

CLASS 5 DIETARY SUPPLEMENTS



**HPRC DIETARY SUPPLEMENTS CLASSIFICATION SYSTEM:
VITAMIN C, VITAMIN E, AND ZINC
AS ANTIOXIDANTS**

Background

The antioxidants zinc and vitamins C and E play an important role in protecting cells and neutralizing free radicals during exercise. Antioxidants are found in many plant-based foods—including green leafy vegetables, citrus fruits, legumes, nuts, grains, seeds, and oils—and are added to commercial foods as well as sports supplements and gels to extend their shelf life.¹

It is well accepted that high-intensity exercise can result in damage to active muscle fibers, which is exhibited by soreness, stiffness, and a reduction in the force-producing capability of the muscle (muscle fatigue).² Exercise produces reactive oxygen species, or free radicals, and it has been hypothesized that antioxidants enhance performance by scavenging these radicals.³

But there is no evidence to date that exercise-induced free radicals in skeletal muscle are harmful to human health, and it is also not known if vigorous exercise/training increases the need for dietary antioxidants.^{3,4}

Research on antioxidants and exercise is plentiful, but studies focus on various antioxidant combinations and doses, with mixed results. For example, ultramarathoners who were given 1000 mg of supplemental vitamin C and 300 mg of supplemental vitamin E for six weeks demonstrated that the antioxidants completely inhibited exercise-induced lipid peroxidation (i.e., degradation of these cell components) but did not prevent muscle damage and had no effect on inflammatory markers.⁵ A review of vitamin E supplementation and exercise that included earlier studies with dose ranges from 300 to 900 mg/day concluded that vitamin E does not appear to decrease exercise-induced lipid peroxidation in humans.⁶ Finally, ultramarathoners who took 1500 mg of supplemental vitamin C for seven days experienced no effect on lipid peroxidation after ultramarathon.⁷

More research is needed on non-vitamin antioxidants such as zinc and N-actyl-cysteine (NAC). The benefits of zinc supplementation to physical performance have not been established, but zinc has been shown to have potential benefits for diseases affecting soldiers, including diarrhea, respiratory diseases, malaria, and leishmaniasis (a parasitic disease transmitted by sandflies).⁸⁻¹⁰ Several studies have shown that NAC delays muscle fatigue only during submaximal exercise but has no effect on muscle fatigue during VO_{2max} exercise.¹¹ It should be noted that these studies used IV preparations, and data regarding benefits are mixed.^{12,13}

Overall, antioxidant supplementation is not needed when consuming a healthy, balanced diet, but when athletes follow a low-fat diet, restrict their energy intakes, or limit dietary intake of fruits, vegetables, and whole grains, they are at greatest risk for poor antioxidant intakes.⁹

Dose Range and Upper Limit

Food and Nutrition Board DRIs^{14,15}

RDA & Upper Limit:			
	RDA Men 19-50	RDA Women 19-50	Upper Limit (UL)
Antioxidant			
Vitamin C (mg)	90	75	2000
Vitamin E (d-alpha-tocopherol; mg / IU)	15 / 22.4	15 / 22.4	1000 / 1500
Zinc (mg)	11	8	40

Doses Used In Randomized Clinical Trials: Vitamin C doses of 1000 to 1500 mg/day have been used with ultramarathoners,^{5,7} and vitamin E dosing has ranged from 300 to 900 mg/day.^{5,6} Zinc has not been used in RCTs with respect to physical performance.

Toxicology Data:

Zinc. 80 – 450 mg/day¹⁶

Vitamin C. Very low toxicity¹⁶

Vitamin E. Insufficient data

Evaluation of Potential Benefits

Limited scientific evidence suggests that antioxidant supplementation would enhance physical performance during military tasks or supports recommending these supplements to athletes or other physically active individuals.^{3,4,9}

Potential Detrimental Effects on...

Military Performance: Overall, there are no detrimental effects if consumption from diet and supplements is below daily Upper Limits (UL). However, recent studies indicate that antioxidant supplementation with high levels of vitamins E and C (i.e., ~16 times higher than the RDA for adults) may actually hinder the adaptive processes to exercise.³

Military Survivability: High doses of vitamin C, vitamin E, and zinc compromise GI tolerance, resulting in diarrhea, nausea, abdominal cramps, and other gastrointestinal disturbances.^{16,17}

High doses of vitamin E can inhibit clotting time and impair vision.¹⁷

Other Health Risks

Vitamin C. Possible adverse effects with intakes greater than 2,000 mg include diarrhea and other gastrointestinal disturbances.¹⁴

Vitamin E. When used in high doses, exceeding the tolerable upper intake level, vitamin E can result in significant side effects and may increase the risk of hemorrhagic stroke.¹⁷

Zinc. High doses, above the UL, may increase the risk of copper deficiency, flu-like symptoms, nausea, vomiting, fatigue, neuropathy, metallic taste, kidney and stomach damage, and other side effects.¹⁷

Interactions with Medications or Other Bioactive Substances

Vitamin E.¹⁷ Because vitamin E inhibits platelet aggregation/adhesion, it should be avoided by anyone taking anticoagulant/antiplatelet drugs, herbs, or supplements. Supplements that should be used with caution in conjunction with vitamin E include beta-carotene, iron, omega-6 fatty acids, vitamin A, and vitamin K. Drugs with a possibility of a minor interaction when taken along with vitamin E include chemotherapy, cyclosporine, cytochrome P450 3A4 substrates, statins, niacin, and warfarin (Coumadin).

Vitamin C.¹⁷ Acetaminophen and NSAIDs (including aspirin) may have minor interactions with vitamin C. Additional possible moderate drug interactions include aluminum, chemotherapy, estrogens (including oral contraceptives), fluphenazine (Prolixin), statins (e.g., Zocor), niacin, protease inhibitors, and warfarin (Coumadin). Some supplements that contain vitamin C (e.g., acerola, Cherokee rosehip, and rosehip) should be taken with caution not to exceed the tolerable intake level of vitamin C (see Multivitamins and Minerals monograph). Other supplements that could interact unfavorably with vitamin C include chromium, copper, grapeseed, iron, and vitamin B12.

Zinc.¹⁷ EDTA supplements should be taken with caution, as EDTA and its salts can cause zinc depletion, even when supplemental zinc is taken. Supplemental phytic acid may have a similar effect. Other supplements to be taken with caution when taking zinc include bromelain, calcium, copper, folic acid, iron, magnesium, manganese, and riboflavin. Drugs that could interact moderately with zinc include cisplatin, penicillamine, quinolone antibiotics, and tetracycline antibiotics.

For details of these and other potential interactions, visit the Natural Medicines Comprehensive Database.¹⁷

Withdrawal Effects

No data found.

Concern and Benefit Estimate (see Dietary Supplement Risk Matrix)

Benefit Potential: Low

Risk (safety concern): Minimal

Classification score: 5

Supplementing an otherwise balanced diet with antioxidants or supplements that contain high doses of antioxidants should be done with caution, as mega-dosing can be detrimental to health.^{3,4}

References

1. AIS Sports Nutrition, Australian Institute of Sport. Antioxidant Vitamins C and E. Fact Sheets: Group A Supplements 2009; http://www.ausport.gov.au/ais/nutrition/supplements/supplement_fact_sheets/group_a_supplements/antioxidant_vitamins_c_and_e. Accessed October 03, 2011.
2. McGinley C, Shafat A, Donnelly AE. Does Antioxidant Vitamin Supplementation Protect against Muscle Damage? Sports Med. 2009;39(12):1011-32.
3. Stear SJ, Burke LM, Castell LM. BJSM reviews: A-Z of nutritional supplements: dietary supplements, sports nutrition foods and ergogenic aids for health and performance Part 3. Br. J. Sports Med. 2009;43(12):890-2.
4. Powers SK, DeRuisseau KC, Quindry J, Hamilton KL. Dietary antioxidants and exercise. J. Sports Sci. 2004;22(1):81-94.
5. Committee on Optimization of Nutrient Composition of Military Rations for Short-term High-stress Situations, Committee on Military Nutrition Research. Nutrient Composition of Rations for Short-Term, High-Intensity Combat Operations. Washington, DC: Food and Nutrition Board, Institute of Medicine; 2005.
6. Viitala P, Newhouse IJ. Vitamin E supplementation, exercise and lipid peroxidation in human participants. Eur. J. Appl. Physiol. 2004;93(1-2):108-15.
7. Nieman DC, Henson DA, McAnulty SR, McAnulty L, et al. Influence of vitamin C supplementation on oxidative and immune changes after an ultramarathon. J. Appl. Physiol. 2002;92(5):1970-7.
8. McClung JP, Scrimgeour AG. Zinc: An Essential Trace Element with Potential Benefits to Soldiers. Milit. Med. 2005;170(12):1048-52.
9. Rodriguez NR, DiMarco NM, Langley S. Nutrition and Athletic Performance. Medicine & Science in Sports & Exercise. 2009;41(3):709-31.
10. Volpe SL. Minerals as Ergogenic Aids. Current Sports Medicine Reports. 2008;7(4):224-9.
11. Powers SK, Jackson MJ. Exercise-Induced Oxidative Stress: Cellular Mechanisms and Impact on Muscle Force Production. Physiological Reviews. 2008;88(4):1243-76.
12. Kelly MK, Wicker RJ, Barstow TJ, Harms CA. Effects of N-acetylcysteine on respiratory muscle fatigue during heavy exercise. Respiratory Physiology & Neurobiology. 2009;165(1):67-72.
13. Silva LA, Silveira PC, Pinho CA, Tuon T, et al. N-acetylcysteine supplementation and oxidative damage and inflammatory response after eccentric exercise. Int. J. Sport Nutr. Exerc. Metab. 2008;18(4):379-88.
14. Panel on Dietary Antioxidants and Related Compounds, Subcommittees on Upper Reference Levels of Nutrients and Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids. Washington, DC: Food and Nutrition Board, Institute of Medicine, National Academy of Sciences; 2000.
15. Panel on Micronutrients, Subcommittees on Upper Reference Levels of Nutrients and Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Washington, DC: Food and Nutrition Board, Institute of Medicine, National Academy of Sciences; 2001.
16. Office of Dietary Supplements, National Institutes of Health. Vitamin C, Vitamin E, and Zinc. Dietary Supplement Fact Sheets 2011; <http://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional> <http://ods.od.nih.gov/factsheets/VitaminE-HealthProfessional> <http://ods.od.nih.gov/factsheets/Zinc-HealthProfessional>. Accessed October 03, 2011.
17. Jellin J, Gregory, PJ, eds. Vitamin C, Vitamin E, and Zinc. Natural Medicines Comprehensive Database 2011; <http://www.naturaldatabase.com>.