

Tart cherry and pomegranate supplementations enhance recovery from exercise-induced muscle damage: a systematic review

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ABSTRACT: Phenolic compounds have antioxidant and anti-inflammatory properties and may prevent inflammation and oxidative stress as well as help the athletes to recover from exercise-induced muscle damage (EIMD). Tart cherry (TC) and pomegranate (PG) are two fruits with high content of polyphenols. Their antioxidant and anti-inflammatory properties have recently attracted substantial interest for their potential to reduce strength loss and promote recovery from EIMD. The aims of this review are (1) to summarise the effects of tart cherry and pomegranate supplementation on oxidative stress, inflammation and recovery, and (2) to outline the differences found in supplementation with tart cherries or pomegranates. SPORTDiscus, PubMed, Web of Science and Scopus were searched according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis and 25 studies were included. The existing evidence suggests that both types of supplementation are good strategies to accelerate recovery of functional performance variables, perceptual variables and inflammation but PG supplementation shows better recovery of oxidative stress. However, positive effects are more likely: 1) when supplementation starts some days before muscle damage is induced and finishes some days after, for a total period of at least 8/10 days, 2) with pronounced muscle damage of the muscles involved, and 3) when total phenolic content is at least 1000 mg/day. This review may help to optimise TC or PG supplementation practice to improve post-exercise recovery.

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INTRODUCTION

Strenuous muscular exercise increases production of reactive oxygen species (ROS), free radicals and non-radical reactive molecules, which may lead to oxidative stress, inflammation and cellular damage [1–3]. This exercise-induced muscle damage is characterized by a temporary loss of force production and delayed onset muscle soreness (DOMS), which have a negative impact on exercise performance [4–6].

Exercise-induced muscle damage (EIMD) has been described as a two-phase process [5]. The first phase is the initial muscle damage caused by strenuous exercise and involves mechanical disruption to sarcomeres and oxidative stress due to an increase in the production of ROS. This muscle damage triggers an inflammatory response associated with secondary muscle damage and remodelling, which may delay the complete recovery of muscle function [6–10].

This is why supplementation with antioxidant and anti-inflammatory nutrients may play an important role in optimizing recovery, attenuating oxidative stress, inflammation and muscle soreness and

improving strength recovery [9], which would be beneficial for athletes' performance.

Antioxidant and anti-inflammatory treatments including ibuprofen and non-steroidal anti-inflammatory drugs (NSAIDs) have been traditionally used to reduce inflammation and DOMS [11, 12]. However, due to their gastrointestinal, renal and cardiovascular adverse effects [5], there is increasing interest in dietary strategies to reduce inflammation and promote recovery.

Recent nutritional research has focused on supplementation with natural nutrients with high concentration of phenolic compounds [13]. These compounds have antioxidant and anti-inflammatory properties and may prevent exercise-induced muscle damage, attenuate inflammation and oxidative stress as well as help the athletes to recover from the oxidative stress produced by free radicals [14–16].

Under physiological conditions a balanced diet is sufficient to keep the balance between oxidants and antioxidants while during intensive physical activities there is an increase in oxidant molecules

that points to a failure of the antioxidative system [15]. The polyphenolic compounds contain a number of hydroxyl groups attached to ring structures, conferring antioxidant properties to these compounds that can exert a protective effect by scavenging free radicals or as iron or copper chelating agents [15, 16]. They can also inhibit the activity of the enzymes responsible for ROS production and indirectly stimulate the expression of antioxidant enzyme genes, such as those for superoxide dismutase or glutathione peroxidase [16].

Tart cherry (TC) and pomegranate (PG) are two fruits whose juices have been widely used as supplementation in sports due to their high levels of polyphenols [8, 17, 18]. Their antioxidant and anti-inflammatory properties have recently attracted substantial interest for their potential to reduce strength loss and promote recovery from EIMD [8, 17, 18]. Polyphenol supplementation with TC or PG may reduce damage induced by oxidative stress and lipid peroxidation, leading to improvements in plasma antioxidant status and reducing cellular inflammation and muscle pain [17–21].

Of the various polyphenol-rich foods studied so far, TC and PG have arguably shown the most potential for promoting recovery from EIMD [8]. However, some studies have shown somewhat equivocal results. In their review, Vitale *et al.* [17] state that it appears that TC has significant anti-inflammatory and antioxidant effects with promising results for athletes, but a consensus on those effects has not been reached. Ammar *et al.* [18] suggest that PG supplementation could be a more effective treatment to improve performance and muscle recovery than other polyphenol-rich foods such as tart cherries, but further research is required.

Due to the increasing interest in tart cherry or pomegranate supplementation, there have been some important studies carried out in the last 2/3 years not included in the last reviews. Therefore, the aims of this review are (1) to summarize the effects of tart cherry and pomegranate supplementation on oxidative stress, inflammation and recovery, including the results of recent studies, and (2) to outline the differences found in supplementation with tart cherries or pomegranates.

MATERIALS AND METHODS

The protocol for this systematic review was designed in accordance with the Preferred Reporting of Systematic Reviews and Meta-Analyses (PRISMA) statement [22].

Inclusion and exclusion criteria

The studies included in this systematic review needed to fulfil the following inclusion criteria: (i) research conducted with human participants, (ii) original articles in peer-reviewed publications, (iii) original studies that had investigated a tart cherry or pomegranate supplementation intervention on muscle damage and recovery, (iv) research conducted with control/placebo groups, and (v) articles published between January 2005 and September 2019. Exclusion criteria were: (i) research conducted with animals, (ii) conferences or posters from congress, (iii) non-English articles, and (iv) systematic reviews or meta-analyses.

Search strategy

The following electronic databases were searched from January 2005 to September 2019: SPORTDiscus, PubMed, Web of Science and Scopus. The search strategy was limited to publications in English. The following search terms were used for tart cherry articles: (tart cherry OR Montmorency cherry) (Title) AND (muscle damage (All Fields) OR oxidative stress (All Fields) OR recovery (All Fields) OR exercise (All Fields) OR muscle pain (All Fields)). The following search terms were used for pomegranate articles: (pomegranate OR *punica granatum* or ellagitannin) (Title) AND (muscle damage (All Fields) OR oxidative stress (All Fields) OR recovery (All Fields) OR exercise (All Fields) OR muscle pain (All Fields)). Additional hand searching of the reference lists of identified papers and previously published systematic reviews was conducted.

Data extraction

Two of the four authors independently did the literature search, the data extraction and the quality assessment. All disagreements in opinion were resolved by a consensus meeting. The titles of the initial search were screened. Then the abstracts of all the potential articles were screened to decide whether they met the inclusion criteria. Finally, eligible full-text articles were reviewed. The following data were extracted from each study: first author name, year of publication, the intervention and placebo group characteristics, dosage of supplements, supplementation duration and exercise protocol to induce muscle damage. The outcomes extracted were the effects of supplementation on functional performance variables, perceptual variables, markers of inflammation and markers of oxidative stress.

Quality assessment

The PEDro scale was used to assess the quality of the selected studies. The PEDro scale is based on the Delphi list developed by Verhagen *et al.* [23] and is a reliable and objective tool that helps identify which studies are likely to be externally valid (criterion 1), internally valid (criteria 2–9) and could have sufficient statistical information to make their results interpretable (criteria 10 and 11) [18]. Points are only awarded when a criterion is clearly satisfied, and criterion one, which relates to external validity, is not used to calculate the PEDro score. Each manuscript was assessed by two of the four authors and discrepant results were resolved through a consensus meeting.

From previous studies [24, 25], a score of 9–10 on the PEDro scale was considered to be “high quality”, scores of 5–8 were considered to be “moderate quality” and studies that scored below 5 were considered to be “low quality”. All the studies included in this review were “moderate quality” or “high quality” studies.

RESULTS

Overall 625 studies were identified through initial database search (126 with tart cherry supplementation and 499 with pomegranate supplementation). After screening the titles and removing the duplicates

TABLE 1. Characteristics of the studies with TC supplementation.

Study	Subjects	Groups	Age (years) (mean ± sd)	Phenolic content/ number cherries per day	Duration	Exercise protocol to induce muscle damage
Connolly et al. [33]	Male college students	14 (TC) 14 (PLA)	22 ± 4 COD	1200 mg/100 cherries	8 days (exercise on day 4)	2 sets of 20 maximal eccentric contractions of the elbow
Howatson et al. [35]	Male and female marathon runners	10 (TC) 10 (PLA)	37 ± 13 38 ± 5	1200 mg/100 cherries	8 days (exercise on day 6)	Marathon race
Kuehl et al. [21]	Healthy male and female runners	28 (TC) 26 (PLA)	38.2 ± 8.5 32.2 ± 9.8	1200 mg/100 cherries	8 days (exercise on day 8)	3 running segments of the Hood to Coast relay race (26.3 ± 2.5 km)
Botwell et al. [31]	Well-trained male athletes (high-intensity intermittent sports)	10 (TC) 10 (PLA)	27.8 ± 1.6 COD	180 cherries	10 days (exercise on day 8)	Single leg intensive knee extensor training session
Bell et al. [28]	Well trained male cyclists	8 (TC) 8 (PLA)	----- -----	180 cherries	7 days (exercise on days 5, 6 and 7)	A prolonged, high-intensity, stochastic cycling task, 109 min.
Bell et al. [29]	Male trained cyclists	8 (TC) 8 (PLA)	----- -----	180 cherries	7 days (exercise on day 5)	A prolonged, high-intensity, stochastic cycling task, 109 min.
Levers et al. [36]	Resistance trained males	11 (TC) 12 (PLA)	21.18 ± 3.34 20.58 ± 1.78	991 mg	10 days (exercise on day 8)	10 sets of 10 repetitions barbell back squat at 70% of RM
Bell et al. [30]	Semi-professional male soccer players	8 (TC) 8 (PLA)	----- -----	180 cherries	7 days (exercise on days 5, 6 and 7)	12 repetitions of 20 m sprint + adapted Loughborough Inter-mittent Shuttle test
Levers et al. [13]	Endurance trained runners or triathletes	11 (TC) 16 (PLA)	20.82 ± 1.89 22.44 ± 4.86	991 mg	10 days (exercise on day 8)	Half marathon race
McCormick et al. [37]	Highly trained male Water Polo players	9 (TC) 9 (PLA)	18.6 ± 1.4 COD	270 cherries	6 days (exercise at the end of day 6)	Match simulation
Beals et al. [27]	Recreationally active male and female subjects	15 (TC) 14 (PLA)	25.9 ± 9.3 24.6 ± 2.8	733 mg	12 days (exercise on day 5)	Maximal isokinetic concentric/eccentric contractions of the quadriceps until fatigue
Hillman et al. [34]	Recreationally active male and female subjects	8 (TC) 8 (PLA)	----- -----	90 cherries	10 days (exercise on day 7)	5 sets of 20 drop jumps
Brown et al. [32]	Physically active females	10 (TC) 10 (PLA)	----- -----	180 cherries	8 days (exercise on day 5)	15 repetitions of 30 m sprint
Abbott et al. [26]	Professional male soccer players	10 (TC) 10 (PLA)	19 ± 1 COD	200 cherries	3 days (exercise after the match on day 1)	Soccer match
Lamb et al. [8]	Non-resistance trained men	12 (TC) 12 (PLA)	IQR: 22.0–33.0 IQR: 22.5–32.0	180 cherries	9 days (exercise on day 5)	5 sets of 10 unilateral maximal eccentric elbow flexions (non dominant arm)

Abbreviations: TC: tart cherry; PLA: placebo; COD: crossover design; IQR: interquartile range.

a total of 35 studies were selected for screening the abstracts (22 with tart cherry supplementation and 13 with pomegranate supplementation). Thirteen studies did not fulfil inclusion criteria and were excluded. Therefore, a total of 22 studies were selected for full text review. Four studies were added from other sources and a total of 26 studies were finally included in the current review: 15 with tart cherry supplementation [8, 13, 21, 26–37] and 11 with pomegranate supplementation [8, 38–47]. One study [8] was repeated because it had two intervention groups, one with TC supplementation and another with PG supplementation. Hence, the total number of studies was actually 25. A summary of this process can be seen in Figure 1.

The characteristics of the 15 studies with TC supplementation have been summarized in Table 1. The sample size ranged from 8 to 28 participants in each group. The TC dosage was very different across the included studies and it was the equivalent to 90 to 270 whole Montmorency tart cherries per day or had a total phenolic content from 590 mg to 1200 mg (~ 100 cherries) per day. The intervention period ranged from 3 days to 12 days. The protocol to induce muscle damage was also very different across the studies. The participants had very different training levels: with no special

requirements (1), non-resistance trained subjects (1) recreationally active subjects (3), resistance trained subjects (1), professional or semi-professional endurance runners (3), well-trained cyclists (2) and professional or semi-professional high-intensity intermittent athletes (rugby, football, taekwondo or water polo) (4).

The characteristics of the 11 studies with PG supplementation have been summarized in Table 2. The sample size ranged from 6 to 17 participants in each group. The PG dosage was very different across the included studies. Only 8 studies specified the total phenolic content, which ranged from 600 to 3840 mg per day. One study did not specify the exact PG dosage but we estimated that it was lower than 200 mg of polyphenols per day [47]. The intervention period ranged from 2 days to 2 months. The protocol to induce muscle damage was also very different across the studies. The participants had very different training levels: with no special requirements (1), no regular physical activity (1), non-resistance trained subjects (2) recreationally active subjects (1), resistance trained subjects (1), endurance trained subjects (1), professional rowers (1), elite weight-lifters (2). One study only specified that the subjects were athletes [42].

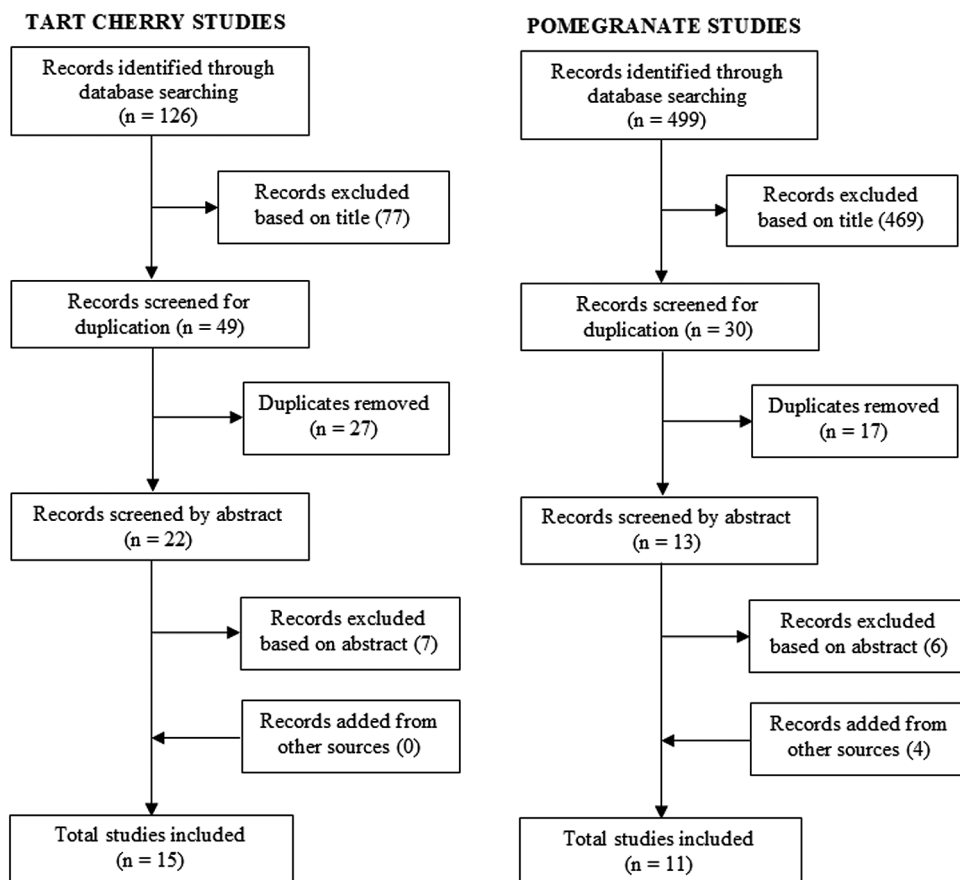


FIG. 1. Flowchart of the search strategy.

TABLE 2. Characteristics of the studies with PG supplementation.

Study	Subjects	Groups	Age (years) (mean \pm sd)	Phenolic content per day	Duration	Exercise protocol to induce muscle damage
Trombold et al. [45]	Healthy recreationally active males	16 (PG) 16 (PLA)	22.2 \pm 1.4 COD	1300 mg	9 days (exercise on day 5)	2 sets of 20 maximal eccentric elbow flexions
Trombold et al. [46]	Resistance trained men	17 (PG) 17 (PLA)	21.9 \pm 2.4 COD	1242 mg	15 days (exercise on day 8)	3 sets of 20 maximal eccentric elbow extensions/6 sets of 10 110% RM eccentric knee extensions
Machin et al. [42]	Non resistance trained men	15 (PG 1x) 15 (PG 2x) 15 (PLA)	----- ----- -----	650 mg (1x) 1300 mg (2x)	8 days (exercise on day 4)	20 min downhill running + 40 reps bilateral isotonic 1RM eccentric contractions elbow flexors
Mazani et al. [43]	male athletes	14 (PG) 14 (PLA)	19.07 \pm 1.07 19.78 \pm 0.89	-----	14 days (exercise on day 14)	Exhaustive exercise running on treadmill at 70% maximal HR
Naghizadeh-Baghi et al. [44]	Healthy male athletes	14 (PG) 14 (PLA)	19 \pm 1 20 \pm 0.89	-----	14 days (exercise on day 14)	Severe physical activity (once)
Al-Dujaili et al. [38]	Healthy males and females with no regular physical activity	12 (PG) 12 (PLA)	22.1 \pm 4.6 22.8 \pm 5.1	842.5 mg	7 days (exercise on day 8)	30 minutes moderate treadmill exercise (50% Wmax)
Fuster-Muñoz et al. [41]	Endurance trained male athletes	6 (PG) 6 (PGD) 10 (PLA)	35.2 \pm 8.5 37.5 \pm 11.4 33.3 \pm 9.0	2200 mg (PG) 1100 mg (PGD)	21 days (normal exercise training)	Endurance based training more than 1 h per session and more than 3 sessions per week
Ammar et al. [39]	Male elite weightlifters	9 (PG) 9 (PLA)	21 \pm 0.5 COD	3840 mg + 2560 pre-exercise	2 days (exercise on day 3)	1 h and 45 minutes of habitual training program
Ammar et al. [40]	Male elite weightlifters	9 (PG) 9 (PLA)	21 \pm 1 COD	3840 mg + 2560 pre-exercise	2 days (exercise on day 3)	1 h and 45 minutes of habitual training program
Urbaniak et al. [47]	Male rowers of the polish national team	10 (PG) 9 (PLA)	20.08 \pm 0.86 20.90 \pm 0.95	< 200 mg	2 months (exercise before/ after supplementation)	2000 m rowing at maximal pace
Lamb et al. [8]	Non-resistance trained men	12 (PG) 12 (PLA)	IQR: 21.0–32.5 IQR: 22.5–32.0	1758 mg	9 days (exercise on day 5)	5 sets of 10 unilateral maximal eccentric elbow flexions (non dominant arm)

Abbreviations: PG: pomegranate; PGD: pomegranate diluted; PLA: placebo; RM: repetition maximum; COD: crossover design; IQR: interquartile range.

TABLE 3. Variables measured and summary of findings of the studies with TC supplementation.

Study	Functional performance variables and perceptual variables	Biochemical markers of inflammation and oxidative stress	Significant differences in TC group (vs PLA group).
Connolly et al. [33]	Relaxed elbow angle, MIVCEF. Pain and muscle tenderness of the elbow flexors. Measurements: baseline and 24, 48, 72 and 96 h post	-----	< MIVCEF loss post (overall treatment effect) < pain post (overall treatment effect) > MIVCKE 24 h and 48 h post
Howatson et al. [35]	MIVCKE. DOMS of the quadriceps. Measurements: baseline, pre, post and 24 h and 48 h post	CRP, IL-6. UA, TAS, MDA, PC. Measurements: baseline, pre, post and 24 h and 48 h post	< CRP 24 h and 48 h post < UA post and 24 h post > TAS pre, post and 24 h and 48 h post < MDA 48 h post
Kuehl et al. [21]	Pain	-----	< Pain post exercise > Recovery of MIVCKE at 24 and 48 h post
Botwell et al. [31]	MIVCKE. DOMS of the quadriceps. Measurements made baseline, pre-exercise, post-exercise and 24 and 48 h post	CRP; TNit, PC, TAS. Measurements made pre-exercise, post-exercise and 24 and 48 h post	< PC 24 h and 48 h post < CRP in all time points (trends)
Bell et al. [28]	-----	TNF- α , IL-1 β , IL-6, IL-8, CRP. LOOH. Measurements: baseline and pre/post each trial (days 5, 6 and 7)	< LOOH in all trial period < IL-6 following trial 2 and 3 < CRP after baseline > MIVCKE 24 h, 48 h and 72 h post
Bell et al. [29]	CE, MIVCKE, 6-s PCP. DOMS of the lower limb. Measurements: baseline and 24 h, 48 h and 72 h post trial	TNF- α , IL-1 β , IL-6, IL-8, CRP. LOOH. Measurements: baseline, pre/post trial and 1 h, 3 h, 5 h, 24 h, 48 h and 72 h post trial	< IL-6 post (overall treatment effect) < CRP in all time points < DOMS (trends)
Levers et al. [36]	IKEMVC. DOMS of the quadriceps. Measurements: baseline (not DOMS), pre and 60 min, 24 h and 48 h post	IL-2, 4, 5, 6, 7, 8, 10, 12p70, 13, TNF- α , IFN- γ , GM-CSF. Tbil, SOD, TAS, MDA, NT. Measurements: baseline, pre, and 60 min, 24 h and 48 h post	< DOMS post, 24 h and 48 h post > MIVCKE, CMJ 24 h, 48 h, 72 h post
Bell et al. [30]	20 m sprint, 5–0–5 agility test, CMJ, MIVCKE. DOMS of the lower limb. Measurements: baseline and 24 h, 48 h and 72 h post trial	TNF- α , IL-1 β , IL-6, CRP. LOOH. Measurements: baseline, pre/post trial and 1 h, 3 h, 5 h, 24 h, 48 h and 72 h post trial	< DOMS, 20 m sprint time, 5–0–5 agility test time across 72 h post < IL-6 (overall treatment effect)
Levers et al. [13]	DOMS of the quadriceps. Measurements: pre and 60 min, 24 h and 48 h post	IL-1 β , 2, 4, 5, 6, 7, 8, 10, 12p70, 13, TNF- α , IFN- γ , GM-CSF. Tbil, UA, SOD, TAS, MDA, NT. Measurements: baseline, pre and 60 min, 24 h and 48 h post	< IL-2, IL-13 post, 24 h and 48 h post < IL-6 post > TAS 48 h post < DOMS pre
McCormick et al. [37]	On-water VJ test, 10 m sprint, repeat sprint test, WIST, TQR. DOMS of the overall body. Measurements: day 1 and 7	IL-6, CRP. Measurements: day 6 and 7 UA, F2-IsoP. Measurements: baseline, day 6 pre and post, and day 7	No significant differences between groups
Beals et al. [27]	ROM of the knee, IKEMVC. Muscle tenderness, muscle pain of the quadriceps, Measurements: baseline, post and 24 h, 48 h, 72 h and 168 h post	TNF- α , IFN- γ , IL-1 β , IL-6, IL-8, IL-10, IL-12p70. Measurements: baseline, post and 24 h, 48 h, 72 h and 168 h post	No significant differences between groups

TABLE 3. Continue.

Study	Functional performance variables and perceptual variables	Biochemical markers of inflammation and oxidative stress	Significant differences in TC group (vs PLA group).
Hillman et al. [34]	CMJ, ROM of the knee flexors. DOMS of the lower limb. Measurements: 6 days and 24 h pre, post and 24 h, 48 h and 72 h post	MPO, ORAC. Measurements: 6 days and 24 h pre, post and 24 h, 48 h and 72 h post	> ORAC at 48 h post
Brown et al. [32]	SRT, CMJ, RSI, MIVCKE. DOMS and pain of the lower limb. Measurements: pre, post and 24 h, 48 h and 72 h post	CRP. Measurements: baseline, pre, post and 24 h, 48 h and 72 h post	> CMJ across 72 h post < DOMS (trends)
Abbott et al. [26]	CMJ, RSI, SW. DOMS. Measurements: 2 days pre-match and 12 h, 36 h and 60 h post	-----	No differences between groups
Lamb et al. [8]	MIVCEF, ROM of the elbow. DOMS of the elbow flexors. Measurements: pre, post and 24 h, 48 h, 72 h and 96 h post	-----	No differences between groups

Abbreviations: MIVCEF: maximal isometric voluntary contraction of the elbow flexors; DOMS: muscle soreness; MIVCKE: maximal isometric voluntary contraction of the knee extensor; IKEMVC: isokinetic knee extension maximal voluntary contraction; CE: cycling economy; PCP: peak cycling power; CMJ: countermovement jump; VJ: vertical jump; WIST: Water Polo Intermittent Shuttle Test; TQR: total quality of recovery; ROM: range of motion; SRT: sit and reach test (for hamstrings stiffness and flexibility); RSI: reactive strength index; SW: subjective wellbeing; CRP: C-reactive protein; IL: interleukin; UA: uric acid; TAS: total antioxidant status; MDA: malondialdehyde; PC: protein carbonyls; TNit: total nitrotyrosine; TNF- α : tumor necrosis factor alpha; LOOH: lipid hydroperoxides; IFN- γ : interferon- γ ; GM-CSF: granulocyte-macrophage colony-stimulating factor; Tbil: total bilirubin; SOD: superoxide dismutase; NT: nitrotyrosine; F2-IsoP: F2 isoprostane; MPO: myeloperoxidase; ORAC: oxygen radical absorbance capacity; pre: pre-exercise; post: post-exercise; TC: tart cherry; PLA: placebo.

Effects of supplementation on functional performance variables

Twelve studies analysed the effects of TC supplementation on any of the following functional performance variables: maximal isometric voluntary contraction of the elbow flexors (MIVCEF), maximal isometric voluntary contraction of the knee extensor (MIVCKE), isokinetic knee extension maximal voluntary contraction (IKEMVC), cycling economy (CE), peak cycling power (PCP), countermovement jump (CMJ), on-water vertical jump test (VJ), Water Polo Intermittent Shuttle Test (WIST), total quality of recovery (TQR), range of motion (ROM), relaxed elbow angle, sit and reach test for hamstring stiffness and flexibility (SRT) and reactive strength index (RSI). Two studies measured MIVCEF, five studies evaluated MIVCKE and two studies measured IKEMVC. Five of these studies found significantly better recovery of these variables after exercise in the TC group (vs PLA). Two studies assessed CMJ height and only one of them found a significantly higher CMJ after exercise in the TC group (vs PLA). The complete summary of findings for functional performance variables in TC intervention studies can be seen in Table 3.

Four studies analysed the effects of PG supplementation on any of the following functional performance variables: MIVCEF, MIVCKE

and ROM. Four studies analysed MIVCEF and three of them found significantly better post-exercise recovery in the PG group (vs PLA). Two studies measured MIVCKE and only one of them found significantly better post-exercise recovery in the PG group (vs PLA). The complete summary of findings for functional performance variables in PG intervention studies can be seen in Table 4.

Effects of supplementation on perceptual variables

Fourteen studies analysed the effects of TC supplementation on any of the following perceptual variables: muscle soreness (DOMS); muscle tenderness, pain intensity and subjective wellbeing (SW). Eleven studies assessed muscle soreness (DOMS) and four of them found that DOMS were significantly lower (or showed a tendency to lower values) after exercise in the TC group (vs PLA). Three studies measured muscle pain and two of them found that pain intensity was significantly lower after exercise in the TC group (vs PLA). The complete summary of findings for perceptual variables in TC intervention studies can be seen in Table 3.

Five studies analysed the effects of PG supplementation on DOMS (perceptual variable) and three of them found that DOMS were

TABLE 4. Variables measured and summary of findings of the studies with PG supplementation.

Study	Functional performance variables and perceptual variables	Biochemical markers of inflammation and oxidative stress	Significant differences in PG group (vs PLA group).
Trombold <i>et al.</i> [45]	MIVCEF. DOMS of the elbow flexors. Measurements made baseline, pre-exercise and 2, 24, 48, 72 and 96 h post	IL-6, CRP. Measurements made baseline and 2, 24, 48, 72, and 96 h post	> recovery of MIVCEF from 24 h to 72 h post < DOMS of the elbow flexors 2 h post
Trombold <i>et al.</i> [46]	MIVCEF, MIVCKE. DOMS of the elbow flexors and knee extensors. Measurements: pre and 2 h, 24 h, 48 h, 72 h, 96 h and 168 h post	-----	> MIVCEF post (overall treatment effect) < DOMS of the elbow flexors post (overall treatment effect)
Machin <i>et al.</i> [42]	MIVCEF, MIVCKE. DOMS of knee extensors and elbow flexors. Measurements: pre and 2 h, 24 h, 48 h, 72 h and 96 h post	-----	> MIVCEF in PG 1x and PG 2x post (overall treatment effect) > MIVCKE in PG 1x and PG 2x post (overall treatment effect)
Mazani <i>et al.</i> [43]	-----	MMP2, MMP9, CRP, CP levels. TAC, SOD, GPX, MDA, Zn levels. Measurements: baseline, pre and post	< MMP2, MMP9, CRP pre > GPX, SOD, TAC and < MDA pre < MMP2, MMP9, CP post > GPX, SOD post and < MDA post
Naghizadeh-Baghi <i>et al.</i> [44]	-----	PON1, ARE, TAC, MDA, GLU, SOD, GPX. Measurements: baseline, pre and post	> ARE, GPX, SOD, TAC, GLU pre < MDA pre > ARE, GPX, SOD, TAC post < MDA post
Al-Dujaili <i>et al.</i> [38]	-----	MDA. Measurements: before and after supplementation (both post-exercise)	Only pre-post comparison: (not between-groups comparisons) < MDA in PG, not changes in PLA
Fuster-Muñoz <i>et al.</i> [41]	-----	CRP. PC, MDA, sE-S. Measurements: day 0 and day 22	< PC, MDA in PG and PG diluted post
Ammar <i>et al.</i> [39]	DOMS of knee extensors/elbow flexors. Measurements: 48 h post	CRP. Measurements: pre, post and 48 h post	< DOMS of knee extensors 48 h post < CRP post
Ammar <i>et al.</i> [40]	-----	CAT, GPX, MDA, UA, Tbil. Measurements: pre, post and 48 h post	> CAT, GPX, UA, Tbil post < MDA post > CAT, GPX, UA, Tbil, MDA decrease 48 h post
Urbaniak <i>et al.</i> [47]	-----	IL-6, HEP. TAC, UA. Measurements: pre, post and 24 h post	> TAC 24 h post
Lamb <i>et al.</i> [8]	MIVCEF, ROM of the elbow. DOMS of the elbow flexors. Measurements: pre, post and 24 h, 48 h, 72 h and 96 h post	-----	No differences between groups

Abbreviations: MIVCEF: maximal isometric voluntary contraction of the elbow flexors; MIVCKE: maximal isometric voluntary contraction of the knee extensor; DOMS: muscle soreness; ROM: range of motion; MPP2: metalloproteinase 2; MPP9: metalloproteinase 9; CRP: C-reactive protein; CP: ceruloplasmin; TAC: total antioxidant capacity; SOD: superoxide dismutase; GPX: glutathione peroxidase; MDA: malondyaldehyde; PON1: Paraoxonase 1; ARE: Arilesterase; GLU: glutathion; PC: protein carbonyls; sE-S: Se-Selectin; CAT: catalase; UA: uric acid; Tbil: total bilirubin; IL: interleukin; HEP: hepcidin; pre: pre-exercise; post: post-exercise; PG: pomegranate; PLA: placebo.

significantly lower at any time after exercise in the PG group (vs PLA). The complete summary of findings for perceptual variables in PG intervention studies can be seen in Table 4.

Effects of supplementation on markers of inflammation

Ten studies analysed the effects of TC supplementation on any of the following inflammatory markers: C-reactive protein (CRP), interleukin (IL) 1 β , 2, 4, 5, 6, 7, 8, 10, 12p70 and 13, tumour necrosis factor alpha (TNF- α), interferon- γ (IFN- γ) and granulocyte-macrophage colony-stimulating factor (GM-CSF). Seven studies measured CRP levels and three of them found a significantly lower post-exercise CRP level in the TC group (vs PLA). Eight studies evaluated IL-6 levels and four of them found a significantly lower post-exercise IL-6 level in the TC group (vs PLA). The complete summary of findings for markers of inflammation in TC intervention studies can be seen in Table 3.

Five studies analysed the effects of PG supplementation on any of the following inflammatory markers: metalloproteinase 2 (MPP2), metalloproteinase 9 (MPP9), CRP, ceruloplasmin (CP), IL-6 and hepcidin (HEP). One of them found significantly lower levels of MPP2, MPP9 and CP after exercise in the PG group (vs PLA) and another study showed significant lower values of CRP in the PG group (vs PLA). The complete summary of findings for markers of inflammation in PG intervention studies can be seen in Table 4.

Effects of supplementation on markers of oxidative stress

Nine studies analysed the effects of TC supplementation on any of the following markers of oxidative stress: uric acid (UA), total antioxidant status (TAS), malondialdehyde (MDA), protein carbonyls (PC), total nitrotyrosine (TNit), lipid hydroperoxides (LOOH), total bilirubin (Tbil), superoxide dismutase (SOD), nitrotyrosine (NT), F2 isoprostane (F2-IsoP), myeloperoxidase (MPO) and oxygen radical absorbance capacity (ORAC). Three studies measured UA levels but only one of them found significantly lower levels of UA after exercise in the TC group (vs PLA). Four studies evaluated TAS and two of them found significantly higher values after exercise in the TC group (vs PLA). Three studies assessed MDA levels but only one found significantly lower levels of MDA 48 h after exercise in the TC group (vs PLA). Three studies measured LOOH levels but only one of them found significant lower levels of LOOH after exercise in the TC group (vs PLA). The details of the effects of TC supplementation on markers of oxidative stress have been summarized in Table 3.

Six studies analysed the effects of PG supplementation on any of the following markers of oxidative stress: total antioxidant capacity (TAC), SOD, glutathione peroxidase (GPX), MDA, paraoxonase 1 (PON1), arylesterase (ARE), glutathione (GLU), PC, sE-selectin (sE-S), catalase (CAT), UA and Tbil. Four studies measured MDA levels and three of them found significantly lower levels in the PG group (vs PLA). The fourth study did not make between-groups comparisons but found significantly lower MDA levels after exercise vs pre-exercise only in the PG group. Three studies evaluated TAC

levels and the three of them found significantly higher CAT levels after exercise in the PG group (vs PLA). Two studies assessed GPX levels and both of them found significantly higher values after exercise in the PG group (vs PLA). Two studies measured UA levels but only one of them found a significantly higher increase in UA levels in PG (vs PLA). The details of the effects of PG supplementation on markers of oxidative stress have been summarized in Table 4.

Methodological quality of studies

The methodological quality scores of the fifteen studies with TC supplementation can be seen in Table 5. The scores of the eleven studies with PG supplementation can be seen in Table 6.

Quality scores ranged from five to nine (of a maximum of ten), with a mean PEDro score of 7.27 ± 1.29 for studies with TC supplementation and 6.55 ± 1.44 for studies with PG supplementation. 16 studies failed to have a concealed allocation, 12 studies failed to achieve similar baseline values for the primary outcome measure and 21 studies did not have blinding of all assessors who measured at least one key outcome. Only 5 studies were deemed high quality while the rest were considered to be of moderate quality.

DISCUSSION

TC and PG supplementation may aid exercise performance and recovery by mitigating oxidative stress and inflammation due to their high content of polyphenols. However, the types and distribution of polyphenols in TC and PG are not the same and, in addition, the polyphenols in the human diet are not necessarily the most active within the body, either because they have a lower intrinsic activity or because they are poorly absorbed from the intestine, highly metabolized or rapidly eliminated [48]. Knowledge of the types and bioavailability of polyphenols in those two fruits is necessary to evaluate their biological activity within target tissues [49].

However, the exact polyphenol composition of the supplementation servings is not provided in most articles and the bioavailability of the phenolic compounds depends on many factors, such as food processing, food matrix, food diet and the individual subject [49]. For these reasons the discussion of this systematic review will be carried out considering only the total phenolic content per day (or the equivalent in number of cherries per day).

Effects of supplementation on functional performance and perceptual variables

Twelve studies with TC supplementation analysed any functional performance variable and six of them [29–33, 35] found significantly better recovery of any of those variables after exercise in the TC group (vs PLA). Four studies with PG supplementation analysed any functional performance variable and three of them [42, 45, 46] found significantly better recovery of any of those variables after exercise in the PG group (vs PLA).

Therefore, there were six studies with TC supplementation and one with PG supplementation that, apparently, did not find any

TABLE 5. Methodological quality of the studies with TC supplementation assessed with the PEDro scale.

Items	Connolly et al. [33]	Howatson et al. [35]	Kuehl et al. [21]	Botwell et al. [31]	Bell et al. [28]	Bell et al. [29]	Levers et al. [36]	Bell et al. [30]	Levers et al. [13]	McCormick et al. [37]	Beals et al. [27]	Hillman et al. [34]	Brown et al. [32]	Abbott et al. [26]	Lamb et al. [8]
1. Eligibility criteria were specified	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2. Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)	+	-	-	+	-	-	-	+	-	+	+	+	-	+	+
3. Allocation was concealed	+	-	-	-	-	-	-	-	-	+	+	-	-	+	+
4. The groups were similar at baseline regarding the most important prognostic indicators	+	+	-	+	+	+	+	+	+	+	-	-	-	+	-
5. There was blinding of all subjects	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
6. There was blinding of all therapists who administered the therapy	-	-	-	+	+	+	+	+	+	+	+	-	+	+	+
7. There was blinding of all assessors who measured at least one key outcome	-	-	-	-	-	-	-	-	-	-	+	-	-	+	+
8. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+
9. All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
10. The results of between-group statistical comparisons are reported for at least one key outcome	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
11. The study provides both point measures and measures of variability for at least one key outcome	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Total score	7	6	5	8	7	7	7	8	6	9	9	6	6	9	9

TABLE 6. Methodological quality of the studies with PG supplementation assessed with the PEDro scale.

Items	Trombold et al. [45]	Trombold et al. [46]	Mazani et al. [43]	Machin et al. [42]	Naghizadeh-B. et al. [44]	Fuster-Muñoz et al. [41]	Al-Dujaili et al. [38]	Ammar et al. [39]	Ammaret al. [40]	Urbaniak et al. [47]	Lamb et al. [8]
1. Eligibility criteria were specified	+	+	+	+	+	+	+	+	+	+	+
2. Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)	+	+	+	+	+	+	+	-	-	+	+
3. Allocation was concealed	+	+	-	-	-	-	-	+	+	-	+
4. The groups were similar at baseline regarding the most important prognostic indicators	-	-	+	+	+	-	-	-	-	+	-
5. There was blinding of all subjects	+	+	-	+	-	+	+	-	-	-	+
6. There was blinding of all therapists who administered the therapy	+	+	-	+	-	+	-	-	-	-	+
7. There was blinding of all assessors who measured at least one key outcome	-	-	-	-	-	+	-	-	-	-	+
8. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	+	+	+	+	+	-	+	+	+	+	+
9. All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"	+	+	+	+	-	+	+	+	+	+	+
10. The results of between-group statistical comparisons are reported for at least one key outcome	+	+	+	+	+	+	-	+	+	+	+
11. The study provides both point measures and measures of variability for at least one key outcome	+	+	+	+	+	+	+	+	+	+	+
Total score	8	8	6	8	5	7	5	5	5	6	9

potential nutritional aid in TC or PG supplementation with regard to functional performance variables.

Fourteen studies analysed the effects of TC supplementation on any perceptual variable and seven of them [13, 21, 29, 30, 32, 33, 36] found significantly better recovery (or a tendency) of any of those variables after exercise in the TC group (vs PLA). Five studies analysed the effects of PG supplementation on perceptual variables and three of them [39, 45, 46] found that DOMS were significantly lower at any time after exercise in the PG group (vs PLA). Therefore, there were seven studies with TC supplementation and two with PG supplementation that, apparently, did not find any potential nutritional aid in TC or PG supplementation with regard to perceptual variables.

There are some potential factors that may have masked the ergogenic effect of those supplementations in most studies: 1) The reviewed studies included subjects with different training levels (recreationally to elite athletes) and lower muscle damage following exercise are registered in well trained subjects; 2) The total phenolic content per day was too low or the supplementation period was too short; 3) The muscle damage protocol did not effectively induce pronounced muscle damage.

However, four studies present contradictory results. Botwell *et al.* [31] and Howatson *et al.* [35] found significant differences between groups for any functional performance variable but not for perceptual variables. The participants in these studies were well-trained athletes who regularly performed the exercises used to induce DOMS, and it is probable that due to the repeated bout effect the authors were not able to induce enough muscle soreness. As stated by Botwell *et al.* [31], this fact may have limited the ability to detect any effect of the supplementation.

Levers *et al.* [36] found significant differences for DOMS and not for functional performance variables and Machin *et al.* [42] found significant differences for functional performance variables but not for DOMS. The possible explanation for a reduction of DOMS not accompanied with improvements in muscle function and vice versa remains unclear and supports the presumption that the muscle damage protocol was not sufficiently intense [50].

Thus, even with some contradictory results, there is moderate evidence that, with a sufficient degree of muscle damage, a long enough supplementation period with enough total phenolic content per day, TC or PG supplementation may be effective to accelerate recovery of functional performance and perceptual variables after EIMD. After reviewing the articles included in this review, we can suggest that neither of the two types of supplementation is superior to the other with regard to recovery of functional performance or perceptual variables.

Effects of supplementation on markers of inflammation

Ten studies analysed the effects of TC supplementation on any inflammatory marker. Six of them [13, 28–31, 35] found significantly better recovery (or a tendency) of any of those variables after exercise in the TC group (vs PLA). The other four [27, 32, 36, 37] did not

find significant differences between groups. The low dosage of phenolic compounds and a low initial muscle damage could be the reasons for the results found by Beals *et al.* [27] and Levers *et al.* [36] because they supplemented with 733 mg/day and 991 mg/day and the subjects experienced only a decline in muscle strength after exercise of ~3% and ~18%, respectively. McKormick *et al.* [37] gave the same two potential explanations for their results: the low phenolic content per day of their supplementation protocol and the low mechanical strain induced by a water polo match simulation in highly trained water polo players. The supplementation used by Brown *et al.* [32] was not low in phenolic compounds but they stated that the repeated-sprint protocol used did not appear to induce a large inflammatory response.

Five studies analysed the effects of PG supplementation on any inflammatory marker, but only two of them [39, 43] found significantly better recovery of any of those variables after exercise in the PG group (vs PLA). The other three [41, 45, 47] did not find significant differences between groups. However, Fuster-Muñoz *et al.* [41] used an habitual training programme as the protocol to create muscle damage and maybe they did not effectively induce pronounced muscle damage. The muscle damage protocol used by Urbaniak *et al.* [47] was 2000 m rowing at maximal pace but it took place during the competitive period when the body of a well-trained athlete is adapted to cover that distance even twice in a single day, leading to a lack of statistically significant changes in inflammatory marker concentrations [47]. In the study conducted by Trombold *et al.* [45] the muscle mass involved in the protocol was small and maybe it was not sufficient to elevate a marker of systemic inflammation.

Therefore, even if the results are not conclusive, it appears that TC or PG supplementation with enough content of phenolic compounds per day may accelerate recovery of inflammatory markers after a pronounced inflammatory response to EIMD. We do not find conclusive results to believe that one type of supplementation is superior to the other with regard to inflammatory response.

Effects of supplementation on markers of oxidative stress

Nine studies analysed the effects of TC supplementation on any marker of oxidative stress and five of them [13, 28, 31, 34, 35] found significantly better recovery of any of those variables after exercise in the TC group (vs PLA). The other four [29, 30, 36, 37] did not find significant differences between groups. Bell *et al.* [29, 30] did not find significant differences between groups in LOOH but they found significant differences in inflammatory markers. Moreover, Bell *et al.* [28] found significant differences between groups in LOOH with exactly the same supplementation period, dosage and muscle damage protocol as Bell *et al.* [29]. These results suggest that the use of LOOH as a measure of oxidative stress may not be the best option, which is confirmed by Palmieri & Sblendorio [51]. Levers *et al.* [36] and McKormick *et al.* [37] supplemented with a low quantity of phenolic compounds per day and the subjects experimented a low

initial level of muscle damage. These two reasons may explain why antioxidant activity was not affected by supplementation.

There is one study with contradictory results: Hillman et al. [34] found higher values in ORAC after exercise in the supplementation group (vs PLA) but did not find differences for the rest of the measured variables. However, they concluded that the muscle damage protocol used induced only mild symptoms of muscle damage and maybe the total phenolic content of each serving was too low to elicit recovery of all the variables that changed after exercise [34].

Six studies analysed the effects of PG supplementation on any marker of oxidative stress and all of them [38, 40, 41, 43, 44, 47] found significantly better recovery of any of those variables after exercise in the PG group (vs PLA). However, Fuster-Muñoz et al. [41] and Urbaniak et al. [47] did not find significant differences between groups in markers of inflammation, probably because the muscle damage protocol induced only mild symptoms of muscle damage but it was enough to provide significantly better recovery of markers of oxidative stress in the TC group (vs PLA).

Hence, it also appears that TC or PG supplementation with enough content of phenolic compounds per day may accelerate recovery of markers of oxidative stress after a pronounced inflammatory response to EIMD. However, given that all the studies with PG supplementation found better recovery of markers of oxidative stress, even with low phenolic content of the servings and a low initial muscle damage, we suggest that PG supplementation is more effective in promoting post-exercise oxidative stress recovery after EIMD than TC supplementation. The most likely reason is the different bioavailability of the phenolic contents in PG and TC because they are both rich sources of anthocyanins, but their profiles of other polyphenols differ [8].

Limitations

The findings from this review must be treated with caution due to 1) the heterogeneity in study design across included studies, 2) the small sample sizes of some studies, leading to low statistical power, 3) the high number of studies that scored only 5/6 points in the PEDro scale, and 4) the low number of studies with PG supplementation evaluating functional performance variables, perceptual variables and markers of inflammation.

There are some other limitations that may affect outcomes. Some of the studies used a crossover design which may have attenuated the response of the body to intense exercise due to the repeated bout effect. Most of the crossover studies have a wash-out period of at least two weeks and used different limbs for each trial, minimizing any repeated bout effect. However, the protective effect is not always isolated to the specific muscle/limb and can last for more than 2 weeks [31]. Another important consideration when a cross-over design is carried out is that the beneficial effect of the supplementation can persist for more than two weeks and can also affect outcomes in the second supplementation arm of the study [18].

It is also important to note that the purpose of the different studies was not always the same. Some of the studies were carried out

with untrained individuals while others were carried out with elite athletes. Moreover, some of the studies with well-trained individuals analysed the influence of supplementation on recovery from habitual training sessions while others analysed the influence on recovery from an extremely intense bout of exercise.

Some studies controlled the background diet while others did not and the subjects consumed their habitual diet, which could be rich in polyphenols, possibly affecting results. The dietary records should be included in the studies to take into account this extra polyphenol intake.

Finally, there are some inconsistencies regarding the total phenolic content of the supplements: the same supplement analysed by three different laboratories showed great differences in the total phenolic content. Subtle differences in the analysis methods might contribute to differences in the total phenolic content but great variations are probably due to inter-batch differences [52], which make it essential to analyse the supplements before the interventions and not to use the results reported from previous analysis.

CONCLUSIONS

Despite some conflicting results, after reviewing the 25 studies included in this systematic review, we can conclude that TC supplementation and PG supplementation are effective nutrients to promote recovery after EIMD. We suggest that both types of supplementation have approximately the same potential to accelerate recovery of functional performance variables, perceptual variables and inflammation but the results show better recovery of oxidative stress with PG supplementation. However, new investigations comparing these two types of supplementation with exactly the same total polyphenol content are needed.

Based on the results of the studies assessed, positive effects are more likely: 1) when supplementation starts some days before muscle damage is induced and finishes some days after, for a total period of at least 8/10 days, and 2) with pronounced muscle damage of the muscles involved.

Due to the inconsistencies found in the studies included in this review regarding the total phenolic content of the supplements, further research is needed to determine the optimal dosage, and we strongly recommend future researchers to analyse the supplements before the interventions. We also recommend that future studies include at least two variables to measure performance, inflammation and oxidative stress to confirm the potential positive effects on recovery after EIMD.

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Declaration of interest

The authors report no conflict of interest.

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