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Nutritional Supplementation and High-Intensity Exercise: A Systematic Review

I Gusti Ayu Indira Pratiwi[1]*, Agustinus I Wayan Harimawan[2]

[1]Faculty of Medicine, Udayana University, Bali, Indonesia

[2]Department of Clinical Nutrition, Faculty of Medicine, Udayana University
Prof. Dr. I.G.N.G. Ngoerah Hospital, Denpasar, Bali, Indonesia

*Corresponding author details: I Gusti Ayu Indira Pratiwi; indirapratiwi87@yahoo.co.id

ABSTRACT

High-intensity interval training and resistance training provide significant benefits for physical performance but may induce oxidative stress and inflammation. Nutritional strategies have been proposed to mitigate these effects. This systematic review aimed to evaluate the effects of nutritional supplementation combined with high-intensity interval training or resistance training on oxidative stress, inflammatory markers, recovery, and performance outcomes in healthy adults. A systematic search was conducted in PubMed, Scopus, and Web of Science. Eligible studies included randomized controlled trials in humans investigating nutritional supplementation in combination with high-intensity interval training or resistance training. Study selection followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Six studies met the inclusion criteria. Polyphenol supplementation combined with resistance training improved muscle mass and maximal oxygen uptake but showed limited anti-inflammatory effects. Acute L-citrulline supplementation increased nitric oxide and antioxidant enzyme activity after high-intensity interval training. Green tea combined with high-intensity interval training reduced interleukin-6, interleukin-1 beta, and galanin while enhancing antioxidant activity in obese older adults. Vitamins C and E reduced muscle damage and hemolysis in elite athletes. Probiotics improved recovery and reduced inflammatory responses. Nutritional supplementation, particularly L-citrulline and polyphenols, shows potential to enhance antioxidant defense, reduce inflammation, and support recovery when combined with high-intensity interval or resistance training.

Keywords: high-intensity interval training; nutritional supplementation; antioxidants; inflammatory response

INTRODUCTION

High-intensity interval training and resistance training are widely recognized for improving maximal oxygen uptake, mitochondrial biogenesis, muscle hypertrophy, insulin sensitivity, and cardiometabolic profiles. Recent evidence continues to confirm that structured high-intensity exercise enhances aerobic capacity and metabolic health in both trained and untrained adults. These adaptations are primarily mediated through mitochondrial and cellular signaling pathways that enhance metabolic efficiency and skeletal muscle function [1,2]. However, acute and chronic exposure to high-intensity workloads also increases reactive oxygen species production, lipid peroxidation, and inflammatory signaling, including activation of nuclear factor kappa B and elevation of pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-alpha [2,3]. While moderate oxidative stress is essential for physiological adaptation, excessive redox imbalance may impair recovery, increase delayed onset muscle soreness, and potentially compromise long-term performance [4].

Nutritional supplementation has been proposed as a strategy to modulate oxidative stress and inflammation during high-intensity exercise. Recent randomized controlled trials have investigated antioxidants, polyphenols, vitamins C and E, amino acids such as L-citrulline, and probiotics for their potential to enhance endogenous antioxidant defenses and attenuate inflammatory responses. Polyphenols and flavonoids found in plant-based foods may exert antioxidant and anti-inflammatory effects through modulation of cellular signaling pathways such as Nrf2 activation and inhibition of oxidative stress–induced inflammatory cascades [5–7]. In addition, supplementation with L-citrulline may improve nitric oxide availability and vascular function, potentially enhancing exercise performance and recovery [8,9]. Probiotic supplementation has also gained attention for its potential to influence immune responses, gut health, and metabolic adaptations associated with intensive training [10,11].

Some studies report improvements in oxidative biomarkers, recovery indices, and performance outcomes, whereas others suggest limited benefits or possible attenuation of adaptive signaling when antioxidant doses are excessive [4,12].

Despite increasing research interest within the past decade, findings remain inconsistent due to variations in supplementation type, dosage, duration, participant characteristics, and exercise protocols. Differences in study design and methodological approaches have contributed to heterogeneous outcomes regarding antioxidant capacity, inflammatory biomarkers, and exercise performance following supplementation [13]. This heterogeneity creates a gap in consolidated evidence regarding the overall efficacy of supplementation combined with high-intensity interval or resistance training.

Therefore, this systematic review aims to synthesize current randomized clinical evidence published within the last decade to clarify the effects of nutritional supplementation on oxidative stress, inflammatory markers, recovery, and performance outcomes in healthy adults undergoing high-intensity interval or resistance training.

METHODS

Eligibility criteria were defined using the Population, Intervention, Comparator, and Outcome (PICO) framework to ensure methodological rigor and clinical relevance. The population included healthy or physically active adults aged 18–72 years without diagnosed chronic diseases. The intervention comprised acute or long-term nutritional supplementation administered in combination with high-intensity interval training (HIIT) or resistance-based training protocols. The comparator consisted of placebo-controlled groups or identical exercise protocols without supplementation. Primary outcomes included biomarkers of oxidative stress, inflammatory markers, and exercise performance indicators. Studies were included if they were conducted in humans and used randomized controlled trial (RCT) or controlled clinical trial designs with quantitative outcome reporting. Studies were excluded if they involved animal or in vitro models, observational designs, populations with chronic diseases, or failed to report relevant oxidative, inflammatory, or performance-related outcomes.

RESULTS AND DISCUSSION

This study was conducted as a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021) (Table 1). A total of 526 records were identified through database searching. After removing 48 duplicates, 478 records remained for title and abstract screening. Of these, 46 articles were selected for full-text assessment. Following eligibility evaluation, 40 articles were excluded due to inappropriate study design, irrelevant outcomes, or unsuitable populations. Ultimately, six studies met the inclusion criteria and were included in the final synthesis.

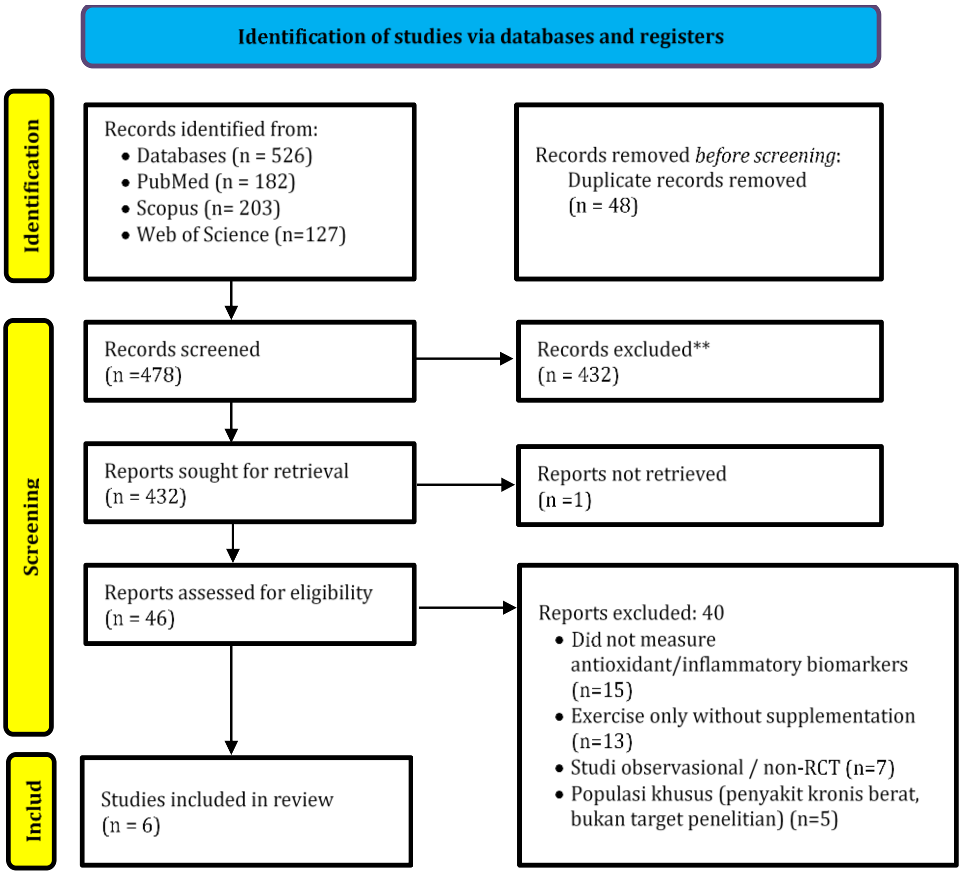

FIGURE 1: PRISMA Flow Chart Diagram.

A systematic literature search was conducted in PubMed, Scopus, and Web of Science between January 2025 and August 2025. The search strategy combined keywords and Boolean operators as follows: ("high-intensity interval training" OR HIIT) AND ("resistance training" OR strength training) AND (antioxidant OR "vitamin C" OR "vitamin E" OR polyphenols OR probiotics OR "L-citrulline").

The methodological framework was structured to ensure transparency in study selection, data extraction, and quality appraisal. The eligibility criteria were determined using the Population, Intervention, Comparator, and Outcome (PICO) framework. The population included healthy or physically active adults aged 18–72 years without diagnosed chronic diseases. The intervention consisted of acute or chronic nutritional supplementation administered in combination with high-intensity interval training (HIIT) or resistance training. The comparator was placebo or an identical exercise protocol without supplementation.

Primary outcomes included biomarkers of oxidative stress, inflammatory markers, recovery indices, and exercise performance parameters, which are commonly used indicators to evaluate physiological responses to high-intensity exercise and nutritional interventions [2,4]. Oxidative stress biomarkers such as reactive oxygen species production, lipid peroxidation markers, and antioxidant enzyme activity are widely used to assess redox balance during exercise [2,4]. Inflammatory outcomes included circulating cytokines such as interleukin-6 and other immune mediators associated with exercise-induced inflammatory responses [3]. Exercise performance parameters included measures of endurance capacity, strength, and time-trial performance, which have been frequently evaluated in studies examining ergogenic supplementation strategies [14] (Table 1).

TABLE 1: Characteristics of studies that meet eligibility criteria.

Study	Population	Intervention	Duration	Primary Biomarkers	Main Findings
Flensted-Jensen et al., 2025	Young adults	Polyphenol supplementation	6–8 weeks	SOD, IL-6, TNF-α	↑ Antioxidant capacity, ↓ inflammation
Valaei et al., 2022	Young men	12 g acute L-citrulline	Single session	SOD, GPx, CAT, NOx	↑ Antioxidant enzymes & nitric oxide, ↓ oxidative stress
Naghizadeh et al., 2023	Obese older adults	HIIT ± 450 mg green tea/day	8 weeks	TRX-1, PON1, IL-1β, IL-6, Galanin	Combination most effective: ↑ antioxidants, ↓ inflammation
Chou et al., 2018	Taekwondo athletes	Vitamin C 2000 mg + Vitamin E 1400 IU (4 days)	Simulated competition	CK, Myoglobin, hemolysis markers	↓ Muscle damage & inflammation
Żychowska et al., 2021	Older women	Daily vitamin C + exercise	6 weeks	IL-6, IL-10, CRP, CCL2	Trend toward ↓ IL-6, ↑ IL-10; not statistically significant
Chen et al., 2024	Middle-aged obese women	TWK10 probiotic + HIIT	8 weeks	VO_2max, waist circumference, metabolic markers	↑ Aerobic capacity, ↓ waist circumference, synergistic effect

Risk of Bias

The methodological quality of included randomized controlled trials was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool (Sterne et al., 2019). The domains evaluated included: (1) randomization process, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of outcomes, and (5) selective reporting.

Each study was categorized as low risk, some concerns, or high risk of bias according to the RoB 2 algorithm. If non-randomized studies were identified, risk of bias was planned to be assessed using the Newcastle-Ottawa Scale, evaluating selection, comparability, and outcome assessment domains (Table 2).

TABLE 2: Risk of Bias.

Study	Randomization Process	Deviations from Intended Intervention	Missing Outcome Data	Measurement of Outcome	Selective Reporting	Overall Risk of Bias
Żychowska et al. (2021) – Vitamin C for 6 weeks in older adults	Some concerns	Low risk	Low risk	Low risk	Some concerns	Low to some concerns
Chou et al. (2018) – Vitamin C + E in Taekwondo athletes	Some concerns	Low risk	Some concerns	Low risk	Some concerns	Low to some concerns
Chen et al. (2024) – Probiotic + HIIT in middle-aged women	Low risk	Low risk	Low risk	Low risk	Some concerns	Low risk
Flensted-Jensen et al. (2025) – Polyphenols + RT + HIIT	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Valaei et al. (2022) – L-Citrulline	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Naghizadeh et al. (2023) – HIIT + Green Tea in obese older adults	Some concerns	Moderate risk	Some concerns	Low risk	Some concerns	Some concerns

Description of Included Studies

The six included trials collectively examined the interaction between nutritional supplementation and high-intensity exercise from three primary mechanistic perspectives: (1) antioxidant modulation, (2) inflammatory regulation, and (3) performance and recovery outcomes. These mechanisms are closely related to the physiological adaptations induced by intensive exercise, particularly the balance between oxidative stress and antioxidant defense systems (Nikolaidis et al., 2012; Powers & Jackson, 2008). Despite differences in population characteristics and supplementation protocols, a consistent pattern emerged suggesting that combined interventions tend to produce more pronounced physiological effects than exercise or supplementation alone. This synergistic interaction may occur because nutritional compounds can modulate cellular signaling pathways involved in redox balance, inflammation, and metabolic regulation [6,15].

The included studies demonstrate that nutritional supplementation combined with exercise interventions may positively influence inflammatory responses and metabolic outcomes across different populations. Interventions such as high-intensity interval training (HIIT) combined with green tea extract, vitamin C and vitamin E supplementation, polyphenols with resistance training, and probiotic supplementation with HIIT were evaluated over durations ranging from 4 days to 12 weeks. Bioactive compounds such as green tea catechins and polyphenols have been reported to exert antioxidant and anti-inflammatory effects by reducing oxidative damage and regulating immune signaling pathways [13,16]. Most studies reported reductions in pro-inflammatory biomarkers, including IL-1β and IL-6, alongside increases in anti-inflammatory markers such as IL-10, which are commonly associated with exercise-induced immune modulation [17].

Additionally, several interventions showed improvements in metabolic profiles, reduced muscle damage, and enhanced body composition (Table 3). These findings are consistent with previous evidence suggesting that antioxidant and probiotic supplementation may support recovery processes and metabolic adaptation during high-intensity training [10,11].

Antioxidant Modulation

Across studies evaluating antioxidant responses, both polyphenol-based and amino acid-based supplementation demonstrated measurable enhancement of endogenous antioxidant defense systems. Exercise-induced oxidative stress activates cellular antioxidant pathways, including enzymatic defenses such as superoxide dismutase, catalase, and glutathione peroxidase [2,4]. Polyphenol supplementation combined with resistance training resulted in significant reductions in malondialdehyde levels and moderate increases in antioxidant enzyme activity (Cohen's d ≈ 0.5–0.8), indicating attenuation of exercise-induced oxidative stress. Polyphenols and flavonoids have been shown to exert antioxidant effects by modulating redox-sensitive signaling pathways and enhancing endogenous antioxidant defenses [6,16,18].

Similarly, acute L-citrulline supplementation prior to high-intensity interval training significantly increased superoxide dismutase and glutathione peroxidase activity, alongside elevated nitric oxide metabolites. L-citrulline is known to increase nitric oxide bioavailability through the arginine–nitric oxide pathway, which may improve vascular function and cellular redox balance during exercise [9]. The magnitude of catalase response was also greater compared with placebo, suggesting enhanced redox buffering capacity during acute high-intensity stress. These findings are consistent with previous reports demonstrating that L-citrulline supplementation may support antioxidant capacity and exercise performance during intense training conditions [8].

Green tea polyphenols combined with high-intensity interval training further reinforced this pattern, demonstrating significant increases in thioredoxin reductase-1 and paraoxonase-1. Catechins found in green tea are widely recognized for their antioxidant and anti-inflammatory properties and have been associated with improvements in metabolic and cardiovascular health [13,19,20]. Collectively, these findings indicate that bioactive compounds may amplify adaptive antioxidant signaling when administered in conjunction with structured high-intensity exercise, potentially enhancing redox homeostasis and recovery following intense workloads [4].

Inflammatory Response

The anti-inflammatory effects varied in magnitude depending on supplementation type and duration. Exercise-induced inflammation is a physiological response to muscle contraction and tissue stress, characterized by the release of cytokines and activation of immune signaling pathways [3]. The strongest and most consistent reductions in inflammatory biomarkers were observed in studies combining polyphenol-rich interventions with high-intensity training, where significant decreases in interleukin-1 beta and interleukin-6 were documented. Polyphenols and flavonoids are known to exert anti-inflammatory effects by modulating oxidative stress–related pathways and inhibiting pro-inflammatory signaling cascades [6,13,16].

Short-term high-dose vitamin C and E supplementation in elite athletes undergoing repeated high-intensity competition significantly reduced muscle damage markers (creatine kinase and myoglobin) and attenuated systemic inflammatory indices, including platelet-to-lymphocyte ratio. Antioxidant vitamins have been widely investigated for their capacity to reduce exercise-induced oxidative stress and inflammation, particularly during periods of intense or repeated competition [4,21]. These findings suggest that antioxidant loading may provide protective effects under extreme competitive stress conditions by limiting excessive oxidative damage and inflammatory activation [22].

In contrast, medium-term vitamin C supplementation in older women produced only modest, non-significant trends toward decreased interleukin-6 and increased interleukin-10 gene expression. Previous studies indicate that aging individuals often exhibit chronic low-grade inflammation and altered redox balance, which may influence the responsiveness to antioxidant interventions [4,23]. This suggests that antioxidant effects may be dose-, duration-, and population-dependent, particularly in aging individuals characterized by low-grade chronic inflammation and altered immune regulation .

Performance and Recovery Outcomes

Performance-related outcomes demonstrated a clearer synergistic pattern when supplementation was combined with high-intensity interval training. Exercise performance adaptations are strongly influenced by metabolic efficiency, mitochondrial function, and vascular responses during repeated high-intensity workloads [2,4]. The probiotic *Lactiplantibacillus plantarum* TWK10, when paired with structured interval training, improved aerobic capacity and reduced anthropometric markers compared with either intervention alone. Previous research has suggested that probiotic supplementation may influence exercise performance by improving gut microbiota composition, immune responses, and metabolic efficiency during training [10,11,24].

Green tea combined with high-intensity interval training improved maximal oxygen uptake and reduced body fat percentage, indicating concurrent metabolic and functional adaptation. Catechins present in green tea have been associated with enhanced fat oxidation, improved metabolic regulation, and antioxidant effects that may support training adaptation [13,19]. L-citrulline enhanced nitric oxide availability, which may contribute mechanistically to improved vascular perfusion and recovery efficiency during intense exercise [9,25]. Increased nitric oxide production has been linked to improved blood flow and oxygen delivery to skeletal muscle, which may support endurance performance and recovery processes [8].

TABLE 3: Subgroup analysis of the effects of nutritional supplementation on inflammation.

Author (Year)	Population	Intervention	Duration	Inflammatory Biomarkers	Main Findings
Naghizadeh et al., 2023	Obese older adults	HIIT + green tea extract	8 weeks	IL-1β, IL-6, Galanin	Significant reductions in IL-1β, IL-6, and
Chou et al., 2018	Taekwondo athletes	Vitamin C (2000 mg) + Vitamin E (1400 IU)	4 days (competition period)	CK, Myoglobin, hemolysis markers	Reduced muscle damage and acute
Żychowska et al., 2021	Healthy older adults	Daily vitamin C + health-oriented	6 weeks	IL-6, IL-10, CRP, CCL2	Decreased IL-6 and increased IL-10, but
Flensted-Jensen et al., 2025	Healthy older adults	Polyphenols (MitoActive) + RT +	12 weeks	IL-10, IFN-γ, TNF-α	Polyphenols attenuated acute inflammatory
Chen et al., 2024	Middle-aged obese women	TWK10 + HIIT	8 weeks	Not cytokine-specific	Improved metabolic profile and body

Taken together, the included studies demonstrate that supplementation strategies targeting antioxidant and inflammatory pathways may enhance physiological adaptation to high-intensity exercise. These adaptations may occur through modulation of oxidative stress signaling pathways, immune responses, and vascular function during training [3,7]. However, effects appear to be context-dependent and influenced by participant characteristics, supplementation dosage, duration, and exercise modality. Combination strategies generally yielded stronger and more consistent benefits than single interventions, supporting the hypothesis that nutritional modulation may act synergistically with high-intensity training stimuli rather than independently driving adaptation.

SUBGROUP ANALYSIS

Antioxidant Effects of Nutritional Supplementation during HIIT

The subgroup analysis of antioxidant-related outcomes demonstrates that the magnitude and consistency of redox modulation differ substantially according to supplementation type, timing, and exercise context (Table 4). Exercise-induced oxidative stress activates multiple cellular antioxidant systems that regulate the balance between reactive oxygen species production and detoxification during high-intensity workloads [2,4]. Across the included trials, the most robust antioxidant effects were observed in interventions targeting enzymatic defense pathways directly involved in reactive oxygen species detoxification.

Acute L-citrulline supplementation (12 g prior to high-intensity interval training) produced the clearest enzymatic response, with significant elevations in superoxide dismutase, glutathione peroxidase, and nitric oxide metabolites. This coordinated upregulation suggests enhanced endogenous antioxidant activation rather than passive radical scavenging. L-citrulline has been shown to increase nitric oxide bioavailability through the arginine–nitric oxide metabolic pathway, which may improve vascular function and redox homeostasis during exercise [9]. The concurrent increase in nitric oxide bioavailability also indicates improved endothelial function and perfusion, potentially facilitating more efficient oxidative stress resolution during early recovery phases. These findings support the concept that targeted amino acid supplementation may amplify adaptive redox signaling in the acute phase of high-intensity exercise [8]

Similarly, the combination of high-intensity interval training with green tea extract resulted in significant increases in thioredoxin reductase-1 and paraoxonase-1, both critical components of cellular antioxidant defense. Unlike direct antioxidant supplementation, polyphenol-rich interventions appear to function as modulators of redox-sensitive transcription pathways, potentially enhancing intrinsic antioxidant capacity through hormetic mechanisms [6,7]. Polyphenols and flavonoids are known to activate signaling pathways associated with antioxidant gene expression and cellular protection against oxidative stress [5,18]. The consistent elevation of enzymatic biomarkers in this context suggests a synergistic interaction between exercise-induced oxidative stimuli and polyphenol-mediated redox signaling amplification.

In contrast, high-dose vitamin C and E supplementation demonstrated a predominantly protective, rather than adaptive, antioxidant profile. While significant reductions in muscle damage and hemolysis were observed during acute competitive stress, direct enhancement of endogenous antioxidant enzyme systems was not consistently reported. Antioxidant vitamins are known to reduce oxidative damage and inflammation during intense exercise; however, their role in stimulating endogenous adaptive responses remains controversial [4,22]. This pattern aligns with the notion that high-dose exogenous antioxidants may primarily attenuate oxidative injury rather than stimulate endogenous defense pathways. Evidence from endurance training studies suggests that excessive antioxidant supplementation may even blunt exercise-induced cellular adaptations by interfering with redox-sensitive signaling processes [26].

Medium-term vitamin C supplementation in older adults further illustrates this distinction. Despite theoretical antioxidant benefits, no significant increases in plasma antioxidant capacity were observed. Instead, modulation was more evident at the level of inflammatory gene expression, suggesting that antioxidant effects may be secondary and population-dependent, particularly in aging individuals characterized by baseline low-grade inflammation (Żychowska et al., 2021; Nikolaidis et al., 2012).

Interventions combining polyphenols with resistance training and high-intensity interval training, as well as probiotic supplementation with *Lactiplantibacillus plantarum* TWK10, demonstrated stronger effects on metabolic fitness and aerobic performance than on classical oxidative biomarkers. These findings imply that certain supplements may exert indirect antioxidant benefits through improvements in mitochondrial efficiency and metabolic regulation rather than direct enzymatic activation [11,24,27]. Improved metabolic efficiency and mitochondrial function during exercise may reduce excessive reactive oxygen species generation, thereby contributing indirectly to better oxidative balance and recovery [1,28].

TABLE 4: Subgroup analysis of the effect of nutritional supplementation on HITT related to antioxidant outcomes.

Author (Year)	Population	Intervention	Duration	Antioxidant Biomarkers	Main Findings
Valaei et al., 2022 (L-Citrulline)	Young men	12 g acute L-citrulline before HIIT	Single session	SOD, GPx, CAT, NOx	Significant increases in SOD, GPx, and NOx;
Naghizadeh et al., 2023 (HIIT + Green Tea)	Obese older adults	HIIT + green tea extract	8 weeks	TRX-1, PON1	Significant increases in TRX-1 and PON1;
Chou et al., 2018 (Vitamin C & E)	Taekwondo athletes	Vitamin C (2000 mg) + Vitamin E (1400 IU)	4 days	CK, Myoglobin (oxidative stress	Reduced muscle damage associated with
Żychowska et al., 2021 (Vitamin C 1000	Healthy older adults	Daily vitamin C + health-oriented	6 weeks	TAS/TAC, gene expression	No significant improvement in
Flensted-Jensen et al., 2025 (Polyphenols +	Healthy older adults	Polyphenols (MitoActive) + RT +	12 weeks	Systemic oxidative status	No significant antioxidant effect;
Chen et al., 2024 (Probiotic TWK10 +	Middle-aged obese women	TWK10 + HIIT	8 weeks	No direct antioxidant biomarkers	Improvements in metabolic profile and

The present systematic review highlights that the interaction between nutritional supplementation and high-intensity exercise is highly context-dependent, with effects varying according to supplement type, dosage, duration, and population characteristics. While several interventions demonstrated improvements in oxidative or inflammatory biomarkers, the magnitude and clinical relevance of these effects differed substantially. Exercise-induced oxidative stress and inflammatory signaling are key mediators of physiological adaptation, but excessive imbalance may impair recovery and performance [2,4].

Flensted-Jensen et al. (2025) reported that polyphenol supplementation combined with resistance training improved muscle strength, muscle size, and maximal oxygen uptake in older adults [29]. However, anti-inflammatory effects were modest, suggesting that the primary driver of physiological improvement was exercise-induced adaptation rather than supplementation alone. This finding aligns with previous mechanistic evidence indicating that flavonoids may reduce oxidative stress and inflammation by modulating redox-sensitive signaling pathways and scavenging reactive species [6,16,18]. Polyphenols may also influence gene expression involved in antioxidant defense systems, thereby enhancing endogenous cellular protection against oxidative stress [15]. Nonetheless, variability in bioavailability and metabolic processing of polyphenols may partly explain inconsistent outcomes across human trials. Thus, polyphenols appear to potentiate training adaptations, but their independent effect is strongly influenced by individual metabolic context.

Acute L-citrulline supplementation (12 g) prior to high-intensity interval training significantly enhanced nitric oxide bioavailability and endogenous antioxidant enzyme activity. Citrulline is converted to arginine, thereby promoting nitric oxide synthesis and improving vascular perfusion [9,25]. Enhanced blood flow facilitates metabolic waste clearance and may attenuate oxidative accumulation during high-intensity efforts. These findings are consistent with prior research demonstrating improvements in exercise performance and metabolic responses following citrulline supplementation [8,30]. Importantly, most available data focus on short-term administration, and long-term adaptation effects remain insufficiently explored. Whether chronic supplementation sustains redox enhancement without attenuating adaptive signaling warrants further investigation, particularly in trained athletes and aging populations.

The synergistic interaction between green tea extract and high-intensity interval training observed by Naghizadeh and Hemati Farsani (2023) further supports the concept of exercise–nutrient synergy [31]. Epigallocatechin gallate, the principal catechin in green tea, has been shown to attenuate lipid peroxidation and enhance antioxidant defense systems [13,19,20]. In this trial, combined intervention significantly reduced pro-inflammatory cytokines such as interleukin-6 and interleukin-1 beta, whereas green tea alone did not produce comparable effects. This pattern suggests that oxidative stimuli generated by high-intensity training may act as a trigger for polyphenol-mediated redox signaling amplification, consistent with hormetic adaptation theory [28].

High-dose vitamin C and E supplementation demonstrated protective effects in acute competitive settings. Chou et al. (2018) reported significant reductions in creatine kinase, myoglobin, and hemolysis in elite Taekwondo athletes during repeated high-intensity matches [21]. These findings support the established biochemical roles of water-soluble vitamin C and lipid-soluble vitamin E in neutralizing free radicals within aqueous and membrane environments [32,33]. However, long-term high-dose antioxidant supplementation remains controversial. Experimental evidence suggests that excessive exogenous antioxidants may blunt mitochondrial biogenesis and endogenous adaptive responses induced by exercise [26].

Therefore, while short-term antioxidant loading may be advantageous during intense competition phases, chronic high-dose use during training periods aimed at physiological adaptation should be approached cautiously.

In older women, six weeks of daily vitamin C supplementation (1000 mg/day) combined with health-oriented exercise resulted in non-significant trends toward decreased interleukin-6 and increased interleukin-10 expression [23]. Although statistical significance was not achieved, the direction of change suggests potential immunomodulatory effects. Given that aging is characterized by chronic low-grade inflammation, modulation of interleukin-6 and interleukin-10 pathways may be clinically relevant. The absence of strong effects may reflect insufficient duration or dose-specific responsiveness. Previous literature indicates that antioxidant intake can influence redox-sensitive transcription factors such as nuclear factor kappa B and nuclear factor erythroid 2-related factor 2 (Ma, 2013; Morgan & Liu, 2011), implying that gene-level modulation may require longer exposure [3,7].

Probiotic supplementation, particularly *Lactiplantibacillus plantarum* TWK10, demonstrated improvements in metabolic recovery and endurance when combined with high-intensity interval training [10]. Mechanistically, probiotics may enhance gut barrier integrity and modulate systemic immune responses through interactions between the gut microbiota and skeletal muscle metabolism [24]. In athletes, probiotic supplementation has also been associated with improved immune function and reduced incidence of illness during intensive training periods [11]. Thus, probiotic supplementation appears to exert indirect anti-inflammatory and recovery-enhancing effects rather than direct antioxidant amplification.

Collectively, the evidence suggests that supplementation strategies may function through distinct mechanistic pathways: acute redox enhancement (L-citrulline), hormetic signaling amplification (polyphenols and green tea), protective radical scavenging (vitamins C and E), or systemic inflammatory modulation via the gut–muscle axis (probiotics). Importantly, supplementation does not universally enhance adaptation; instead, its benefit depends on training phase, physiological status, and dosage strategy. Future research should prioritize longer-term trials, dose–response analyses, and mechanistic endpoints to clarify optimal integration of nutritional supplementation within high-intensity training paradigms.

This systematic review provides a comprehensive synthesis of current clinical evidence regarding the interaction between nutritional supplementation and high-intensity exercise. One of the main strengths of this review lies in its focus on randomized controlled trials involving human participants, which increases the reliability of the findings compared with observational evidence.

In addition, the review integrates multiple mechanistic domains, including oxidative stress modulation, inflammatory responses, metabolic adaptation, and exercise performance outcomes. By combining evidence from different supplementation strategies such as amino acids, antioxidant vitamins, polyphenols, and probiotics, this review provides a broader understanding of how nutritional interventions may influence physiological responses to high-intensity training.

Despite these strengths, several limitations should be considered when interpreting the findings. First, the number of eligible studies included in the analysis was relatively small, which limits the overall strength of the conclusions. Second, substantial heterogeneity was observed among studies in terms of supplementation dosage, intervention duration, training protocols, participant characteristics, and outcome measurements. This variability prevented the conduct of a quantitative meta-analysis and required reliance on narrative synthesis. Third, most studies evaluated short-term interventions, making it difficult to determine the long-term effects of supplementation on exercise adaptation and metabolic health. Finally, differences in bioavailability, absorption, and metabolic processing of bioactive compounds such as polyphenols may partly explain inconsistencies across studies.

The findings of this review have several practical implications for athletes, physically active individuals, and clinicians involved in exercise and sports nutrition. Nutritional supplementation may provide additional benefits when integrated with structured high-intensity training programs, particularly in supporting antioxidant defense, moderating inflammatory responses, and facilitating recovery. Acute supplementation strategies, such as L-citrulline or polyphenol-rich compounds like green tea extract, appear to be particularly effective in improving redox balance and physiological responses during intense exercise sessions.

In competitive or high-load training phases, short-term antioxidant supplementation with vitamins C and E may help reduce exercise-induced muscle damage and inflammatory responses, potentially supporting recovery between repeated bouts of intense activity. However, caution should be exercised when considering long-term high-dose antioxidant supplementation during training periods aimed at physiological adaptation, as excessive antioxidant intake may interfere with endogenous redox signaling and mitochondrial adaptations.

Probiotic supplementation represents another promising strategy, particularly through its influence on the gut–muscle axis and systemic immune regulation. Improvements in metabolic efficiency, immune resilience, and recovery may indirectly enhance training tolerance and performance outcomes. Overall, supplementation strategies should be individualized based on training phase, athlete characteristics, and specific performance goals rather than applied universally.

CONCLUSION

This systematic review demonstrates that selected nutritional supplements, including vitamins C and E, polyphenols, L-citrulline, green tea extract, and probiotics, may enhance antioxidant defense, modulate inflammatory responses, and support recovery when combined with high-intensity interval or resistance training. The evidence suggests that the benefits are most evident when supplementation is integrated with structured exercise stimuli, highlighting a synergistic interaction rather than a strong independent effect of supplements alone. Acute interventions, particularly L-citrulline and green tea combined with high-intensity training, appear to produce more consistent improvements in redox-related biomarkers, whereas other supplements primarily exert protective or metabolic-supportive roles.

Despite these promising findings, the overall strength of evidence remains constrained by the limited number of trials, variability in study design, short intervention durations, and heterogeneous outcome measures. These factors limit generalizability and prevent firm conclusions regarding optimal dosage, timing, and long-term effectiveness. Future well-designed randomized controlled trials with larger samples, longer follow-up periods, and standardized biomarkers are required to establish clearer evidence-based recommendations for integrating nutritional supplementation within high-intensity training programs.

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