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Meta-analysis

Effect of vitamin C supplementation on post-exercise recovery: A systematic review and meta-analysis of randomized double-blind placebo trials

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SUMMARY

Introduction: Exercise-induced oxidative stress and inflammation may impair recovery and performance. Vitamin C, a potent antioxidant, has been proposed to attenuate exercise-induced muscle damage and modulate inflammatory and oxidative biomarkers during recovery.

Methods: A systematic review and meta-analysis were conducted in accordance with PRISMA guidelines and registered in PROSPERO (CRD42024594742). Twelve randomized controlled trials involving adult participants exposed to different exercise protocols were included. Vitamin C supplementation, administered in various forms, was compared with placebo. Primary outcomes were inflammatory (CRP, IL-6) and oxidative stress (MDA) biomarkers. Risk of bias was assessed using the RoB 2.0 tool, and certainty of evidence was evaluated using the GRADE framework.

Results: Pooled analyses showed no significant effects of vitamin C supplementation on IL-6 (MD = 0.00; 95 % CI: −0.25 to 0.25; p = 1.00; 2 trials, n = 31) or MDA (MD = −0.59; 95 % CI: −1.99 to 0.81; p = 0.41; 3 trials, n = 41). A significant reduction was observed for CRP (MD = −0.44; 95 % CI: −0.66 to −0.22; p = 0.0001; 2 trials, n = 52). Heterogeneity was substantial for MDA (I^2 = 80 %) but negligible for IL-6 and CRP (I^2 = 0 %). Risk of bias was predominantly rated as "some concerns" or "high." According to GRADE, the certainty of evidence was low for IL-6 and CRP and very low for MDA due to risk of bias and imprecision.

Conclusion: Based on a very limited number of small randomized trials, vitamin C supplementation does not appear to consistently modify post-exercise inflammatory or oxidative stress biomarkers. However, the available evidence is characterized by low to very low certainty, substantial methodological limitations, and imprecision. Therefore, these findings should be interpreted with caution and considered hypothesis-generating, underscoring the need for larger, high-quality, well-controlled trials.

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1. Introduction

Strenuous physical activity is a powerful physiological stimulus able to generate substantial metabolic and mechanical stress on skeletal muscle tissue, mainly when the exercise bout involves high intensity, unaccustomed loads, or prolonged duration [1]. Intense exertion has been identified as a potential trigger for rare but serious adverse events, whereas non-pharmacological interventions may mitigate these risks [2–5]. These stressors collectively contribute to a cascade of acute physiological disturbances, including reduced muscle contractile capacity, transient impairments in neuromuscular function, and the familiar phenomenon of delayed onset muscle soreness (DOMS), which usually emerges 24–72 h post-exercise. DOMS is extensively considered a hallmark of exercise-induced muscle damage and reflects structural disruptions such as sarcomere overstretching, Z-line streaming, and changes in excitation–contraction coupling [6–9].

At the biochemical level, strenuous exercise triggers a marked increase in the production of Reactive Oxygen Species (ROS), arising from multiple intracellular sources with mitochondrial electron leakage, (Nicotinamide adenine dinucleotide phosphate (reduced form) NADPH oxidase activation, xanthine oxidase, and infiltrating immune cells [10–12]. Even though low to moderate reactive oxygen species (ROS) generation is critical for redox signaling and adaptive processes, excessive accumulation overwhelms endogenous antioxidant defenses, encouraging a state of oxidative stress. This redox imbalance encourages lipid peroxidation, protein oxidation, and Deoxyribonucleic acid (DNA) damage, which can worsen muscle fatigue and lengthen recovery [13].

Managing and optimizing these physiological reactions, balancing the necessity for sufficient stress to induce training adaptations against the risk of excessive damage or prolonged recovery, remains a central focus in sports science, clinical rehabilitation and performance optimization [14–16]. Strategies to modify these responses include nutritional interventions, recovery modalities, antioxidant supplementation, exercise periodization, and targeted rehabilitation protocols. Understanding the mechanistic groundworks of exercise-induced oxidative and inflammatory responses is thus vital for developing evidence-based methods that enhance recovery while preserving long-term adaptability [17].

With this in mind, vitamin C (Ascorbic Acid), a vital water-soluble antioxidant, has been widely projected as a nutritional countermeasure owing to its ability to directly neutralize ROS, thus hypothetically mitigating oxidative stress and the subsequent inflammatory cascade [18]. Key biomarkers of this response include Malondialdehyde (MDA), a typical measure of lipid peroxidation and oxidative damage, and inflammatory cytokines such as Interleukin-6 (IL-6) and C-reactive protein (CRP) [19–21].

Still, the effectiveness of vitamin C supplementation in controlling post-exercise recovery remains highly controversial. An earlier trial demonstrated a protective antioxidant effect, displaying a reduction in markers such as MDA (Boohloli et al., 2012). Equally, others indicated no beneficial effect on crucial inflammatory markers (IL-6, CRP) [39,40] and, judgmentally, some studies advise that excessive ROS scavenging could interfere with obligatory muscle adaptations, possibly delaying muscle function recovery [36].

Although previous reviews have addressed antioxidant supplementation in exercise contexts or reported broad performance-related outcomes, they have largely synthesized heterogeneous biomarkers or physiological endpoints without a focused quantitative meta-analytic assessment of the most consistently reported inflammatory (IL-6, CRP) and oxidative stress (MDA) markers specifically within the post-exercise recovery period and under controlled, double-blind, placebo-controlled trial conditions [22,23].

Clarifying whether vitamin C supplementation modulates biochemical responses associated with post-exercise recovery is essential for informing evidence-based strategies for athletes, coaches, and healthcare professionals [24]. Given the heterogeneity and inconsistent findings reported across individual trials, a comprehensive quantitative synthesis is warranted to estimate the overall magnitude and direction of the effects of vitamin C on post-exercise inflammatory and oxidative stress–related responses. Therefore, the present study aimed to systematically review and meta-analyze randomized, double-blind, placebo-controlled trials evaluating the impact of vitamin C supplementation on biochemical markers related to inflammation and oxidative stress following exercise in adult populations.

2. Methods

2.1. Protocol and registration

This review was performed following the guidelines set by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [25] and has been registered in the PROSPERO database under the identifier CRD42024594742.

2.2. Eligibility criteria

The selected studies were sourced from peer-reviewed journals and published between the inception of each database and November 2025. Inclusion and exclusion parameters were recognized founded on the PICOS framework (Population, Intervention, Comparison, Outcomes, and Study Design), and encompassed:

1. (P) Adults aged 18 years or older, classified as apparently healthy or with stable, well-controlled chronic conditions as defined by each original study, who were exposed to a structured or experimentally controlled exercise protocol (acute bout or short-term training) designed to elicit measurable physiological stress and post-exercise recovery responses, with exercise modality, intensity, duration, and frequency explicitly described;
2. (I) Studies in which the intervention group received vitamin C as a dietary supplement, administered exclusively via the oral route in clearly defined pharmaceutical dosage forms (e.g., capsules, tablets, or powdered formulations), provided either before exercise, after exercise, or in both periods, and delivered acutely or chronically in temporal proximity to a single exercise bout or structured training program explicitly designed to assess post-exercise recovery responses, irrespective of exercise modality. We also included trials in which vitamin C was administered as part of whole foods, fruit-derived beverages, or non-standardized extracts were not considered eligible;
3. (C) Comparison groups consisted of participants receiving a placebo under identical exercise and recovery conditions;
4. (O) Outcomes were restricted to biomarkers directly related to post-exercise recovery, including indicators of muscle damage, oxidative stress, and inflammatory activity measured before and after exercise or during the defined recovery window following exercise exposure; studies reporting biomarkers unrelated to exercise-induced stress or recovery processes were excluded;
5. (S) Eligible studies were randomized, placebo-controlled trials, including both parallel-group and crossover designs, employing single-, double-, or triple-blind methodologies. Crossover designs were eligible but not mandatory. When crossover trials

were included, data were preferentially extracted using within-participant comparisons when sufficient information was available, appropriately accounting for the paired nature of the data. If paired analyses were not feasible or if carryover effects could not be confidently excluded, only post-intervention data were extracted and the study was analyzed as a parallel-group trial. Only articles published in peer-reviewed journals and master's theses written in English were considered eligible. Conference abstracts, doctoral dissertations, descriptive or observational studies, case reports, editorials, and review articles were excluded.

2.3. Information source, search strategy and study selection

The literature search was performed across the Lilacs, CINAHL, MEDLINE/PubMed (via the U.S. National Library of Medicine), Scopus, and Web of Science databases by submitting a set of predefined keywords "Ascorbic Acid" OR "Magnorbin" OR "Vitamin C" OR "L-Ascorbic Acid" OR "Ascorbate" OR "Ascorbicum" OR "Hybrin" AND "Exercise" OR "Physical Activity" OR "Strengthening Program" OR "Training" OR "Rehabilitation" OR "Habilitation" OR "Post-exercise recovery" (Supplementary file: Search strategy).

2.4. Screening and selection process

All identified records were imported into the Rayyan QCRI platform (Qatar Computing Research Institute, Qatar) for duplicate detection and removal. Title and abstract screening was independently conducted by four reviewers to enhance sensitivity and minimize the risk of missing eligible studies at this initial stage. Full-text eligibility assessment was subsequently performed by the same reviewers, with disagreements resolved through discussion and, when necessary, consultation with a fifth senior reviewer to achieve consensus. Data extraction was then carried out independently by two reviewers using a standardized extraction form, as this phase involves a more detailed and structured assessment of predefined variables. Any discrepancies identified during data extraction were resolved through consensus discussion between the two reviewers, with arbitration by a third senior reviewer when required. After final confirmation of eligible studies, the research team collectively evaluated the feasibility and appropriateness of conducting a meta-analysis based on data availability and methodological homogeneity.

2.5. Data collection and extraction

Information extracted from each primary study included details such as authorship, study design, participant characteristics, intervention type, and exercise protocols, which were compiled into a summary table. When key data were absent, corresponding authors were contacted to obtain clarification or further information. Data extraction was independently performed by at least two reviewers. If no response was received from the study authors, data displayed in graphical format were extracted using the Web Plot Digitizer® tool. Biomarkers related to muscle damage, oxidative stress, and inflammation were recorded as means and standard deviations (SD). When studies reported values in terms of standard error (SE) or confidence intervals (CI), these were converted to SD for consistency.

2.6. Data items

The review focused on extracting data concerning biomarkers of muscle damage, oxidative stress, and inflammation to enable comparison pre- and post-intervention (immediately and 2 h following exercise cessation). Additional variables—such as participant characteristics, intervention details, and funding sources—were also retrieved from the included studies. Data that were unclear or unavailable after efforts to retrieve them were excluded from the analysis.

2.7. Risk of bias assessment

Risk of bias was evaluated via the Cochrane Risk of Bias tools [26], implemented through the Review Manager software (RevMan 5.4.1). The assessment addressed six domains:

1. Randomization process
2. Deviations from intended interventions
3. Absent outcome data
4. Measurement of outcomes
5. Selection of reported results
6. Overall risk of bias

Each domain was rated as "low risk," "some concerns," or "high risk", consistent with the criteria outlined by [26]. The evaluation was independently completed by two reviewers. In cases where judgments differed, a third reviewer was consulted to resolve discrepancies. Potential bias-related variables—such as publication bias and selective outcome reporting—were similarly considered. All reviewers endured formal training in risk of bias assessment before the analysis.

2.8. Certainty of evidence (GRADE assessment)

The GRADE framework (GRADE Working Group, 2004) was enforced to assess the certainty and quality of the evidence. This method prioritizes randomized controlled trials as high-level evidence, while similarly factoring in study design, execution quality, and any limitations impacting reliability [27]. The GRADEpro GDT v4® software (McMaster University, Ontario, Canada) was required to create a Summary of Findings table.

2.9. Qualitative synthesis (systematic review)

A narrative synthesis was conducted to systematically describe how each included study was designed and implemented, acknowledging the intentional breadth of populations and clinical contexts examined. Although the included studies encompassed diverse conditions such as obesity, chronic heart failure, susceptibility to common cold incidence, and vascular health, all were unified by the assessment of inflammatory, oxidative, or endothelial biomarkers measured in relation to exercise exposure or recovery-related physiological stress. Key methodological characteristics and outcome data were summarized narratively and in tabular form. This approach was adopted to capture shared recovery-relevant biological pathways across heterogeneous populations, while recognizing that the diversity of study contexts may introduce a degree of indirectness in relation to strictly defined post-exercise recovery biomarkers.

2.10. Quantitative synthesis and effect measures (meta-analysis)

After study selection, the team assessed whether a meta-analysis was appropriate. When applicable, data on muscle damage, oxidative stress, and inflammatory markers were pooled. The meta-analysis relied on pre- and post-intervention measurements and included all relevant exercise protocols. For the purposes of this review, post-exercise was defined as assessments conducted

immediately after exercise cessation or within up to 2 h following the end of the exercise bout.

Statistical heterogeneity was quantified via the I^2 statistic, interpreted as: 0 %–29 %: may not be important, 30 %–49 %: moderate heterogeneity, 50 %–74 %: substantial heterogeneity, 75 %–100 %: considerable heterogeneity [28, 29].

Significance was determined at the level $p < 0.05$ (<5 %) for overall effect sizes. If the necessary dispersion values (SD, CI, SE, p-values) were absent, change SDs were calculated accordingly. Meta-analysis results were offered as weighted mean differences (MD) with 95 % confidence intervals and p-values, and displayed by means of forest plots. A random-effects model was applied to account for between-study variability and enhance generalizability [30]. All statistical procedures were executed via RevMan 5.4.1.

3. Results

3.1. Description of participant characteristics

Across the twelve included studies, participant characteristics varied substantially with respect to age, sex, training status, and health condition, reflecting a broad range of populations exposed to exercise-related physiological stress [40]; Boohloli et al., 2012; [31–38,41,42].

Most trials enrolled young to middle-aged adults, with mean ages ranging from approximately 21 to 40 years in studies involving healthy or recreationally active individuals (Boohloli et al., 2012; [32,34,35,37,41,42]. In contrast, two studies included older or clinical populations, namely overweight or obese adults with type 2 diabetes mellitus (mean age 53 ± 7 years [38]; and patients with chronic heart failure (mean age 65.6 years; [31].

Sex distribution was heterogeneous. Several studies recruited male-only samples, particularly those involving endurance or resistance exercise protocols [40]; Boohloli et al., 2012; [33,34,36]. Other trials included mixed-sex samples, especially in obese or clinical populations [32,35,38], while [41] focused exclusively on healthy young women.

Participants also differed in training status and baseline physical fitness. Studies ranged from untrained or recreationally active individuals (Boohloli et al., 2012 [37,41]; to well-trained recreational athletes participating in competitive endurance events [40]. Exercise modalities included aerobic running, treadmill walking, resistance exercise, eccentric contractions, cycling, and forearm isometric exercise, reflecting diverse physiological demands imposed on the participants.

Sample sizes were generally modest, ranging from 11 to 49 participants, with most trials enrolling between 20 and 30 individuals per study. Randomized, placebo-controlled designs predominated, including both parallel-group and crossover trials, ensuring within-study comparability of participant characteristics between intervention and control conditions.

3.2. Study selection

A total of 1403 records were acknowledged completed using database searches, with no further records obtained from registers. After eliminating 319 duplicates, 1084 unique records were screened founded on title and abstract, resulting in the exclusion of 1055 studies. Twenty-nine reports were retrieved for full-text assessment, all of which were successfully obtained. Following eligibility evaluation, 17 reports were omitted for the subsequent reasons: combination of vitamin C with other interventions ($n = 9$), not being a randomized controlled trial ($n = 5$), inclusion of participants under 18 years of age ($n = 1$), lack of relevant outcome ($n = 1$), or nonappearance of a placebo group ($n = 1$). Thus, 12 studies achieved the inclusion criteria and were incorporated into the final review. The selection and screening process followed the PRISMA guidelines, as illustrated in Fig. 1.

3.3. Results of individual studie

Twelve studies examined the effects of vitamin C supplementation on physiological responses to exercise, encompassing heterogeneous populations, supplementation protocols, and exercise modalities, as detailed in Table 1 (see Fig. 2). The findings can be thematically organized into inflammatory and immune responses, oxidative stress and redox balance, neuromuscular recovery and perceptual outcomes, and vascular or cardiovascular responses.

Regarding inflammatory and immune responses, the evidence was mixed and highly context-dependent. In recreationally trained middle-aged men [40], showed that 500 mg/day of vitamin C for 15 days increased plasma ascorbate concentrations but did not attenuate exercise-induced increases in IL-6 or IL-10 mRNA or protein following a competitive 15 km run. Similarly, [41]; in healthy young women supplemented with 500 mg/day for two weeks, reported no between-group differences in inflammatory markers following 30 min of running, despite exercise-related changes in oxidative parameters. In contrast [33], observed that in young men performing high-intensity resistance exercise, 500 mg/day for two weeks prevented the post-exercise increase in CRP seen in the placebo group, although no significant changes were observed in blood pressure or lactate between groups. [42]; studying healthy young men with marginal vitamin C status over eight weeks, reported modest increases in self-reported physical activity and a reduced incidence and duration of upper respiratory tract infections, suggesting indirect immune-related benefits rather than direct modulation of exercise-induced inflammation.

With respect to oxidative stress and antioxidant capacity, several studies reported reductions in lipid or protein oxidation markers, although results were not uniform. Boohloli et al. (2012) demonstrated that supplementation with 500 mg/day for 14 days significantly reduced serum MDA concentrations and increased total antioxidant capacity following 30 min of running at 75 % of oxygen maximal uptake (VO_2max) in untrained young men, without affecting IL-6 or leukocyte counts [34]. showed that doses of 500–1000 mg/day for two weeks attenuated post-exercise protein carbonyl formation after treadmill running at 75–80 % VO_2max, while other oxidative stress markers, including glutathione and thiobarbituric acid reactive substances, remained unchanged. Conversely [36], found no effect of 1000 mg/day for eight weeks on oxidative stress markers, muscle damage indices, or recovery following downhill running in trained men.

Findings related to neuromuscular recovery and perceptual outcomes were inconsistent [35]. reported that high-dose vitamin C supplementation (3 × 1000 mg/day for eight days) did not reduce strength loss, soreness, pain perception, or range-of-motion deficits following eccentric elbow flexor exercise in young adults. In contrast [32], observed that obese adults supplemented with 500 mg/day for four weeks exhibited significantly lower heart rate and ratings of perceived exertion during a standardized treadmill walk, along with reduced fatigue scores, despite no differences in weight loss or respiratory exchange ratio compared with placebo.

In addition, although [42] reported outcomes using incidence and relative risk metrics, this does not reflect an observational design. Rather, these measures were applied to dichotomous clinical outcomes (occurrence of respiratory tract infections) within a randomized, double blind, placebo-controlled trial framework. The use of epidemiological effect measures in this

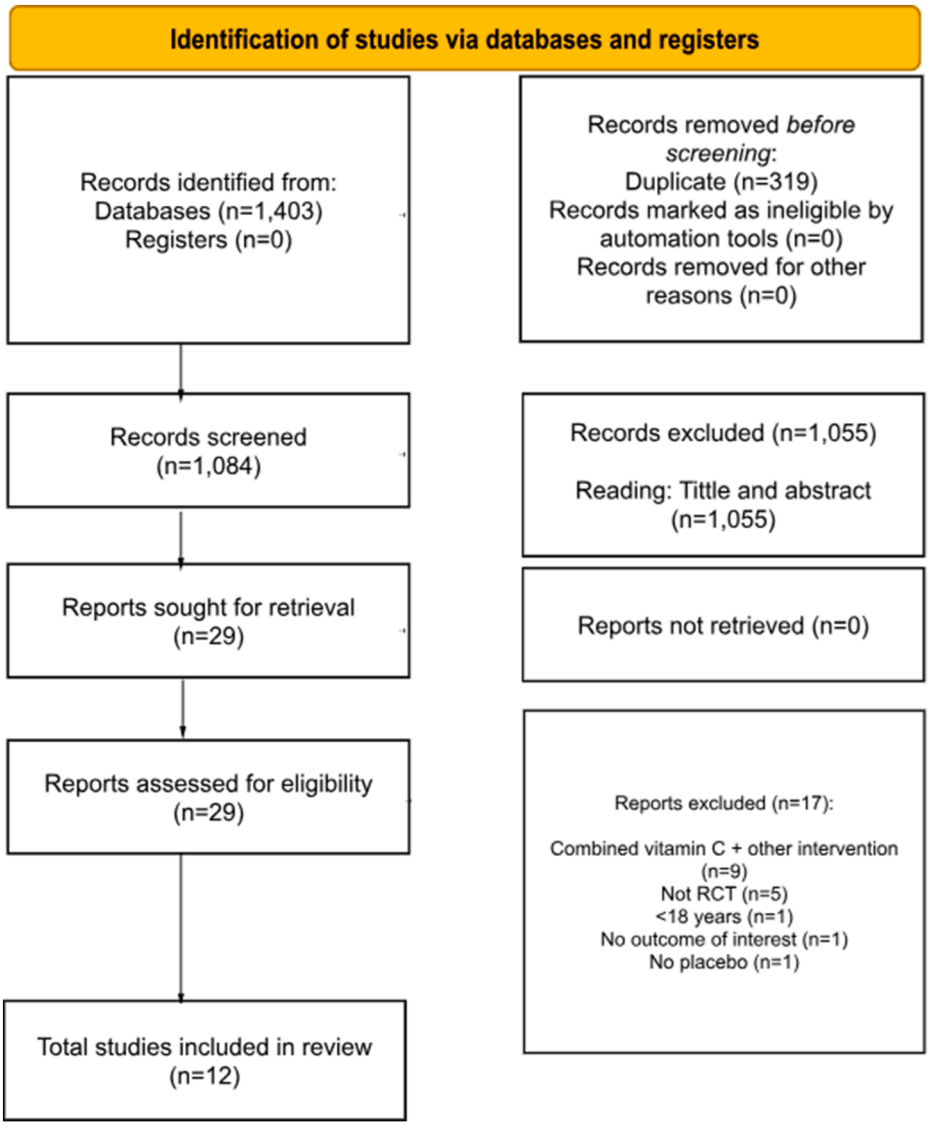

Fig. 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only.

context is methodologically appropriate and does not conflict with the experimental nature of the study. Accordingly [42], should be consistently interpreted as an interventional clinical trial, with relative risk serving as an outcome metric rather than a descriptor of study design.

Finally, studies evaluating vascular and cardiovascular responses suggested potential benefits in specific clinical or physiological contexts. Caruana and Marshall (2015) showed that a single oral dose of 2000 mg vitamin C enhanced post-contraction vasodilatory responses during normoxic conditions in recreationally active men, although this effect was abolished under hyperoxic exposure. In patients with chronic heart failure [31], reported that supplementation with 4000 mg/day for four weeks improved endothelial function, left ventricular ejection fraction, and 6-min walk distance in a crossover design. Additionally, Boonthongkaew et al. (2021), studying overweight or obese adults with type 2 diabetes, found that vitamin C co-supplementation (1000 mg/day) during six weeks of low-intensity cycling increased plasma ascorbate concentrations and enhanced antioxidant capacity compared with placebo, although no differences in post-exercise blood pressure responses were observed.

3.4. Baseline vitamin C status

Baseline plasma vitamin C (ascorbate) concentrations varied substantially across the randomized trials that explicitly reported this variable, indicating marked heterogeneity in participants' initial vitamin C status. In the trial by [41]; baseline plasma vitamin C levels were low in both groups, averaging 11.3 ± 3.3 μmol/L in the supplementation group and 9.6 ± 11.7 μmol/L in the placebo group, values compatible with hypovitaminosis C.

Similarly [32], enrolled obese adults with suboptimal vitamin C status, reporting baseline plasma ascorbate concentrations indicative of marginal deficiency prior to supplementation.

In contrast, other trials included participants with adequate baseline vitamin C levels [42]. restricted inclusion to individuals with plasma vitamin C concentrations below 45 μmol/L, with mean baseline values in the low-to-adequate range, thereby targeting a population with marginal vitamin C status rather than overt deficiency.

[40] reported baseline plasma vitamin C concentrations within the adequate physiological range in both placebo and supplemented groups, consistent with the well-nourished and highly trained status of the participants.

Table 1
Description of the characteristics of the study population of articles by author and year, sample, age (years), intervention, control and outcomes.

Author/Years	Study Design	Sample	Age (years)	Intervention	Control	Outcomes	Funding
[40]	Randomized, double-blind, placebo-controlled trial.	31 male recreational well-trained athletes. Intervention group: n = 15. Control group: n = 16.	Intervention group: 37.2 ± 5.4 years. Control group: 39.5 ± 5.6 years.	Exercise: Duration: One-time 15-km run. Modality: Running in a competitive event Intensity: Average HR ~163–165 bpm, Max HR ~178–182 bpm Frequency: One session (post-supplementation) Vitamin C: Dosage: 500 mg/day (250 mg, twice daily). Duration: 15 days Form: Oral capsules	Identical capsules containing microcrystalline cellulose.	No effect on IL-6 or IL-10 (both mRNA and protein levels) in plasma or blood mononuclear cells. No effect on cortisol, markers of oxidative stress (MDA, LOOH), or muscle damage (CK, AST). Exercise increased IL-6 and IL-10 levels, but vitamin C did not influence these responses.	Not mentioned.
Boohloli et al., 2012	Double-blind, placebo-controlled study.	16 healthy, non smoking, untrained young men Intervention group: n = 8. Control group: n = 8.	Intervention group: 21.1 ± 0.8 years. Control group: 22.1 ± 0.6 years.	Exercise: 30-min running at 75%VO2máx Vitamin C: Dosage: 500 mg/day (2 h before exercise) Form: Oral capsules	Identical capsules containing lactose	Increased plasma concentrations of vitamin C before and after exercise affected MDA after exercise compared to placebo group. Vitamin C did not show any effect on IL-6 and inflammatory mark-ers such as total leukocytes, neutrophils, lym-phocytes and CRP. Moderate dose vitamin C supplementation possibly alleviated lipid peroxidation and muscle damage but not inflammatory responses after 30-min running at 75 % VO2max.	Not mentioned.
[38]	Randomized, double-blind, placebo-controlled cross-over study	24 participants (20 women and four men). Were included in the study and 20 patients (16 women and four men) completed the study. Patients were overweight to obese and had low physical fitness, with type 2 diabetes mellitus	Participants were 53 ± 7 years	Exercise: low-intensity Duration: 6 weeks Type: cycling exercise at 33 % of peak oxygen consumption for 20 min. Vitamin C: 1000 mg ascorbic acid. Form: Oral capsules	Identical capsules containing 1000 mg of Daucus carota dry root.	Differences of blood pressure between resting before and within 60 min after exercise were not observed in both Vitamin C and placebo arm. Plasma ascorbate concentration significantly higher at rest before and immediately after low-intensity exercise at post-Vitamin C supplementation than at post-placebo	Not mentioned.
[37]	A cross-over study.	11 males with a body mass index of 23.0 ± 0.7. They were all recreationally active. None of them smoked. None had a history of cardiovascular or respiratory disorder except	Male subjects aged 21.1 ± 0.8	Exercise: static forearm contraction at 60 % MVC for 2 min by using a handgrip dynamometer Vitamin C: Doses: 2000 mg Form: lemon-flavoured,	Identical lemonades: Tasting sessions held prior to the study indicated they were indistinguishable.	There were no significant differences between baseline values of any of the recorded variables (of MABP, HR, FBF and FVC) after placebo or vitamin C,	Not mentioned.

		for two subjects who had childhood asthma. None took vitamin supplements of any kind, including vitamins C or E.		efferves-cent vitamin C (Boots Pharmacy, UK), dissolved in Cloudy Lemonade (Somerfield plc) or Lemonade alone. Both were taken through a drinking straw to reduce the risk of recog-nizing the lemonade containing vitamin C;		in the absence or presence of hyperoxia.	
[36]	Randomized, double blind, placebo-control	20 active males, non smoking, non-smokers and free from any known illnesses as ascertained Intervention group: n = 10. Control group: n = 10	Placebo group: 22·1 ± 0.4 (years) Ascorbic acid group: 24·2 ± 1.5 (years)	Exercise: downhill running of 30 min Intensity: sub-maximal intensity Duration: 14 days Vitamin C: Doses: 1 g ascorbic acid Form: Oral capsules	Identical capsules containing lactose	There were no significant differences (P.0·05) in heart rates, VO2max, ratings of perceived exertion, RER, minute ventilation and run speed between the two groups.	Not mentioned.
[35]	Randomized, placebo-control.	24 subjects (male and female) Intervention group: n = 12. Control group: n = 12	Placebo group: 22.6 ± 4.6 (years) Treatment: 22.3 ± 3.9 (years)	Exercise: 2 × 20 eccentric elbow extensions Vitamin C:3 × 1000 mg/day during 8 days	3 × 50 mg/day of glucose during 8 days	There were no significant between group differences in response to any of the aforementioned variables: strength loss, point tenderness, elbow flexor range of motion, subjective pain.The results of this study suggest that a VC supplementation protocol of 3 × 1000 mg/day for 8 days is ineffective in protecting against selected markers of delayed onset muscle soreness.	
[34]	were randomly assigned in a counter-balanced design, placebo-controlled trial.	Twelve males age 18 to 35 y volunteered as subjects.	the volunteers were 25.0 ± 1.4 years old.	Exercise: Each subject performed 30 min of running at 75–80 % of VO2max at the end of 2 wk of each treatment. Prior to and immediately after exercise, blood was drawn. Vitamin C: Vitamin C (VC) was taken either 250 mg/ twice per or 500 mg/twice per d with a minimum of 2 wk between treatmets.	The supple-ments were supplied by CIBA Pharmaceuticals (Edison, NJ).	Therefore, vitamin C supplementation had no influence on these parameters during and immediately following the exercise. There was a similar significant increase in the ratio of oxidized to total glutathione after exercise independent of treatment. Vitamin C did not alter the exercise-induced response.	Not mentioned.
[33]	Randomized, double-blinded, placebo-controlled trial.	20 young men, divided into vitamin C supplementation (n = 10) and placebo (n = 10) groups.	Supplement: 38.2 ± 3.7 years. Placebo: 39.4 ± 3.6 years.	Exercise: Exercise session involved one session of resistance exercise, which was carried out after two weeks of supplementation. Resistance exercise included five exercises of three sets of eight repetitions with 80 % of repetitions maximum (1RM) for bench press, leg extension, lateral pull down, lying leg curl and	maltodextrin was similarly prepared in capsules and provided to placebo group. Maltodextrin is a white powder made from starch	that levels of C -reactive protein, lactate and systolic and diastolic blood pressure were not significantly changed in participants after supplementation. C -reactive protein levels significantly increased only in placebo group immediately post resistance exercise and 24 h post exercise.	This study was adapted from a MSc thesis approved by the Marivan Branch, Islamic Azad University, with scientific and financial supports.

(continued on next page)

Table 1 (*continued*)

Author/Years	Study Design	Sample	Age (years)	Intervention	Control	Outcomes	Funding
				triceps pushdown. vitamin C: Vitamin C supplement group received 500 mg d - 1 of vitamin C in capsules.		The unique statistically significant difference between the two groups included a significant increase in level of C -reactive protein in placebo group immediately post resistance exercise.	
[31]	This was a cross-over, randomized controlled trial.	A total of 37 subjects with chronic heart failure. Group I (n = 19), Group II (n = 18).	mean age was 65.6.	Exercise: Exercise capacity was evaluated by the total distance of 6-min walk test (6MWT). Group I (n = 19) received vitamin C 4000 mg daily for four weeks and followed by placebo for six weeks. Group II (n = 18) received placebo for six weeks and followed by vitamin C 4000 mg daily for four weeks.	Not mentioned.	There was a statistic difference in brachial diameter change percentage, baseline flow, and peak flow while using antioxidant supplementation compared to when they are not using antioxidant supplementation. there was a significant difference in LVEF while using antioxidant supplementation. There was a statistical increase in 6MWT while using antioxidant supplementation.	Not mentioned.
[32]	Randomized, placebo-controlled trial.	Twenty obese adults (4 men and 16 women).	intervention group: 37.4 3.3 years. Control group: 32.5 4.3 years.	Exercise: Then, at the start of the trial and at trial week 4, a 60-min treadmill walk at 50 % of VO2max was performed to determine the effects of vitamin C supplementation on exercise heart rate, RPE, and RER. Rested (no exercise for 48 h) and fasted (no food or drink with the exception of water for 10 h). After the collection of a blood sample, participants were fitted with a heart rate monitor, a respiratory mask, and a two-way non-rebreathing valve and asked to walk on a motorized treadmill for 60 min Vitamin C: receive 500 mg of vitamin C (VC) or placebo (CON) daily for 4 wk while adhering to a vitamin C–controlled, calorie-restricted diet. Feelings.	CON participants consumed a placebo capsule daily.	Heart rate and the Ratings of Perceived Exertion during exercise was significantly decreased in the VC versus the CON group. the two groups lost similar amounts of weight (w4 kg), and the respiratory exchange ratio was not altered by group. The general fatigue score decreased 5.9 U for the VC group versus a 1.9U increase for the CON group.	Not mentioned.

[42]	Randomized, double-blind, placebo-control led trial. eight-week trial	Healthy non- smoking 28 adult men Vitamin C (n = 15) Placebo (n = 13)	Intervention group: 23.0 ± 3.1 years. Control group: 23.2 ± 4.3 years.	Vitamin C: to ingest two capsules daily in a divided dose (morning and evening). Vitamin C capsules (500 mg vitamin C per capsule, Twinlab C-500 CAPS, American Fork, UT, USA). Exercise: Participants were provided a booklet at the start of the study that contained the Wisconsin Upper Respiratory Symptom Survey-21, the Godin Leisure-Time Exercise Questionnaire, and a short food frequency measure.	were identical in appearance to the placebo capsules that contained white flour.	Fasting plasma vitamin C concentrations were raised significantly for the vitamin C group versus the placebo group at week 4. Physical activity increased slightly in the vitamin C group compared to the placebo group in the first four weeks of the trial. however, at weeks 5–6 and weeks 7–8, physical activity increase more markedly in the vitamin C versus placebo groups.	Not mentioned.
[41]	The aim of this double blind randomized controlled trial.	Forty-nine healthy young women randomly assigned into 500 mg day^{1}vitamin C supplement (n = 25) or placebo (n = 24) groups for two weeks.	Intervention group: 24.000 + 3 years. Control group: 23.000 ± 2 years.	Exercise: Then they ran with a 5–6 km h intensity for 30 min.Two subjects together (one person from supplement group and one person from placebo group) initiated to run. Third blood samples were taken immediately (2–3 min) after running. Vitamin C: Subjects were randomly assigned to either vitamin C (500 mg day [1] or placebo (500 mg day [1] lactose) for two weeks.	placebo (500 mg day [1] lactose). Vitamin C and lactose were prepared in capsule forms.	Vitamin C and energy intakes were not statistically different between groups. Before and after exercise comparison indicated that there is significant decrease in MDA and increase in TGSH in S and P groups. There were significant differences in relation to plasma vitamin C concentration after intervention and after exercise between groups.	Not mentioned.

Legend: HR – Heart Rate; Max HR – Maximum Heart Rate; VO_2max/VO_2max – Maximal Oxygen Uptake; MVC – Maximal Voluntary Contraction; IL-6 – Interleukin-6; IL-10 – Interleukin-10; mRNA – Messenger Ribonucleic Acid; MDA – Malondialdehyde; LOOH – Lipid Hydroperoxides; CK – Creatine Kinase; AST – Aspartate Aminotransferase; CRP – C-Reactive Protein; FBF – Forearm Blood Flow; FVC – Forearm Vascular Conductance; MABP – Mean Arterial Blood Pressure; RER – Respiratory Exchange Ratio; RPE – Rating of Perceived Exertion; 1RM – One-Repetition Maximum; 6MWT – Six-Minute Walk Test; LVEF – Left Ventricular Ejection Fraction; TGSH – Total Glutathione; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; MBP – Mean Blood Pressure; VC – Vitamin C; bpm – Beats Per Minute.

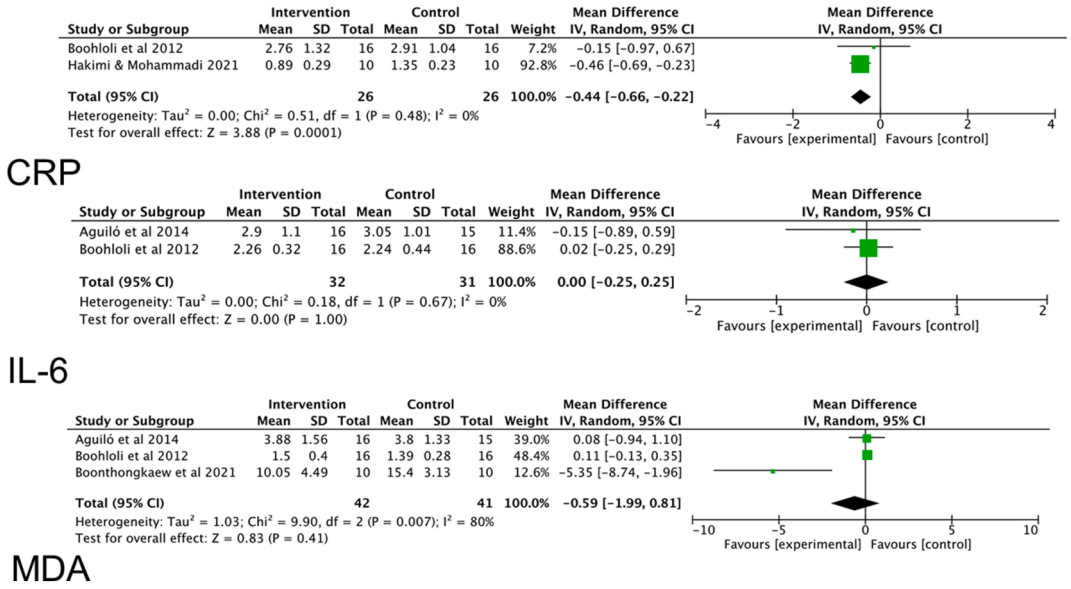

Fig. 2. Meta-analysis for overall effects of vitamin C an exercise on interleukin 6 (IL-6), C reactive protein (CRP) and malondialdehyde (MDA).

Likewise, Boohlooli et al. (2012) measured plasma vitamin C at baseline and showed comparable pre-intervention concentrations between groups, followed by significant post-supplementation increases only in the vitamin C arm.

Other trials, including those by [33–35,37]; and [31]; did not report baseline plasma vitamin C concentrations, limiting interpretation regarding participants' initial vitamin C status and its potential moderating effect on physiological and oxidative stress outcomes.

3.5. Pharmacological aspects

Across the included studies, vitamin C was consistently administered as ascorbic acid, the biologically active and water-soluble form of the vitamin, using standardized oral pharmaceutical formulations. Most trials employed capsules or tablets, ensuring precise dose control and minimizing variability related to absorption or co-ingested bioactive compounds [32,34–36,40,41]; Boohloli et al., 2012). No study utilized parenteral, sublingual, or non-oral routes of administration.

Daily doses ranged from 500 mg to 4000 mg, delivered either as a single bolus dose or as fractionated administrations throughout the day. Fractionated dosing was commonly adopted in short-term supplementation protocols to maintain plasma ascorbate concentrations near saturation. For example [40], administered 500 mg/day divided into two 250 mg capsules over 15 days, with the final dose ingested the evening before a 15 km running competition, thereby ensuring elevated systemic vitamin C availability during exercise and early recovery. Similarly, Boohloli et al. (2012) provided 500 mg/day for 14 days prior to an acute treadmill exercise bout at 75 % VO_2max, using a single daily oral dose.

Several studies employed acute supplementation strategies, particularly when vascular or redox outcomes were of interest. [37]; for instance, administered a single oral dose of 2000 mg vitamin C approximately 2 h before experimental testing to examine post-contraction vasodilatory responses. In contrast, most investigations adopted chronic supplementation protocols lasting from 2 to 8 weeks, designed to evaluate cumulative effects on oxidative stress, inflammatory markers, neuromuscular recovery, or cardiovascular function [31,33,34,36,38,42].

High-dose regimens were also implemented in specific contexts [35]. used 3000 mg/day, administered as three 1000 mg doses, over eight days to assess effects on delayed-onset muscle soreness, while [31] provided 4000 mg/day for four weeks in patients with chronic heart failure, reflecting a therapeutic rather than ergogenic intent. Despite these higher doses, administration remained oral and pharmaceutically standardized.

Importantly, none of the included studies evaluated vitamin C derived from whole foods, fruit juices, or non-standardized extracts, nor did they combine vitamin C with other antioxidants within the intervention arm.

3.6. Synthesis of results

The meta-analysis assessed the effects of vitamin C supplementation on inflammatory and oxidative stress biomarkers, together with C-reactive protein (CRP), interleukin-6 (IL-6), and malondialdehyde (MDA), across several clinical trials. The focus on CRP, IL-6, and MDA was primarily determined by data availability and methodological comparability across the included studies. Although several trials reported additional exercise recovery–related outcomes, such as creatine kinase (CK), delayed onset muscle soreness (DOMS), or strength and functional performance measures, these outcomes were assessed using heterogeneous protocols, non-uniform time points, or incomparable measurement scales. As a result, pooling these outcomes in a quantitative meta-analysis was not methodologically appropriate. In contrast, CRP, IL-6, and MDA were the only biomarkers consistently reported across multiple eligible trials with sufficient methodological alignment to allow quantitative synthesis. Therefore, the emphasis on these biomarkers reflects a data-driven analytical decision rather than an intentional exclusion of functional or clinical recovery outcomes, and it defines the narrow but methodologically robust scope of the present meta-analysis.

For CRP, the analysis included two studies with a combined total of 52 participants. The pooled results revealed a statistically significant reduction in CRP levels following vitamin C supplementation, with a mean difference (MD) of −0.44 (95 % CI: −0.66, −0.22; p = 0.0001), and no heterogeneity (I^2 = 0 %).

Regarding IL-6, two studies (n = 31) were analyzed. The overall MD was 0.00 (95 % CI: −0.25, 0.25), showing no significant difference between intervention and control groups (p = 1.00; I^2 = 0 %). These results advocate that vitamin C supplementation does not significantly impact IL-6 levels, indicating a limited impact on this specific inflammatory cytokine.

For MDA, an oxidative stress marker, three studies (n = 41) were included. The pooled estimate revealed a non-significant reduction in MDA levels (MD = −0.59; 95 % CI: −1.99, 0.81; p = 0.41), with substantial heterogeneity between the studies (I^2 = 80 %). This variability suggests that differences in study design, dosage, or participant characteristics may have influenced the results.

3.7. Risk of bias

The risk of bias varied across the included studies, with differences observed in randomization procedures, adherence to interventions, outcome measurement, and reporting practices. Overall, most studies were judged to have some concerns, while a few presented high or low risk of bias (Fig. 3).

Randomization Process (D1)

All studies, except Caruana & Marshall (2015), adequately described their randomization procedures, including sequence generation and allocation concealment, and were thus rated as low risk [37]. presented some concerns owing to limited methodological detail on the randomization process.

Deviations from Intended Interventions (D2)

All studies (100 %) were rated as low risk for deviations from intended interventions, as there was no evidence that participants or investigators deviated from the assigned protocols or that such deviations influenced the study outcomes.

Missing Outcome Data (D3)

Every study demonstrated low risk for missing outcome data. Data loss was minimal or well-documented, and no significant differences between groups were attributed to absent data.

Measurement of Outcomes (D4)

Most studies (75 %) were classified as low risk, employing validated and standardized measurement tools suitable for their objectives. But, [33,37]; and [31] presented some concerns owing to unclear blinding of assessors or incomplete descriptions of measurement reliability.

Selection of Reported Results (D5)

The highest risk of bias was observed in this domain. Several studies, including [40]; Boohloli et al. (2012), and [34]; were rated as high risk due to the absence of pre-specified analysis plans and possible selective outcome reporting. Others, such as [37,42]; demonstrated some concerns related to insufficient reporting transparency.

Overall Bias

When all domains were considered [38], was the only study rated as low overall risk of bias. Most studies (75 %) were classified as having some concerns, while a smaller portion (25 %) demonstrated high risk, mainly due to selective reporting and limited methodological clarity. Overall, the evidence base is moderately reliable, but care is advised when interpreting results from studies with incomplete reporting or potential outcome selection bias.

3.8. GRADE assessment

The GRADE assessment designated that the overall certainty of evidence regarding the effects of vitamin C supplementation on inflammatory and oxidative stress markers ranged from low to very low, primarily as a result of concerns related to risk of bias, imprecision, and inconsistency across studies (Table 2).

- CRP: The evidence for CRP was classified as low certainty. Even though inconsistency, indirectness, and imprecision were not serious, the risk of bias by reason of selective reporting restricted the strength of this evidence.
- IL-6: The certainty of evidence was rated as low, reflecting serious risk of bias owing to selective reporting and imprecision linked to wide confidence intervals. Nevertheless, inconsistency and indirectness were not considered serious, as the studies evaluated similar populations and intervention protocols.
- MDA: Certainty of evidence was graded as very low, driven by serious concerns about risk of bias, very serious inconsistency (I^2 = 80 %), and imprecision resulting from overlapping

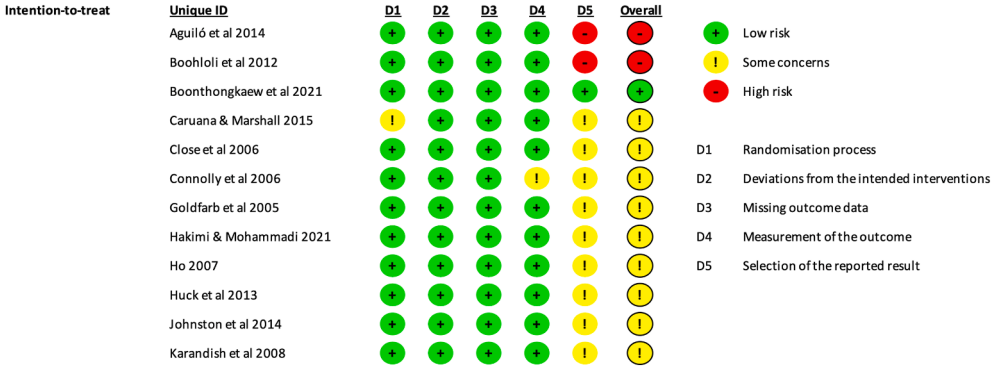

Fig. 3. Cochrane risk of bias tool.

Table 2
Levels of evidence analysis via (GRADE Working Group, 2004).

Outcome	No. of Studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Certainty of Evidence
IL-6	2	Serious[a]	Not serious	Not serious	Serious[b]	Low
MDA	3	Serious[a]	Very serious[c]	Not serious	Serious[b]	Very low
CRP	2	Serious[a]	Not serious	Not serious	Not serious	Low

[a] Selection of the Reported Result.
[b] Presence and absence of effect.
[c] $I^2 = 80$ %.

confidence intervals. These factors advocate substantial variability among studies assessing oxidative stress through MDA levels.

Overall, the GRADE analysis emphasizes that current findings on the anti-inflammatory and antioxidant effects of vitamin C should be interpreted with caution, as the existing evidence is restricted by methodological weaknesses and variability across studies.

4. Discussion

4.1. Summary of main findings

This systematic review and meta-analysis of randomized controlled trials aimed to evaluate the effect of vitamin C supplementation on post-exercise recovery, concentrating on key inflammatory and oxidative biomarkers. The pooled analysis exposed no significant effect of vitamin C supplementation on the inflammatory markers interleukin-6 and MDA. Yet, a statistically significant reduction was detected for the inflammatory marker C-reactive protein (CRP). However, these findings should be interpreted with considerable caution due to the limited number of studies and small sample sizes contributing to each pooled analysis. Only two trials contributed data to the CRP and IL-6 meta-analyses, and three trials to the MDA analysis, resulting in low total sample sizes (CRP n = 52; IL-6 n = 31; MDA n = 41). Such sparse evidence substantially limits statistical power and increases susceptibility to random error, thereby reducing the stability and reliability of the pooled effect estimates. Consequently, the observed reduction in CRP should be viewed as preliminary rather than definitive, and the absence of significant effects for IL-6 and MDA cannot be interpreted as conclusive evidence of no effect. Overall, the small evidence base underscores the fragility of the pooled estimates and precludes strong or generalized conclusions regarding the effectiveness of vitamin C supplementation on post-exercise inflammatory and oxidative stress biomarkers.

4.1.1. Clinical vs. statistical significance

The pooled analysis exposed distinct patterns across the inflammatory and oxidative biomarkers. For CRP, the meta-analysis demonstrated a clear and statistically significant reduction preferring the intervention (MD = −0.44; 95 % CI: −0.66 to −0.22; p = 0.0001), with no evidence of heterogeneity ($I^2 = 0$ %).

In contrast, IL-6 showed no significant overall effect, along with no heterogeneity. The wide confidence interval and variability among studies indicate that the intervention's impact on IL-6 is unclear and likely inconsistent across different experimental conditions. Equally, MDA, a key marker of lipid peroxidation [43–45], exhibited no significant pooled reduction, with substantial homogeneity across studies. This suggests that the intervention does not produce detectable improvements in oxidative stress as quantified by MDA.

Taken together, although a small statistically significant reduction in CRP was observed, this finding should be interpreted cautiously given the low to very low certainty of the evidence and the methodological limitations of the included trials. The absence of corresponding changes in IL-6 and MDA limits the strength of inference regarding a consistent anti-inflammatory or anti-oxidative effect. Inflammation and oxidative stress represent interconnected components of the post-exercise recovery response; therefore, changes confined to a single biomarker, particularly in the absence of corroborating effects on related pathways, may not reflect a robust or clinically meaningful modulation of recovery-related physiological processes.

4.1.2. Biological plausibility

The statistically significant reduction in CRP observed in the meta-analysis (MD = −0.44; 95 % CI –0.66 to −0.22) is biologically plausible, given that CRP is a downstream acute-phase inflammatory protein known to respond rapidly to alterations in systemic inflammatory and oxidative stress burden [46–50]. However, this isolated finding should be interpreted with caution. While it may suggest a potential anti-inflammatory association of the intervention, the absence of consistent effects across related biomarkers and the limited certainty of the evidence preclude firm conclusions regarding a clinically meaningful modulation of inflammatory or redox-related pathways.

Yet, the absence of significant effects on IL-6 and MDA designates that this anti-inflammatory response is not accompanied by broader modulation of upstream cytokine signaling or oxidative lipid damage. IL-6, a key cytokine released rapidly in response to muscular contraction and metabolic stress, often serves as an early initiator of the inflammatory cascade; its stability across studies suggests that the intervention does not markedly alter the primary inflammatory trigger associated with exercise [51].

Also, the null effect on MDA implies that the intervention does not importantly attenuate oxidative membrane damage, reinforcing the conception that the drop in CRP may reflect a limited or downstream anti-inflammatory shift rather than a wide-ranging improvement in redox status. Taken together, these results recommend a selective effect on CRP without concomitant changes in IL-6 or oxidative stress, signifying that the biological impact of the intervention may be uncertain and not fully extend across the interconnected oxidative–inflammatory pathways activated by exercise.

4.2. Evidence level

Founded on the GRADE assessment, the certainty of the evidence was rated as Low for IL-6 and CRP and Very Low for MDA, reflecting substantial limitations across key methodological domains. For all three biomarkers, the evidence was downgraded owing to serious risk of bias, primarily affiliated to selective outcome reporting and inadequately described analytical plans, that undermine confidence in the internal validity of the included trials. The assessment of IL-6 and CRP was further weakened by

imprecision, as reflected in wide confidence intervals and small sample sizes thus restricting the ability to detect clinically significant changes or confirm true null effects.

The certainty of evidence for MDA was demoted even further, to Very Low, because of very serious inconsistency, marked by substantial heterogeneity across studies ($I^2 = 80$ %). This erraticism advocates that differences in study design, vitamin C dosage, participant characteristics, or exercise protocols may be influencing the direction and magnitude of the effect. When combined with inaccuracy and risk of bias, the reliability of the pooled findings becomes highly uncertain.

These restrictions have important consequences for interpretation. Low or very low-certainty evidence indicates that the true effect of vitamin C supplementation may be considerably different from the estimated effect reported in the meta-analysis. In practical terms, this means that even statistically significant findings, for example the reduction observed for CRP, should be interpreted with care, as the underlying evidence base lacks the methodological rigor needed to support firm conclusions. Equally, non-significant results for IL-6 and MDA cannot be taken as definitive evidence of no effect, as the existing data are too uncertain to exclude significant benefits or harms.

Overall, the GRADE ratings advise that the present literature does not provide a stable foundation upon which to construct clinical or performance-related recommendations regarding vitamin C supplementation for modulating post-exercise inflammatory or oxidative biomarkers. Considerable improvements in trial quality, reporting transparency, sample size, and protocol consistency are vital before high-confidence conclusions can be formulated about the physiological relevance or clinical utility of vitamin C in this context.

4.3. Heterogeneity among studies

The meta-analysis established markedly different heterogeneity patterns across biomarkers, each carrying central implications for interpretation and clinical relevance. CRP exhibited no heterogeneity ($I^2 = 0$ %), indicating that both included trials produced nearly identical effect estimates despite variations in sample size, exercise modality, and supplementation duration. This high degree of reliability suggests that the response of CRP to vitamin C supplementation is stable across different experimental conditions. Clinically, such uniformity infers that, even if the direction of effect is very slight, changes in CRP are predictable and unlikely to vary substantially across populations or exercise contexts.

Similar to CRP, IL-6 exhibited no heterogeneity ($I^2 = 0$ %), indicating that all included studies reported highly reliable effect estimates despite differences in exercise modality, supplementation duration, and participant characteristics. This uniformity advises that vitamin C exerts a reliably insignificant effect on IL-6 responses across experimental conditions. Clinically, the lack of variability reinforces the interpretation that vitamin C supplementation does not implicitly modulate early-phase cytokine signaling after exercise. Given that IL-6 is a pivotal upstream mediator involved in initiating inflammatory cascades and coordinating metabolic recovery (Pedersen & Febbraio, 2008), the consistent null findings suggest that vitamin C is unlikely to affect the core inflammatory triggers that shape post-exercise recovery, irrespective of population or training status.

In contrast, MDA demonstrated considerable heterogeneity ($I^2 = 80$ %), reflecting notable discrepancies in oxidative stress outcomes among the included studies. This high variability probably stems from important methodological and physiological differences, such as variation in exercise intensity, antioxidant status, baseline oxidative load, or timing of biomarker measurement. From a clinical perspective, this inconsistency introduces considerable uncertainty in interpreting the antioxidant potential of vitamin C. Since MDA is a key indicator of lipid peroxidation and membrane oxidative damage, widely divergent results indicate that vitamin C's impact on oxidative stress may depend heavily on contextual factors, potentially benefiting some individuals or exercise models while producing negligible effects in others. Accordingly, no reliable clinical decision can be drawn regarding vitamin C's ability to attenuate oxidative damage in a predictable or generalizable manner.

Taken together, these heterogeneity patterns offer important insight into the true scope of vitamin C's physiological impact. The complete reliability observed for both CRP and IL-6 indicates that vitamin C produces extremely stable and expectable effects, or lack thereof, across diverse exercise models and participant profiles. While the CRP response suggests a slight downstream anti-inflammatory influence, the equally consistent null effect for IL-6 supports that vitamin C does not implicitly alter early-phase cytokine signaling that drives the initiation of the inflammatory cascade. In contrast, the large variability surrounding MDA reveals that vitamin C's potential role in modifying oxidative stress is highly context-dependent and inconsistent across studies, preventing any reliable clinical interpretation of its antioxidant efficacy. All in all, these results establish that any physiological benefits of vitamin C supplementation are restricted, biomarker-specific, and inadequately robust to justify broad clinical recommendations for enhancing post-exercise recovery.

4.4. Comparison with previous literature

The findings of this systematic review and meta-analysis offer a nuanced perspective on the role of vitamin C in post-exercise recovery. Although a slight statistically significant reduction in CRP was observed, no significant effects were identified for IL-6 or MDA. These mixed findings both align with and diverge from previous studies, underscoring the heterogeneity of reported outcomes in the existing literature and the need for cautious interpretation.

The observed reduction in CRP is broadly consistent with findings from individual studies, such as [33]; who reported lower CRP levels and improved lactate tolerance following vitamin C supplementation in overweight men undergoing resistance training. Similarly, Boohloli et al. (2012) reported reductions in oxidative stress markers, including MDA, after vitamin C intake. However, while these studies provide supportive context, the overall body of evidence remains heterogeneous. Taken together, these findings suggest a possible association between vitamin C supplementation and modulation of inflammatory responses—particularly downstream acute-phase proteins such as CRP—but do not allow firm conclusions regarding a consistent or clinically meaningful anti-inflammatory effect across different populations and exercise protocols.

Nevertheless, the lack of effect on IL-6, a key upstream inflammatory cytokine, supports the results of [39,40]; who both found that vitamin C did not significantly modify exercise-induced cytokine responses. This underpins the impression that vitamin C may not hinder the initial stages of inflammatory signaling but may act later in the inflammatory cascade.

Regarding MDA, this review observed a non-significant overall effect with substantial heterogeneity, reflecting variability in study protocols, participant characteristics, and supplementation regimens. This contrasts with some earlier trials, such as [34,36]; which demonstrated modest antioxidant effects on protein carbonyls and other oxidative biomarkers. Yet, these effects were not consistently replicated across studies, suggesting that vitamin C's

antioxidant influence may be context-dependent, more pronounced in populations with oxidative stress vulnerabilities, such as those with poor glycemic control or low baseline vitamin C status [38,42].

Interestingly, some research has warned against high-dose antioxidant supplementation during training [35,36]. raised concerns that antioxidants like vitamin C might attenuate beneficial training adaptations by blunting reactive oxygen species (ROS) signals required for muscle remodeling. These perspectives add complexity to the interpretation of results: even when oxidative stress markers such as MDA are reduced, since changes may not translate to improved functional recovery and might even delay performance adaptation.

Finally, while earlier reviews [22–24] have discussed antioxidant supplementation broadly, they often lacked a focused meta-analytic synthesis of vitamin C's effects on these specific biomarkers. This current review fills that gap, offering a targeted quantitative assessment and confirming the low certainty of evidence for IL-6 and CRP, and very low certainty for MDA as stated by the GRADE framework.

Overall, this study both confirms and challenges prior evidence, highlighting the limited and unpredictable impact of vitamin C supplementation on biochemical recovery markers. These results underline the need for more robust, well-controlled trials to clarify vitamin C's efficacy in athletic and clinical populations.

4.5. Implications of baseline vitamin C status

An important methodological consideration emerging from this review is the heterogeneity—and frequent absence—of baseline plasma vitamin C assessment across the included trials. Baseline vitamin C status is a critical determinant of physiological responsiveness to supplementation, given the saturable intestinal absorption, renal threshold regulation, and nonlinear plasma–tissue kinetics of ascorbate. Individuals with marginal or deficient baseline vitamin C levels are more likely to exhibit measurable biochemical and functional responses, whereas supplementation in vitamin C–replete individuals may yield minimal or null effects [52].

In the present evidence base, only a subset of trials quantified baseline plasma vitamin C concentrations, revealing substantial variability in participants' nutritional status. Studies enrolling individuals with low or marginal baseline levels would tend to report greater post-supplementation increases in plasma ascorbate and, in some cases, modest reductions in oxidative stress or downstream inflammatory markers. Conversely, trials involving well-nourished or trained participants with adequate baseline vitamin C concentrations would generally reported no meaningful effects on inflammatory cytokines or oxidative stress biomarkers following exercise. This pattern suggests a potential ceiling effect, whereby additional vitamin C intake confers limited physiological benefit once plasma saturation is achieved.

The absence of baseline vitamin C data in several trials represents a key source of indirectness and may partially explain the inconsistent findings observed across outcomes, particularly for oxidative stress markers. Without accounting for initial vitamin C status, it is not possible to determine whether null effects reflect true inefficacy of supplementation or simply supplementation of already replete individuals. This limitation also constrains subgroup or dose–response analyses and reduces the interpretability of pooled estimates.

4.6. Limitations of this review

The primary restrictions of this review stem from the inherent methodological weaknesses of the primary literature, specifically the low overall quality and high heterogeneity. Across the included trials, several recurring methodological issues, such as unclear randomization procedures, erratic reporting of analytical plans, lack of assessor blinding, and selective outcome reporting, resulted in widespread "some concerns" and "high-risk" classifications in the risk-of-bias assessment. These weaknesses directly contributed to the downgrading of the certainty of evidence in the GRADE evaluation, mostly for IL-6 and MDA, where both imprecision and inconsistency were major concerns.

Another important limitation arises from the extensive variability in study protocols. The included trials differed noticeably in exercise modality (aerobic, resistance, maximal vs. submaximal exertion), sample characteristics (trained athletes, sedentary adults, individuals with obesity, and patients with chronic diseases), duration of supplementation (single dose to eight weeks), and vitamin C dosage (500 mg–4000 mg/day). Such heterogeneity complicates direct comparison across trials and possibly contributed to the considerable variability observed in oxidative stress outcomes, particularly for MDA ($I^2 = 80$ %). This variability advocates that contextual factors, such as baseline oxidative load, participant training status, and timing of biomarker assessment, may heavily impact the effect of vitamin C, but the existing evidence base lacks the granularity required to explore these moderators through subgroup analyses.

Moreover, the ongoing debate about the physiological role of reactive oxygen species (ROS) presents an interpretive challenge. Since ROS are not solely harmful by-products but also crucial signaling molecules essential for muscle remodeling, mitochondrial biogenesis, and long-term adaptation, the theoretical benefit of antioxidant supplementation remains contentious. The scientific research literature advises that excessive ROS scavenging may blunt key adaptive pathways, in theory impairing training responses even when biochemical markers such as MDA appear reduced. Given that some included studies indicated attenuated training adaptations with antioxidant use, any isolated reduction in oxidative biomarkers observed within individual trials must be interpreted carefully and not automatically considered advantageous.

Also, this review cannot exclude the likelihood of publication bias. The body of evidence is comparatively small, and several included trials lacked pre-registered protocols or detailed statistical analysis plans, raising the possibility that unfavorable or null findings may have been underreported. Selective reporting was one of the most problematic domains in the risk-of-bias assessment, further intensifying the possibility that relevant outcomes, mostly oxidative stress markers beyond MDA, were inconsistently presented across trials.

Importantly, chronic diseases were not ignored in the study selection process. Two included trials and deliberately enrolled clinical populations, specifically individuals with type 2 diabetes mellitus (Boonthongkaew et al., 2021) and patients with chronic heart failure (Ho 2007). These studies were retained because their primary focus was the evaluation of exercise-related inflammatory and oxidative stress biomarkers rather than disease-specific clinical outcomes. Their inclusion was therefore justified on mechanistic grounds, as they addressed biological responses to exercise and supplementation that are relevant across both healthy and clinical populations. Nevertheless, the presence of these populations contributes to indirectness and was considered when interpreting the overall findings.

An additional limitation concerns the insufficient control and reporting of dietary intake and concurrent supplement use across the included trials. The majority of studies did not implement rigorous dietary standardization or objective dietary assessment methods. Instead, several trials merely instructed participants to maintain their habitual eating patterns throughout the

intervention period. Moreover, the use of concomitant antioxidant supplements or micronutrients with potential redox-modulating properties was rarely monitored or explicitly reported. This lack of dietary and supplement control may have influenced baseline antioxidant status and attenuated or obscured the isolated effects of vitamin C supplementation on inflammatory and oxidative stress biomarkers. Importantly, this issue reflects a structural limitation of the existing primary literature rather than a methodological shortcoming of the present review. The absence of standardized dietary control underscores the need for future trials to incorporate detailed nutritional assessment and stricter control of co-supplementation when investigating antioxidant interventions in exercise settings.

Finally, the possible influence of baseline vitamin C status must be recognized. Some studies, such as [42]; propose that individuals with marginal or insufficient vitamin C levels may experience more marked physiological responses to supplementation. Yet, most included trials neither reported nor controlled for baseline ascorbate concentrations, preventing meaningful interpretation of whether supplementation primarily benefits deficient individuals or exerts broader effects. This oversight represents a significant breach, as the physiological relevance of vitamin C supplementation cannot be disconnected from participants' nutritional status.

Collectively, these restrictions emphasize the fragility of the current evidence base and underline the necessity for rigorously designed, adequately powered, and transparently reported randomized trials before firm decisions can be made about the true role of vitamin C in post-exercise recovery.

4.7. Implications for practice

Given the lack of a steady, significant effect on critical inflammatory and oxidative biomarkers and the low certainty of the evidence, routine vitamin C supplementation for the primary purpose of enhancing post-exercise recovery founded on these markers cannot be recommended. In other words, while the biochemical rationale behind using vitamin C as an antioxidant is deep-rooted, the actual translation into meaningful physiological or performance benefits remains tenuous. Clinicians, trainers, and athletes should be aware that while the antioxidant effect of vitamin C is clear in a biochemical sense, its practical or functional benefit is doubtful.

Besides, this uncertainty must be weighed against the potential for vitamin C supplementation to affect adaptive signaling pathways. Exercise-induced ROS play a dual role: while they contribute to oxidative stress, they similarly act as essential signaling molecules that promote long-term adaptive responses such as mitochondrial biogenesis and muscle remodeling. By scavenging these ROS, vitamin C may inadvertently blunt these beneficial training adaptations.

As a result, the decision to use vitamin C as a routine supplement should be approached with care. It is crucial to consider individual training goals, the specific context of use, and whether the potential dampening of adaptive signaling outweighs any marginal biochemical benefits. In summary, while vitamin C is not fundamentally harmful, its routine use as a recovery enhancer should be carefully evaluated, and different strategies that support both antioxidant defense and adaptive signaling should be prioritized.

4.8. Recommendations for future research

Future research must prioritize the development and execution of high-quality randomized clinical trials with rigorously defined protocols, standardized reporting procedures, and adequate sample sizes to ensure sufficient statistical power, mostly important given the substantial heterogeneity detected in the current evidence base. To support internal validity, future studies should not only control for key confounders but also adopt uniform criteria for exercise modality, training intensity, and participant characteristics.

A crucial procedural improvement involves systematically assessing and reporting participants' baseline vitamin C status. Without this information, it remains impossible to determine whether supplementation benefits only persons with marginal or deficient levels or whether it confers measurable effects even among those with adequate nutritional intake. In addition, future trials should incorporate functional performance outcomes, such as exercise capacity, recovery kinetics, and muscle function, alongside biochemical markers. This multidimensional method would permit researchers to regulate whether changes in oxidative or inflammatory biomarkers translate into improvements in real-world performance or recovery.

Further emphasis should be placed on delineating do se–response relationships and identifying the optimal timing and duration of supplementation. Comprehending whether acute, chronic, or peri-exercise dosing yields the most reliable and physiologically relevant effects is vital for minimizing the latent risk of attenuating beneficial training-induced adaptations. In the end, future work should aim to elucidate not only whether vitamin C supplementation is effective but for whom, under what conditions, and with what clinical or functional significance.

5. Conclusion

In summary, the available evidence from randomized controlled trials suggests that vitamin C supplementation does not consistently modify post-exercise inflammatory or oxidative stress biomarkers. Although a statistically significant reduction in CRP was observed, this finding is based on only two small trials and should be interpreted as preliminary, particularly given the low certainty of evidence and the presence of methodological limitations. Likewise, the absence of significant effects on IL-6 and MDA should not be interpreted as definitive evidence of no effect, as these analyses were supported by very small sample sizes and very low certainty evidence. Overall, the extremely limited number of included trials, high risk of bias, and imprecision substantially restrict the strength of any conclusions. Therefore, current findings should be viewed as hypothesis-generating rather than confirmatory, and no firm clinical or performance-related recommendations regarding vitamin C supplementation for post-exercise recovery can be made based on the existing evidence.

Data availability

The data from this study are available at: https://drive.google.com/drive/u/1/folders/1ATSO6z5ppWprayWSJG1XdkYqEcmrcjLI

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