

REVIEW

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Effect of curcumin supplement or placebo in delayed onset muscle soreness: a systematic review and meta-analysis

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Abstract

Background: There are multiple strategies that have been suggested to attenuate delayed onset muscle soreness (DOMS). Curcumin has been shown to reduce exercise-induced oxidative stress (OS) and inflammation. However, currently, there is still controversy.

Main body of the abstract: We conduct this meta-analysis according to the PRISMA guidelines. Relevant studies were included from Medline and Scopus from the date of inception to May 04th, 2021 that reported VAS score, blood markers (creatinine kinase (CK), tumor necrotic factor (TNF)- α and interleukin (IL)-6) and range of motion of either group. There were total of 13 studies including 202 and 176 persons in curcumin and placebo group. The unstandardized mean difference (UMD) of VAS muscle soreness in post-exercise, 1, 2, 3 and 4 days was -0.12 (95% CI $-0.46, 0.22$), -0.38 ($-0.83, 0.08$), -0.67 ($-1.19, -0.16$), -0.86 ($-1.38, -0.34$), -0.81 ($-1.27, -0.36$) and -1.24 ($-1.50, -0.99$) scores lower in curcumin when compared to placebo. The UMD of CK was -11.07 (95% CI $-24, 1.86$), -37.51 ($-68.04, -6.97$), -45.40 ($-95.67, 4.86$), -53.33 ($-128.11, 21.45$), -90.98 ($-173.45, -8.51$) and 117.84 ($-338.69, 574.37$) lower in curcumin when compared to placebo. No statistically significant differences were noted for IL-6, TNF- α and ROM between two groups.

Short conclusion: This meta-analysis suggested that curcumin supplement reduced delayed onset muscle soreness and CK after exercise in 1, 2, 3, and 4 days when compared to placebo. However, TNF and IL were not affected by curcumin ingestion.

Level of evidence I.

Keywords: DOMS, Curcumin, Exercise-induced muscle soreness, Meta-analysis

Background

Delayed onset muscle soreness (DOMS) normally occurs approximately 1 to 2 days after the unaccustomed activity and eccentric muscle contraction, with a symptom of muscle soreness and discomfort (Kim and So 2019; Mizumura and Taguchi 2016; Lewis et al. 2012).

Normally, DOMS is one symptom of exercise-induced muscle damage (EIMD) (Howatson and Someren 2008). Researchers have proposed several hypotheses for the etiology of DOMS previously such as lactic acid, muscle spasms, muscle damage, and inflammatory response, whereas novel hypotheses include Toll-like receptor 4 activation, increased levels of neurotrophic factors such as nerve growth factors and glial cell line-derived neurotrophic factors; however, the exact cause of DOMS remains unclear (Urai et al. 2013; Ota et al. 2013; Cheung et al. 2003; Smith 1991; Yoon et al. 2020). Delayed onset

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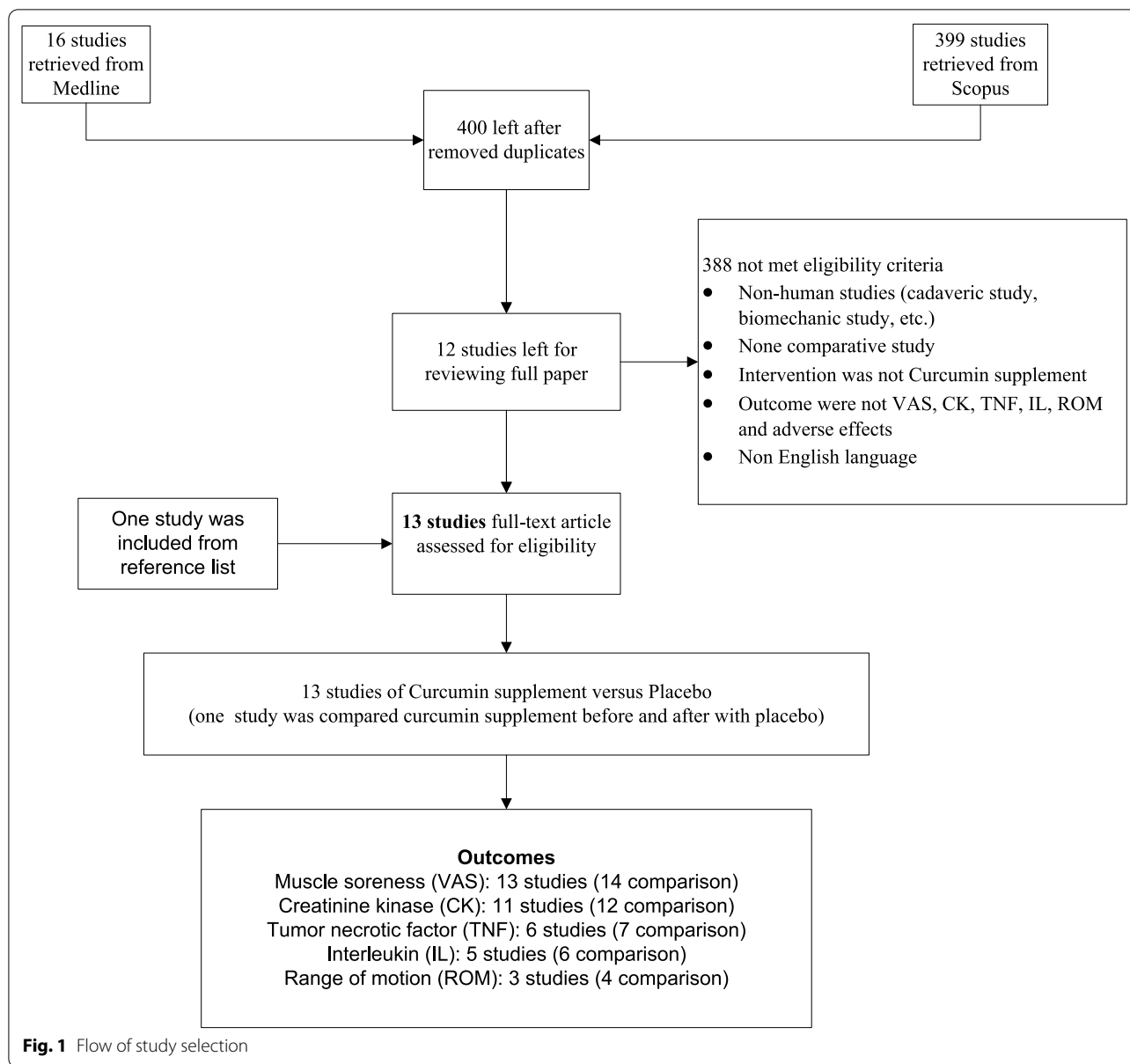


Fig. 1 Flow of study selection

muscle soreness (DOMS) is a combination of muscle pain and stiffness occurring several hours after unaccustomed exercise, particularly when eccentric muscle activity is involved, it can induce muscle damage (Tanabe et al. 2019; Clarkson et al. 1992). An inflammatory response and the reactive oxygen species (ROS) production were triggered by this mechanical stress. The reason behind this process is that the mechanical stress promotes the activation of transcription factors such as nuclear factor- κ B (NF- κ B), and it would result in limiting an athlete's performance and daily activities (García-López et al. 2007). EIMD can be manifested by prolonged decline in muscle strength, reduction in range of motion

(ROM), swelling, DOMS and an increase in blood muscle proteins, including creatine kinase (CK) activity (Clarkson et al. 1992; García-López et al. 2007; Tiidus 1998; Warren et al. 1999; Takahashi et al. 1994). Muscle function impairment caused by damaged and its subsequent inflammatory responses may reduce the ability to perform daily training and reduce athletic performance. Therefore, post-exercise muscle damage should be prevented or minimized (Tanabe et al. 2019). At present, multiple strategies have been treated to attenuate DOMS such as hyperbaric oxygen, anti-inflammatory medication, massage, cryotherapy, homeopathy, stretching, electrotherapeutic modalities, ultrasound, rest, and light

Table 1 Characteristics of included studies

Author	Year	Country	N	nc	np	RCT	N (men)	BMI	Preparation	Exercise	Age (mean)	Dose	Outcome
Drobnic F	2014	Spain	19	9	10	Parallel	19	24.6	Meriva	Downhill running	35.4	1 g bid	VAS CK
Nicol LM	2015	New Zealand	17	17	17	Crossover	17	-	Capsules	Leg press	33.8	2.5 gm bid	VAS CKTNF IL
Tanabe Y	2015	japan	14	14	14	Crossover	14	22	Theracurmin	Elbow flexor	23.5	150 mg bid	VAS CKTNF IL ROM
McFarlin BK	2016	USA	28	14	14	Parallel	10	22.5	Longvida	Leg press	19.5	200, 400, 1000 mg	VAS CKTNF IL
Naknhostin-Roochi B	2016	Iran	10	10	10	Crossover	10	25.6	Theracurmin	squat exercises	25	150 mg	VAS CK
Basham SA	2019	USA	20	20	20	Crossover	20	26.7	CurcuFresh	Leg press	21.7	1.5 g	VAS CKTNF
Amalraj A	2020	India	30	15	15	Parallel	12	23.3	AB	Downhill running	36	500 mg	VAS CK
Jäger R	2019	USA	63	42	21	Parallel	31	25.6	CurcuWIN	Downhill running	21	50, 200 mg	VAS
Tanabe Y	2019	japan	24	16	8	Parallel	24	22.1	Theracurmin	Elbow flexor	28.3	180 mg 7 day	VAS CK ROM
Tanabe Y scan	2019	japan	20	10	10	Parallel	20	23.5	Theracurmin	Elbow flexors	28.75	180 mg	VAS CKTNF IL ROM
Cardaci TD	2020	USA	23	11	12	Parallel	11	24.6	UPS	Treadmill	21.13	2 g	VAS
Mallard AR	2020	New Zealand	27	13	14	Parallel	27	25.6	Lipisperse	LL resistance	26	427 mg	VAS CKTNF IL
Hillman AR	2021	USA	22	11	11	Parallel	17	25.4	Capsules	Plyometric	21.5	475 mg	VAS CK

UPS ubiquitin proteasome system, LL lower limb, AB aurea biolabs

Table 2 Risk of bias assessment

Author	Sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective outcome report
Drobnic F	Y	Y	Y	Y	Y
Nicol LM	Y	Y	N	Y	Y
Tanabe Y	U	N	N	Y	Y
McFarlin BK	Y	Y	Y	Y	Y
Naknhostin-Roohi B	U	N	Y	Y	Y
Basham SA	U	N	Y	Y	Y
Amalraj A	Y	Y	Y	Y	Y
Jäger R	Y	Y	Y	Y	Y
Tanabe Y	U	N	N	Y	Y
Tanabe Y scan	U	N	N	Y	Y
Cardaci TD	Y	Y	Y	Y	Y
Mallard AR	Y	Y	Y	Y	Y
Hillman AR	Y	Y	Y	Y	Y

exercise. Nutritional interventions with antioxidant and anti-inflammatory properties are frequently reported to reduce DOMS.

Curcumin is a natural polyphenolic substance extracted from turmeric. It has various physiological effects, such as membrane protective effects, as well as anti-inflammatory and antioxidant responses (Thapa et al. 2013; Hatcher et al. 2008). These mechanisms have been reported to suppress the activity of NF- κ B, thereby suppressing the expression of IL-6 and tumor necrotic factor TNF- α (Cho et al. 2007; Aggarwal et al. 2006), which is a modulating factor for cytokines and cyclooxygenase (COX) (Thapa et al. 2013; Hatcher et al. 2008; Cho et al. 2007; Aggarwal et al. 2006; Chun et al. 2003). Therefore, these actions are considered to have a positive effect on DOMS. However, outcomes (muscle soreness, CK, TNF- α , IL-6 and ROM) of the curcumin and placebo are inconsistent. Some studies show benefit with intake of curcumin supplement (Tanabe et al. 2019, 2015; Hillman et al. 2021), while other studies do not (Nicol et al. 2015; McFarlin et al. 2016; Drobnic et al. 2014; Mallard and Briskey 2020; Jäger et al. 2019; Ms et al. 2020). A previous meta-analysis (Fang and Nasir 2021) found that the efficacy of curcumin in reducing CK serum levels and muscle soreness index among adults, however, it included a study that combined curcumin and piperine supplement and compared to placebo, which should be excluded. Moreover, the previous meta-analyses did not assess other relevant outcomes (TNF- α , IL-6 and ROM), importance sources of heterogeneity (e.g., preoperative exercise, age, and dosage of curcumin supplement) with subgroup analysis and publication biases were not assessed. Furthermore, some of the other randomized

controlled trial studies (RCTs) (Hillman et al. 2021; Mallard and Briskey 2020; Amalraj et al. 2020; Cardaci et al. 2020) that have since been published were not included. Therefore, this meta-analysis of curcumin supplement versus placebo was conducted. This study aims to update the comparisons between curcumin supplement and placebo of muscle soreness and CK and adds comparisons of TNF- α , IL-6 and ROM.

Main text

Search strategy and data sources

This review was conducted according to the transparent reporting of systematic reviews and meta-analyses (PRISMA guideline 2009). The search was performed in two databases: PubMed and Scopus; from the date of inception to May 04th, 2021. The keywords were used as following search terms: ((Delayed onset muscle soreness) OR (DOMS)) AND (curcumin)). Manual search for reference lists of all included studies was screened for further eligible articles identification. The studies were screened independently by two authors (J.M. and P.K.) against the eligibility criteria based on titles and abstracts using bibliographical software package, EndNote version X7. Disagreements were resolved regarding inclusion and exclusion criteria of a study with a third author (J.K.)

Inclusion criteria

Studies were included if they met the following criteria: (a) RCT and quasi-RCT studies; (b) studies that reported outcomes as following: muscle soreness index (VAS), creatinine kinase (CK); tumor necrotic factor-alpha (TNF- α), interleukin-6 (IL-6) and range of motion (ROM); (c) studies that compared clinical outcomes between

Table 3 Comparisons of VAS between curcumin supplement and placebo

Author	Curcumin			Placebo		
	N	Mean	SD	N	Mean	SD
<i>(a) VAS preexercise</i>						
Nicol LM	17	0	0	17	0	0
Tanabe Y	14	0.68	0.91	14	0.34	0.57
McFarlin BK	14	0.16	0.53	14	0.21	0.63
Naknhostin-Roohi B	10	5.93	0.19	10	5.93	0.37
Basham SA	20	3.089	0.206	20	3.795	0.206
Amalraj A (VAS 0–4)	15	2.91	0.36	15	2.65	0.459
Jäger R (200 mg)	21	0	0	21	0	0
Tanabe Y (pre)	8	0.833	0.625	8	1.04	0.94
Tanabe Y (post)	8	1.04	1.25	8	–	–
Tanabe Y scan (0–10) pre	10	0.676	0.795	10	0.636	0.477
Tanabe Y scan (0–10) post	10	0.954	1.113	10	1.193	1.113
Mallard AR (0–10)	13	0.375	0.625	14	0.375	0.5
Hillman AR	11	0.149	0.223	11	1.334	2.074
UMD (95% CI)				– 0.12 (– 0.46, 0.22)		
<i>(b) VAS post-exercise</i>						
Nicol LM	17	2	1.5	17	1.75	1.75
Tanabe Y	14	1.36	1.48	14	1.42	1.59
Jäger R (50 mg)	–	2.97	1.73	21	–	–
Jäger R (200 mg)	21	2.14	0.99	21	2.97	1.81
Tanabe Y (pre)	8	1.04	0.833	8	1.56	1.87
Tanabe Y (post)	8	1.46	1.88	8	–	–
Tanabe Y scan (0–10) pre	10	0.795	0.795	10	1.113	2.385
Tanabe Y scan (0–10) post	10	1.431	1.67	10	1.749	1.749
Mallard AR (0–10)	13	3	2.5	14	2.5	2.25
Hillman AR	11	0.963	1.334	11	2.963	2.963
UMD (95%CI)				– 0.38 (– 0.83, 0.08)		
<i>(c) VAS at 24 h</i>						
Nicol LM	17	2.87	1.33	17	3	2
Tanabe Y	14	4.32	2.5	14	4.77	1.82
McFarlin BK	14	3.53	0.32	14	4.84	0.63
Naknhostin-Roohi B	10	6.48	0.09	10	6.85	0.19
Jäger R (50 mg)	–	5.36	1.81	21	–	–
Jäger R (200 mg)	21	3.63	0.99	21	5.53	1.65
Tanabe Y (pre)	8	4.375	1.458	8	4.69	2.29
Tanabe Y (post)	8	3.44	1.46	8	–	–
Tanabe Y scan (0–10) pre	10	3.975	1.272	10	3.657	1.272
Tanabe Y scan (0–10) post	10	4.216	1.91	10	3.897	1.67
Mallard AR (0–10)	13	1.625	1.813	14	2.188	1.875
Hillman AR	11	2.667	1.778	11	4.667	3.482
UMD (95%CI)				– 0.67 (– 1.19, – 0.16)		
<i>(d) VAS at 48 h</i>						
Drobnic F	9	2.33	0.79	10	3.06	7.9
Nicol LM	17	2.2	1.33	17	3.2	2.2
Tanabe Y	14	5.45	2.05	14	5.97	2.27
McFarlin BK	14	5.26	0.42	14	6.95	0.63
Naknhostin-Roohi B	10	6.67	0.19	10	8.33	0.19
Jäger R (50 mg)	–	4.289	1.98	21	–	–

Table 3 (continued)

Author	Curcumin			Placebo		
	N	Mean	SD	N	Mean	SD
Jäger R (200 mg)	21	3.88	0.99	21	4.289	2.23
Tanabe Y (pre)	8	7.083	1.667	8	5.94	2.6
Tanabe Y (post)	8	4.89	1.67	8	–	–
Tanabe Y scan (0–10) pre	10	6.519	0.954	10	5.724	1.272
Tanabe Y scan (0–10) post	10	5.408	1.83	10	6.208	1.67
Cardaci TD	11	4.66	1.58	12	6.12	1.58
Mallard AR (0–10)	13	0.813	0.876	14	1.25	0.875
Hillman AR	11	2.667	1.852	11	5.408	3.26
UMD (95% CI)				–0.86 (–1.38, –0.34)		
<i>(e) VAS at 72 h</i>						
Tanabe Y	14	4.66	2.5	14	5	2.5
McFarlin BK	14	1.89	0.42	14	3.89	0.63
Naknhostin-Roohi B	10	6.85	0.09	10	7.96	0.19
Basham SA	20	2.5	0.206	20	2.912	0.206
Jäger R (50 mg)	–	1.65	1.73	21	–	–
Jäger R (200 mg)	21	1.73	0.91	21	1.4	1.65
Tanabe Y (pre)	8	6.04	1.35	8	6.15	1.46
Tanabe Y (post)	8	4.06	1.25	8	–	–
Tanabe Y scan (0–10) pre	10	5.565	1.272	10	5.247	1.749
Tanabe Y scan (0–10) post	10	4.77	1.83	10	6.758	0.875
Mallard AR (0–10)	13	0.188	0.438	14	0.5	0.375
Hillman AR	11	1.112	1.186	11	4.445	3.112
UMD (95%CI)				–0.81 (–1.27, –0.36)		
<i>(f) VAS at 96 h</i>						
Tanabe Y	14	2.84	2.95	14	3.3	2.61
McFarlin BK	14	0.53	0.32	14	1.79	0.63
Amalraj A (VAS 0–4)	15	1.122	0.56	15	2.35	0.51
Tanabe Y (pre)	8	3.54	1.67	8	5.31	2.71
Tanabe Y (post)	8	3.33	1.88	8	–	–
Tanabe Y scan (0–10) pre	10	3.18	1.749	10	3.419	1.749
Tanabe Y scan (0–10) post	10	3.737	1.988	10	6.042	1.272
UMD (95%CI)				–1.24 (–1.50, –0.99)		

curcumin supplement and placebo; (d) There had adequate data for extracted and pooled. We excluded studies if they were using a combination of intervention besides curcumin supplement, experimental and animal studies, reviews, letters to editor, or case reports and non-English languages studies.

Data extraction and methodology quality assessment

The data were extracted from each study through structured data extraction forms by two reviewers (N.R. and P.P.), using data extraction forms. The items extracted were baseline characteristics of the study that included average age, sex, study design, mean follow-up time and dose of curcumin. Clinical outcomes data (number of

subjects, means, and SD of VAS and CK) between groups were extracted and followed by data extraction of frequencies (adverse effect) between treatment groups. In case of any disagreements in opinion, a third author (J.M.) decision would be required. Quality assessment was performed by two authors (N.R. and P.P.) according to the Cochrane Collaboration tool for evaluating the risk of bias in order to avoid the distortion of the meta-analysis outcomes (Liberati et al. 2009). RCT studies were assessed by risk of bias followed by the PRISMA guideline recommendation based on sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of

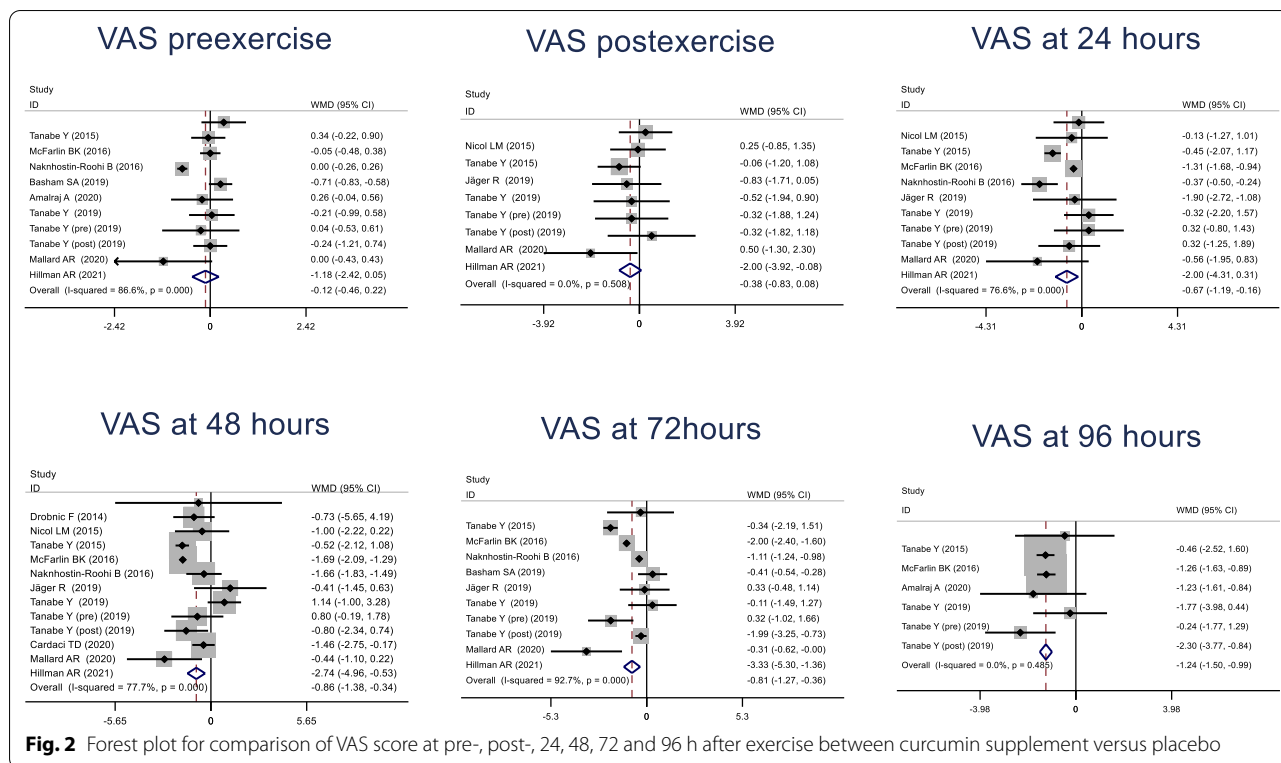


Fig. 2 Forest plot for comparison of VAS score at pre-, post-, 24, 48, 72 and 96 h after exercise between curcumin supplement versus placebo

bias. Any conflicts between reviewers for quality assessment were settled by third reviewer (J.K.).

Outcomes of interest

The outcomes were VAS of muscle soreness, CK, TNF- α , IL-6 and ROM. The measurement of those outcomes was the same as reported in the original studies, which were VAS of muscle soreness (0–10); lower values are equivalent to better outcomes. For CK, TNF- α , IL-6, lower values are equivalent to better outcomes. For ROM, higher values are equivalent to better outcomes.

Statistical methods

For continuous data, data were pooled as unstandardized mean difference (UMD) with 95% confidence interval (CI). The heterogeneity across the studies was assessed using Q statistic and I² statistic for quantifying the degree of heterogeneity. I² value equal to 0% is considered as no, 25% as low, 50% as moderate and 75% as high heterogeneity. The statistical significance for heterogeneity was set with a P value < 0.10. A random-effect model was used if I² > 25, otherwise a fixed effects model was applied. In order to explore the cause of heterogeneity, meta-regression was applied in the meta-regression model. According to the results of meta-regression, sensitivity analyses were performed by leave-one-out to assess the robustness of a pooled conclusion. The funnel plots and Egger

test were used to assess the publication bias (Palmer et al. 2020; Egger et al. 1997). The metatrim and fill method was used to estimate the number of studies that might be missing and to adjust the pooled estimate (Duval and Tweedie 2000). Data were analyzed using STATA version 15.0 (StataCorp. 2017). P value < 0.05 was considered statistically significant. P value of < 0.10 was considered as a threshold of significant heterogeneity.

Results

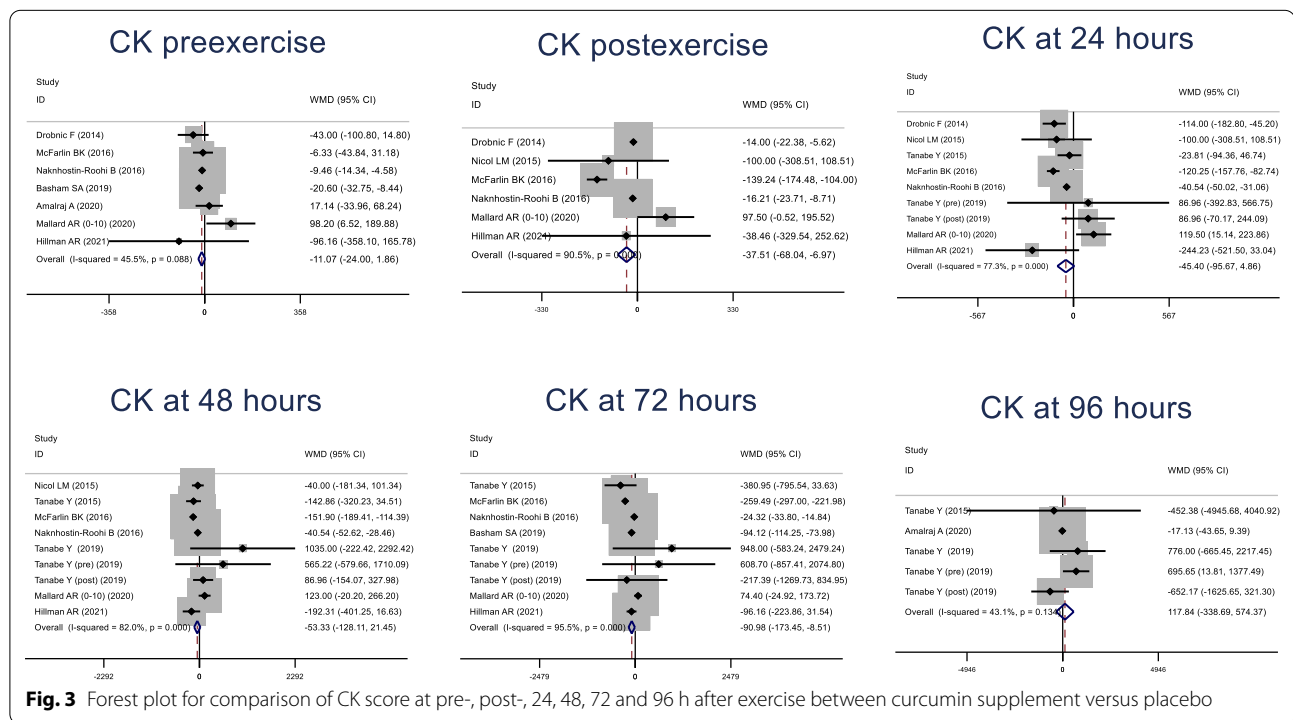
We identified 16 and 399 studies from Medline and Scopus, respectively (Fig. 1); 15 studies were duplicated, leaving 400 studies to review titles and abstracts. Of these, 12 full papers and a study, which was identified from the reference list, were reviewed and leaving a total of 13 studies for data extraction. Characteristics of the 13 studies (Tanabe et al. 2019, 2015; Hillman et al. 2021; Nicol et al. 2015; McFarlin et al. 2016; Drobnic et al. 2014; Mallard and Briskey 2020; Jäger et al. 2019; Ms et al. 2020; Amalraj et al. 2020; Cardaci et al. 2020; Nakhostin-Roohi et al. 2016) are described in Table 1. All studies were RCTs. Nine studies were parallel design, while four studies were crossover design. All 13 studies (Tanabe et al. 2019, 2015; Hillman et al. 2021; Nicol et al. 2015; McFarlin et al. 2016; Mallard and Briskey 2020; Jäger et al. 2019; Ms et al. 2020; Amalraj et al. 2020; Cardaci et al. 2020; Nakhostin-Roohi et al. 2016) were reported of post-exercise muscle

Table 4 Comparisons of CK between curcumin supplement and placebo

Author	Curcumin			Placebo		
	N	Mean	SD	N	Mean	SD
<i>(a) CK preexercise</i>						
Drobnic F	9	193	64.18	10	236	64.18
McFarlin BK	14	88.61	50.63	14	94.94	50.63
Naknhostin-Roohi B	10	36.49	6.76	10	45.95	4.05
Basham SA	20	214.7	14.7	20	235.295	23.53
Amalraj A	15	129.79	93.06	15	112.65	39.18
Mallard AR (0–10)	13	278.6	144.3	14	180.4	90.6
Hillman AR	11	230.77	288.47	11	326.93	336.54
UMD (95% CI)					– 11.07 (– 24.00, 1.86)	– 11.07 (– 24.00, 1.86)
<i>(b) CK post-exercise</i>						
Drobnic F	9	250	9.3	10	264	9.3
Nicol LM	17	100	300	17	200	320
McFarlin BK	14	234.18	44.3	14	373.42	50.63
Naknhostin-Roohi B	10	67.57	10.82	10	83.78	5.405
Mallard AR (0–10)	13	329.1	147.8	14	231.6	107.2
Hillman AR	11	326.93	307.71	11	365.39	384.62
UMD (95%CI)					– 37.51 (– 68.04, – 6.97)	
<i>(c) CK at 24 h</i>						
Drobnic F	9	579	76.4	10	693	76.4
Nicol LM	17	100	300	17	200	320
Tanabe Y	14	23.809	95.238	14	47.619	95.238
McFarlin BK	14	151.9	50.63	14	272.15	50.63
Naknhostin-Roohi B	10	68.92	10.82	10	109.46	10.82
Tanabe Y	8	344	647	8	0	0
Tanabe Y (pre)	10	260.87	608.696	10	173.913	478.261
Tanabe Y (post)	10	130.435	217.391	10	43.478	130.435
Mallard AR (0–10)	13	380.3	166.1	14	260.8	99.9
Hillman AR	11	255.77	326.93	11	500	336.54
UMD (95%CI)					– 45.40 (– 95.67, 4.86)	
<i>(d) CK at 48 h</i>						
Nicol LM	17	50	220	17	90	200
Tanabe Y	14	47.619	59.524	14	190.476	333.333
McFarlin BK	14	139.24	50.63	14	291.14	50.63
Naknhostin-Roohi B	10	75.68	10.82	10	116.22	16.21
Tanabe Y	8	1164	1810	8	129	129
Tanabe Y (pre)	10	1000	1652.174	10	434.783	826.087
Tanabe Y (post)	10	304.348	173.913	10	217.391	347.826
Mallard AR (0–10)	13	348.5	249.4	14	225.5	88
Hillman AR	11	211.54	134.62	11	403.85	326.94
UMD (95%CI)					– 53.33 (– 128.11, 21.45)	
<i>(e) CK at 72 h</i>						
Tanabe Y	14	452.38	214.286	14	833.333	761.905
McFarlin BK	14	145.57	50.63	14	405.06	50.63
Naknhostin-Roohi B	10	78.38	10.82	10	102.7	10.82
Basham SA	20	200	35.29	20	294.118	29.412
Tanabe Y	8	1681	2069	8	733	776
Tanabe Y (pre)	10	1608.696	1913.043	10	1000	1391.304

Table 4 (continued)

Author	Curcumin			Placebo		
	N	Mean	SD	N	Mean	SD
Tanabe Y (post)	10	826.087	1086.957	10	1043.478	1304.348
Mallard AR (0–10)	13	285.4	125	14	211	138.3
Hillman AR	11	192.31	115.39	11	288.47	182.7
UMD (95%CI)					- 90.98 (- 173.45, - 8.51)	
					- 90.98 (- 173.45, - 8.51)	
<i>(f) CK at 96 h</i>						
Tanabe Y	14	309.524	333.333	14	761.905	8571.43
Amalraj A	15	107.76	41.63	15	124.89	31.84
Tanabe Y	8	2026	1724	8	1250	1164
Tanabe Y (pre)	10	1869.565	169.552	10	1173.913	1086.957
Tanabe Y (post)	10	1086.957	1173.913	10	1739.13	1043.478
UMD (95%CI)					117.84 (- 338.69, 574.37)	



soreness using VAS. Indirect markers of muscle damage were reported using CK in 11 studies (Tanabe et al. 2019, 2015; Hillman et al. 2021; Nicol et al. 2015; McFarlin et al. 2016; Drobnic et al. 2014; Mallard and Briskey 2020; Ms et al. 2020; Amalraj et al. 2020; Nakhostin-Roohi et al. 2016), TNF- α in six studies (Tanabe et al. 2019, 2015; Nicol et al. 2015; McFarlin et al. 2016; Mallard and Briskey 2020; Ms et al. 2020) and IL-6 in five studies (Tanabe et al. 2019, 2015; Nicol et al. 2015; McFarlin et al. 2016; Mallard and Briskey 2020). Post-exercise ROM was reported in three studies (Tanabe et al. 2019, 2015). Mean

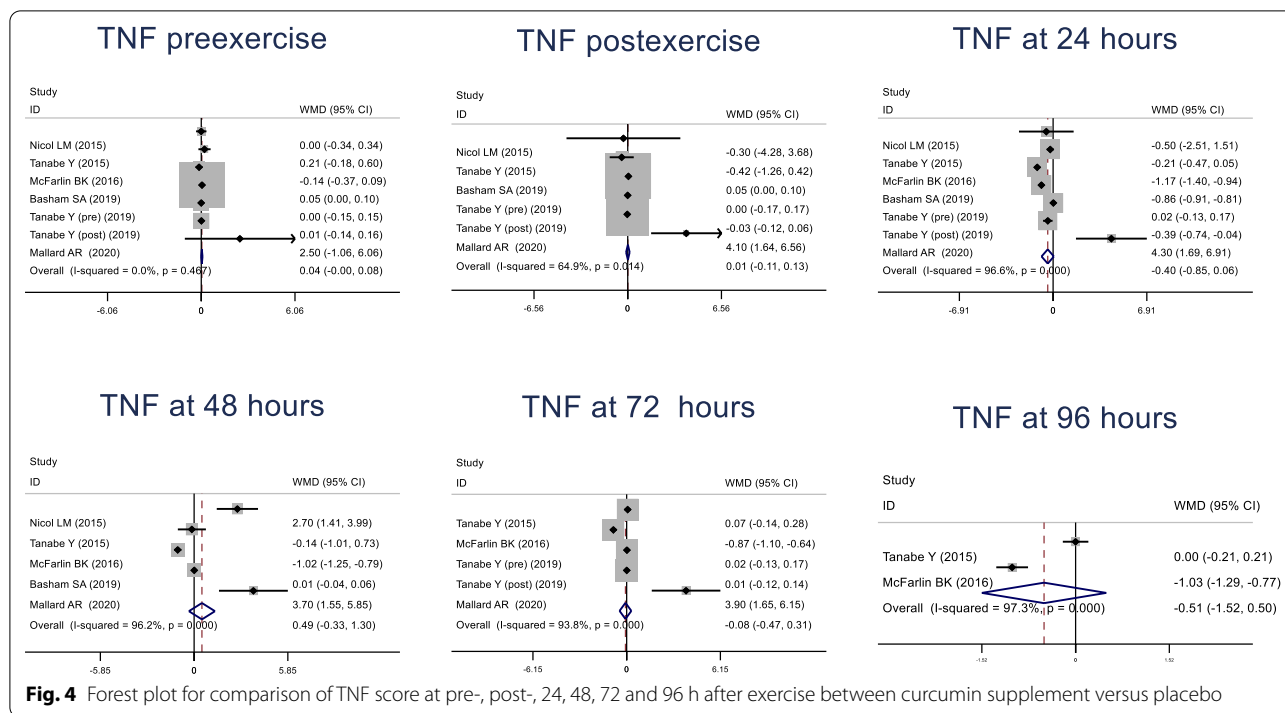
age and BMI of participants varied from 19.5 to 36 years and 22 to 26.2, respectively. Eight studies reported percentages of male gender 100 percent. While four studies reported percentages of male gender from 36 to 77 percent. Eight studies were active exercise, while five studies were resistive exercise.

Risk of bias in included studies

Risk of bias is described in Table 2. Among 13 studies, no selective outcome reporting and incomplete outcome

Table 5 Comparisons of TNF between curcumin supplement and placebo

Author	Curcumin			Placebo		
	N	Mean	SD	N	Mean	SD
<i>(a) TNF preexercise</i>						
Nicol LM	17	-0.5	0	17	-0.5	0
Tanabe Y	14	1.83	0.7	14	1.62	0.28
McFarlin BK	14	3.73	0.22	14	3.87	0.37
Basham SA	20	1.17	0.1	20	1.12	0.04
Tanabe Y (pre)	10	0.63	0.18	10	0.63	0.17
Tanabe Y (post)	10	0.59	0.16	10	0.58	0.18
Mallard AR	13	8	5.5	14	5.5	3.7
UMD (95% CI)				0.04 (-0.00, 0.08)		
<i>(b) TNF post-exercise</i>						
Nicol LM	17	2.5	2.5	17	2.8	8
Tanabe Y	14	1.55	0.42	14	1.97	1.55
Basham SA	20	1.14	0.1	20	1.09	0.04
Tanabe Y (pre)	10	0.61	0.19	10	0.61	0.19
Tanabe Y (post)	10	0.59	0.11	10	0.62	0.09
Mallard AR	13	7.5	3.4	14	3.4	3.1
UMD (95%CI)				0.01 (-0.11, 0.13)		
<i>(c) TNF at 24 h</i>						
Nicol LM	17	1.5	1.4	17	2	4
Tanabe Y	14	1.62	0.35	14	1.83	0.35
McFarlin BK	14	3.58	0.22	14	4.75	0.37
Basham SA	20	0.1	0.1	20	0.96	0.04
Tanabe Y (pre)	10	0.58	0.19	10	0.56	0.14
Tanabe Y (post)	10	0.16	0.54	10	0.55	0.17
Mallard AR	13	8.4	4.1	14	4.1	2.6
UMD (95%CI)				-0.40 (-0.85, 0.06)		
<i>(d) TNF at 48 h</i>						
Nicol LM	17	3.5	0.5	17	0.8	2.66
Tanabe Y	14	2.04	0.77	14	2.18	1.48
McFarlin BK	14	3.73	0.22	14	4.75	0.37
Basham SA	20	1.08	0.1	20	1.07	0.07
Mallard AR	13	7.2	3.5	14	3.5	1.9
UMD (95%CI)				0.49 (-0.33, 1.30)		
<i>(e) TNF at 72 h</i>						
Tanabe Y	14	1.83	0.28	14	1.76	0.28
McFarlin BK	14	3.73	0.22	14	4.6	0.37
Tanabe Y (pre)	10	0.58	0.18	10	0.56	0.15
Tanabe Y (post)	10	0.59	0.13	10	0.58	0.17
Mallard AR	13	7.4	3.5	14	3.5	2.3
UMD (95%CI)				-0.08 (-0.47, 0.31)		
<i>(f) TNF at 96 h</i>						
Tanabe Y	14	1.83	0.28	14	1.83	0.28
McFarlin BK	14	3.65	0.22	14	4.68	0.44
UMD (95%CI)				-0.51 (-1.52, 0.50)		



report, followed by blinding (9/13), sequence generation (8/13) and allocation concealment (8/13).

Outcomes

VAS of muscle soreness at pre- and post-exercise, 24, 48, 72 and 96 h

The mean values of VAS of muscle soreness between curcumin and placebo in post-exercise person at pre- and post-exercise, 24, 48, 72 and 96 h are shown in Table 3 and Fig. 2. The pooled UMD was -0.12 (95% CI -0.46, 0.22), -0.38 (-0.83, 0.08), -0.67 (-1.19, -0.16), -0.86 (-1.38, -0.34), -0.81 (-1.27, -0.36) and -1.24 (-1.50, -0.99), i.e., mean VAS muscle soreness was approximately -0.7, -0.9, -0.8 and -1.2 score statistically significant difference between two groups at 24, 48, 72 and 96 h (Table 3; Fig. 2). Separately fitting preoperative exercise, age, sex, and body mass index and dosage of curcumin supplement at baseline in a meta-regression analysis and none of the co-variables could explain the heterogeneity. Egger’s test and a contour funnel plot did not suggest any evidence of publication bias.

CK at pre- and post-exercise, 24, 48, 72 and 96 h

The mean values of CK between curcumin and placebo in post-exercise person at pre- and post-exercise, 24, 48, 72 and 96 h are shown in Table 4 and Fig. 3. The UMD was -11.07 (95% CI -24, 1.86), -37.51 (-68.04, -6.97), -45.40 (-95.67, 4.86), -53.33

(-128.11, 21.45), -90.98 (-173.45, -8.51) and 117.84 (-338.69, 574.37) U/L, i.e., mean CK was approximately -38 and -91 U/L statistically significant difference between two groups at post-exercise and 72 h (Table 4; Fig. 3). None of the co-variables could explain the heterogeneity. Egger’s test and a contour funnel plot did not suggest any evidence of publication bias.

TNF-α at pre- and post-exercise, 24, 48, 72 and 96 h

The mean values of TNF-α between curcumin and placebo in post-exercise person at pre- and post-exercise, 24, 48, 72 and 96 h are shown in Table 5 and Fig. 4. The UMD was -0.04 (95% CI -0.00, 0.08), 0.01 (-0.11, 0.13), -0.40 (-0.85, 0.06), 0.49 (-0.33, 1.30), -0.08 (-0.47, 0.31) and -0.51 (-1.52, 0.50) pg/mL, i.e., mean TNF-α was not significant difference between two groups at post any time point. Egger’s test and a contour funnel plot did not suggest any evidence of publication bias.

IL-6 at pre- and post-exercise, 24, 48, 72 and 96 h

The mean values of IL-6 between curcumin and placebo in post-exercise person at preexercise, 24, 48, 72 and 96 h are shown in Table 6 and Fig. 5. UMD was -0.03 (95% CI -0.35, 0.32), -0.46 (-1.12, 0.02), -0.49 (-1.52, 0.54), -0.29 (-0.72, 0.14) and -1.00 (-1.83, -0.16) pg/mL, i.e., mean IL-6 was approximately -1 pg/mL statistically significant difference between two groups at 96 h. None of the co-variables could explain the heterogeneity.

Table 6 Comparisons of IL between curcumin supplement and placebo

Author	Curcumin			Placebo		
	N	Mean	SD	N	Mean	SD
<i>(a) IL preexercise</i>						
Nicol LM	17	0	0	17	0	0
Tanabe Y	14	0.85	0.14	14	0.7	0.14
McFarlin BK	14	2.84	0.41	14	3.51	0.68
Tanabe Y scan pre	10	2.66	0.41	10	2.33	0.25
Tanabe Y scan post	10	2.58	0.41	10	2.62	0.66
Mallard AR (0–10)	13	12.1	10.1	14	10.1	22
UMD (95% CI)					−0.03 (−0.35, 0.32)	
<i>(b) IL at 24 h</i>						
Nicol LM	17	0	0	17	0.42	1.875
Tanabe Y	14	0.77	0.21	14	1.13	0.56
McFarlin BK	14	2.36	0.41	14	3.72	0.68
Tanabe Y scan pre	10	2.7	0.5	10	3.11	0.99
Tanabe Y scan post	10	2.99	0.33	10	2.7	0.86
Mallard AR (0–10)	13	13.5	10.7	14	10.7	11.1
UMD (95%CI)					−0.46 (−1.12, 0.02)	
<i>(c) IL at 48 h</i>						
Nicol LM	17	0.56	1.03	17	0	0
Tanabe Y	14	0.92	0.28	14	0.92	0.42
McFarlin BK	14	2.5	0.34	14	3.58	0.68
Mallard AR (0–10)	13	14.4	12	14	12	11.6
UMD (95%CI)					−0.49 (−1.52, 0.54)	
<i>(d) IL at 72 h</i>						
Tanabe Y	14	0.92	0.42	14	1.27	0.56
McFarlin BK	14	2.64	0.41	14	3.45	0.68
Tanabe Y scan pre	10	3.15	0.58	10	2.82	0.62
Tanabe Y scan post	10	2.53	0.82	10	2.78	0.49
Mallard AR (0–10)	13	12.2	11.6	14	11.7	10
UMD (95%CI)					−0.29 (−0.72, 0.14)	
<i>(e) IL at 96 h</i>						
Tanabe Y	14	1.76	2.53	14	1.9	1.97
McFarlin BK	14	2.3	0.41	14	3.51	0.68
UMD (95%CI)					−1.00 (−1.83, −0.16)	

Egger's test and a contour funnel plot did not suggest any evidence of publication bias.

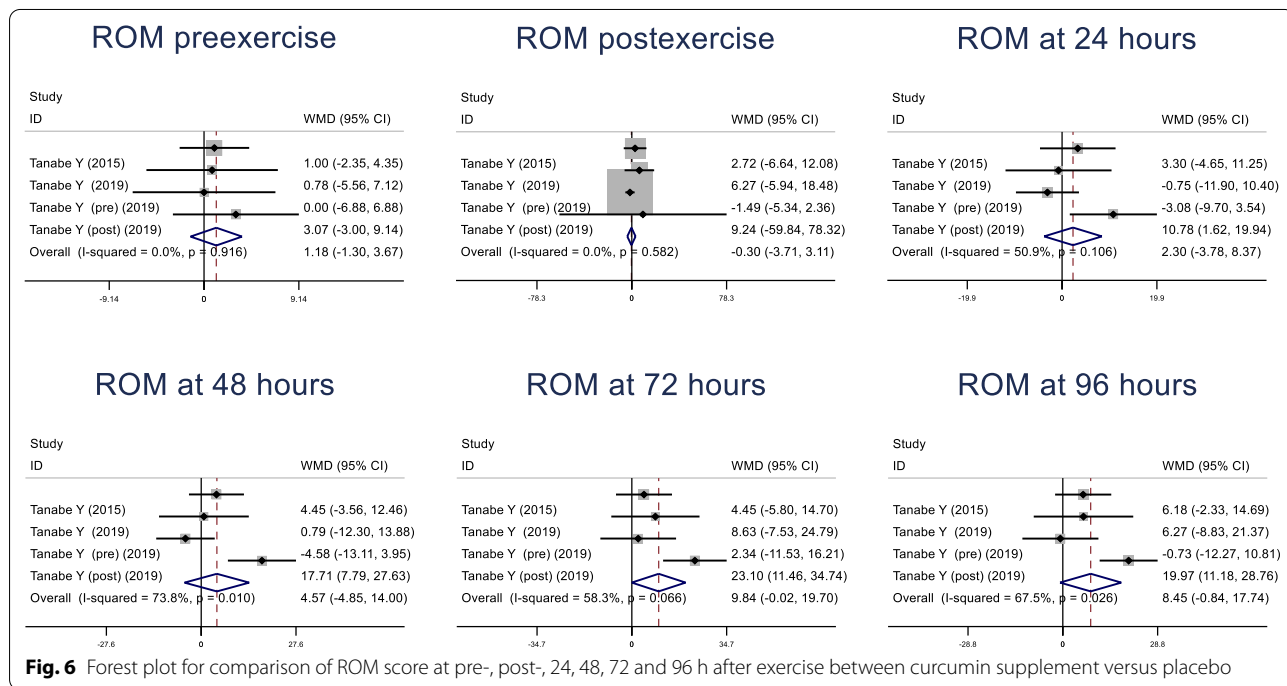
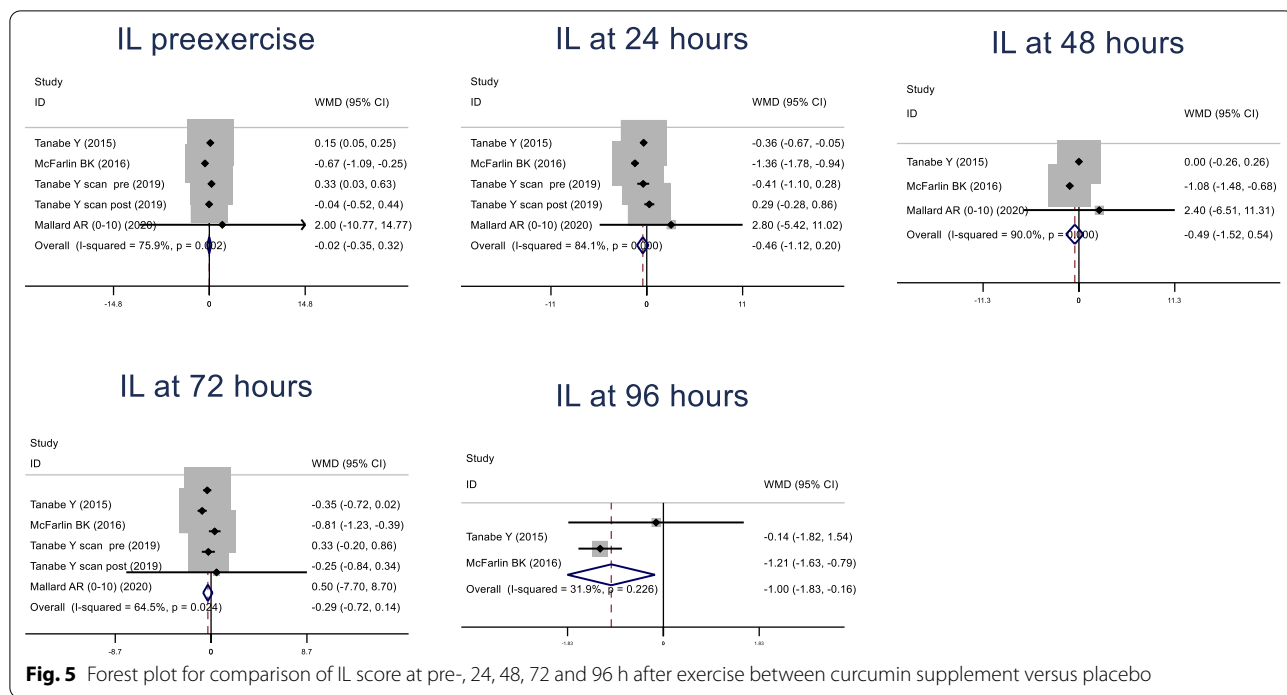
ROM at pre- and post-exercise, 24, 48, 72 and 96 h

The mean values of ROM between curcumin and placebo in post-exercise (eccentric elbow flexion) person at pre- and post-exercise, 24, 48, 72 and 96 h are shown in Table 7 and Fig. 6. The UMD was 1.18 (95% CI −1.30, 3.67), −0.30 (−3.71, 3.11), 2.30 (−3.78, 8.37), 4.57 (−4.85, 14.00), 9.84 (−0.02, 19.70) and 8.45 (−0.84, 17.74) pg/mL, i.e., mean ROM had no statistically significant difference between two groups. Egger's test and a

contour funnel plot did not suggest any evidence of publication bias.

Discussion

This review suggested that persons who took curcumin supplement before exercise have pain score of about 1 score lower than those who took placebo in and post-exercise at 1, 2, 3 and 4 days. For indirect markers of muscle damage, the persons who took curcumin supplement before exercise have lower CK, TNF and IL score than those who took placebo. However, TNF and IL have no statistically significant difference between those two



groups. In terms of ROM, no difference between the two groups in all follow-up time was shown. After all outcomes were pooled and the sources of heterogeneity were explored by meta-regression analysis, the differences of all co-variables were shown to have no effect on all outcomes.

From a review of previous meta-analysis (Fang and Nasir 2021), curcumin has efficacy in reducing CK serum levels and muscle soreness index among adults. Therefore, curcumin may be known as a priority EIMD recovery agent in interventions. However, previous meta-analyses have limitations as following: Included one study

Table 7 Comparisons of ROM between curcumin supplement and placebo

Author	Curcumin			Placebo		
	N	Mean	SD	N	Mean	SD
<i>(a) ROM preexercise</i>						
Tanabe Y	14	134	4	14	133	5
Tanabe Y	8	136.47	4.71	8	135.69	7.84
Tanabe Y (pre)	10	133.85	9.24	10	133.85	6.16
Tanabe Y (post)	10	136.92	6.93	10	133.85	6.93
UMD (95% CI)					1.18 (− 1.30, 3.67)	
<i>(b) ROM post-exercise</i>						
Tanabe Y	14	115.03	12.64	14	112.31	12.64
Tanabe Y	8	116.86	6.27	8	110.59	16.47
Tanabe Y (pre)	10	116.2	5.39	10	117.69	3.08
Tanabe Y (post)	10	119.28	110.77	10	110.04	12.32
UMD (95% CI)					− 0.30 (− 3.71, 3.11)	
<i>(c) ROM at 24 h</i>						
Tanabe Y	14	116.76	12.07	14	113.46	9.196
Tanabe Y	8	112.98	10.98	8	113.73	11.76
Tanabe Y (pre)	10	109.23	5.39	10	112.31	9.23
Tanabe Y (post)	10	119.28	9.23	10	108.5	11.55
UMD (95%CI)					2.30 (− 3.78, 8.37)	
<i>(d) ROM at 48 h</i>						
Tanabe Y	14	118.48	12.64	14	114.03	8.62
Tanabe Y	8	106.67	12.55	8	105.88	14.11
Tanabe Y (pre)	10	103.11	6.16	10	107.69	12.31
Tanabe Y (post)	10	118.51	9.23	10	100.8	13.08
UMD (95%CI)					4.57 (− 4.85, 14.00)	
					4.57 (− 4.85, 14.00)	
<i>(e) ROM at 72 h</i>						
Tanabe Y	14	119.06	12.64	14	114.61	14.94
Tanabe Y	8	106.67	17.25	8	98.04	15.69
Tanabe Y (pre)	10	106.19	16.94	10	103.85	14.62
Tanabe Y (post)	10	120.05	10.77	10	96.95	15.38
UMD (95%CI)					9.84 (− 0.02, 19.70)	
<i>(f) ROM at 96 h</i>						
Tanabe Y	14	122.51	11.49	14	116.33	11.49
Tanabe Y	8	109.8	18.82	8	103.53	10.98
Tanabe Y (pre)	10	110.04	9.24	10	110.77	16.16
Tanabe Y (post)	10	123.85	9.23	10	103.88	10.77
UMD (95%CI)					8.45 (− 0.84, 17.74)	

(Delecroix et al. 2017) that reported a combination of curcumin and piperine, which is not equal to curcumin alone; did not explore the outcomes such as IL, TNF and ROM of curcumin when compared to placebo.

This study has several strengths. First of all, this study included 13 studies in the pooling of all important clinical outcomes of curcumin supplement and placebo. Secondly, we explore the possible causes of heterogeneity, when covariate data at baseline are available. Publication bias for each outcome was assessed. However,

there are some limitations in this study. The scope of this study does not include other important outcomes such as adverse effects and cost-effective analysis, since there are incomplete data. Finally, only English publications were considered in this study. At present, more than one supplement is consumed before exercise to reduce pain after playing sports (EIMD or DOMS). This may be more effective than using one alone, but there is no comparative research yet. In the future, there should be more RCT studies to responding to playing sports effectively.

Moreover, further RCT studies that assess combine effect of cost-effective analysis should be performed.

Conclusion

To conclude, curcumin supplement has reduced muscle soreness and CK after exercise after 1, 2, 3, and 4 days when compared to placebo. On the other hand, TNF and IL were not affected by curcumin ingestion. Further RCT studies that assess cost-effective analysis should be performed.

Abbreviations

DOMS: Delayed-onset muscle soreness; ROS: Reactive oxygen species; NF- κ B: Nuclear factor- κ B; ROM: Range of motion; CK: Creatine kinase; IL: Interleukin; TNF: Tumor necrotic factor; COX: Cyclooxygenase; RCTs: Randomized controlled trial studies; VAS: Visual analog score; SD: Standard deviation; UMD: Unstandardized mean difference.

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Authors' contributions

NR was responsible for the conception and design research, collection data, analysis and interpretation results of the data, prepared figure, drafting manuscript. PP was responsible for the collection research data and assembly of data. JM was responsible for manuscript writing; JM edited and revised manuscript for important intellectual contents; and JM contributed to final approval of the article. KC was responsible for the collection research data and assembly of data. JK was responsible for the conception and design, and JK supervised in analysis and interpretation data, edited and revised manuscript, critical revision of the manuscript, approved final version of manuscript and statistical expertise. All authors have read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Declarations

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing of interests

None.

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