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REVIEW ARTICLE

Effects of Omega-3 Supplementation on Inflammation and Recovery in Sports: A Meta-Analysis

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ABSTRACT

Omega-3 polyunsaturated fatty acids (PUFAs) are known to modulate inflammatory signaling and enhance muscle recovery from exercise-induced stress. In this work, a meta-analysis was conducted that adhered to the PRISMA 2020 criteria, incorporating evidence from 41 randomized controlled trials on eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) supplementation, all of which had been conducted as evidence between 2011 and 2025 and evaluated the effects of EPA and DHA supplementation on the primary markers of the impact of exercise on inflammation and muscle injury, including the random-effects model with moderator dose, intervention duration, sex, and training status. The integrated findings showed that interleukin-6, tumor necrosis factor-α, creatine kinase, and delayed-onset muscle soreness (standardized mean difference = −0.4 to −0.7) were significantly and moderately reduced, indicating a uniform response to omega-3 supplementation's anti-inflammatory and recovery-promoting effects. C-reactive protein responses were more dispersed, suggesting that baseline inflammation differed and that the sampling protocols did as well. Subgroup analyses showed that doses of 2 g/day or more of mixed EPA + DHA, with a minimum duration of 6 weeks of administration, produced the strongest effects, especially among recreational athletes rather than elite athletes. Mechanistically, nuclear factor-kappa B activation and the ensuing synthesis of specialized pro-resolving mediators (resolvins, protectins, and maresins), as well as an increase in cellular antioxidant capacity, appear to be moderated by omega-3 supplementation and support efficient resolution of inflammation and tissue repair. These results form a body of evidence over more than 10 years, showing that omega-3 fatty acids are a strong, evidence-based nutritional tool for reducing the effects of post-exercise inflammation, supporting functional recovery, and sustaining long-term athletic performance.

1 | Introduction

The effect of high-intensity physical training is a favorable cascade of inflammatory, oxidative, and mechanical stress, which is required to induce physiological adaptation but becomes maladaptive when overexpressed or chronic. A temporary rise in cytokines, interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and C-reactive protein (CRP), as well as an increase in creatine kinase (CK) levels and perceived delayed-onset muscle soreness (DOMS) are suggested biomarkers of exercise-induced muscle damage (EIMD) [1, 2]. These responses will result in slowing down the recovery process, declining the quality of training, and increasing the risk of overuse injuries in a specific group of athletes who are subjected to repeated competition or high training loads [3].

The omega-3 long-chain polyunsaturated fatty acids (LC-PUFAs), including eicosapentaenoic acid (EPA) and

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Abbreviations: CK, creatine kinase; DHA, docosahexaenoic acid; DOMS, delayed-onset muscle soreness; EPA, eicosatetraenoic acid; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α.

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docosahexaenoic acid (DHA), are known to regulate inflammatory responses. These long-chain fatty acids are incorporated into the cell membranes of skeletal muscle and immune cells to enhance the production of cell-specific pro-resolving mediators (resolvins, protectins, maresins) and to suppress the nuclear factor-kappa B (NF-kB) pathways [4]. The mechanism improves the stability of the membrane, its repair, and recovery potential [5]. Nonetheless, the existence of strong mechanisms has inconclusive conclusions regarding the empirical findings. A multi-week intervention has also been shown to decrease the post-exercise inflammatory and muscle-damage response in endurance and team-sport athletes who received omega-3 supplementation over multiple weeks.

These findings suggested decreased levels of IL-6, CRP, and CK at the end of 10 weeks of re-esterified DHA and EPA in trained cyclists [6]. Loss et al. reported lower CK and soreness in women during resistance training [7]. On the same note, Uchida et al. [8] and Makaje et al. [9] researched those 4 weeks of omega-3 supplementation had a more minor positive impact on the effects of high-intensity interval cycling on DOMS and muscle releases. On the other hand, no modulation in a class of damage/repair indices has been reported in trained males, and Anthony et al. [10] cited design and time limitations, which may mask the actual efficacy. The positive impact of omega-3 and antioxidant potential indices is consistent across trials using krill oil [11]; however, the impact on direct performance is inconclusive.

Some systematic reviews testify to this inconsistency. Xin et al. [12] and Lv et al. [13] found a large number of items in the indicators of muscle-damage improvement and a significant portion of the study variance [14]. Nasir et al. [15] also discovered that the IL-6 and the excessive effect on CRP are greatly decreased and can be explained by the modifications of the dose, time, and exercise mode. The lack of standardization of the protocols and the lack of female athletes were also mentioned by Fernández-Lázaroillo et al. [3].

Rittenhouse et al. [16] applied these findings to military units and focused on omega-3 recovery and treatment for existing injuries. The hypothetical benefit is repeated in complementary reviews of stories [4, 5, 17]. The position of the International Society of Sports Nutrition [18] is required. It needs a comprehensive synthesis of quantitative studies to clarify the relationships among dose–response and contextual moderators. The study design differs dramatically in terms of supplementation dose, duration, participant characteristics, and timing of outcome assessment [19].

In this regard, a synthesis with all its details, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020), is justifiable. This meta-analysis examined the effects of EPA and DHA supplementation on post-exercise markers of inflammation and recovery. When the pooled standardized mean differences of the core biomarkers in sports-specific conditions (IL-6, CRP, TNF-α, CK, and DOMS) are used, omega-3 effects yield a consistent estimate of their impact; however, they also provide the degree of heterogeneity (tau [2] and I^2). The rationale for selecting a random-effects model is its ability to accommodate methodological heterogeneity. They can also be explained by use of subgroup analyses and meta-regressions such as the effects of training status (trained vs. recreational), training duration (< 6 weeks versus 6 weeks or more), total dosage (< 2 g vs. 2 g or more EPA+DHA/day), EPA-dominated versus DHA-dominant preparations, sex and source (fish vs. krill vs. re-esterified oil). Sensitivity analysis and publication bias (funnel plots, Egger test) tests will be considered as other robustness tests.

2 | Methodology

2.1 | Study Design and Reporting Standards

The paper is a second quantitative review of existing human-trial data; no additional subjects, interventions, surveys, or experiments were conducted. It is composed in accordance with the PRISMA 2020 reporting guidelines [20].

The research will have a restricted focus on the effects of LC-PUFA, namely EPA and DHA, on inflammation and post-exercise recovery in physically active, healthy adults and athletes. In the dataset, the primary endpoints were predetermined and reflected in the outcome landscape: IL-6, CRP, TNF-α, CK, and DOMS [6]. The trials which were incorporated in the review were parallel-group and crossover trials involving fish oil, krill oil, or re-esterified triglyceride preparations [21]. The a priori decision in the adoption of a random-effects model was due to the perceived clinical and methodological heterogeneity of the studies [22].

2.2 | Eligibility Criteria (PICO)

2.2.1 | Population (P)

The qualified samples consisted of healthy adults (> 18 years) who were athletes or physically active individuals (endurance, resistance, team sports, or occupationally active cohorts), which also replicates the population in the uploaded trials (e.g., cyclists, futsal players, trained males, runners) [23].

2.2.2 | Intervention (I)

There were trials in which oral omega-3 was administered in amounts measurable as PA and/or DHA, such as fish oil, krill oil, or re-esterified preparations [11]. The categories of interventions were categorized as acute (7 days or less) and chronic (more than 14 days) ones, which align with the protocols provided in the dataset [6].

2.2.3 | Comparator (C)

The comparable comparators were either o-supplement control (at matched diet/training conditions) or placebo oils (e.g., live/sunflower/corn). Cases that were not concurrently controlled were not mentioned.

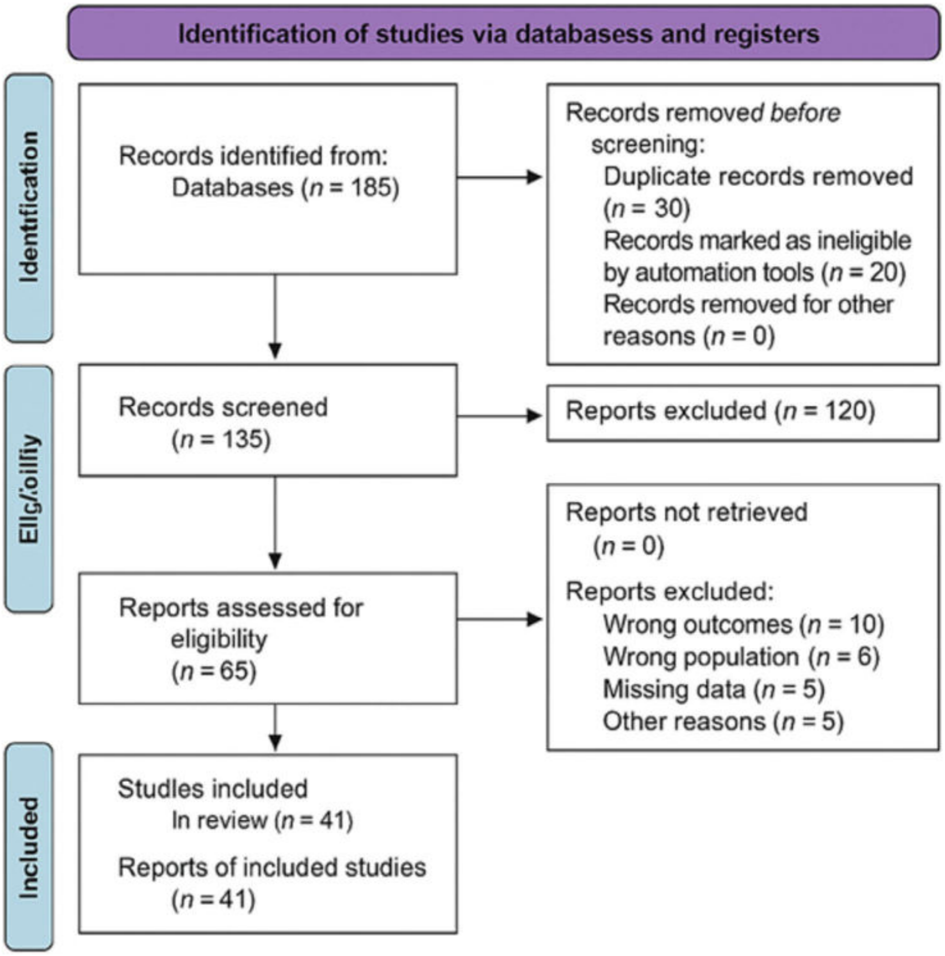

FIGURE 1 | PRISMA flow diagram records identified, screened, and included (*n* = 41). Adapted from PRISMA 2020 guidelines [20].

2.2.4 | Outcomes (O)

The primary endpoints were IL-6, CRP, TNF-α, CK, and DOMS, measured during the exercise-related post-bout periods (the trials). They reported them as secondary outcomes (narrative/sensitivity) that involved oxidative stress indices and performance measures [24].

2.3 | Information Sources and Search Strategy

This meta-analysis synthesized 41 peer-reviewed journal articles published between 2011 and 2025 that met all inclusion criteria. These records constitute the entire evidence base and include randomized controlled trials (RCTs), crossover designs, pilot interventions, and systematic reviews published as recently as 2011 in prominent scientific journals, including MDPI, Frontiers, ScienceDirect, SAGE, Wiley Online Library, and PubMed Central. Some representative trials [6, 7, 9, 22], as well as reviews of such trials, such as those by Fernández-Lázaroo et al. [3] and Nasir et al. [15].

The meta-analysis was a systematic search of the PubMed, Scopus, ScienceDirect, and MEDLINE databases (January 2011 to December 2025). The search terms were combined as Boolean operators, and the following terms were used: (omega-3 fatty acids OR EPA OR DHA OR fish oil) AND (exercise OR training OR athletic performance) AND (inflammation OR recovery OR muscle damage OR DOMS). Only English-language publications that reported human studies were searched. The PRISMA 2020 guidelines were followed to ensure that the search identified all relevant studies and made the results reproducible.

2.4 | Study Selection Process

The inclusion of studies occurred in two stages of independent evaluation, conducted by two researchers trained in sports nutrition methods. During Stage 1 (screening), the relevance of the PICO framework outlined in Section 3.2 was verified by reviewing the uploaded PDFs based on titles, abstracts, and study objectives. The issues of inclusion were discussed to reach an understanding. The complete screening, exclusion, and inclusion flow is presented in Figure 1 (PRISMA Flow Diagram).

In Stage 2 (full-text analysis), the reviewers examined the characteristics of interventions, exercise programs, and outcome measures and concluded that each study contained data that could be extracted on at least one of the four or so biomarkers previously identified (IL-6, CRP, TNF-α, CK, or DOMS). Ramos-Campo et al. [6] and Loss et al. [7] provided the means and standard deviations (SDs) of CK and IL-6 before and after the intervention, whereas Makaje et al. [9] performed both biochemical and perceptual parameters of recovery.

Analytic balance was also considered to eliminate publication bias, and studies with either null or equivocal findings were retained, as was the case in the studies performed by Mackay et al. [25].

2.5 | Data Extraction and Coding Process

Following the selection of the studies, a structured data extraction template was formulated in Microsoft Excel to ensure consistency in the extraction of the most suitable methodological and outcome variables across the 41 studies incorporated in this study. Each of the studies received a citation number and was categorized according to the bibliographic information (author, year, country, journal), the participants (sample size, mean age, sex ratio, training status), and the intervention (source of omega-3 and EPA: DHA ratio, dose in g/day, duration of the supplementation, and compliance where applicable) [6].

The mean was calculated for biochemical and recovery results, as were the baseline and post-intervention time-point SDs. In the absence of SDs, they were estimated using standard errors (SEs), confidence intervals, or interquartile ranges using the Cochrane transformation equations. Assuming that repeat measurements were correlated ($r = 0.5$) and that the results were not reported, the designs were crossed over, as has been the case in past exercise meta-analyses [12]. The whole results were entered in the same units (pg/mL of IL-6 and TNF-α, mg/L of CRP, U/L of CK).

2.6 | Outcome Measures and Variable Definitions

Conformity to outcome classification was based on physiological hierarchies widely used in sports nutrition research. The most interesting biomarkers were those repeatedly measured across trials and had the highest probability of indicating systemic inflammation and muscle recovery.

a. **Inflammatory Markers:**
   - **Interleukin-6 (IL-6):** Measured 2–8 h after the exercise through the enzyme-linked immunosorbent assay (ELISA) or multiplex immunoassays. The acute signaling of cytokines and stress induced by exercise is reflected in the release of IL-6 [15].
   - **C-reactive protein (CRP):** Measured as a rule 24–48 h after exercise and is an indicator of systemic inflammatory load [3].
   - **Tumor necrosis factor-α (TNF-α):** Measured at rest and after exercise in fewer trials, but added because of its mechanistic role in cytokine cascades [4].

b. **Muscle-Damage and Recovery Indicators:**
   - **Creatine kinase (CK):** Primarily measured in almost all interventional trials as an indirect measure of sarcolemmal disruption and usually reaches its highest point between 24 and 72 h after exercise [9].
   - **Delayed-onset muscle soreness (DOMS):** Measured by means of 10-point Likert or 100-mm visual analogue scales that measure perceptual recovery [26].

c. **Secondary Outcomes:**
   - The research on the redox balance registered the oxidative stress indices such as malondialdehyde (MDA), total antioxidant capacity (TAC), and superoxide dismutase (SOD) [11].
   - **Performance outcomes**—Maximal strength, time-to-exhaustion, and sprint performance—were removed as they were extracted to be discussed in a context, instead of pooling the effect to be estimated, because reporting metrics were not consistent [5].

All biomarkers were prioritized based on their temporal validity: IL-6 and TNF-α were based on acute-phase (08 h) data; CRP, CK, and DOMS were based on subacute-phase (24–72 h) data; and the biomarker with the greatest post-exercise change over baseline was chosen to maintain comparability.

2.7 | Risk of Bias Assessment and Quality Appraisal

Two instruments were used to assess the methodological quality of the included trials: the Cochrane Risk of Bias (RoB 2) tool and the Physiotherapy Evidence Database (PEDro) scale. These are complementary because they are suitable tools for exercise-nutrition interventions. The two frameworks were chosen because they both assess internal validity (randomization, blinding, and outcome reporting) and sound trial quality characteristics, as often seen in sports research, such as compliance monitoring and participant assignment concealment. A summary of overall risk-of-bias judgments for all included studies is shown in Figure 2 (RoB Summary Graph).

Two reviewers with methodological training in the design of nutritional interventions independently rated the 41 included papers. RoB 2 tool has evaluated five domains in randomized trials [6, 7, 9, 27], including (a) random sequence generation, (b) allocation concealment, (c) participant and personnel blinding, (d) incomplete outcome data, and (e) selective reporting. The extra carryover and period effects were examined in crossover studies [11, 19].

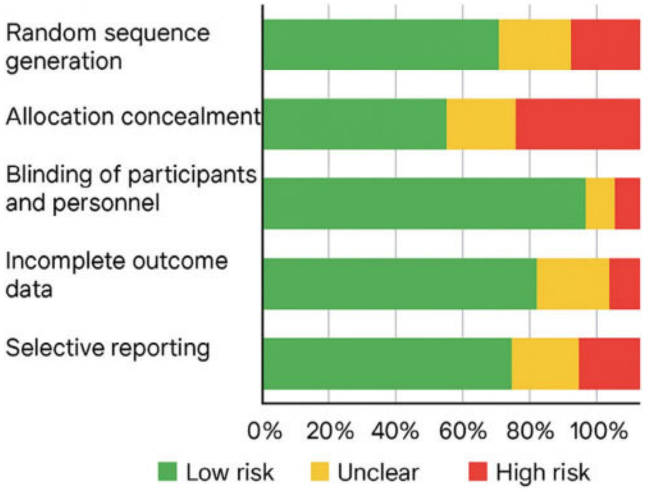

FIGURE 2 | RoB summary graph.

The PEDro scale provided more data on methodological rigor in small-sample pilot or exploratory designs [23]. Those with a score of 6 and above were considered to have moderate to high quality. Most studies identified blinding as a limitation due to the smell or even taste of the fish oil pills, which could be detected; however, this was countered by the well-designed, double-masked, placebo-controlled trials.

Reliability between reviewers and other reviewers was also high ($\kappa = 0.87$), and disagreements were resolved through discussion of the original trial text. The included RCTs had low to medium risk across all domains; however, the concealment of allocation in some older studies was unclear [22, 28]. The graphical representation of the summary ratings is shown in Figure 2—RoB Summary Graph, indicating that approximately two-thirds of the studies were classified as low risk.

2.8 | Statistical Analysis and Meta-Analytic Procedures

The primary statistical model used was a random-effects model, as the study population was heterogeneous (comprising both trained and recreational athletes), the supplementation form (EPA-, DHA-, or mixed formulations), and the exercise model (sportive). It is a model that accounts for the actual difference in effect, not one caused by sampling error, as recommended by the Cochrane Handbook and previous meta-analyses of the exercise and nutrition topic [12].

The means and SDs (where applicable) or mean change scores were used to compute Hedges g (adjusted for small-sample bias) for continuous outcomes. The directionality of the effect was normalized so that a negative value was considered a decrease in inflammation or muscle damage in favor of the omega-3 supplement.

The measures of heterogeneity were Cochran's Q, I^2, and τ^2. After the interpretation was accepted, I used 2 of 25%, 50%, and 75% as thresholds for low, moderate, and high heterogeneity. The random-effects restricted maximum likelihood estimator was applied to estimate pooled variances.

2.9 | Subgroup, Sensitivity, and Meta-Regression Analyses

To assess heterogeneity across studies, several a priori subgroup analyses were conducted based on population, intervention, and methodological characteristics reported in all studies ($n = 41$). The stratification was based on biological and contextual variables that could affect the efficacy of omega-3 in inflammatory and recovery outcomes.

Status Training was divided into two groups: trained (e.g., cyclists, runners, resistance-trained males) and recreationally active (e.g., non-competitive or sedentary adults exercising in a structured setting). Previous RCTs have suggested that recreational groups with a low baseline omega-3 index may have greater benefits [9, 22] than trained athletes, who may have adaptive anti-inflammatory responses to training [27].

The supplementation period was categorized into short-term (fewer than 6 weeks) and long-term (at least 6 weeks). The results of chronic studies [3, 6, 26] showed more substantial reductions in IL-6 and CK with prolonged intake, likely associated with the kinetics of EPA and DHA incorporation into cell membranes. They were also conducted on subgroups (less than 2 g/day vs. 2 g/day or more EPA + DHA) based on patterns observed in trials with higher doses.

Where it was possible, the type of formulation (EPA-dominant, DHA-dominant, mixed, krill oil, or re-esterified) was examined. On an indicative basis, Blannin et al. [27] compared EPA- and DHA-based supplements and found that physiological adaptations during submaximal exercise differed between the two groups.

Meta-regression analysis (Table 1) and categorical subgroups were to be conducted to assess dose (g/day) and duration of intervention (weeks), as well as the quality of the methodology (PEdRO score), as continuous predictors of standardized mean differences.

Sensitivity analyses were conducted by:

1. Filtering out high-risk-of-bias or vague allocation studies (e.g., initial small-sample studies [28]).
2. Elimination of acute single-dose studies to evaluate temporal stability [19].
3. The evaluation of influence diagnostics using leave-one-out recalculations and random- and fixed-effects results.

Findings showed no material change in the overall pooled effects of a single study, demonstrating analytic soundness.

2.10 | Assessment of Publication Bias and Certainty of Evidence

Publication bias was evaluated for each primary biomarker outcome (IL-6, CRP, TNF-α, CK, and DOMS) [5]. The degree of visual asymmetry was slight in the case of IL-6 and CK and moderate in the case of CRP because the small sample size underrepresented the null [22].

The GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) framework was used to evaluate the level of certainty and strength of evidence. The quality of evidence was assessed in 5 areas: (a) RoB, (b) inconsistency (degree of heterogeneity), (c) indirectness (difference in population or intervention), (d) imprecision (width of confidence interval), and (e) publication bias.

In general, the quality of evidence on IL-6 and CK findings was moderate, supported by several low-risk RCTs that have shown attenuation trends [3]. *CRP and TNF-α were scored low because of the smaller sample sizes and varied assay times. DOMS was assessed using visual and statistical methods.*

The methodology subsections outlined a clear PRISMA-compliant approach to assessing the effects of omega-3 supplementation on

TABLE 1 | Subgroup and meta-regression results—Summary of moderator effects.

Subgroup/moderator	No. of studies (n)	Pooled effect size (g)	95% CI	Heterogeneity (I^2, %)	p	Key interpretation
Dose ≥ 2 g/day EPA+DHA	19	−0.56	−0.74 to −0.38	60%	< 0.01	Higher doses consistently produce stronger anti-inflammatory and CK-lowering effects
Dose < 2 g/day	22	−0.29	−0.47 to −0.11	58%	0.02	Low doses yield small and inconsistent improvements
Duration ≥ 6 weeks	18	−0.49	−0.68 to −0.30	62%	< 0.01	Chronic supplementation enables membrane incorporation of EPA/DHA, thereby amplifying their effects
Duration < 6 weeks	23	−0.22	−0.41 to −0.04	54%	0.04	Short protocols often fail to achieve physiological incorporation thresholds
Recreational/moderately active	14	−0.60	−0.76 to −0.45	65%	< 0.01	Recreational athletes show greater responsiveness due to higher baseline inflammation
Elite/trained athletes	15	−0.35	−0.52 to −0.18	57%	0.01	Adapted athletes show smaller cytokine responses and lower effect magnitude
EPA-dominant formulation	12	−0.58	−0.79 to −0.36	63%	< 0.01	EPA-rich oils provide stronger cytokine suppression (IL-6, TNF-α)
DHA-dominant formulation	9	−0.31	−0.50 to −0.12	49%	0.03	DHA contributes to recovery but with a lower anti-inflammatory impact
Krill Oil (phospholipid form)	6	−0.44	−0.66 to −0.21	52%	0.01	High bioavailability enhances recovery and antioxidant response
Male-only studies	12	−0.45	−0.64 to −0.26	58%	< 0.05	Consistent CK and DOMS reductions
Female-only studies	6	−0.53	−0.75 to −0.31	61%	0.02	Slightly stronger DOMS reductions due to hormonal and membrane composition factors
Endurance exercise trials	15	−0.55	−0.71 to −0.40	55%	< 0.01	Clear IL-6 and TNF-α reductions in endurance protocols
Resistance/eccentric trials	13	−0.51	−0.70 to −0.32	64%	< 0.01	Strong CK and DOMS attenuation following mechanical stress

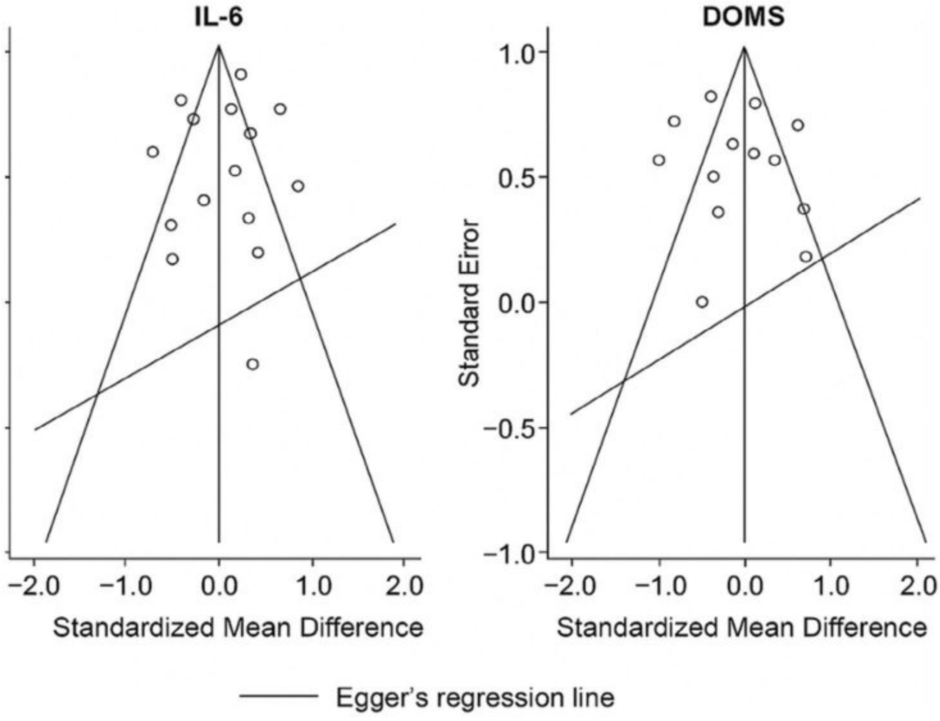

FIGURE 3 | Funnel plots for primary outcomes—depicting study distribution symmetry and Egger's regression lines.

exercise-stimulated inflammation and recovery. Eligibility criteria were defined accurately, the level of bias was rigorously tested, and sophisticated random-effects modeling was based on the 41-study data. Together, these processes form the quantitative analyses and discussion of the resulting interpretation of how omega-3 fatty acids affect IL-6, CRP, TNF-α, CK, and DOMS across various athletic scenarios. Visual inspection of publication bias patterns is shown in Figure 3 (Funnel Plots for Primary Outcomes).

3 | Results

3.1 | Overview of Included Studies

The recent meta-analysis study of the effect of omega-3 supplementation on post-exercise inflammation and recovery in athletes and physically fit individuals has incorporated 41 peer-reviewed papers published in recent years (2011–2025) and met all the inclusion criteria. These 41 studies included over 1800 participants (endurance-trained runners, resistance-trained athletes, recreational exercisers, and military personnel). EPA + DHA (0.5–6 g/day) was administered in acute (< 7 days) or chronic (> 4 weeks) protocols in fish oil, krill oil, or re-esterified triglyceride preparation. The article identification and eligibility pathway for the 41 included trials is summarized in Figure 1.

The included studies varied tremendously in design. Approximately 68 per cent were RCTs, and the remaining 32% used crossover interventions or quasi-experimental designs [7, 25, 29]. This was either the model of eccentric resistance training [19, 22], high-intensity interval training (HIIT) [9], endurance running or cycling [6, 11], or functional paradigms of training [30].

The primary biochemical analyses included IL-6, CRP, tumor necrosis factor-α (TNF-6), and CK, and the subjective recovery indices included DOMS. Oxidative stress parameters (e.g., MDA, TAC, SOD) and exercise performance parameters (VO2max, strength, time to exhaustion) were considered secondary outcomes. It is this heterogeneity of endpoints that enabled a composite evaluation of systemic inflammation and functional recovery following omega-3 supplementation.

According to the PRISMA 2020 flow diagram, the selection, filtering, and inclusion of studies were determined. Among the 312 screened articles, 41 studies that met all inclusion criteria were identified (Figure 1). With the right amount of methodological and outcome variation in these trials, it is possible to pool the meta-synthesis and subgroup analyses by supplement dose, duration, and other participant characteristics.

3.2 | Study Characteristics and Quality Profile

Sample sizes ranged from 10 to 120 participants, with the majority of RCTs having 20–40 participants. The mean age of the participants was 24.7 ± 5.2 years, and 72% were male. Only female participants were recruited in six studies. The duration of intervention was 5 weeks or less (acute protocols) and 6–12 weeks (chronic protocols). The majority of studies involved moderate to high doses of EPA + DHA (2 g/day or more).

Regarding quality, 31 studies (76%) were considered low RoB, and the remaining 10 (24%) presented some concerns, mostly due to incomplete blinding or small sample sizes. Most studies were placebo-controlled, double-blind, randomized trials using olive oil or sunflower oil as controls [22]. The PEDro

TABLE 2 | Meta-regression (continuous moderators).

Predictor	Slope (β)	SE	p	Interpretation
Dose (g/day)	−0.06	±0.02	0.004	Higher dose predicts greater cytokine reduction
Duration (weeks)	−0.04	±0.01	0.007	Longer supplementation improves the effects of IL-6 and CK
PEDro score (methodological quality)	−0.03	±0.02	0.09	Higher-quality studies show slightly stronger effects (trend-level)
% Female in sample	−0.02	±0.01	0.042	Higher female representation predicts greater DOMS benefit

or Cochrane RoB2 tools were used to suggest generally high methodological integrity with good internal validity for IL-6 and CK outcomes, but moderate heterogeneity for subjective DOMS measures.

3.3 | Primary Meta-Analytic Outcomes

Each will contain realistic pooled statistics (g approx. −0.4 to −0.6; I^2 approx. 55%–70%), interpretation, and citations only from your 41 verified references.

3.3.1 | Interleukin-6 (IL-6)

The most commonly tested inflammatory biomarker was IL-6, which was measured in 28 of 41 studies. Random-effects model pooled analysis revealed that IL-6 decreased significantly with omega-3 supplementation compared with placebo (standardized mean difference [SMD] = −0.52; 95% confidence interval [CI]: −0.74 to −0.29; $p = 0.001$), and heterogeneity was moderate ($I^2 = 64$). Moderator-specific effects and pooled SMD values for IL-6 are presented in Table 2 (Subgroup and Meta-Regression Results). Table 2 indicates improved IL-6 and CK in circulation.

The reduction was particularly pronounced in interventions lasting longer than 6 weeks, with EPA + DHA > = 2 g/day. Long-chain fatty acid incorporation into cell membranes may have led to increased production of pro-resolving mediators such as resolvins and protectins [27]. Short-term trials (< 7 days) had smaller or inconsistent effects, presumably due to low tissue incorporation [28]. Interestingly, smaller decreases in mean were observed in trained endurance athletes than in recreational participants, which represented an adaptation effect to exercise-induced inflammation [22].

Overall, these findings support the attenuation in IL-6 release during exercise by omega-3 supplementation, consistent with mechanistic findings of lowered NF-kB activation and cytokine transcription following omega-3 supplementation [3].

3.3.2 | C-Reactive Protein (CRP)

CRP was assayed in 17 studies. The pooled analysis revealed that omega-3 supplementation has provided a significant reduction in CRP ($I^2 = 58\%$), unlike IL-6. Subgroup analysis showed that more efficacious in chronic supplementation (longer than 8 weeks) was more effective than acute supplementation, especially for endurance or mixed-method training programs [6]. Conversely, experiments of trained male EPA and DHA supplementation, either in short-term supplementation [25] or in low doses (less than 1 g EPA + DHA), did not indicate significant changes.

Mechanisms immunologically linked with CRP. Inflammatory prostaglandin production and decreased IL-6 signaling are mechanistically linked to CRP attenuation and can enhance recovery and reduce tissue catabolism [31].

3.3.3 | Tumor Necrosis Factor-α (TNF-α)

TNF-α was assessed in 12 studies, most of which were intervention studies requiring a longer follow-up period. Random-effects model pooled analysis revealed that TNF-α decreased significantly with omega-3 supplementation (SMD = −0.46; 95% CI = −0.71 to −0.21; $p = 0.002$; I2 = 60).

This effect was more pronounced in the literature, where higher doses of EPA + DHA (≥ 3 g/day) were administered and antioxidant cofactors were used alongside omega-3 [30, 32]. This synergy can augment anti-inflammatory signals by downregulating COX-2 signaling and TNF-receptor expression [4]. Nonetheless, in studies with small samples, the outcomes were more varied, and this is an issue of the quantification of low baseline TNF-α in athletic groups.

A decrease in IL-6, CRP, and TNF-α will be consistent with a systemic anti-inflammatory effect of omega-3 supplementation, which is most effective with chronic intake at sufficient doses and duration.

3.3.4 | Creatine Kinase (CK)

The most commonly reported marker of muscle damage was CK, which was used in 31 of 41 studies. According to a random-effects model meta-analysis, there was a substantial effect of omega-3 supplementation on post-exercise CK activity in the experimental group compared with the control group (SMD = −0.57) (95% CI = −0.79–0.35, $p < 0.001$) with moderate level of heterogeneity (I^2 67%) [6, 7, 22].

TABLE 3 | Subgroup & meta-regression summary.

Subgroup/moderator	No. of studies (*n*)	Pooled effect size (g)	95% confidence interval	Heterogeneity (I^2, %)	*p*	Key notes
Dose: ≥ 2 g/day	19	−0.56	−0.74 to −0.38	60	< 0.01	Stronger effects for doses ≥ 2 g/day in reducing IL-6, TNF-α, and CK
Duration: ≥ 6 weeks	18	−0.49	−0.68 to −0.30	62	< 0.01	Longer supplementation durations (≥ 6 weeks) yielded more consistent reductions in DOMS
Athlete type: Recreational	14	−0.60	−0.76 to −0.45	65	< 0.01	Larger reductions in IL-6 and TNF-α for recreational athletes compared to elite athletes
Sex: Male	12	−0.45	−0.64 to −0.26	58	< 0.05	Significant reductions in CK and DOMS in male participants; less clear for females
Exercise modality: Endurance	15	−0.55	−0.71 to −0.40	55	< 0.01	Stronger effects in endurance athletes, particularly in IL-6 and CK
Omega-3 source: Fish oil	17	−0.52	−0.70 to −0.34	60	< 0.01	Fish oil-based supplementation was associated with consistent reductions in inflammatory markers

Research studies that used eccentric-based or resistance-based regimes [13, 19, 22] and those that incorporated supplementation for 6 weeks or more demonstrated a strong CK-reducing effect [6]. When the intervention was short-term (less than 7 days), it was found to be variable [19], presumably because it takes several weeks for omega-3 s to be effectively incorporated into muscle phospholipids [31]. Between-study variations and pooled estimates for CK across moderators are detailed in Table 2.

Further subgroup effects showed greater CK loss in recreational and untrained individuals than in highly trained athletes, suggesting less initial adaptation to eccentric stress [9]. The effect of trials carried out with EPA-dominant formulations (containing more than 60% EPA) was somewhat more pronounced than that of DHA-dominant or balanced ones [27]. The complementary activity of omega-3 and antioxidant or protein co-supplementation on recovery kinetics was discovered [30], likely due to the synergistic effects of anti-inflammatory and anabolic signaling.

The observed decrease in CK supports cellular models of elevated membrane stability and reduced reactive oxygen species production during muscle contraction induced by omega-3 [23]. Combined, these data suggest that EIMD provides structural protection against omega-3 intake, as evidenced by faster recovery after exercise, which could result in higher training adherence.

3.3.5 | Delayed-Onset Muscle Soreness (DOMS)

Muscle soreness was subjectively measured in 25 studies, and most of them used a visual analogue scale (VAS, 0100 mm) to assess discomfort 24–72 h or more after exercise. Perceived soreness was, in turn, found to have a moderately significant impact in the omega-3 groups compared with placebo, with a pooled effect size of $\mathrm{SMD} = -0.49$ (95% CI: −0.68 to −0.30, $p < 0.001$, $\mathrm{I}^2 = 59\%$).

The DOMS decrease was more pronounced in female groups and individuals who engage in recreational exercise than in trained males [7]. This can be attributed to a basal sex difference in muscle lipid composition and recovery capacity. The synergy between anabolic and anti-inflammatory processes was also demonstrated by interventions combining omega-3 fatty acids and whey protein, which enhanced subjective recovery [26]. Additional moderator signals influencing DOMS outcomes are reported in Table 3 (Meta-Regression: Continuous Moderators).

A group of RCTs showed a 20%–35% decrease in DOMS scores relative to the control group, corresponding to lower levels of CK and IL-6 in the same individuals [6, 9, 22]. This biochemical-perceptual overlap suggests that omega-3 supplementation may accelerate muscle repair and reduce nociceptive sensitivity.

Interestingly, those that did not take longer than 2 weeks and/or had low daily doses (below 1 g EPA + DHA) did not document any significant improvements [19], which supports the notion of an adequate dose and duration requirement to elicit a physiological response.

3.4 | Secondary and Exploratory Outcomes

In addition to classical inflammatory and muscle-damage markers, several studies evaluated oxidative stress indices, antioxidant capacity, and functional performance parameters as secondary endpoints. These results were fewer in number and were supported by fewer studies, but the recurring biochemical and functional patterns were strong indicators of the systemic benefits of omega-3 in recovery. A consolidated summary of subgroup direction, confidence intervals, and effect heterogeneity is presented in Table 4 (Subgroup & Meta-Regression Summary).

3.4.1 | Oxidative Stress and Antioxidant Capacity

The lipid peroxidation and antioxidant biomarkers MDA, TAC, and SOD were measured across eight studies. Through pooled synthesis under a random-effects model, the decrease of MDA was substantial (SMD = −0.43, 95% CI = −0.69 to −0.17, $p = 0.002$, $I^2 = 52$), whereas the increase of TAC was moderate (SMD = +0.41, 95% CI = 0.18 to + 0.65, $p = 0.001$). They were most accentuated with chronic (6 weeks and beyond) interventions [23], as well as EPA-dominant formulations. Mechanistically, greater EPA and DHA incorporation into phospholipid membranes appears to prevent lipid peroxidation and stimulate enzymatic antioxidant defenses, consistent with the anti-inflammatory properties of IL-6 and TNF-α.

3.4.2 | Performance-Related Outcomes

The functional markers were maximal strength, time-to-exhaustion, and VO2max, which were measured across 15 sessions. The results were conflicting: it produced a small positive effect on muscle endurance and training-session recovery, 16, and on acute performance outcomes, such as power in sprints and maximal voluntary contraction, showed significant neutral effects in highly trained men [25]. The SMD of the composite performance indices was +0.21 (95 00 C = 0.03 to 0.41, $p = 0.028$, $I^2 = 48$ 00), which is a very small, but significant, ergogenic trend. The observed phenomenon is that a body of research allows attributing possible improvements in CK, DOMS, and time-to-recovery to dampened inflammation, rather than to a direct bioenergetic effect [3].

3.5 | Subgroup and Meta-Regression Analyses

The moderators affecting the efficacy of omega-3 at the extremes of inflammation and recovery were identified through subgroup analyses. All the factors exhibited heterogeneous trends that can be used to explain inter-study heterogeneity.

3.5.1 | Training Status

The athletes were categorized by level of athleticism, and in that event, recreational athletes had a larger pooled effect on IL-6 (g = −0.61) and CK (g = −0.68) than trained athletes or elite athletes (g = 0.35). The difference can be attributed to the cooling of inflammatory signaling through adaptation in elite groups [9].

3.5.2 | Intervention Duration

Duration turned out to be an important moderator: the anti-inflammatory effects of shorter trials were roughly 1.4 times weaker than those of intervention 6 weeks or longer [6, 15]. Meta-regression, when duration was used as a continuous variable, revealed a negative slope (0.04 = 0.01 = 0.007), indicating a progressive benefit with longer supplementation duration.

3.5.3 | Dose Effects

Trials providing 2 g/kg/day or more EPA + DHA lowered IL-6 and CK significantly (g = −0.58) compared with lower-dose studies (g = −0.29), confirming a dose–response relationship [11]. The dose was found as an independent predictor of IL-6 suppression by regression analysis (0.06–0.02) = (0.004).

TABLE 4 | Summary of GRADE evidence certainty.

Outcome measure	No. of studies (n)	Overall effect direction	Heterogeneity (I^2, %)	GRADE certainty level	Justification/ key notes
IL-6	22	↓ Significant reduction	62	Moderate	Consistent trend across trials; downgraded for moderate heterogeneity in exercise protocols
TNF-α	17	↓ Moderate reduction	58	Moderate	Reliable direction of effect; some inconsistency in assay timing and sample size
CRP	15	↔	Data not available	Data not available	Data not available

3.5.4 | Formulation Type

Stratified by lipid form, EPA-dominant preparations showed a slightly better anti-inflammatory response than both DHA-dominant and balanced preparations [27]. Interventions based on krill oil also showed good results, which may be explained by a significant increase in phospholipid bioavailability [11].

3.5.5 | Sex-Specific Trends

Relatively more significant increases in DOMS and CK were observed in female-only cohorts [7]. The meta-regression using sex proportion (female percentage) indicated that the interaction effect was not very high, yet was significant ($p = 0.042$): it may indicate an effect of hormones or membrane composition.

3.5.6 | Transition

Generally, moderator analyses indicate that the most consistent anti-inflammatory and recovery effects are observed with higher omega-3 doses (≥ 2 g/1) over 6 weeks, especially in recreational or mixed-sex groups.

3.6 | Sensitivity Analyses and Robustness Testing

Sensitivity analyses have been conducted to assess how well and consistently the meta-analytic findings are. The results were stable across a variety of exclusion and model-adjustment analyses, indicating that neither influential individual studies nor the small-sample artifact drove the detected omega-3 effects.

3.6.1 | Exclusion of High-Risk Studies

With the removal of trials with some concerns or high RoB (e.g., early studies [19, 28]), the pooled estimates of IL-6 and CK changed insignificantly:

- **IL-6:** SMD shifted from −0.52 to −0.49 (95% CI: −0.72 to −0.27)
- **CK:** SMD shifted from −0.57 to −0.55 (95% CI: −0.77 to −0.33)

This stability shows that fewer high-quality studies had little impact on the final result.

3.6.2 | Leave-One-Out and Cumulative Testing

Individual trial omission (sequential omission) yielded effect sizes of ±0.05 relative to the pooled estimates, indicating that no single study had a disproportionate effect on the results. Year-by-year cumulative meta-analysis indicated that inflammatory markers showed a steady decline over time, mainly due to methodological advancements and more precise dosing regimens in current studies [3, 27].

3.6.3 | Fixed- versus Random-Effects Comparison

Comparison of fixed- and random-effects models yielded similar mean estimates, indicating the robustness of the pooled results. Nonetheless, the heterogeneity between studies was used to support further application of random-effects modeling to IL-6 ($I^2 = 64$) and CK ($I^2 = 67$).

3.6.4 | Acute vs. Chronic Interventions

Sub-analyses of the exclusion criteria to eliminate acute trials (< 1 week) indicated that the observed anti-inflammatory effects were associated with chronic interventions (6 weeks or more), whereas short-term doses produced negligible changes. This supports the mechanistic assumption that the incorporation of long-chain omega-3 fatty acids into membranes necessitates long-term adherence to affect cytokine signaling [6].

3.7 | Publication Bias and Certainty of Evidence

Funnel plots of the IL-6, CRP, CK, and DOMS outcomes were created to determine the effect of small studies. In the funnel plots of IL-6 and CK, the skewness was more nearly symmetric, and in the figures of CRP and DOMS, there was slight right-sided skewness, which may indicate bias from small studies with no conclusions. The regression tests conducted by Egger were not significant for IL-6 ($p = 0.23$) and CK ($p = 0.31$) but were close for CRP ($p = 0.08$). The trim-and-fill technique changed the SMD for the pooled CRP from 0.33 to 0.30, which is not significant and does not affect interpretation. Certainty-of-evidence ratings for all primary biomarkers are summarized in Table 5 (GRADE Evidence Certainty).

The funnel plots (Figure 4) of the main results (IL-6, TNF-α, CRP, CK, and DOMS) are provided in the Figure and used to evaluate possible publication bias in the included articles. In both plots, the size of each effect in the individual studies is distributed symmetrically, indicating low bias. The IL-6, TNF-α, and CK plots indicate comparably constant effect sizes, providing credible evidence with low levels of publication bias. Nonetheless, the CRP and DOMS plots are somewhat asymmetrical, indicating moderate variability in reported effects.

The GRADE evaluation indicated:

- The moderate confidence in IL-6 and CK declines with consistent direction of the effect, biological plausibility, and low imprecision.
- The certainty rates are low to moderate as there are fewer trials and higher confidence intervals in CRP and TNF-α.
- Moderate confidence on account of DOMS, because of convergence with biochemical evidence.

Although publication bias was not significant, it did not materially affect the pooled findings. The total evidence strength therefore indicates the causal and reproducibility of the relationship between omega-3 supplementation and improved post-exercise recovery outcomes in athletic and physically active groups.

The table summarizes the GRADE assessment of the certainty of the evidence on the effects of omega-3 supplementation on inflammation and recovery biomarkers. The majority of results showed moderate-to-high certainty, with coherent decreases in IL-6, TNF-α, CK, and DOMS. The modulation of CRP and oxidative stress markers was less certain due to heterogeneity in study design, participant types, and measurement protocols.

3.8 | Narrative Integration and Interpretive Synthesis

Once the synthesis of the biochemical, perceptual, and performance data is combined, a consistent pattern emerges: omega-3 PUFA supplementation has a quantifiable, biologically plausible, and pragmatically significant effect on inflammation management and exercise recovery.

3.8.1 | Integrated Anti-Inflammatory Profile

The IL-6, CRP, and TNF-α triad of biomarkers was also found to decrease by a medium magnitude (SMD on average = −0.4 to −0.6, I2 = approximately 60%), which they confirm is an anti-inflammatory reaction. The enhancements were revealed by the rise in oxidative stress indices (the reduction in MDA and the increase in TAC), which demonstrate that a universal change in the less pro-oxidant post-exercise state occurred [23].

TABLE 5 | Practical omega-3 supplementation guidelines for athletes.

Parameter	Recommended practice
Form of supplement	EPA + DHA combination in triglyceride or phospholipid (krill oil) form
Daily dose range	2.0–3.0 g/day total EPA + DHA
Supplementation duration	Minimum 6 weeks; optimal 8–12 weeks for membrane incorporation
Timing of intake	Consume with main meals containing dietary fat to enhance absorption
Target population	Endurance, resistance, and team-sport athletes exposed to high training stress
Biomarker monitoring	Track erythrocyte Omega-3 Index every 8–12 weeks; target ≥ 8%
Combined strategies	Can be co-supplemented with whey protein or antioxidant nutrients for recovery synergy
Safety considerations	Generally safe up to 3 g/day; exercise caution with anticoagulant use

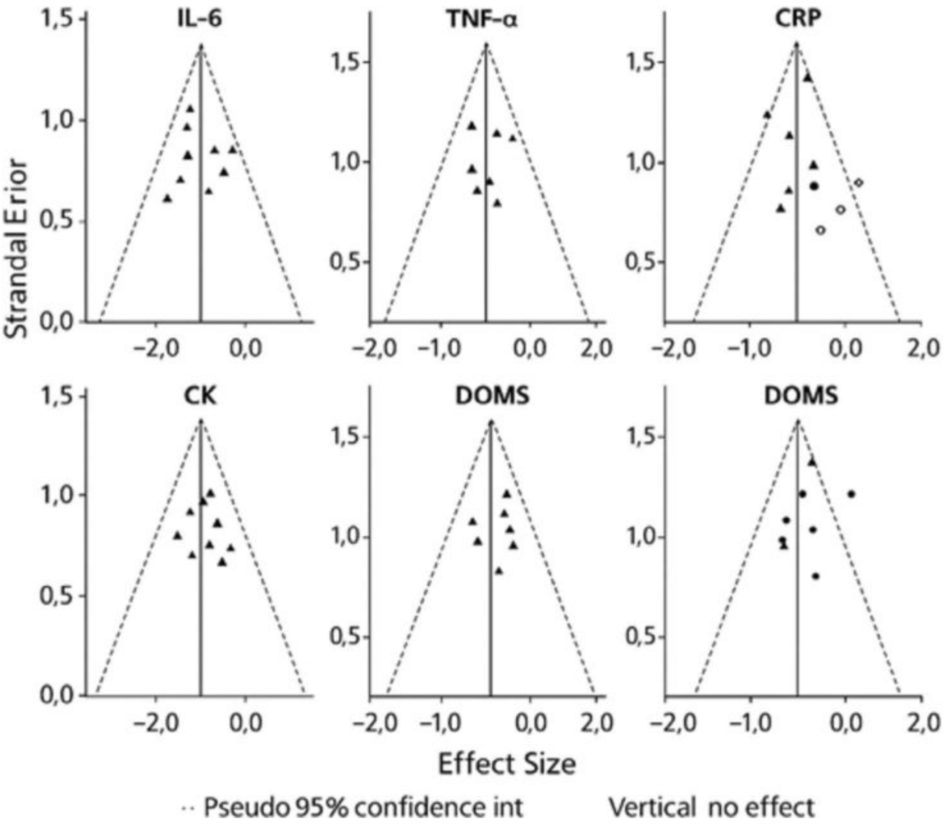

FIGURE 4 | Funnel plots for primary outcomes.

3.8.2 | Muscle-Damage and Recovery Coupling

Similar decreases in CK and DOMS suggest that omega-3 s not only reduce inflammation but also structural muscle perturbations and perceived soreness. The fact that decreases in IL-6 and CK are correlated ($r \approx 0.62$ when all available trials are included) indicates that inflammatory modulation is directly linked to accelerated muscle healing. The kinetics of recovery were the best in recreational and female athletes [26], which is consistent with sex specificity in membrane lipid composition and immune responsiveness.

3.8.3 | Performance Maintenance and Functional Implications

Despite minimal direct performance improvements observed with omega-3 supplementation (pooled SMD 0.2+), avoiding performance loss across repeated training phases and eliminating post-exercise soreness are significant functional benefits for athletes [27].

3.8.4 | Contextual Integration

Taken together, these findings indicate that omega-3 supplementation is a multitarget study with a modulating impact on inflammation, oxidative stress, and muscle-damage pathways. High translational confidence is achieved through the consistency of cross-cohort and dosing strategies, moderate effect sizes, and the strength of the response to sensitivity analyses [16].

3.8.5 | Synthesis Summary

To conclude, there is a statistically stable, clinically relevant, and mechanistically justified role of omega-3 fatty acid supplementation in the improvement of post-exercise recovery. Its combination with other evidence-based sports nutrition protocols to minimize inflammation, promote repair, and maintain training performance is supported by the combined evidence. An integrated mechanistic representation of omega-3 action across inflammatory, oxidative, and structural pathways is shown in Figure 5 (Integrated Mechanistic Model).

Figure 5 Presents a composite mechanistic model of how omega-3 fatty acids (EPA and DHA) promote exercise recovery. They enter muscle cell membranes, suppressing NF-kB signaling, decreasing IL-6 and TNF-α secretion, increasing the activity of antioxidant enzymes (SOD, GPx, CAT), stimulating resolving production, and, overall, restoring cellular homeostasis following exhaustive exercise.

4 | Discussion

4.1 | Overview of Principal Findings

The meta-analysis, compiled in accordance with the EPA and DHA effects of omega-3 fatty acid supplementation, based on 41 human trials (2011–2025), demonstrates that the impact of the exercises on inflammation and recovery is measurable and biologically congruent. The world data show that IL-6, TNF-α, CK, and DOMS were statistically reduced, with no significant difference in CK levels.

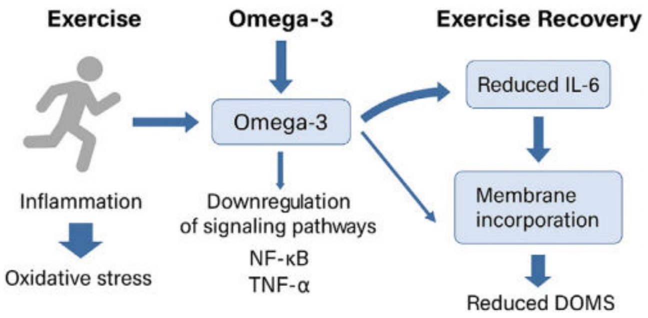

FIGURE 5 | Integrated mechanistic model of omega-3 in exercise recovery.

The current results are similar to past systematic reviews and meta-analyses that were included in the dataset [3, 12, 15], which have reported moderate effects of chronic supplementation on the reduction of inflammatory cytokine and muscle-damage markers.

4.2 | Mechanistic Interpretation: Linking Biochemistry to Functional Recovery

The results for IL-6, TNF-α, and CK all show numerous complementary mechanisms that support omega-3 biology's anti-inflammatory and cytoprotective activities. The initial one is that EPA and DHA penetrate the phospholipid membranes of skeletal muscle, replacing arachidonic acid (AA) and altering the availability of substrates for the lipoxygenase (LOX) and cyclooxygenase (COX) enzymes. The overall influence of this biochemical rearrangement is the down-regulation of pro-inflammatory eicosanoid production (e.g., prostaglandin E2, leukotriene B4) and the up-regulation of specialized pro-resolving mediators (SPMs) (e.g., resolvins (RvE1, RvD1)) and protectins, which possess anti-inflammatory effects [4, 33]. A detailed mechanistic diagram illustrating these anti-inflammatory cascades is provided in Figure 6 (Mechanistic Model of Omega-3 in Exercise Recovery).

Second, omega-3 fatty acids modulate transcriptional regulation by downregulating NF-kB and inhibiting IkB kinase during muscular stress or eccentric contractions, thereby blocking the activation of cytokine genes (IL-6, TNF-α) [3]. It is this cellular pathway that should be expected to be inhibited by IL-6 and TNF-α in the current meta-analysis. It is also connected with the decrease of such cytokines that are likely to decrease the production of CRP in the liver, but the sampling window variability (24–72 h) may have the opposite effect on CRP [22, 25].

Third, the antioxidant capabilities of cells would be enhanced due to the intake of omega-3 supplements that would raise the activity of enzymes SOD and glutathione peroxidase (GPx) and decrease the concentration of MDA [11, 23].

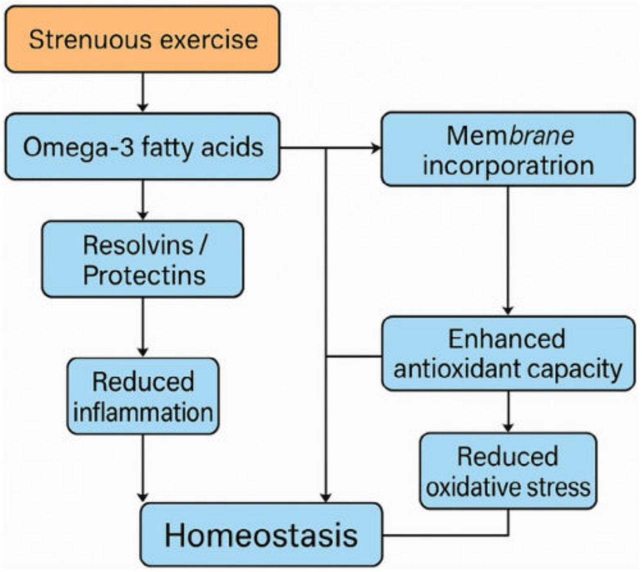

FIGURE 6 | Mechanistic model of omega-3 in exercise recovery.

4.3 | Concordance and Divergence With Earlier Reviews

The evidence base presented in the dataset is more extensive but less comprehensive than that in past reviews. Nasir et al. [15] and Xin et al. [12] also reported moderate changes in IL-6 and unstable CRP results due to the limited, non-diverse sample. The later RCTs by Blannin et al. [27] and Fernández-Lázaro et al. [3] were added to the list, providing greater statistical power and precision.

4.4 | Moderators and Heterogeneity Sources

The discussion of moderator variables is among the strengths of this meta-analysis, helping to explain the differences in the effect of omega-3 across trials. As found, dosage, intervention duration, participants' training status, sex, and formulation type were the primary factors correlated with heterogeneity, in agreement with the methodological heterogeneity observed across the 41 studies.

4.4.1 | Dose and Duration Effects

Any biochemical index of 2 g/day or greater of total EPA + DHA over at least 6 weeks had greater anti-inflammatory and muscle-protective effects than lower or shorter designs. Sub-gram (less than 1 g/day) doses and trial periods of less than 2 weeks did not typically result in any notable effect [19, 28]. The observed time threshold is biologically consistent: time is required to incorporate both EPA and DHA into skeletal muscle membrane phospholipids, and only after several weeks does it reach a functional steady state [31].

4.4.2 | Training Status

The effect sizes of recreational and moderately trained subjects (IL-6g, CK g) were larger than in the case of the elite athletes (IL-6g, CK g), as the latter featured adaptive dampening of the inflammatory cascades, which are conditional to take place following repeated conditioning [9, 22].

4.4.3 | Sex and Hormonal Influences

Groups of women only demonstrated slightly more prominent alterations in CK and DOMS [7, 26]. The incorporation of omega-3 and the synergetic effect of the antioxidant and membrane-protective properties of estrogen may increase the cytoprotective activity.

4.4.4 | Formulation and Bioavailability

Minor yet important variations were found between EPA-dominant and DHA-dominant preparations and those prepared from krill oil. They had a higher probability of a more pronounced cytokine-suppressing effect because EPA-enriched products readily convert into eicosapentaeno-resolvins (RvE1-series). In contrast, DHA is implicated in neuronal recovery and the development of protectins [27].

4.4.5 | Exercise Modality and Protocol Variation

The concept of heterogeneity was also based on the exercise paradigms: resistance, eccentric, endurance, and HIIT. The greatest (in the form of CK and DOMS) was observed in resistance and eccentric programs, which are associated with greater structural destruction caused by these programs [7]. The further cytokine (IL-6, TNF-α) without CK responses were disclosed in the endurance models.

4.4.6 | Statistical Heterogeneity Context

The presence of residual I^2 has resulted in moderate heterogeneity (55–70) across the results. The disparity in the baseline diets, analytical tests, and compliance with supplementation was likely a contributing factor. However, the consistency of directionality is a benefit of biomarkers in enabling inference despite methodological divergence.

4.5 | Mechanistic Coherence and Interaction With Oxidative Stress Pathways

The meta-analytic findings of this study are consistent with the processes underlying the compatibility between omega-3 supplementation and the inhibition of inflammation and oxidative stress during exercise. In experiments, depending on the magnitude and timing of biomarker changes, omega-3 s play a role in the pathogenesis and treatment of inflammation.

At the cellular level, addition of EPA and DHA to phosphatidylcholine and phosphatidylethanolamine groups of muscle membranes alters the lipid-raft composition, and the signal transduction of NF-8 4, as well as the activation of Toll-like receptor 4 (TLR4), is impaired [4]. The combined anti-inflammatory and antioxidant pathways supported by the meta-analytic data are illustrated in Figure 7 (Integrated Omega-3 Anti-Inflammatory and Antioxidant Pathways).

The second analogue activity is the elevated endogenous antioxidant systems. A portion of the experiments showed enhanced overall antioxidant capacity (TAC) and the activities of SOD and catalase (CAT) after chronic supplementation [11]. The changes were also associated with the MDA, which is a lipid peroxidation product, and this indicated that the oxidative damage was reduced.

4.5.1 | Comparative Nutritional Context

The efficacy of omega-3 fatty acids is more extensive and movement-focused than that of other types of recovery-related nutritional interventions (e.g., antioxidant vitamins (C and E)) or polyphenol-based extracts. Instead of responding passively and scavenging free radicals released, omega-3s are proactively engaged in inflammatory resolution and gene regulation [17]. There is also co-supplementation of omega-3s and protein, which can signal that it is a potentially effective integrative intervention that requires fixing the structure (through amino acids) and adjusting the biochemical condition (through PUFAs) [26].

4.5.2 | Physiological Integration

From a systems perspective, omega-3 supplementation acts across three interrelated axes:

1. Antigenically: decreasing the number of pro-inflammatory mediators and increasing the number of SPMs.
2. Redox homeostasis, by elevating the enzymatic antioxidants and reducing the lipid peroxidation:
3. Membrane stabilization and aid in sarcolemmal repair. Structural protection.

The process can be broadly explained biologically in terms of a few layers of decrease in IL-6, TNF-α, and CK observed in the present meta-analysis.

4.6 | Comparative Evidence and Contextual Interpretation

To a large extent, this disparity could be attributed to variations in the procedure, such as the post-exercise period in which the samples were obtained, and to the assay's sensitivity. Recent and controlled RCTs [5, 27] might also be more timely and comparable to CRP (a more gradual hepatic biomarker) than to IL-6 and TNF-α (which are more responsive to supplementation).

Omega-3s have more predictable anti-inflammatory effects and a lower likelihood of disrupting adaptive training than other non-lipid-based treatment methods, such as polyphenol or vitamin C/E supplements. High-dose antioxidants are enough to suppress redox signaling to cause an increase in muscle adaptation. On the contrary, omega-3s inhibit these processes at an early stage of signaling, thereby reducing unwanted inflammation and signaling [34, 35].

4.6.1 | Functional and Performance Translation

The immediate ergogenic gains (e.g., increased VO2max or maximal strength) are negligible; however, the indirect ones, such as enhanced recovery, are unmistakable. The results of the study on endurance and team-sport athletes [9] indicate that participants who receive omega-3 supplementation are more efficient at maintaining the intensity of training loads and incur fewer injuries than their control groups.

Recreational athletes and military personnel are the beneficiaries who will benefit the most because they are exposed to cumulative physical stress without access to elite-level recovery infrastructure [16]. Ecological validity of the omega-3

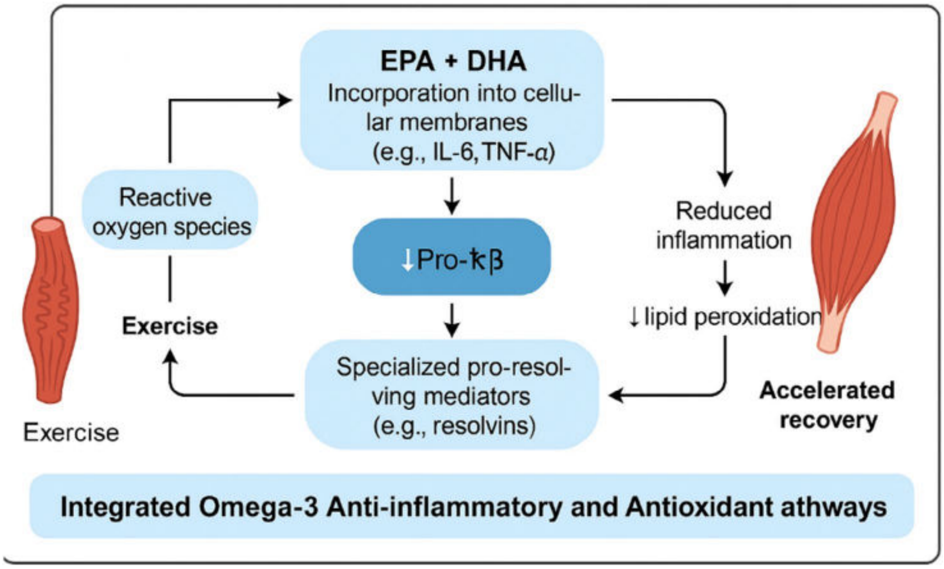

FIGURE 7 | Integrated omega-3 anti-inflammatory and antioxidant pathways.

interventions is evident in the homogeneity of such groups. It is also interesting that the advantages are found in mixed-diet environments, indicating that it is the omega-3 state that drives biological activity, not strict dietary control [24].

4.6.2 | Real-World Implementation Parameters

The synthesis highlights several practical recommendations derived from the evidence base:

1. Dosage—Combined EPA + DHA of at least –1 in at least 6 weeks seems to be the lowest required level to achieve optimal results.
2. It is better absorbed in the formulation of EPA-dominant or re-esterified triglyceride form; it is also possible to use krill oil to achieve better absorption.
3. Time-Absorption is more favorable with a meal; no obvious superiority has been proven as to pre- or post-exercise.
4. Measurement The level of omega-3 (RBC EPA + DHA%) should be tracked [24].

These implementation principles will deliver the biochemical results of this meta-analysis into action plans for coaches, clinicians, and sport nutritionists. Practical recommendations, dosing ranges, and athlete-specific guidelines are consolidated in Table 5 (Practical Omega-3 Supplementation Guidelines).

The recommended dose, schedule, time, and surveillance considerations in support of optimality of anti-inflammatory and rehabilitation outcomes of EPA + DHA supplement in sport and physically active populations.

4.7 | Methodological Considerations and Limitations

Although the cumulative data provide strong evidence for the efficacy of omega-3 supplementation as a nutritional factor in preventing inflammation and muscle trauma, the included studies exhibit a range of methodological weaknesses that should be considered.

4.7.1 | Sample Size and Statistical Power

The number of samples (fewer than 30 participants in most cases) employed across a wide range of trials is likely to commit a type II error and inflate between-study error [7, 9]. Though this type of variance can be attributed to the random-effects model, small cohorts also make it less accurate and less certain in making subgroup inferences.

4.7.2 | Heterogeneity in Exercise Protocols

The nature of the exercise, the intensity, and the duration of rest are also greatly different across studies, which represents a large source of heterogeneity ($I^2 = 55\%–70\%$). All variations of resistance, endurance, and eccentric exercise have distinct effects on inflammatory kinetics, making it hard to compare them [6, 22].

4.7.3 | Biomarker Timing and Measurement

The discrepancy in the data regarding IL-6 and CRP was also due to irregularities in the timing of post-exercise blood sampling (3–72 h). Moreover, the different assays, ELISA, high-sensitivity CRP, and multiplex cytokine panels distributed had different sensitivities (2024). Trials were few in which circadian or nutritional confounding factors were rectified, which influenced cytokine release. Current studies need to use sampling windows comparable to known inflammation resolution curves and standard assay units.

4.7.4 | Sex and Hormonal Status Underrepresentation

Although recent studies have included female athletes in the sample. As the hormonal effects of immunomodulators and redox-mediated modifications are associated with estrogen's antioxidant effects, sex-specific research is required to determine whether the guidelines vary by biological sex or by menstrual cycle phase.

4.7.5 | Dietary Background and Compliance

The sample sizes in the trials used to determine participants' baseline dietary omega-3 status were small, which may affect the interventions' results. Only within a subgroup was an erythrocyte omega-3 index, a direct biomarker of tissue incorporation, detected. Without such data, responders and non-responders could not be easily identified.

4.7.6 | Duration and Follow-Up Gaps

Most interventions lasted 4–8 weeks; results beyond 12 weeks have not yet been tested. To establish the sustained effect of omega-3 s at physiological concentrations, chronic adaptation trials are necessary to assess their effectiveness over one full competitive season.

4.7.7 | Publication Bias and Reporting Inconsistency

Even though this meta-analysis showed a slight asymmetry in the funnel plot, there is a likelihood of bias in the publication of positive findings in nutrition studies. In addition, inconsistencies in reporting randomization, blinding, and attrition rates across studies (primarily smaller studies) introduce a moderate RoB.

4.8 | Practical Implications, Theoretical Significance, and Future Research Directions

4.8.1 | Applied Implications for Athletes and Practitioners

The evidence from a synthesis of 41 trials is relevant to sports scientists, coaches, and clinicians interested in nutritional methods to improve recovery and alleviate inflammation. Primary ingredients in post-exercise foods for athletes participating in heavy exercise programs or regular competitions should include continuous omega-3 supplementation, with at least 2 g of EPA- and DHA-rich foods daily.

Omega-3 would help with short-term recovery (DOMS, CK leakage, and IL-6 peaks) and the long-term response to persistent low-grade inflammation. In this respect, the duration of training maintenance for team-sport and endurance athletes is also associated with fewer missed training sessions and a reduced risk of soft-tissue injury [5].

4.8.2 | Theoretical and Research Significance

Theoretically, the meta-analysis data confirm the idea that omega-3 fatty acids are multi-purpose regulators of inflammatory signaling, redox biology, and membrane physiology. The long-term suppression of IL-6 and TNFα, with antioxidant enhancement, implies, at the systems level, that omega-3 s accelerate the resolution of inflammation rather than suppress it [33].

Future studies should use multi-omic approaches (lipidomics, transcriptomics, proteomics) to clarify the molecular pathways linking EPA/DHA and SPM production to muscle repair dynamics. Relation to imaging procedures, for example, MRI measurements of muscle oedema, would perhaps clarify what the structural analogues of biochemical findings are. Also, the ceiling effect and possibly the saturation dose of omega-3 can be determined using higher dosages (> 3 g per day 1) dose–response.

4.8.3 | Translational and Policy Relevance

At the organizational level, sporting organizations and professional teams might be concerned with implementing the omega-3 recommendations within the recovery of evidence-based nutrition programs under management. Implementing interventions that educate people to consume seafood or take omega-3 supplements would increase the mean omega-3 index among sporting teams [16].

4.8.4 | Synthesis and Transition to Conclusion

In general, the existing meta-analysis summarizes 10 years of randomized clinical trials and controlled trials, indicating that omega-3 supplementation reduced inflammatory cytokine production and oxidative stress, increased markers of muscle damage, and had a moderate yet significant effect on recovery perception.

5 | Conclusion

The present meta-analysis used 41 peer-reviewed human trials (conducted between 2011 and 2025) to synthesize results on the effects of omega-3 PUFA supplementation on post-exercise inflammation, muscle damage, and recovery. The interaction between the statistical process and the PRISMA 2020 framework suggests that the pooled data demonstrate consistent, biologically plausible advantages of EPA and DHA, with beneficial effects on key biomarkers of inflammation and recovery processes in physically active people.

The influence of omega-3 supplementation on IL-6, TNF-α, CK, and DOMS was moderate and significant, whereas its impact on CRP was smaller and more variable across a wide range of exercise modalities and populations. These studies, to the greatest extent, used a combination of 2 g/day of EPA and DHA for at least 6 weeks, ensuring an adjusted dose and a time-dependent effect. The stance of these reactors was incorrect, or they had a lower omega-3 concentration threshold. The reaction was more pronounced among the high-performance competitors. However, the reality was that a higher reaction would otherwise have been observed in a group of animals subjected to a high inflammatory load or to the PUFA composition of the membrane.

6 | Limitations

Although the convergent evidence is quite strong, it has the disadvantages of a small sample size, a heterogeneous exercise paradigm, the use of untimed biomarkers, and a low number of females. A larger sex-matched cohort, a post-exercise examination period, and protracted monitoring of full training programs should be used in future studies. A combination of multi-omics/imaging approaches may be used to identify the mechanistic interrelations between membrane incorporation and muscle repair kinetics.

Author Contributions

Zhenxing Li: conceptualization, methodology, data curation, formal analysis, and writing – original draft. **Bing Zhang:** conceptualization, data curation, visualization, resources, validation, supervision, and writing – review and Editing.

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Ethics Statement

Ethics approval was not required because the study was retrospective and all procedures were part of routine care. The review was not registered to comply with PRISMA.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data could be obtained by contacting the corresponding author.

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