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Antioxidants in Sport: Exercise-Induced Oxidative Stress, Dietary Strategies, and Performance Outcomes – A Review

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Abstract

Background. Exercise induces reactive oxygen species (ROS) production, triggering both adaptive signaling and potential oxidative damage in skeletal muscle. While moderate ROS generation promotes beneficial training adaptations, including mitochondrial biogenesis and improved insulin sensitivity, excessive antioxidant supplementation may paradoxically blunt these adaptive responses.

Aim. This narrative review examines current evidence on exercise-induced oxidative stress, the role of dietary antioxidants, and the efficacy of supplementation strategies in athletic populations.

Material and methods. Systematic search of PubMed, Scopus, and Web of Science using keywords: "exercise", "oxidative stress", "antioxidants", "vitamins C and E", "polyphenols", "CoQ10", "melatonin", "recovery". Priority given to randomized controlled trials, meta-analyses, and mechanistic reviews.

Results. Chronic high-dose vitamins C (≥1000 mg/day) and E (≥400 IU/day) blunt mitochondrial and antioxidant adaptations without clear performance benefits. Polyphenol-rich foods (berries, cherries, pomegranate, blackcurrant) enhance recovery and reduce soreness. Coenzyme Q10 (100–300 mg/day) and melatonin (3–20 mg/day) provide modest benefits for recovery and oxidative stress without impairing adaptations. Food-based or combined antioxidant sources outperform isolated high-dose supplements.

Conclusions. For most athletes, an optimal strategy is a high-quality, plant-rich diet rather than chronic high-dose supplementation. Food-first approaches with fresh fruits, vegetables, whole grains, legumes, and seeds effectively manage exercise-induced oxidative stress. Targeted, short-term polyphenol-rich interventions around competition or intense training may aid recovery without hindering adaptations. Routine use of large doses of vitamins C and E is not recommended and may impair training responses.

Keywords: exercise-induced oxidative stress, antioxidant supplementation, training adaptations, reactive oxygen species, athletic performance, dietary antioxidants, mitochondrial biogenesis, insulin sensitivity, polyphenols.

1. Introduction

Regular physical training is a cornerstone of health promotion and disease prevention, conferring well-documented cardiovascular, metabolic, and psychological benefits (1-3). However, intense and prolonged exercise generates substantial increases in reactive oxygen species (ROS) production in skeletal muscle, leading to transient oxidative stress (1,2). This exercise-induced oxidative stress has prompted widespread adoption of dietary antioxidant supplementation to reduce oxidative damage and enhance performance.

The paradox of exercise and oxidative stress lies in the dual nature of ROS. While excessive ROS production causes lipid and protein peroxidation and muscle damage, moderate ROS production serves as a crucial signaling molecule that triggers adaptive responses to training. These ROS-mediated adaptations include upregulation of the endogenous antioxidant enzyme defense system (superoxide dismutase, glutathione peroxidase, catalase), mitochondrial biogenesis via PGC-1α activation, and improvements in insulin sensitivity and glucose uptake (1,4,5).

Recent evidence demonstrates that high-dose supplementation with non-enzymatic antioxidants, particularly vitamins C and E, may paradoxically blunt beneficial training adaptations (1,3,17-19). This counterintuitive finding has shifted scientific consensus toward a more nuanced understanding: the optimal strategy may not be maximal ROS suppression, but rather maintenance of physiological redox balance through natural, food-based sources (2,5,6).

Research objective. To synthesize current evidence on exercise-induced oxidative stress, evaluate the efficacy and safety of various antioxidant supplementation strategies, and provide practical recommendations for athletes and physically active individuals.

2. Mechanisms of Exercise-Induced Oxidative Stress and Adaptive Responses

2.1. Sources and Production of Reactive Oxygen Species During Exercise

During physical exercise, oxygen consumption increases 10- to 20-fold in active skeletal muscle, leading to enhanced aerobic metabolism and elevated ROS production. Major cellular sources of ROS generation during muscle contraction include mitochondria (primary site), xanthine oxidase, NADPH oxidase, and immune cells, including macrophages, monocytes, and neutrophils. Reactive oxygen species encompass superoxide anion ($O_2^{\bullet -}$), hydroxyl radical ($HO^{\bullet}$), peroxyl radical ($RO_2^{\bullet}$), and hydrogen peroxide (H_2O_2) (2). High-intensity exercise also increases reactive nitrogen species (RNS), including nitric oxide (NO) and peroxynitrite ($ONOO^-$) (1,2).

2.2. The Antioxidant Defense System

The human body maintains redox balance through integrated enzymatic and non-enzymatic antioxidant defenses (1,4):

Enzymatic antioxidants:

- **Superoxide dismutase (SOD)**: Catalyzes dismutation of superoxide to hydrogen peroxide; exists in cytosolic (SOD1) and mitochondrial (SOD2) forms (1).
- **Glutathione peroxidase (GPx)**: Converts hydrogen peroxide and organic hydroperoxides to water using reduced glutathione (GSH) as substrate (1).

- **Catalase (CAT)**: Converts hydrogen peroxide directly to water and oxygen in peroxisomes and mitochondria (1).

Non-enzymatic antioxidants from dietary sources include vitamin C, vitamin E, β-carotene, glutathione, α-lipoic acid, coenzyme Q10, and polyphenolic compounds (2,5,6).

2.3. The Hormesis Hypothesis: ROS as Signaling Molecules

Contemporary exercise physiology recognizes that moderate ROS production acts as a hormetic signal—a low-dose stressor activating adaptive defense mechanisms (1,4). ROS-mediated activation of redox-sensitive signaling pathways (NF-κB, MAPK cascades) promotes transcription of genes encoding antioxidant enzymes and stress-response proteins (1,4). Recent comprehensive analysis by Powers et al. (25) demonstrates that contraction-induced ROS production is essential for achieving full benefits of exercise-induced adaptation in skeletal muscle, with ROS triggering signaling pathways that regulate mitochondrial biogenesis and expression of mitochondrial proteins and antioxidant enzymes.

During endurance training, ROS activates AMPK and calcium-dependent signaling cascades that phosphorylate PGC-1α, a master transcriptional coactivator of mitochondrial biogenesis (1,4). PGC-1α promotes expression of nuclear respiratory factors and mitochondrial transcription factor A (Tfam), leading to enhanced mitochondrial DNA replication and synthesis of new, more efficient mitochondria that produce fewer ROS per ATP generated (1,4).

ROS signaling also enhances glucose uptake and insulin sensitivity through multiple pathways: (1) AMPK activation promotes GLUT4 translocation to cell membrane, (2) ROS-derived nitric oxide stimulates endothelial-dependent vasodilation, and (3) PGC-1α regulates insulin-sensitizing gene expression (1,4,5).

3. Antioxidant Supplementation: Effects on Adaptations to Exercise Training

3.1. High-Dose Vitamin C and E: Blunting of Adaptations

A landmark randomized controlled trial by Ristow et al. (17) demonstrated that 4 weeks of endurance training increased insulin sensitivity, adiponectin, PGC-1α expression, and endogenous antioxidant enzymes; these adaptations were largely blunted in participants receiving vitamin C (1000 mg/day) plus vitamin E (400 IU/day). Importantly, this blunting effect is associated with chronic supplementation throughout the training period; acute single-dose post-exercise vitamin C intake does not substantially impair the adaptive response (19).

Gomez-Cabrera et al. (19) showed in Wistar rats that vitamin C supplementation (0.24 mg/cm²) during endurance training markedly decreased both SOD2 and GPx mRNA expression, directly suppressing the adaptive antioxidant response. Braakhuis et al. (18) found that, in trained endurance athletes, vitamin C supplementation (1000 mg/day) decreased SOD activity post-exercise and reduced catalase activity in erythrocytes compared to placebo.

In humans, Paulsen et al. (26) conducted a double-blind RCT (n=54) receiving 1000 mg vitamin C + 235 mg vitamin E daily for 11 weeks of endurance training, finding blunted increases in cytosolic PGC-1α and mitochondrial COX4 protein in vastus lateralis, alongside reduced CDC42 and MAPK1 expression—confirming the blunting effect observed in animal studies.

Mankowski et al. (1) and Mason et al. (3) concluded, in comprehensive reviews, that chronic high-dose vitamin C and E supplementation does not consistently improve performance or recovery and can blunt key training adaptations at the molecular and systemic levels. No

convincing evidence supports the ergogenic benefits of high-dose antioxidant vitamin supplementation in well-nourished athletes.

3.2. Polyphenolic Compounds and Exercise Recovery

Polyphenols are diverse phytochemicals, including flavonoids, phenolic acids, stilbenes, and lignans, that are abundantly found in plant-derived foods. Unlike isolated vitamins, polyphenols modulate redox-sensitive cell signaling pathways rather than simply quenching ROS, and appear to enhance rather than impair exercise-induced adaptive signaling (4,8).

Key evidence:

- **Blueberry consumption** (McLeay et al.,5): Significantly improved recovery of maximal voluntary contraction strength and reduced muscle soreness 48 hours following eccentric leg exercise compared to placebo.
- **Tart cherry juice** (Howatson et al.,7; Bowtell et al.,20): Multiple trials report reduced strength loss, inflammation, and soreness after marathon running and heavy resistance exercise.
- **Blackcurrant extract** (Lyall et al.,9): Anthocyanin-rich extract taken before and after eccentric exercise improved recovery of muscle function, attenuated soreness, and lowered creatine kinase compared to placebo. A comprehensive 2024 review by Willems et al. (27) synthesizing 17 randomized controlled trials examining anthocyanin-rich blackcurrant supplementation (1.8–3.2 mg/kg, 105–315 mg anthocyanins) found meaningful effects on continuous and intermittent exercise performance and recovery markers, with the largest effects 48–72 hours post-exercise.
- **Polyphenol-rich foods meta-analysis** (Carey et al.,8): Meta-analysis showed polyphenol-rich interventions accelerated recovery of muscle function and reduced delayed onset muscle soreness, with the largest effects 48–72 hours post-exercise. Cao et al. (28) demonstrated that long-term polyphenol consumption expands endogenous antioxidant capacity through Nrf2 pathway activation, explaining why food-based polyphenols enhance rather than blunt training adaptations—a distinct mechanism from acute ROS scavenging by isolated vitamins.

Importantly, polyphenol interventions appear to enhance adaptive responses rather than block them, fitting with a hormetic perspective rather than simple antioxidant "blocking" of exercise signals.

3.3. Coenzyme Q10

Coenzyme Q10 is a lipid-soluble quinone functioning as an electron carrier in the mitochondrial electron transport chain and a membrane-bound antioxidant preventing lipid peroxidation. Unlike vitamins C and E, CoQ10 is synthesized endogenously, and concentrations are tightly regulated; supplementation does not cause excessive antioxidant capacity (10,21).

Leonardo-Mendonça et al. (11) found that resistance-trained athletes receiving CoQ10 supplementation showed significant reductions in oxidative stress biomarkers and muscle damage markers with improved recovery parameters. A systematic review concluded that CoQ10 may modestly improve some performance parameters and oxidative stress markers in certain contexts, with variable dosages and training status.

Short-term co-supplementation with royal jelly and CoQ10 in swimmers improved high-intensity interval exercise performance and reduced lipid peroxidation and markers of muscle

damage compared with placebo, suggesting a potential role in specific high-intensity settings (21).

3.4. Melatonin

Melatonin is a hormone produced by the pineal gland with potent antioxidant and anti-inflammatory properties. Unlike classic free-radical scavengers, melatonin enhances endogenous antioxidant enzyme expression and maintains circadian-rhythm-driven recovery (12).

Ortiz-Franco et al. (13) found that melatonin supplementation (20 mg/day for 4 weeks) in high-intensity trained athletes significantly reduced exercise-induced oxidative damage (DNA damage markers) and improved antioxidant status compared to placebo. Leonardo-Mendonça et al. (11) demonstrated that melatonin supplementation in resistance-trained athletes reduced oxidative stress biomarkers, attenuated muscle damage, and did not impair adaptive responses to training.

San Miguel et al. (14) in a recent systematic review concluded that melatonin supplementation may improve some markers of muscle function and decrease soreness after intense exercise. Melatonin appears not to blunt training adaptations, possibly because its antioxidant mechanism complements rather than suppresses ROS-dependent signaling.

3.5. Combined Antioxidant Formulas and Glutathione

Lee et al. (15) conducted a randomized, double-blinded, crossover trial in 12 middle-aged triathlon athletes examining acute supplementation with combined yeast-derived glutathione (252 mg) and vitamin C (110 mg) versus individual compounds or placebo. Combined VitC+glutathione supplementation produced significantly lower carbon dioxide output, lower respiratory exchange ratio, and higher oxygen pulse during 90 minutes of submaximal cycling, suggesting improved metabolic efficiency.

Glutathione: Aoi et al. (29) conducted an RCT demonstrating that 2 weeks of glutathione supplementation elevated PGC-1α expression and mitochondrial content while reducing exercise-induced acidification, without impairing training adaptations—indicating that synergistic glutathione formulations may enhance recovery through metabolic optimization rather than non-specific ROS quenching.

Combined supplementation increased total hemoglobin concentration in skeletal muscle, reduced blood lactate post-exercise, and increased biological antioxidant potential while decreasing oxidative stress markers. Importantly, individual supplementation with glutathione or vitamin C alone did not produce equivalent benefits, suggesting synergistic effects of combined natural antioxidant compounds (15).

4. Dietary Approaches to Antioxidant Support in Athletes

4.1. The Food-First Strategy: Natural Antioxidants from Whole Foods

Current scientific evidence strongly supports a "food-first" approach to meeting antioxidant requirements in athletes. Regular consumption of a diverse range of fresh fruits, vegetables, whole grains, legumes, beans, sprouts, seeds, and nuts provides a comprehensive array of antioxidants, including vitamins C and E, polyphenols, carotenoids, and mineral cofactors (Cu, Zn, Se, Mn) (2,5,6,22).

The antioxidant content of whole foods exists in natural ratios optimized through evolutionary selection, incorporating complementary phytochemicals that enhance bioavailability and

synergistic activity (2,5,6). For example, vitamin C combined with polyphenols in citrus fruits or berries demonstrates enhanced antioxidant and anti-inflammatory efficacy compared to vitamin C alone.

Athletes following a restricted-antioxidant diet for 2 weeks showed significantly elevated oxidative stress markers following both submaximal and exhaustive exercise (increases of 38%, 45%, and 31% respectively) compared to athletes consuming habitual antioxidant-rich diets. This underscores that trained athletes have elevated antioxidant requirements and benefit substantially from increased dietary antioxidant intake through whole-food sources (2).

4.2. Plant-Based and Mediterranean Dietary Patterns

Emerging research demonstrates that structured dietary patterns emphasizing plant-derived foods offer superior antioxidant support compared to standard Western diets (5,6,22). Mediterranean and plant-based dietary patterns provide exceptionally high total antioxidant capacity.

Ayaz et al. (6) conducted a narrative review concluding that plant-based athletes consuming well-designed diets demonstrate equivalent or superior performance compared to omnivorous athletes, with particular benefits for recovery and management of training-induced inflammation. The high polyphenol content of plant-based diets, combined with adequate intake of micronutrients (Fe, Zn, B12, omega-3), supports both oxidative stress management and training adaptation.

These findings suggest that promotion of plant-forward dietary patterns—while not requiring complete vegetarian adherence—represents an evidence-based strategy for athletes seeking to optimize antioxidant status and training outcomes.

4.3. Minerals and Cofactors for Antioxidant Enzyme Function

The functionality of endogenous antioxidant enzymes depends on adequate dietary intake of mineral cofactors: copper and zinc for Cu/Zn-SOD, selenium for glutathione peroxidase, and manganese for manganese-SOD. Athletes with marginal micronutrient status may experience impaired enzymatic antioxidant defense despite appropriate training (1,2,23).

Current evidence supports micronutrient adequacy through diverse whole-food consumption or, when intake is inadequate, targeted supplementation of deficient micronutrients at recommended dietary allowance (RDA) levels rather than megadose supplementation. Moderate-level zinc/copper supplementation and selenium supplementation have demonstrated benefits, while megadose supplementation offers no additional advantage and may introduce risk of nutrient interactions (1,2,23).

5. Current Guidelines and Practical Recommendations

5.1. Summary of Evidence on Antioxidant Supplementation Efficacy

The weight of current evidence permits the following conclusions:

1. High-dose isolated vitamin C (≥1000 mg/day) and vitamin E (≥400 IU/day) supplementation consistently blunts training-induced adaptations in endogenous antioxidant defenses, mitochondrial biogenesis, and insulin sensitivity without demonstrable benefits for endurance performance (1,3,17–19). These supplements are not recommended for athletes engaged in endurance training.

2. Polyphenol-rich whole foods and supplements (from berries, pomegranate, tea, cocoa) demonstrate benefits for reducing exercise-induced oxidative damage, accelerating recovery from muscle damage, and reducing inflammation without blunting training adaptations (4–9,20). These represent a preferred supplementation strategy compared to isolated vitamins.

3. Coenzyme Q10 and melatonin supplementation at physiologically relevant doses (100–300 mg/day CoQ10, 3–20 mg/day melatonin) show promise for reducing oxidative stress, accelerating recovery, and improving sleep quality without apparent blunting of training adaptations (10–14,21).

4. Combined or synergistic antioxidant formulas derived from food sources (e.g., glutathione+vitamin C, polyphenol complexes) appear more effective than single isolated compounds and do not demonstrate the adaptive-blunting effects seen with megadose single vitamins (15).

5. Micronutrient adequacy (Cu, Zn, Se, Mn) is essential for enzymatic antioxidant function, but megadose supplementation of individual minerals offers no advantage over RDA-level intake through diverse whole-food consumption (1,2,23).

5.2. Practical Recommendations for Athletes and Coaches

Primary Strategy: Emphasize Whole-Food Antioxidant Intake

- Consume a minimum of 8–10 servings daily of colorful fresh fruits and vegetables: dark leafy greens, berries, citrus fruits, tomatoes, peppers, cruciferous vegetables, and allium vegetables (2,5,6).
- Include whole grains, legumes, beans, lentils, nuts, and seeds (2,5,6).
- Incorporate antioxidant-rich plant oils such as extra-virgin olive oil and herbal teas (green tea, white tea) (5,6).

Secondary Strategy: Targeted Supplementation When Appropriate

- **Avoid**: High-dose vitamin C (>500 mg/day) and vitamin E (>400 IU/day) supplementation during intense endurance training phases; these suppress training adaptations without consistent performance benefits (1,3,17–19).
- **Consider**: Polyphenol-rich foods or standardized extracts (anthocyanin-rich berry extracts, green tea extract) for athletes with high training demands or elevated recovery needs (4–9).
- **Consider**: Coenzyme Q10 supplementation (100–300 mg/day) for master's athletes or those with high fatigue accumulation (10,21).
- **Consider**: Melatonin supplementation (3–10 mg, taken 30–60 minutes before bedtime) for athletes with disrupted sleep patterns or circadian misalignment (11,13,14).
- **Ensure**: Adequate micronutrient status through diverse whole-food consumption or targeted supplementation at RDA levels (not megadose) for Cu, Zn, Se, and Mn (1,2,23).

Timing and Duration

- Prioritize antioxidant intake throughout the day from food sources rather than acute peri-exercise supplementation (1,2,3).

- Supplement trials should span ≥4 weeks to assess full training adaptation effects (1,4).

5.3. Special Populations: Older Adults and Athletes with Comorbidities

Older adults with age-related increases in oxidative stress, impaired antioxidant enzyme systems, and comorbidities such as hypertension, insulin resistance, or type 2 diabetes may derive particular benefit from increased dietary antioxidant intake. However, the same principles apply: whole-food-based antioxidant strategies are preferable to high-dose isolated supplements (1,4,24).

Older athletes engaging in regular endurance or resistance training should prioritize antioxidant-rich dietary patterns (Mediterranean, plant-forward) combined with micronutrient adequacy; modest polyphenol supplementation and CoQ10 or melatonin may be considered for those with signs of accumulated training fatigue or sleep disruption (1,4,10,14,24).

6. Future Research Directions

Several important gaps remain in current knowledge regarding antioxidants and exercise:

1. **Optimal dosing and formulations**: Few studies systematically examined dose-response relationships for antioxidant supplementation or compared single-compound versus multi-compound formulations using rigorous methodologies (1,4). Future research should establish evidence-based dosing guidelines.

2. **Long-term supplementation effects**: Most studies examine acute or short-term (4–8 week) supplementation; long-term (≥12 week) effects on training adaptations and performance in diverse athletic populations remain underexplored (1,4).

3. **Individual variability and genetic factors**: Exercise-induced oxidative stress and antioxidant responses show substantial individual variation, likely reflecting genetic differences in antioxidant enzyme expression; future studies should characterize individual differences and develop personalized supplementation strategies (1,4).

4. **Older and master athletes**: Research on antioxidant supplementation in older athletes is limited; future studies should prioritize this population, which may have distinct antioxidant requirements (1,4,24).

5. **Sex-based differences**: Few studies examined sex-based differences in exercise-induced oxidative stress and responses to antioxidant supplementation; future research should characterize potential sex differences (15).

6. **Specific antioxidant compounds**: While polyphenols, CoQ10, and melatonin show promise, additional research on emerging compounds (astaxanthin, pterostilbene, resveratrol) and their effects on oxidative stress and training adaptations in humans is needed (4,8,9). Stilbene compounds, including resveratrol and pterostilbene (a dimethoxy-resveratrol analogue), represent a particularly promising class of emerging antioxidants. Zhang et al. (30) synthesized evidence on resveratrol and pterostilbene, demonstrating that high-dose resveratrol (150 mg/kg) extended time-to-exhaustion during intense exercise via SIRT1-PGC-1α upregulation, with pterostilbene showing preliminary evidence for superior potency. These observations suggest that stilbene compounds merit further investigation in human populations.

7. Conclusion

Exercise-induced oxidative stress is a dual-edged phenomenon: moderate ROS production serves essential signaling functions, promoting training adaptations, including mitochondrial biogenesis, upregulation of enzymatic antioxidants, and improved insulin sensitivity; yet excessive ROS generation causes cellular damage and impairs contractile function. Current evidence demonstrates that high-dose supplementation with isolated antioxidant compounds, particularly vitamins C and E at megadose levels (≥1000 mg C or ≥400 IU E daily), paradoxically blunts beneficial training adaptations without consistent improvements in athletic performance.

In contrast, a whole-food-based dietary approach emphasizing diverse fresh fruits, vegetables, whole grains, legumes, seeds, and nuts provides comprehensive and synergistic antioxidant and phytochemical support without risk of over-suppressing adaptive signaling. Plant-based and Mediterranean dietary patterns offer particularly robust antioxidant benefits. When supplementation is necessary—as in athletes with high training demands, poor recovery, or circadian disruption—evidence supports polyphenol-rich extracts, coenzyme Q10, and melatonin as safer choices than high-dose isolated vitamins, with particular benefits for recovery and reducing muscle damage.

Micronutrient adequacy at RDA levels, achieved through whole-food consumption, remains essential for optimal enzymatic antioxidant defense. The emerging consensus—that "less is more" when it comes to isolated antioxidant supplementation, but that dietary emphasis on whole antioxidant-rich foods is universally beneficial—represents a significant paradigm shift in nutritional support for athletes. This evidence-based, individualized approach optimizes both performance and long-term health.

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Author Contributions:

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