects on recovery of some aspects of muscle function 24h after physical activity. Decreased loss of mean power during sprint for the CG ($-1.77 \pm 7.25\%$; 1277 ± 153W), compared to placebo ($-13.6 \pm 13.0\%$; 1130 ± 241W) (Effect size $= -1.12$; CI 90% =-1.86 - −0.29).	–
McFarlin et al. (2016)	Before, 1 d, 2 d, 3 and 4 d after: Muscle soreness; CK; Inflammatory cytokines (IL-6, TNF-α, IL-8, IL-10).	Significantly lower increases of CK (−48%; $p = 0.035$), TNF-α (−25%; $p = 0.028$), and IL-8 (−21%; $p = 0.030$) for the CG, after exercise-induced muscle damage, compared to placebo.	No
Chilelli et al. (2016)	Before and 3 months later: IL-6; TNF-α; CRP; AGE; sRAGE; MDA; PPFA; NEFA.	Significant reduction in the accumulation of total AGEs (-11.59 ± 12.49 vs. 0.15 ± 2.30; $p < 0.001$) and MDA (-0.10 ± 0.006 vs. -0.07 ± 0.03; $p < 0.02$) for the CG, compared to control group.	No
Nicol et al. (2015)	Before, immediately after, 24hrs and 48hrs after: Muscle pain and swelling; Muscle sensitivity; Jumping performance; CK; IL-6; TNF-α.	Curcumin supplementation reduced single-leg muscle pain symptoms in several locations 24 and 48 h after the exercise. CG also displayed lower CK concentration 24 and 48 h after the exercise (−22–29 %; ± 21–22 %) and lower IL-6 24h following the exercise (−20 %; ±18 %). No significant differences in TNF-α. Improved muscle performance (determined by the increased height of the single-leg 1st jump) 24 and 48 h after the resistance exercise (15 %; 90 %CL ± 12 %).	No
Sciberras et al. (2015)	Before, immediately after and 1hr after: Curcumin's plasmatic concentration; IL-6; TNF-α; IL1-RA; IL-10; Cortisol; CRP. Before: Psychological stress.	CG reported higher amount of "better than usual" results, with respect to training stress, when compared to placebo and control groups.	No

(*continued*)

Table 2. Continued.

Author/year	Outcome variables	Main results	Side effects? (yes/no)
Takahashi et al. (2013)	Immediately after: Curcumin's plasmatic concentration; Heart rate; Perceived exertion; d-ROMs; TRX-1; BAP; GSH; TBARS; GSSG; SOD; CAT; GPX; GR.	CGs displayed lower serum concentrations of d-ROMs ($p = 0.023$) and TRX-1 ($p = 0.047$), and also higher BAP ($p < 0.01$) and GSH ($p = 0.037$) values, compared to the placebo, after the exercise. Immediately after the exercise, the placebo group displayed lower GR values (5.6 ± 0.6), compared to pre-exercise (9.0 ± 1.1) ($p < 0.05$). 2h after the exercise, the placebo group displayed higher GPX values (269.3 ± 9.3), compared to pre-exercise (197.3 ± 36.9) ($p < 0.05$).	-

AGE, advanced glycation end-products; AOPP, advanced oxidation protein products; BAP, biological antioxidant potential; CAT, catalase; CG, curcumin group; CK, creatine kinase; CRP, c reactive protein; d-ROMs, derivatives of reactive oxygen metabolites; FRAP, Ferric Reducing *Antioxidant* Power; GPX, glutathione peroxidase; GR, glutathione reductase; GSH, reduced glutathione; GSSG, oxidized glutathione; H2O2; hydrogen peroxide; HSP 70, heat shock protein 70; I-FABP, intestinal fatty acid binding protein; IκB, inhibitor of kappa beta; IL1-RA, interleukin 1 receptor antagonist; IL-6, interleukin 6; IL-8, interleukin 8; IL-10, interleukin 10; MCP-1, monocyte chemoattractant protein-1; MDA, malondayldehyde; MyD88, myeloid differentiation protein 88; MVC, maximal voluntary contraction; NF-κB, nuclear factor kappa beta; NEFA, composition and non-esterified fatty acid; pAMPK, phosphorylated 5-AMP-activated protein kinase; PBMC, peripheral blood mononuclear cell; pHSF1, p-Heat shock factor 1; pNF-κB, p-Nuclear factor kappa beta; PPFA, plasma phospholipid fatty acid; PSI, physiological strain index; RER, respiratory exchange ratio; ROM, range of motion; SIRT1, sirtuin-1; sRAGE, soluble receptor for AGE; TBARS, thiobarbituric acid reactive substances; TNF-α, tumor necrosis factor alpha; TLR4, toll-like receptor 4; TRX-1, thioredoxin-1; SOD, superoxide dismutase; VCO2, carbon dioxide production; VE, minute ventilation; VO2, oxygen consumption.

Another clinical trial carried out in France, with 10 rugby players supplemented with curcumin + piperine (6 g/day + 60 mg/day – 4 days), also displayed no effects on the reduction of pain or muscle damage (Delecroix et al. 2017).

Muscle recovery and performance

After curcumin supplementation there was a significant improvement in some aspects of muscle recovery and performance in exercise (Table 2). Curcumin supplementation post-resistance exercise (180 mg/day – 4 days) improved the range of movement (ROM) 3–4 days following the exercise in comparison to the placebo group (Tanabe, Chino, Sagayama, et al. 2019), thus substantiating the findings of Tanabe, Chino, Ohnishi, et al. (2019), which suggests that post-exercise supplementation contributed to muscle recovery. Another study (Delecroix et al. 2017) reported lower average loss of power in sprints for the CG (6 g curcumin + 60 mg piperine/day – 4 days) (−1.77 ± 7.25%; 1277 ± 153 W) when compared to the placebo (−13.6 ± 13.0%; 1130 ± 241 W). Nicol et al. (2015) observed improved muscle performance (determined by the increase in the 1st jump height) 24- and 48-hours after resistance exercise (15%; 90% CL ± 12%) in individuals supplemented with curcumin (5 g/day – 5 days). However, no significant difference was observed in relation to perceived exertion between curcumin and placebo groups (Takahashi et al. 2013).

Oxidative stress

With respect to oxidative stress, Chilelli et al. (2016), in their study carried out in Italy with 47 cyclists, showed that the group supplemented with curcumin + *Boswellia serrata* (10 mg/day + 105 mg/day – 3 months) displayed higher reduction of endogenous advanced glycation end products (AGEs) (−11.59 ± 12.49 vs. 0.15 ± 2.30; $p < 0.001$) and malondialdehyde (MDA) (−0.10 ± 0.006 vs. −0.07 ± 0.03; $p < 0.02$) compared to the control group. Takahashi et al. (2013), by their part, in a clinical trial conducted in Japan with 10 males, observed that the groups supplemented with curcumin (90 mg/day and 180 mg/day – 1 day) displayed lower serum concentration of derivatives of reactive oxygen metabolites (d-ROMs) ($p = 0.023$) and thioredoxin-1 (TRX-1) ($p = 0.047$), besides higher values of biological antioxidant potential (BAP) ($p < 0.01$) and reduced glutathione (GSH) ($p = 0.037$) compared to placebo after aerobic exercise (treadmill walking or running at 65% VO2 max). The placebo group, displayed lower values of glutathione reductase (GR) immediately after the exercise, than pre-exercise ($p < 0.05$) and displayed higher values of glutathione peroxidase (GPX) 2 h following the exercise ($p < 0.05$) (Takahashi et al. 2013). In contrast, other studies did not report significant differences between groups in the assessed oxidative stress markers (McAllister et al. 2018; Tanabe, Chino, Ohnishi, et al. 2019) (Table 2).

Psychological and physiological parameters

Curcumin supplementation is also related to beneficial effects in psychological and physiological parameters (thermal and cardiovascular) (Table 2). A double-blind clinical trial conducted in the United Kingdom with 11 practitioners of aerobic physical activity (cycle ergometer) displayed, through a subjective assessment, that the CG (500 mg/day – 4 days) displayed more frequently a "better than usual" result with respect to the psychological stress during training, compared to the placebo and control groups (Sciberras et al. 2015).

Szymanski et al. (2018) observed that the absolute increase of the internal temperature (2.42 ± 0.26 °C vs. 2.13 ± 0.30 °C; $p = 0.019$), average body temperature (2.38 ± 0.24 °C vs. 2.12 ± 0.28 °C; $p = 0.049$), heart rate (39 ± 5 bpm vs. 30 ± 7 bpm; $p = 0.012$) and Physiological Strain Index (PSI) (9.76 ± 0.57 vs. 8.73 ± 0.76; $p = 0.047$) were higher during aerobic exercise in the placebo group, compared to the curcumin supplemented group (500 mg/day – 3 days), although findings are controversial with respect to heart rate (McAllister et al. 2018; Sciberras et al. 2015; Takahashi et al. 2013).

No significant differences were observed for minute ventilation (VE), maximum oxygen uptake (VO_2), carbon dioxide production (VCO_2), respiratory exchange ratio (RER), hydration and skin temperature (Szymanski et al. 2018).

Gastrointestinal function (GI)

Only one study assessed the effect of curcumin supplementation on the improvement of GI function during exercise-induced exertional heat stress (Table 2). In the study by Szymanski et al. (2018), the fatty acid binding protein (I-FABP, GI barrier damage marker) displayed higher elevation after aerobic exercise for the placebo group (after exercise: 87% vs. 58%; 1 h after exercise: 33% vs. 18%) than for the CG (500 mg/day – 3 days).

Side effects

More than half of the studies (n = 6) assessed the presence of side effects in relation to curcumin supplementation and no adverse symptoms or injury to health were reported for the used dosages (Chilelli et al. 2016; Falgiano et al. 2018; McFarlin et al. 2016; Nicol et al. 2015; Sciberras et al. 2015; Szymanski et al. 2018) (Table 2).

Assessment of risk of bias

Although most of the studies were randomized, many did not include the description of the method employed to generate the random sequence, thus hampering the assessment (Delecroix et al. 2017; Falgiano et al. 2018; McAllister et al. 2018; McFarlin et al. 2016; Sciberras et al. 2015; Szymanski et al. 2018; Takahashi et al. 2013; Tanabe, Chino, Ohnishi, et al. 2019; Tanabe, Chino, Sagayama, et al. 2019). Most studies displayed low risk of bias in relation to allocation concealment. With respect to the blinding of participants and personnel, most of the studies were double-blind, thus displaying low risk for this bias, except for Delecroix et al. and Chilelli et al., who did not detail the data about the blinding and were assessed as *unclear* in this regard. As for the blinding of the outcome evaluators, three studies were classified as *unclear* (Chilelli et al. 2016; Delecroix et al. 2017; Tanabe, Chino, Sagayama, et al. 2019). All studies were classified as *unclear* for selective outcome reporting bias, due to insufficient information about the studies' protocols for judgment (Figure 2).

Discussion

This systematic review, according to our knowledge, is the first to gather the available evidence about the effects of curcumin supplementation in sport and exercise in human beings, indicating reduction of inflammation, oxidative stress, muscle pain and damage; improved muscle recovery, sport performance, psychological and physiological responses (thermal and cardiovascular) during training, as well as GI function (Figure 3).

Regular physical activity has many health benefits (Grazioli et al. 2017; Warburton and Bredin 2017). However, high intensity, long duration and short-rest time exercises may lead to severe inflammation, muscle damage and consequently muscle pain (Clarkson, Nosaka, and Braun 1992; Powers et al. 2010; Wagner, Reichhold, and Neubauer 2011), as well as influence immunological response (Walsh et al. 2011), thus enabling the activation of transition factors, increasing the serum concentration of pro-inflammation cytokines and production of extracellular reactive oxygen species (EROs) (Garcia-Lopez et al. 2007).

Although exercise-induced moderate inflammatory responses and EROs are essential for physiological adaptations and muscle regeneration (Clarkson, Nosaka, and Braun 1992; Ferraro et al. 2014; Garcia-Lopez et al. 2007), if not controlled, may lead to delayed onset muscle soreness (DOMS) and decreased sport performance (Powers et al. 2010; Wagner, Reichhold, and Neubauer 2011). Therefore, it is important to resort to strategies to control or minimize muscle damage and inflammatory responses, allowing for fast recovery, particularly for athletes and individuals with intense exercise routine.

There are evidences that curcumin supplementation plays an important role on reduced post-exercise inflammation (McFarlin et al. 2016; Nicol et al. 2015; Szymanski et al. 2018; Tanabe, Chino, Ohnishi, et al. 2019). One of the mechanisms involved is based on its capacity to inhibit transcription factors, such as nuclear kappa B (NF-kB) and activator protein-1 (AP-1), responsible for inducing enzyme expression and secretion (cyclooxygenase-2 (COX-2) and 5-lipoxygenase (LOX-5)) and cytokines (TNF-α and proinflammatory interleukins as IL-1, IL-6, IL-8) activators of the immunological system (Khalaf, Jass, and Olsson 2010; Singh and Aggarwal 1995; Thaloor et al. 1999). However, literature is still controversial with respect to the anti-inflammatory effects of curcumin on physical exercise (Chilelli et al. 2016; Falgiano et al. 2018; Sciberras et al. 2015), and more experimental studies are necessary to clarify this relation.

Recent research, with protocols that used between 0.01 and 6 g/day curcumin, has also shown benefits of the supplementation on the reduction of pain and muscle damage (decreasing serum CK) (Nicol et al. 2015; Tanabe, Chino, Ohnishi, et al. 2019; Tanabe, Chino, Sagayama, et al. 2019), speeding recovery and enhancing sport performance (Delecroix et al. 2017; Tanabe, Chino, Ohnishi, et al. 2019; Tanabe, Chino, Sagayama, et al. 2019). Curcumin, through the modulation of NF-kB activity, an important factor of the inflammatory cascade and regulator of the myogenesis, may support the cellular proliferation and differentiation of myoblasts, enabling the increase of strength and muscle repair (Mourkioti et al. 2006; Thaloor et al. 1999). Thus, it is likely that curcumin has positive therapeutic applications in athletes and physical activity practitioners, either through its anti-inflammatory action or its role in muscle regeneration (Tanabe, Chino, Ohnishi, et al. 2019).

The supplementation of different kinds of antioxidants, including curcumin (Chilelli et al. 2016; Takahashi et al. 2013), has been pointed out as a positive strategy for

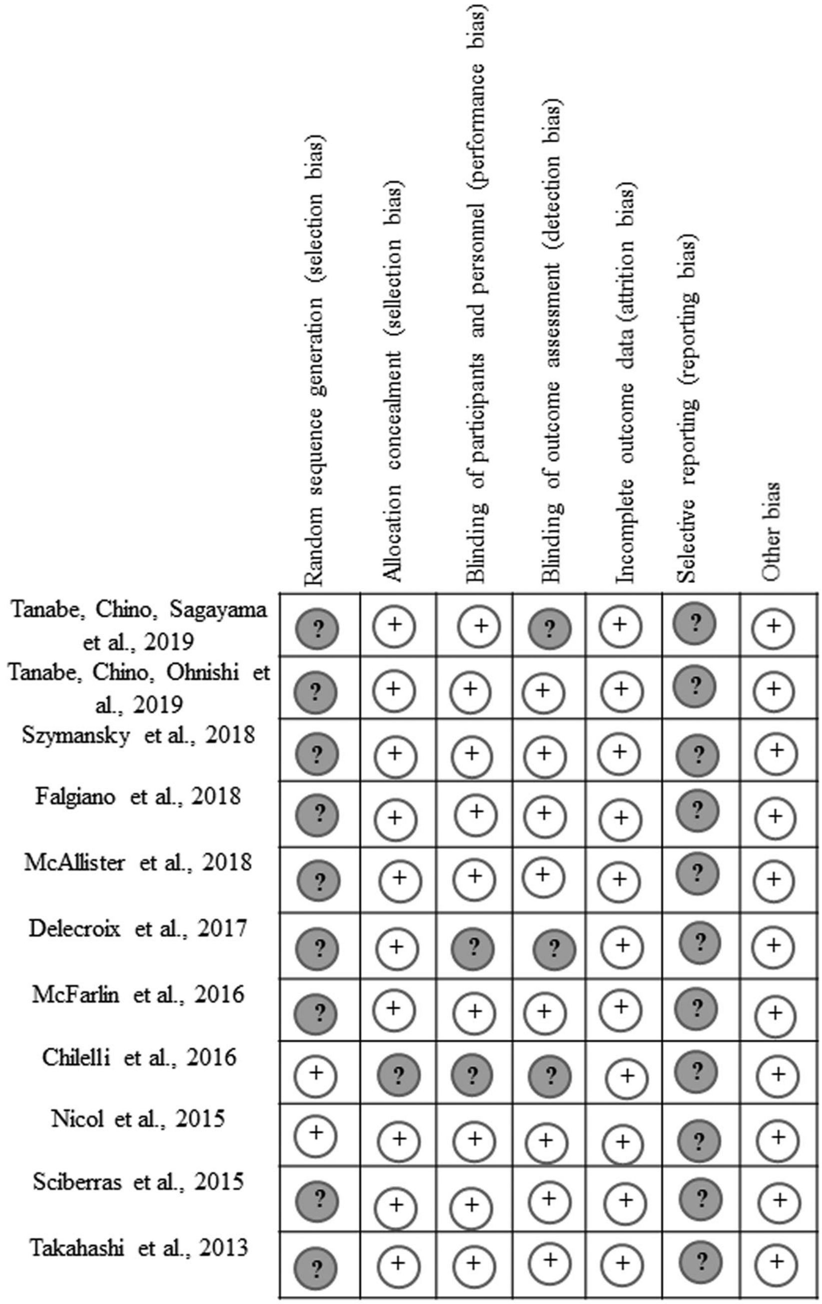

Figure 2. Risk of bias summary: Authors' judgments about each possible risk of bias of the studies included in the review. +, low risk; ?, unclear.

preventing oxidative stress and improving sport performance (Antonioni et al. 2019; Takami et al. 2019). The antioxidant effect of curcumin is related to its capacity of sequestering EROs, precluding lipidic peroxidation and cellular damage, in addition to chelating free radical generator ions (Itokawa et al. 2008). Curcumin is also involved in the modulation of the activity of the GPX enzymes, catalase (CAT) and superoxide dismutase (SOD) in the neutralization of free radicals (Manikandan et al. 2004). In addition, curcumin can suppress the NF-kB metabolism and, consequently, inhibit EROs-generator enzymes, such as COX-2, LOX-5, and xanthine-hydrogenase/oxidase (Khalaf, Jass, and Olsson 2010; Marchiani et al. 2014; Singh and Aggarwal 1995).

McAllister et al. (2018), in their study carried out in the USA with trained males exposed to double stress (mental and physical), did not observe significant effects of curcumin supplementation on the oxidative stress markers after the exercise, just as Tanabe et al. (Tanabe, Chino, Ohnishi, et al. 2019). However, the authors highlighted that their protocol did not induce oxidative stress in their sample, even after exhaustive training, which might explain the absence of treatment effects and, therefore, supplementation would not be necessary.

Another likely justification for the absence of significant results after curcumin supplementation in physical exercise is its low bioavailability, which happens to be a major disadvantage for its clinical application (Anand et al. 2007;

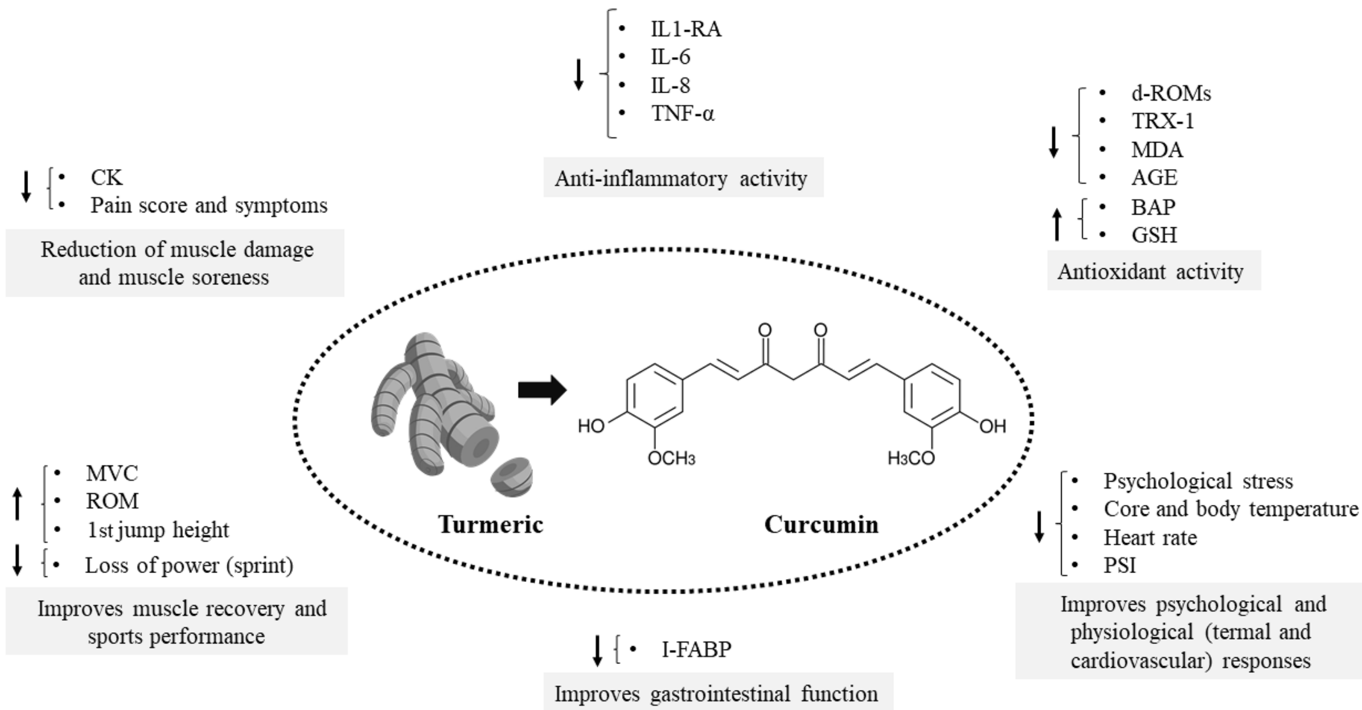

Figure 3. Potential positive effects and molecular targets of curcumin supplementation in exercise. AGE, advanced glycation end-products; BAP, biological antioxidant potential; CK, creatine kinase; d-ROMs, derivatives of reactive oxygen metabolites; GSH, reduced glutathione; I-FABP, intestinal fatty acid binding protein; IL1-RA, interleukin 1 receptor antagonist; IL-6, interleukin 6; IL-8, interleukin 8; MDA, malondayldehyde; MVC, maximal voluntary contraction; PSI, physiological strain index; ROM, range of motion; TNF-α, tumor necrosis factor alpha; TRX-1, thioredoxin-1.

Nelson et al. 2017). Some reasons for its low availability are: reduced absorption, low water solubility, quick metabolism, chemical instability and fast systemic elimination (Anand et al. 2007). Hence, it is important that future studies assess previously whether curcumin's serum concentration has sufficiently increased after supplementation so as to produce biological effects, in addition to resorting to methods which are being developed with the purpose of increasing bioavailability, such as the association of curcumin and piperine, use of nanoparticles, phospholipid complexes and curcumin's structural analogs (safflower oil) (Anand et al. 2007; Prasad et al. 2014; Siviero et al. 2015).

As for the physiological aspects, Szymanski et al. observed lower increase of heart rate in the curcumin-supplemented group during exercise-induced thermal stress. The remaining studies that did not report significant results have resorted to physical exercises in normal thermal conditions (McAllister et al. 2018; Sciberras et al. 2015; Takahashi et al. 2013). It is possible that the reduced heart rate is associated with the action of curcumin in the improvement of endothelial function (Santos-Parker et al. 2017; Szymanski et al. 2018), although the mechanisms have not been completely clarified.

Literature indicates that intense and prolonged physical exercises may lead to disorders in the immune system and in the GI tract (Dokladny, Zuhl, and Moseley 2016; Lim and Mackinnon 2006). These disorders, such as the increased macrophages activity, due to muscle damage, increased pro-inflammatory circulating cytokines, increased intestinal permeability, allowing the passage of gram-negative bacteria and translocation of lipopolysaccharides (LPS) (cell wall component endotoxin of the gram-negative bacteria) for systemic circulation, may enable the development of endotoxemia and hyperthermia (Lim and Mackinnon 2006). In this context, the effects of curcumin supplementation on the reduction of internal and body temperature, on PSI and on the reduction of risk of insolation appear to be secondary to its action in the improvement of GI function, in addition to its anti-inflammatory action (Szymanski et al. 2018).

The existence of investigations addressing the advantages of curcumin supplementation for the health of the GI tract (Ghosh et al. 2018; Lopresti 2018) has raised the hypothesis that the phenolic compound could help reducing gastrointestinal symptoms and intercurrences during training, thus improving sport performance. Szymanski et al. (2018) observed an improvement in the GI function after 3 days of curcumin supplementation. Some of the proposed mechanisms are related to the curcumin's capacity of significantly reduce LPS plasmatic concentration, as well as interleukin-1β (IL-1β) production by the intestinal epithelial cells and reduce the mitogen-activated protein kinase (p38 MAPK), helping the reduction of the disfunction of the intestinal barrier and inflammatory process (Wang, Ghosh, and Ghosh 2017).

In addition to the aforementioned effects, curcumin supplementation seems to be beneficial for neuropsychiatric changes and cognitive functions (Lopresti 2018; Ng et al. 2017; Zhu et al. 2019). However, little is known about its effects during physical exercise. Sciberras et al., after applying the Daily Analysis of Life Demands on Athletes (DALDA) questionnaire, observed that, after supplementation, participants reported feeling better with respect to the causes and symptoms of psychological stress, when compared to the place group. This result paves the way for future investigations on the use of this polyphenol to improve psychological parameters in sport and exercise.

Curcumin has already been approved and listed as "Generally Recognized As Safe" (GRAS) by the US Food and Drug Administration (FDA) (Gupta, Patchva, and Aggarwal 2013). Also, clinical trials assessed its safety and tolerability, by indicating that doses up to 12 g/day are safe for human consumption for a 3-month period (Gupta, Patchva, and Aggarwal 2013; Lao et al. 2006). Among the studies included in the present review, no side effects of curcumin supplementation were reported, and the doses applied were considered safe and tolerable for sport practitioners and athletes.

In this study, some strengths may be highlighted, such as its systematic approach, based on the PRISMA method, peer-review and assessment of the risk of bias through the Cochrane Collaboration tool (Higgins and Green 2008). However, it was not possible to carry out a meta-analysis of the data due to the heterogeneity of the studies. The reduced amount of papers included may also be regarded as a limitation to ensure the benefits of curcumin supplementation in sport and physical exercise in human beings. Nevertheless, this review adds new information to literature and emphasizes the need for further studies on this subject with the purpose of examining the acute and chronic effects of curcumin supplementation in different populations and sports, elucidating the mechanisms involved and establish recommended curcumin dosages in sport.

In conclusion, the evidences presented indicate that curcumin supplementation in human beings is likely safe and beneficial for sport and physical activity, due to the reduction of inflammation and oxidative stress, reduction of pain and muscle damage, improved muscle recovery, sport performance, psychological and physiological responses (thermal and cardiovascular) during training, as well as the GI function. However, curcumin is not yet considered a sports supplement with level A of evidence, therefore, more studies are still needed to confirm the results and establish a safe and effective dosage of supplementation.

Disclosure statement

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References

Ammon, H., and M. Wahl. 1991. Pharmacology of *Curcuma longa*. *Planta Medica* 57 (01):1–7. doi: 10.1055/s-2006-960004.

Anand, P., A. B. Kunnumakkara, R. A. Newman, and B. B. Aggarwal. 2007. Bioavailability of Curcumin: Problems and promises. *Molecular Pharmaceutics* 4 (6):807–18. doi: 10.1021/mp700113r.

Antonioni, A., C. Fantini, I. Dimauro, and D. Caporossi. 2019. Redox homeostasis in sport: Do athletes really need antioxidant support? *Research in Sports Medicine* 27 (2):147–65. doi: 10.1080/15438627.2018.1563899.

Chilelli, N., E. Ragazzi, R. Valentini, C. Cosma, S. Ferraresso, A. Lapolla, and G. Sartore. 2016. Curcumin and *Boswellia serrata* modulate the Glyco-oxidative status and lipo-oxidation in master athletes. *Nutrients* 8 (11):745. doi: 10.3390/nu8110745.

Clarkson, P. M., K. Nosaka, and B. Braun. 1992. Muscle function after exercise-induced muscle damage and rapid adaptation. *Medicine and Science in Sports and Exercise* 24 (5):512–20. http://www.ncbi.nlm.nih.gov/pubmed/1569847.

Davis, J. M., E. A. Murphy, M. D. Carmichael, M. R. Zielinski, C. M. Groschwitz, A. S. Brown, J. D. Gangemi, A. Ghaffar, and E. P. Mayer. 2007. Curcumin effects on inflammation and performance recovery following eccentric exercise-induced muscle damage. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* 292 (6):R2168–R2173. doi: 10.1152/ajpregu.00858.2006.

Delecroix, B., A. E. Abaïdia, C. Leduc, B. Dawson, and G. Dupont. 2017. Curcumin and piperine supplementation and recovery following exercise induced muscle damage: A randomized controlled trial. *Journal of Sports Science & Medicine* 16 (1):147–53. http://www.ncbi.nlm.nih.gov/pubmed/28344463.

Dokladny, K., M. N. Zuhl, and P. L. Moseley. 2016. Intestinal epithelial barrier function and tight junction proteins with heat and exercise. *Journal of Applied Physiology* 120 (6):692–701. doi: 10.1152/japplphysiol.00536.2015.

Falgiano, P. A., T. L. Gillum, Z. J. Schall, H. R. Strag, and M. R. Kuennen. 2018. Dietary curcumin supplementation does not alter peripheral blood mononuclear cell responses to exertional heat stress. *European Journal of Applied Physiology* 118 (12):2707–17. doi: 10.1007/s00421-018-3998-5.

Ferraro, E., A. M. Giammarioli, S. Chiandotto, I. Spoletini, and G. Rosano. 2014. Exercise-induced skeletal muscle remodeling and metabolic adaptation: Redox signaling and role of autophagy. *Antioxidants & Redox Signaling* 21 (1):154–76. doi: 10.1089/ars.2013.5773.

Garcia-Lopez, D., M. J. Cuevas, M. Almar, E. Lima, J. A. DE Paz, and J. Gonz??Lez-Gallego. 2007. Effects of eccentric exercise on NF-[kappa]B activation in blood mononuclear cells. *Medicine & Science in Sports & Exercise* 39 (4):653–64. 10.1249/mss.0b013e31802f04f6.

Ghandadi, M., and A. Sahebkar. 2017. Curcumin: An effective inhibitor of interleukin-6. *Current Pharmaceutical Design* 23 (6):921–31. https://www.ingentaconnect.com/contentone/ben/cpd/2017/00000023/00000006/art00009. doi: 10.2174/1381612822666161006151605.

Ghosh, S. S., H. He, J. Wang, T. W. Gehr, and S. Ghosh. 2018. Curcumin-mediated regulation of intestinal barrier function: The mechanism underlying its beneficial effects. *Tissue Barriers* 6 (1):e1425085. doi: 10.1080/21688370.2018.1425085.

Grazioli, E., I. Dimauro, N. Mercatelli, G. Wang, Y. Pitsiladis, L. Di Luigi, and D. Caporossi. 2017. Physical activity in the prevention of human diseases: Role of epigenetic modifications. *BMC Genomics.* 18 (S8):802. doi: 10.1186/s12864-017-4193-5.

Gupta, S. C., S. Patchva, and B. B. Aggarwal. 2013. Therapeutic roles of curcumin: Lessons learned from clinical trials. *The AAPS Journal* 15 (1):195–218. doi: 10.1208/s12248-012-9432-8.

Hewlings, S., D. Kalman, S. J. Hewlings, and D. S. Kalman. 2017. Curcumin: A review of its' effects on human health. *Foods* 6 (10):92. doi: 10.3390/foods6100092.

Higgins, J. P. T., and S. Green. 2008. Cochrane *handbook for systematic reviews of interventions*. Chichester, England: Wiley-Blackwell. https://books.google.com. br/books?hl=en&lr=&id=

NKMg9sMM6GUC&oi=fnd&pg=PT13&ots= LIXCUZAxA-&sig=FcJjfWft_BHXyRgAszdNlFZsEEI#v=onepage&q&f=false

Huang, W.-C., W.-C. Chiu, H.-L. Chuang, D.-W. Tang, Z.-M. Lee, L. Wei, F.-A. Chen, and C.-C. Huang. 2015. Effect of curcumin supplementation on physiological fatigue and physical performance in mice. *Nutrients* 7 (2):905–21. doi: 10.3390/nu7020905.

Itokawa, H., Q. Shi, T. Akiyama, S. L. Morris-Natschke, and K.-H. Lee. 2008. Recent advances in the investigation of curcuminoids. *Chinese Medicine* 3 (1):11. doi: 10.1186/1749-8546-3-11.

Jurenka, J. S. 2009. Anti-inflammatory properties of curcumin, a major constituent of Curcuma longa: A review of preclinical and clinical research. *Alternative Medicine Review: A Journal of Clinical Therapeutic* 14 (2):141–53. Retrieved fromhttp://www.ncbi.nlm.nih.gov/pubmed/19594223.

Karlapudi, V., A. V. V. Prasad Mungara, K. Sengupta, B. A. Davis, and S. P. Raychaudhuri. 2018. A placebo-controlled double-blind study demonstrates the clinical efficacy of a novel herbal formulation for relieving joint discomfort in human subjects with osteoarthritis of knee. *Journal of Medicinal Food* 21 (5):511–20. doi: 10.1089/jmf.2017.0065.

Kawanishi, N., K. Kato, M. Takahashi, T. Mizokami, Y. Otsuka, A. Imaizumi, D. Shiva, H. Yano, and K. Suzuki. 2013. Curcumin attenuates oxidative stress following downhill running-induced muscle damage. *Biochemical and Biophysical Research Communications* 441 (3):573–8. doi: 10.1016/j.bbrc.2013.10.119.

Khalaf, H., J. Jass, and P.-E. Olsson. 2010. Differential cytokine regulation by NF-κB and AP-1 in Jurkat T-cells. *BMC Immunology* 11 (1):26. doi: 10.1186/1471-2172-11-26.

Kunnumakkara, A. B., D. Bordoloi, C. Harsha, K. Banik, S. C. Gupta, and B. B. Aggarwal. 2017. Curcumin mediates anticancer effects by modulating multiple cell signaling pathways. *Clinical Science (England : 1979)* 131 (15):1781–99. doi: 10.1042/CS20160935.

Kunwar, A., and K. I. Priyadarsini. 2016. Curcumin and its role in chronic diseases. In *Anti-inflammatory Nutraceuticals and Chronic Diseases*, eds. Subash Chandra Gupta, S. Prasad, and B. B. Aggarwal, 1–25. New York: Springer. 10.1007/978-3-319-41334-1_1.

Lao, C. D., M. T. Ruffin, D. Normolle, D. D. Heath, S. I. Murray, J. M. Bailey, M. E. Boggs, J. Crowell, C. L. Rock, and D. E. Brenner. 2006. Dose escalation of a curcuminoid formulation. *BMC Complementary and Alternative Medicine* 6 (1):10. doi: 10.1186/1472-6882-6-10.

Li, H., A. Sureda, H. P. Devkota, V. Pittalà, D. Barreca, A. S. Silva, D. Tewari, S. Xu, and S. M. Nabavi. 2020. Curcumin, the golden spice in treating cardiovascular diseases. *Biotechnology Advances* 38:107343. doi: 10.1016/j.biotechadv.2019.01.010.

Lim, C. L., and L. T. Mackinnon. 2006. The roles of exercise-induced immune system disturbances in the pathology of heat stroke. *Sports Medicine* 36 (1):39–64. doi: 10.2165/00007256-200636010-00004.

Lopresti, A. L. 2018. The problem of curcumin and its bioavailability: Could its gastrointestinal influence contribute to its overall health-enhancing effects? *Advances in Nutrition* 9 (1):41–50. doi: 10.1093/advances/nmx011.

Marchiani, A., C. Rozzo, A. Fadda, G. Delogu, and P. Ruzza. 2014. Curcumin and curcumin-like molecules: From spice to drugs. *Current Medicinal Chemistry* 21 (2):204–22. https://www.ingentaconnect.com/content/ben/cmc/2014/00000021/00000002/art00004. doi: 10.2174/092986732102131206115810.

Mazieiro, R., R. R. Frizon, S. M. Barbalho, and R. D. A. Goulart. 2018. Is curcumin a possibility to treat inflammatory bowel diseases? *Journal of Medicinal Food* 21 (11):1077–85. doi: 10.1089/jmf.2017.0146.

McAllister, M. J., S. A. Basham, H. S. Waldman, J. W. Smith, M. B. Butawan, and R. J. Bloomer. 2018. Effects of curcumin on the oxidative stress response to a dual stress challenge in trained men. *Journal of Dietary Supplements*:1–12. doi: 10.1080/19390211.2018.1515142.

McFarlin, B. K., A. S. Venable, A. L. Henning, J. N. B. Sampson, K. Pennel, J. L. Vingren, and D. W. Hill. 2016. Reduced inflammatory and muscle damage biomarkers following oral supplementation with bioavailable curcumin. *BBA Clinical* 5:72–8. doi: 10.1016/j.bbacli.2016.02.003.

Miłobędzka, J., S. V. Kostanecki, and V. Lampe. 1910. Zur Kenntnis des Curcumins. *Berichte Der Deutschen Chemischen Gesellschaft* 43 (2):2163–70. doi: 10.1002/cber.191004302168.

Manikandan, P., M. Sumitra, S. Aishwarya, B. M. Manohar, B. Lokanadam, and R. Puvanakrishnan. 2004. Curcumin modulates free radical quenching in myocardial ischaemia in rats. *The International Journal of Biochemistry & Cell Biology* 36 (10):1967–80. doi: 10.1016/j.biocel.2004.01.030.

Mizumoto, A., S. Ohashi, M. Kamada, T. Saito, Y. Nakai, K. Baba, K. Hirohashi, Y. Mitani, O. Kikuchi, J. Matsubara, et al. 2019. Combination treatment with highly bioavailable curcumin and NQO1 inhibitor exhibits potent antitumor effects on esophageal squamous cell carcinoma. *Journal of Gastroenterology* 54 (8):687–12. doi: 10.1007/s00535-019-01549-x.

Mollazadeh, H., A. F. G. Cicero, C. N. Blesso, M. Pirro, M. Majeed, and A. Sahebkar. 2019. Immune modulation by curcumin: The role of interleukin-10. *Critical Reviews in Food Science and Nutrition* 59 (1):89–101. doi: 10.1080/10408398.2017.1358139.

Momtazi-Borojeni, A. A., E. Abdollahi, B. Nikfar, S. Chaichian, and M. Ekhlasi-Hundrieser. 2019. Curcumin as a potential modulator of M1 and M2 macrophages: New insights in atherosclerosis therapy. *Heart Failure Reviews* 24 (3):399–409. doi: 10.1007/s10741-018-09764-z.

Mourkioti, F., P. Kratsios, T. Luedde, Y.-H. Song, P. Delafontaine, R. Adami, V. Parente, R. Bottinelli, M. Pasparakis, and N. Rosenthal. 2006. Targeted ablation of IKK2 improves skeletal muscle strength, maintains mass, and promotes regeneration. *Journal of Clinical Investigation* 116 (11):2945–54. doi: 10.1172/JCI28721.

Nelson, K. M., J. L. Dahlin, J. Bisson, J. Graham, G. F. Pauli, and M. A. Walters. 2017. The essential medicinal chemistry of curcumin. *Journal of Medicinal Chemistry* 60 (5):1620–37. doi: 10.1021/acs.jmedchem.6b00975.

Ng, Q. X., S. S. H. Koh, H. W. Chan, and C. Y. X. Ho. 2017. Clinical use of curcumin in depression: A meta-analysis. *Journal of the American Medical Directors Association* 18 (6):503–8. doi: 10.1016/j.jamda.2016.12.071.

Nicol, L. M., D. S. Rowlands, R. Fazakerly, and J. Kellett. 2015. Curcumin supplementation likely attenuates delayed onset muscle soreness (DOMS). *European Journal of Applied Physiology* 115 (8):1769–77. doi: 10.1007/s00421-015-3152-6.

Powers, S. K., J. Duarte, A. N. Kavazis, and E. E. Talbert. 2010. Reactive oxygen species are signalling molecules for skeletal muscle adaptation. *Experimental Physiology* 95 (1):1–9. doi: 10.1113/expphysiol.2009.050526.

Prasad, S., S. C. Gupta, A. K. Tyagi, and B. B. Aggarwal. 2014. Curcumin, a component of golden spice: From bedside to bench and back. *Biotechnology Advances* 32 (6):1053–64. doi: 10.1016/j.biotechadv.2014.04.004.

Priyadarsini, K. 2014. The chemistry of curcumin: From extraction to therapeutic agent. *Molecules* 19 (12):20091–112. doi: 10.3390/molecules191220091.

Ray Hamidie, R. D., T. Yamada, R. Ishizawa, Y. Saito, and K. Masuda. 2015. Curcumin treatment enhances the effect of exercise on mitochondrial biogenesis in skeletal muscle by increasing cAMP levels. *Metabolism* 64 (10):1334–47. doi: 10.1016/j.metabol.2015.07.010.

Sahin, K., R. Pala, M. Tuzcu, O. Ozdemir, C. Orhan, N. Sahin, and V. Juturu. 2016. Curcumin prevents muscle damage by regulating NF-κB and Nrf2 pathways and improves performance: An in vivo model. *Journal of Inflammation Research* Volume 9:147–54. doi: 10.2147/JIR.S110873.

Salehi, B., Z. Stojanović-Radić, J. Matejić, M. Sharifi-Rad, N. V. Anil Kumar, N. Martins, and J. Sharifi-Rad. 2019. The therapeutic potential of curcumin: A review of clinical trials. *European Journal of Medicinal Chemistry* 163:527–45. doi: 10.1016/j.ejmech.2018.12.016.

Santos-Parker, J. R., T. R. Strahler, C. J. Bassett, N. Z. Bispham, M. B. Chonchol, and D. R. Seals. 2017. Curcumin supplementation improves vascular endothelial function in healthy middle-aged and older adults by increasing nitric oxide bioavailability and reducing oxidative stress. *Aging* 9 (1):187–208. doi: 10.18632/aging.101149.

Sciberras, J. N., S. Galloway, A. Fenech, G. Grech, C. Farrugia, D. Duca, and J. Mifsud. 2015. The effect of turmeric (Curcumin) supplementation on cytokine and inflammatory marker responses following 2 hours of endurance cycling. *Journal of the International Society of Sports Nutrition* 12 (1):5. doi: 10.1186/s12970-014-0066-3.

Sharan Patel, S., A. Acharya, R. S. Ray, R. Agrawal, R. Raghuwanshi, and P. Jain. 2019. Cellular and molecular mechanisms of curcumin in prevention and treatment of disease. *Critical Reviews in Food Science and Nutrition* 60 (6):887–53. doi: 10.1080/10408398.2018.1552244.

Singh, S., and B. B. Aggarwal. 1995. Activation of transcription factor NF-kappa B is suppressed by curcumin (diferuloylmethane) (*). *Journal of Biological Chemistry* 270 (42):24995–5000. doi: 10.1074/jbc.270.42.24995.

Siviero, A., E. Gallo, V. Maggini, L. Gori, A. Mugelli, F. Firenzuoli, and A. Vannacci. 2015. Curcumin, a golden spice with a low bioavailability. *Journal of Herbal Medicine* 5 (2):57–70. doi: 10.1016/j.hermed.2015.03.001.

Sun, J., F. Chen, C. Braun, Y.-Q. Zhou, H. Rittner, Y.-K. Tian, X.-Y. Cai, and D.-W. Ye. 2018. Role of curcumin in the management of pathological pain. *Phytomedicine* 48:129–40. doi: 10.1016/j.phymed.2018.04.045.

Szymanski, M. C., T. L. Gillum, L. M. Gould, D. S. Morin, and M. R. Kuennen. 2018. Short-term dietary curcumin supplementation reduces gastrointestinal barrier damage and physiological strain responses during exertional heat stress. *Journal of Applied Physiology* 124 (2):330–40. doi: 10.1152/japplphysiol.00515.2017.

Takahashi, M., K. Suzuki, H. Kim, Y. Otsuka, A. Imaizumi, M. Miyashita, and S. Sakamoto. 2013. Effects of curcumin supplementation on exercise-induced oxidative stress in humans. *International Journal of Sports Medicine* 35 (06):469–75. doi: 10.1055/s-0033-1357185.

Takami, M., W. Aoi, H. Terajima, Y. Tanimura, S. Wada, and A. Higashi. 2019. Effect of dietary antioxidant-rich foods combined with aerobic training on energy metabolism in healthy young men. *Journal of Clinical Biochemistry and Nutrition* 64 (1):79–85. doi: 10.3164/jcbn.18-40.

Talib, W. H., S. A. Al-Hadid, M. B. W. Ali, I. H. Al-Yasari, and M. R. A. Ali. 2018. Role of curcumin in regulating p53 in breast cancer: An overview of the mechanism of action. *Breast Cancer: Targets and Therapy* Volume 10:207–17. doi: 10.2147/BCTT.S167812.

Tanabe, Y., K. Chino, T. Ohnishi, H. Ozawa, H. Sagayama, S. Maeda, and H. Takahashi. 2019. Effects of oral curcumin ingested before or after eccentric exercise on markers of muscle damage and inflammation. *Scandinavian Journal of Medicine & Science in Sports* 29 (4):524–34. doi: 10.1111/sms.13373.

Tanabe, Y., K. Chino, H. Sagayama, H. J. Lee, H. Ozawa, S. Maed, and H. Takaha. 2019. Effective timing of curcumin ingestion to attenuate eccentric exercise-induced muscle soreness in men. *Journal of Nutritional Science and Vitaminology* 65 (1):82–9. doi: 10.3177/jnsv.65.82.

Thaloor, D., K. J. Miller, J. Gephart, P. O. Mitchell, and G. K. Pavlath. 1999. Systemic administration of the NF-κB inhibitor curcumin stimulates muscle regeneration after traumatic injury. *American Journal of Physiology-Cell Physiology* 277 (2):C320–C329. doi: 10.1152/ajpcell.1999.277.2.C320.

Vogel, H., and J. Pelletier. 1815. Curcumin – biological and medicinal properties. *Journal de Pharmacie*, 289. http://www.indsaff.com/10Curcuminbiological.pdf

Wagner, K.-H., S. Reichhold, and O. Neubauer. 2011. Impact of endurance and ultraendurance exercise on DNA damage. *Annals of the New York Academy of Sciences* 1229 (1):115–23. doi: 10.1111/j.1749-6632.2011.06106.x.

Walsh, N. P., M. Gleeson, D. B. Pyne, D. C. Nieman, F. S. Dhabhar, R. J. Shephard, S. J. Oliver, S. Bermon, and A. Kajeniene. 2011. Position statement part two: Maintaining immune health. *Exercise Immunology Review* 17:64–103. http://eir-isei.de/2011/eir-2011-064-article.pdf.

Wang, J., S. S. Ghosh, and S. Ghosh. 2017. Curcumin improves intestinal barrier function: Modulation of intracellular signaling, and organization of tight junctions. *American Journal of Physiology-Cell Physiology* 312 (4):C438–C445. doi: 10.1152/ajpcell.00235.2016.

Warburton, D. E. R., and S. S. D. Bredin. 2017. Health benefits of physical activity: A systematic review of current systematic reviews. *Current Opinion in Cardiology* 32 (5):541–56. doi: 10.1097/HCO.0000000000000437.

Zhu, L.-N., X. Mei, Z.-G. Zhang, Y. Xie, and F. Lang. 2019. Curcumin intervention for cognitive function in different types of people: A systematic review and meta-analysis. *Phytotherapy Research* 33 (3):524–33. doi: 10.1002/ptr.6257.