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Dietary interventions through supplementation with antioxidant compounds

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Abstract

Dietary supplements (DS) are manufactured products consisting of one or more dietary ingredients; they are intended to supplement the diet and provide additional nutrients or other beneficial compounds that are lacking or insufficient in a regular diet. Dietary supplements containing antioxidant compounds have been shown to have positive effects in various (pato)physiological processes, i.e., any condition that is fundamentally redox imbalanced (cardiovascular diseases, cancer, aging, intense exercise). The most common antioxidants in dietary supplements are clearly antioxidant micronutrients such as vitamin C, vitamin E, zinc, and selenium, but also various secondary plant compounds, including polyphenols and carotenoids. The dosage of antioxidants administered through dietary supplements may not always be optimal, so some dietary interventions through supplementation with antioxidant compounds have been shown to have an effect that it is limited, or completely absent. Therefore, any dietary supplementation should be done only under appropriate guidance from health care professionals to ensure that it is safe, effective, and appropriate for the individual's condition and needs.

Key words: dietary intervention, dietary supplements, antioxidant activity, diseases, ageing, athletes

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Introduction

In promoting human health, nutrition is increasingly recognized as an important factor in the prevention and treatment of many non-communicable diseases. Although there is a growing wealth of information available in this field, the trustworthiness of dietary guidelines is often uncertain due to the prevalence of observational studies as the primary source of evidence. Moreover, when randomized clinical trials of nutrition interventions are conducted, the results are often controversial or lack clinical validity because of inherent design limitations (1).

A nutrition intervention refers to a set of interventions aimed at changing an aspect of nutrition in individuals or populations. There are different types of nutrition interventions, and they can be tailored to specific conditions or goals. The World Health Organization (WHO) divides nutrition interventions into four main groups:

1. Behavioral interventions: These interventions aim to change dietary habits through behavior change.
2. Fortification: this involves adding nutrients to the basic foods.
3. Supplementation: This involves administering specific nutrients to specific populations.
4. Regulatory interventions: These interventions aim to regulate specific activities to change diets and improve health (2).

Dietary supplements (DS)

Dietary supplements (DS) are manufactured products that consist of one or more dietary ingredients; they are intended to supplement the diet and provide additional nutrients or other beneficial compounds that are lacking or insufficient in a regular diet. DS are available on the market in a variety of forms, including tablets, capsules, gummy bears, and powders, as well as beverages and energy bars (3). They can increase the absorption of nutrients by providing either naturally derived or synthetic versions of active ingredients. This group of nutrient compounds comprises vitamins, minerals, fatty acids, amino acids, and fiber. In addition, dietary supplements may contain substances that are not essential to life but are marketed for their potential positive effects on the body, such as antioxidant activity. Some of the most common antioxidants found in DS are listed in Table I.

Table I Examples of the most common antioxidants present in dietary supplements

Tabela I Primeri najčešćih antioksidanasa prisutnih u dijetetskim suplementima

Antioxidant compound	**Description**	**Use / Purpose**
Vitamin C	Vitamin C, also known as ascorbic acid, is a powerful antioxidant that protects cells from free radical damage.	It is commonly found in various supplements, especially those aimed at immune system support and overall antioxidant activity.
Vitamin E	Vitamin E refers to a group of fat-soluble products comprised of tocopherols and tocotrienols. It acts as an antioxidant that helps protect cell membranes from oxidative stress.	It is commonly found in supplements that promote heart and skin health.
Selenium	Selenium is a trace element that acts as a cofactor for antioxidant enzymes in the body. It plays a role in neutralizing free radicals.	It is often included in antioxidant formulas or multivitamin supplements.
Zinc	Zinc is a mineral that has an important function in the immune system, DNA synthesis, cell division and wound healing. It is an essential nutrient because it acts as a cofactor for important enzymes involved in the proper functioning of the antioxidant defense system.	It is often included in antioxidant dietary supplements due to its role in supporting overall immune function and cellular health.
β-carotene	β-carotene is a naturally occurring pigment found in fruits and vegetables, especially those with an orange or yellow color. It is a precursor of vitamin A and is classified as a provitamin with antioxidant activity.	It is commonly found in dietary supplements that support healthy skin, vision, and immune function.
Coenzyme Q10 (CoQ10)	CoQ10 is an endogenous antioxidant involved in energy production in cells.	It is commonly supplemented to support heart health and as an antioxidant for overall well-being.
α-lipoic acid	α-lipoic acid is a powerful antioxidant that can act in both water-soluble and fat-soluble environments. It has the ability to regenerate other antioxidants such as vitamins C and E.	It is commonly found in supplements aimed at overall antioxidant support and metabolic health.
Polyphenols	Polyphenols are a class of natural compounds found abundantly in plants. They are known for their antioxidant properties and have been associated with various health benefits.	They are commonly used in dietary supplements because of their ability to combat numerous health issues, including aging and chronic diseases.

Antioxidant compounds in dietary supplements

The antioxidant supplement market size is globally predicted to reach $6,876 million by 2027. The report “Antioxidant Supplement Market Forecast (2022-2027)” covers the antioxidant supplement market in detail from various aspects: by source: natural and synthetic; by ingredient type: vitamins, minerals, botanicals, and others; by function: medicinal and sports nutrition; by formulation: tablets, liquid, capsules, and gummy bears; by distribution channel: supermarket/hypermarket, drugstore, nutrition and health food store, online retailer, and others; and by geography (4).

The concept of antioxidant supplementation is based on the recognition that reactive oxygen species (ROS) and other free radicals play a role in the development of various human diseases by causing oxidative stress. It is believed that reducing oxidative damage may help prevent these diseases.

Antioxidant dietary supplements in cardiovascular diseases (CVD)

Antioxidant DS are of interest in the context of CVD because of their potential to combat oxidative stress, inflammation, and other factors involved in the development of these complex diseases. However, evidence for the efficacy of antioxidant supplements in preventing or treating CVD is mixed, and some studies have shown limited or no effect.

In the Women's Health Study, a large-scale clinical trial of initially healthy women, a group of 39,876 participants took 402 mg of vitamin E from natural sources or a placebo every other day over a 10-year period. The goal of the study was to examine the effects of vitamin E supplementation on serious cardiovascular events and cancer. At the end of the study, results showed that rates of serious cardiovascular events and cancer were not significantly lower in participants taking vitamin E compared to those taking the placebo. However, an interesting result emerged, although this was not the primary endpoint of the study. In the group receiving vitamin E supplementation, all-cause cardiovascular mortality had decreased by a remarkable 24%. Although the primary outcomes of the study did not show a significant effect on cardiovascular events or cancer incidence, the observed reduction in cardiovascular mortality is a significant finding that deserves attention. It suggests a possible beneficial effect of vitamin E supplementation in reducing the risk of cardiovascular-related death. However, further research is needed to validate and understand this finding in detail (5).

Indeed, some studies have indicated potential contributions of vitamin E supplementation in specific subgroups. One notable study conducted in Israel focused on individuals with type 2 diabetes who also shared a genetic predisposition to increased oxidative stress. In this study, vitamin E supplementation (268 mg/day) was shown to significantly reduce coronary heart disease in this particular subgroup. The results of the study suggest that in individuals with type 2 diabetes and a genetic predisposition to increased oxidative stress, vitamin E supplementation may have positive effects in reducing the risk of coronary heart disease. This highlights the potential role of

antioxidants such as vitamin E in mitigating the effects of oxidative stress on cardiovascular health, particularly in vulnerable populations (6).

A recent systematic review analyzed eight studies with a total of 15,445 participants randomized to receive either vitamin C supplementation or placebo. Results showed that the composite endpoint of serious CVD events did not differ significantly between the interventional and placebo groups based on the Physicians Health Study II, which followed participants for eight years. Consistent findings were noted across various outcomes, including all-cause mortality, total myocardial infarction, total stroke, cardiovascular disease mortality, self-reported coronary artery bypass grafting/percutaneous transluminal coronary angioplasty, and self-reported angina. The quality of evidence for these outcomes was generally low or very low because of indirectness, imprecision, and inconsistency. The authors concluded that there is no evidence that vitamin C supplementation reduces CVD risk in healthy persons or in persons at increased risk for cardiovascular disease, based on current evidence (7).

The *Supplementation en Vitamines et Mineraux Antioxydants (SU.VI.MAX)* study examined the effects of a combination of vitamins and minerals with antioxidant properties on the incidence of cardiovascular disease. The study involved 13,017 French men and women who were assigned to either a group that received a single capsule daily containing 120 mg of vitamin C, 30 mg of vitamin E, 6 mg of β-carotene, 100 µg of selenium, and 20 mg of zinc, or a placebo. Participants were followed for a period of seven and a half years. The results obtained showed no significant effect of the vitamin and mineral combination on the overall rate of cardiovascular disease (8).

A recent prospective, randomized, double-blind, placebo-controlled study showed that eight weeks of pomegranate peel polyphenols supplementation had beneficial effects on inflammatory status and oxidative stress biomarkers in diabetic patients. It concluded that polyphenols could be recommended as functional food ingredients that can be considered as dietary and natural remedies with pharmacological properties for the prevention and treatment of diabetics with cardiovascular complications (9).

The pathological features of CVD, such as oxidative stress and inflammation, have been consistently linked to severely suppressed intracellular antioxidant defenses, including low plasma glutathione (GSH) levels. The available evidence suggests that antioxidant dietary supplements, such as coenzyme Q10, selenium, curcumin, omega-3 fatty acids, and vitamins E or D, may have the potential to improve cardiometabolic health in patients with diabetes. The beneficial effects of such dietary interventions seem to be related to their ability to enhance plasma GSH levels and reduce cholesterol, as well as other biomarkers of oxidative stress and inflammation (10).

Most research in this area has focused on the use of single antioxidants as dietary supplements rather than a combination of antioxidants or antioxidants from whole foods. The synergistic effects of antioxidants consumed as a part of a balanced diet may differ from those of isolated supplements. In addition, some studies suggest that the overall dietary pattern, rather than individual antioxidants, may have a greater impact on

cardiovascular health. A diet rich in fruits, vegetables, whole grains and other antioxidant-rich foods is consistently associated with a lower risk of CVD.

Antioxidant dietary supplements in cognition

Studies have been conducted on the effects of antioxidant supplements on cognition. However, similar to CVD, the results are not fully consistent, and further research is needed to draw as comprehensive conclusions as possible.

Researchers conducting a randomized trial called the Physicians' Health Study II administered either a placebo or 50 mg of β-carotene to a group of 5,956 men aged 65 and above. The study revealed that long-term supplementation (at least 15 years) resulted in cognitive improvements (11).

The results of the PREADViSE (The Prevention of Alzheimer's Disease by Vitamin E and Selenium) study suggest that antioxidant supplements with vitamin E (268 mg/day) or selenium (200 µg/day), either alone or in combination, showed no protective effect against dementia compared with a placebo. The study monitored a cohort of more than 3,700 men aged 60 and older over a six-year period. This was the first study to examine the long-term association between antioxidant supplement use and the incidence of dementia in asymptomatic men (12).

Limited evidence suggests that vitamin C may play a role in maintaining cognitive function and reducing the risk of cognitive decline. However, more research is needed to establish a clear link between vitamin C supplementation and cognitive performance.

Regarding cognition, individual response to antioxidant intake may vary, and the effectiveness of these supplements may depend on factors such as age, health status, and genetic factors. In addition, supplements should not replace a healthy diet and lifestyle, which are critical to maintaining cognitive health.

Antioxidant dietary supplements in cancer prevention

Research on the effects of antioxidant supplements on cancer is a complex and ever-evolving field, but the evidence is inconclusive so far. Antioxidants are a popular group of complementary therapies used by cancer patients. These therapies involve the administration of antioxidants through various methods, including dietary interventions, intravenous infusions, or, more commonly, dietary supplements (13).

While certain studies propose that oral antioxidant intake during chemotherapy could enhance patient survival, other research indicates that it might impede the effectiveness of chemotherapeutic treatment. There is a concern that antioxidant therapies may interact with the cytotoxic effects of chemotherapy, potentially reducing adverse side effects and enhancing quality of life, but at the same time compromising the efficacy of cancer treatment (14).

A 2016 review concluded that antioxidant intake may help reduce adverse effects and chemotoxicity associated with chemotherapy. However, the authors noted inconsistencies in the literature on this topic (15). One of the best studied oral antioxidant

preparations is melatonin, which has shown antitumor activity *in vitro* in conjunction with irradiation (16).

For example, a recently published randomized controlled trial comparing chemotherapy regimens in breast cancer found an increased risk of recurrence in women who took antioxidant supplements (vitamins A, C, and E; carotenoids; coenzyme Q10) both before and during chemotherapy. These findings underscore the complex and sometimes contradictory nature of the relationship between antioxidant intake, chemotherapy, and cancer treatment outcomes (17).

Antioxidant dietary supplements in age-related eye diseases

Slowing down or even remission of age-related eye diseases, such as age-related macular degeneration (AMD) and cataracts, could often be in good correlation with antioxidant supplements usage. Antioxidants such as vitamins C and E, beta-carotene, and zinc have been studied in relation to these eye diseases.

A six-year study, the Age-Related Eye Disease Study (AREDS), conducted by the National Eye Institute, found that a specific combination of antioxidants (500 mg vitamin C, 268 mg vitamin E, 15 mg β-carotene, 80 mg zinc, and 2 mg copper; globally known as the AREDS formulation) provided some protection against the progress of advanced AMD, but not cataracts, in individuals at high risk for the disease (18).

Subsequent studies, such as the AREDS2 study, have further investigated the role of antioxidants in AMD. For example, the AREDS2 study examined supplementation of 10 mg of lutein and 2 mg of zeaxanthin in place of β-carotene on late age-related macular degeneration in men and women for up to five years. It discovered a positive but not significant effect of the supplements on AMD (19).

The Cochrane review considered 19 randomized controlled trials and evaluated the efficacy of antioxidant vitamin/mineral supplements (including multivitamins, vitamin E, lutein, zeaxanthin, and zinc) in preventing AMD progression and vision loss compared with placebo or no treatment. The overall results suggest that subjects taking the antioxidant vitamins/minerals were less likely to experience late-stage AMD progression and vision loss than those not taking the supplements. This suggests an affirmation of these supplements in reducing the risk of AMD progression in individuals who are generally well nourished. However, the review also found that individual intake of lutein and zeaxanthin or vitamin E did not show a positive effect on AMD or vision loss. The study suggests that the combination of antioxidant vitamins/minerals as examined in the included studies may be more effective in preventing late-stage AMD and vision loss than the individual components alone (20).

Antioxidant dietary supplements in athletic performance

From ancient times, participants in the Olympic Games believed that the consumption of some food could help them win. For decades, athletes of all sport disciplines have been enthusiastic about the use of antioxidant dietary supplements. Many athletes supplement with antioxidants, believing in their beneficial effect upon fatigue,

muscle damage and immunity. Many athletes strongly believe that the use of antioxidants improves their sports performance, while some evidence suggests that it impairs training adaptation (21). The reason for this lies in the well-known fact that physical activity generates free radicals - reactive oxygen and nitrogen species (RONS), and their production is associated with muscle damage and fatigue, as well as impaired immune function. For this reason, among many sports supplements, antioxidants never lost their popularity. Many studies have been conducted in order to prove their efficiency, and many of them lacked the evidence of efficiency. A clear finding of all these studies is that, if an athlete is deficient in a single antioxidative nutrient, targeted supplementation will result in improvements in their sports performance, and overall health. On the other hand, the interest of manufacturers in the field of sport nutrition has never stopped growing, resulting in the overproduction of numerous multicomponent supplements.

The attention to vitamin C is based on its importance for the immune system (especially in the winter period), as well as in collagen synthesis, and both roles are very important to athletes. Some recommendations go far above RDA values, even up to several grams. High-dose supplementation with vitamin C during exercise training cannot be recommended, because there are few affirmative findings. Moreover, there is growing evidence indicating the potential negative outcomes of antioxidant overuse, and, in particular, vitamin C supplementation on health and performance (22).

The requirements for nutritive antioxidants, in particular vitamins C and E, during exercise training are not supposed to be in excess of 200% of the current recommendations for the general population, dependent on training loads (e.g., intensity, volume and frequency of the training). The general picture that emerges from the available data is that antioxidant intake during exercise training to maintain an appropriate physiological antioxidant status in reference to current recommendations can be achieved through a balanced and well-diversified diet.

Moreover, results from a large clinical trial show that vitamin E supplementation over a long period of time, even at doses below the UL (268 mg/day taken for several years), might increase men’s risk of prostate cancer (23). A very popular antioxidant supplement, coenzyme Q, showed certain mild side effects among the general as well as athlete population, which can include fatigue, insomnia, rashes, nausea, upper abdominal pain, heartburn, sensitivity to light, irritability, dizziness, and headaches (24).

Numerous biological active compounds, besides the well-known antioxidative micronutrients, are being investigated for their potential beneficial role in sport performance. Most of them fall into the category of phytonutrients, *e.g.* phenolic (resveratrol, quercetin) and carotenoid compounds, as well as N- acetyl-cysteine and glisodin – SOD rich cantaloupe melon combined with wheat gliadin (25). For instance, a randomized, double-blind, placebo-controlled study pointed out that polyphenol-rich chokeberry juice had had an impact on attenuating the effect of intensive training in active handball players (26). Moreover, athletes commonly utilize plant-derived polyphenol supplements to counteract the adverse impacts of exercise-induced oxidative stress, expedite the recovery of muscle function, and improve overall performance (27).

Lately, astaxanthin, a carotenoid compound, has grown in popularity in the scientific milieu, as well as among athletes. Orally administrating 4 mg of astaxanthin to young soccer players had a better effect upon immune system function and muscle recovery compared to the placebo group. (28). Further investigation proved that this antioxidative compound could be used in preventing muscle oxidative damage (29).

Should we therefore recommend antioxidant supplementation to athletes? The answer to this question should be negative, as there is no clear scientific evidence for it. Moreover, high dose antioxidant supplements could compromise the physiological adaptation process to stress induced by exercising. Combined antioxidant supplementation showed no pronounced positive effects either (30). Consequently, we can conclude that an optimal nutrition strategy could be the best solution.

Athletes should be advised to consume a diet rich in antioxidants containing a broad variety of fresh fruits, raw and/or steam-cooked vegetables, fruit and vegetable juices, whole grains and nuts. Similarly to the general population, only in certain situations, such as a deficiency in a certain antioxidant nutrient, antioxidant supplementation could be approved by a health care professional.

Caution regarding the antioxidants doses in dietary supplements

Recent research has raised concerns about the routine consumption of antioxidant supplements. Several reputable studies, including meta-analyses, systematic reviews, observational studies, and human intervention trials, have shown that antioxidant multivitamin or multimineral supplements have no beneficial effect on all-cause mortality, cancer, cardiovascular disease, or cognitive function (31–36).

As a matter of fact, some studies have suggested that consuming high doses of specific antioxidant supplements, such as β-carotene, vitamin E, and potentially high doses of vitamin A, could be linked to an elevated risk of all-cause mortality. This is due to the pro-oxidant effects of β-carotene and vitamin E when taken in high doses, particularly in certain populations (37). The large number of dietary supplements does not prevent non-communicable diseases or mortality in the general population without clear evidence of nutrient deficiency (31, 34, 38). These results highlight the limited advantage of antioxidant supplementation, especially in the healthy general population that does not show signs of nutrient deficiency.

The dosage of dietary antioxidants administered via supplements may not always be optimal. Therefore, lower doses or combinations of antioxidants are often more effective than higher doses of single agents (39, 40).

For example, eating foods naturally rich in vitamin C has been shown to reduce oxidative damage in the body, whereas high-dose vitamin C in supplement form alone did not provide the same effect. In one study, daily supplementation with 500 mg of vitamin C over a 6-week period resulted in a 60% increase in plasma vitamin C levels. However, it was also observed that this high dosage resulted in pro-oxidant activity of vitamin C, as evidenced by significantly higher levels of 8-oxoadenine in blood

lymphocyte DNA (41). It is worth noting that a dosage of 1,000 mg of vitamin C for optimal health far exceeds the recommended daily dose of 75-90 mg/day (42).

High concentrations of vitamin E (α-tocopherol) can have pro-oxidant effects both in food and in the body (700 ppm) (43). Similarly, resveratrol, a compound with strong antioxidant capacity, may have pro-oxidant effects in the presence of copper (44). Like any substance, antioxidants can have negative effects when taken in excess. Ingestion of high doses of antioxidants is associated with increased toxicity, leading to pro-oxidant effects or “antioxidant stress” (45).

Conclusion

Certain antioxidant supplements have shown positive effects and efficacy, but it is important to pay attention to appropriate dosing. Many dietary supplements, including vitamins, minerals, and functional ingredients, play an important role in modern health care. However, it is common for supplements to be overused by the general population as a means of improving or maintaining health. Therefore, careful attention must be paid to the dosage of all supplements taken. In conclusion, it should be emphasized that any dietary intervention should only be undertaken under appropriate guidance from healthcare professionals to ensure that it is safe, effective and appropriate for the individual's condition and needs. It is generally recommended to focus primarily on an adequate and balanced diet that includes a variety of antioxidant-rich foods as part of a comprehensive approach to overall health.

References

1. Magni P, Bier DM, Pecorelli S, Agostoni C, Astrup A, Brighenti F, et al. Perspective: Improving Nutritional Guidelines for Sustainable Health Policies: Current Status and Perspectives. Adv Nutr Bethesda Md. 2017 Jul;8(4):532–45.
2. WHO [Internet]. [cited 2023 May 30]. Available from: https://sdghelpdesk.unescap.org/e-library/e-library-evidence-nutrition-actions-elena
3. NIH [Internet]. [cited 2023 May 30]. Available from: https://web.archive.org/web/20200814221351/https://ods.od.nih.gov/factsheets/DietarySupplements-HealthProfessional/
4. Antioxidant Supplement Market Report [Internet]. [cited 2023 May 30]. Available from: https://www.industryarc.com/Research/Global-Antioxidant-Supplement-Market-Research-513321
5. Lee IM, Cook NR, Gaziano JM, Gordon D, Ridker PM, Manson JE, et al. Vitamin E in the Primary Prevention of Cardiovascular Disease and Cancer: The Women’s Health Study: A Randomized Controlled Trial. JAMA. 2005 Jul 6;294(1):56.
6. Milman U, Blum S, Shapira C, Aronson D, Miller-Lotan R, Anbinder Y, et al. Vitamin E Supplementation Reduces Cardiovascular Events in a Subgroup of Middle-Aged Individuals With

Both Type 2 Diabetes Mellitus and the Haptoglobin 2-2 Genotype: A Prospective Double-Blinded Clinical Trial. Arterioscler Thromb Vasc Biol. 2008 Feb;28(2):341–7.

7. Al-Khudairy L, Flowers N, Wheelhouse R, Ghannam O, Hartley L, Stranges S, et al. Vitamin C supplementation for the primary prevention of cardiovascular disease. Cochrane Heart Group, editor. Cochrane Database Syst Rev. 2017 Mar 16;2017(3). doi: 10.1002/14651858.CD011114.pub2
8. Hercberg S, Galan P, Preziosi P, Bertrais S, Mennen L, Malvy D, et al. The SU.VI.MAX Study: A Randomized, Placebo-Controlled Trial of the Health Effects of Antioxidant Vitamins and Minerals. Arch Intern Med. 2004 Nov 22;164(21):2335.
9. Grabež M, Škrbić R, Stojiljković MP, Vučić V, Rudić Grujić V, Jakovljević V, et al. A prospective, randomized, double-blind, placebo-controlled trial of polyphenols on the outcomes of inflammatory factors and oxidative stress in patients with type 2 diabetes mellitus. Rev Cardiovasc Med. 2022 Feb 11;23(2):057.
10. Dludla PV, Ziqubu K, Mabhida SE, Mazibuko-Mbeje SE, Hanser S, Nkambule BB, et al. Dietary Supplements Potentially Target Plasma Glutathione Levels to Improve Cardiometabolic Health in Patients with Diabetes Mellitus: A Systematic Review of Randomized Clinical Trials. Nutrients. 2023 Feb 14;15(4):944.
11. Grodstein F. A Randomized Trial of Beta Carotene Supplementation and Cognitive Function in MenThe Physicians' Health Study II. Arch Intern Med. 2007 Nov 12;167(20):2184.
12. Kryscio RJ, Abner EL, Caban-Holt A, Lovell M, Goodman P, Darke AK, et al. Association of Antioxidant Supplement Use and Dementia in the Prevention of Alzheimer's Disease by Vitamin E and Selenium Trial (PREADViSE). JAMA Neurol. 2017 May 1;74(5):567.
13. Kantor ED, Rehm CD, Du M, White E, Giovannucci EL. Trends in Dietary Supplement Use Among US Adults From 1999-2012. JAMA. 2016 Oct 11;316(14):1464.
14. Poljsak B, Milisav I. The Role of Antioxidants in Cancer, Friends or Foes? Curr Pharm Des. 2019 Mar 29;24(44):5234–44.
15. Yasueda A, Urushima H, Ito T. Efficacy and Interaction of Antioxidant Supplements as Adjuvant Therapy in Cancer Treatment: A Systematic Review. Integr Cancer Ther. 2016 Mar;15(1):17–39.
16. Farhood B, Goradel NH, Mortezaee K, Khanlarkhani N, Salehi E, Nashtaei MS, et al. Melatonin as an adjuvant in radiotherapy for radioprotection and radiosensitization. Clin Transl Oncol. 2019 Mar;21(3):268–79.
17. Ambrosone CB, Zirpoli GR, Hutson AD, McCann WE, McCann SE, Barlow WE, et al. Dietary Supplement Use During Chemotherapy and Survival Outcomes of Patients With Breast Cancer Enrolled in a Cooperative Group Clinical Trial (SWOG S0221). J Clin Oncol. 2020 Mar 10;38(8):804–14.
18. A Randomized, Placebo-Controlled, Clinical Trial of High-Dose Supplementation With Vitamins C and E, Beta Carotene, and Zinc for Age-Related Macular Degeneration and Vision Loss: AREDS Report No. 8. Arch Ophthalmol. 2001 Oct 1;119(10):1417.
19. Chew EY, Clemons TE, SanGiovanni JP, Danis RP, Ferris FL, Elman MJ, et al. Secondary Analyses of the Effects of Lutein/Zeaxanthin on Age-Related Macular Degeneration Progression: AREDS2 Report No. 3. JAMA Ophthalmol. 2014 Feb 1;132(2):142.

20. Evans JR, Lawrenson JG. Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration. Cochrane Eyes and Vision Group, editor. Cochrane Database Syst Rev. 2017 Jul 30;2017(9). doi: 10.1002/14651858.CD000254.pub4
21. Jeukendrup AE, Gleeson M. Sport nutrition. Third edition. Champaign, IL: Human Kinetics; 2019.
22. Gomez-Cabrera MC, Domenech E, Romagnoli M, Arduini A, Borras C, Pallardo FV, et al. Oral administration of vitamin C decreases muscle mitochondrial biogenesis and hampers training-induced adaptations in endurance performance. Am J Clin Nutr. 2008 Jan;87(1):142–9.
23. Klein EA, Thompson IM, Tangen CM, Crowley JJ, Lucia MS, Goodman PJ, et al. Vitamin E and the Risk of Prostate Cancer: The Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA. 2011 Oct 12;306(14):1549.
24. Hidaka T, Fujii K, Funahashi I, Fukutomi N, Hosoe K. Safety assessment of coenzyme Q $_{10}$ (CoQ $_{10}$). BioFactors. 2008;32(1–4):199–208.
25. Dudašova Petrovičova O, Stanković I, Milinković N, Dopsaj V, Đorđević B, Dopsaj M. Effects of 6-Week Supplementation with GliSODin on Parameters of Muscle Damages, Metabolic, and Work Performance at International Level Rowers after Specific Maximal Effort. Biology. 2022 Sep 30;11(10):1437.
26. Petrovic S, Arsic A, Glibetic M, Cikiriz N, Jakovljevic V, Vucic V. The effects of polyphenol-rich chokeberry juice on fatty acid profiles and lipid peroxidation of active handball players: results from a randomized, double-blind, placebo-controlled study. Can J Physiol Pharmacol. 2016 Oct;94(10):1058–63.
27. Bojarczuk A, Dzitkowska-Zabielska M. Polyphenol Supplementation and Antioxidant Status in Athletes: A Narrative Review. Nutrients. 2022 Dec 29;15(1):158.
28. Djordjevic B, Baralic I, Kotur-Stevuljevic J, Stefanovic A, Ivanisevic J, Radivojevic N, et al. Effect of astaxanthin supplementation on muscle damage and oxidative stress markers in elite young soccer players. J Sports Med Phys Fitness. 2012 Aug;52(4):382–92.
29. Brown DR, Gough LA, Deb SK, Sparks SA, McNaughton LR. Astaxanthin in Exercise Metabolism, Performance and Recovery: A Review. Front Nutr. 2018 Jan 18;4:76.
30. Baralic I, Stojmenovic T, Andjelkovic M, Djordjevic B, Dikic N, Radojevic-Skodric S, et al. Effect of combined antioxidant treatment on oxidative stress, muscle damage and sport performance in female basketball players. Srp Arh Celok Lek. 2019;147(11–12):729–35.
31. Angelo G, Drake VJ, Frei B. Efficacy of Multivitamin/mineral Supplementation to Reduce Chronic Disease Risk: A Critical Review of the Evidence from Observational Studies and Randomized Controlled Trials. Crit Rev Food Sci Nutr. 2015 Dec 6;55(14):1968–91.
32. Bjelakovic G, Nikolova D, Gluud C. Antioxidant Supplements to Prevent Mortality. JAMA. 2013 Sep 18;310(11):1178.
33. Fortmann SP, Burda BU, Senger CA, Lin JS, Whitlock EP. Vitamin and Mineral Supplements in the Primary Prevention of Cardiovascular Disease and Cancer: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013 Dec 17;159(12):824–34.
34. Kuszak AJ, Hopp DC, Williamson JS, Betz JM, Sorkin BC. Approaches by the US National Institutes of Health to support rigorous scientific research on dietary supplements and natural products. Drug Test Anal. 2016 Mar;8(3–4):413–7.

35. Myung SK, Ju W, Cho B, Oh SW, Park SM, Koo BK, et al. Efficacy of vitamin and antioxidant supplements in prevention of cardiovascular disease: systematic review and meta-analysis of randomised controlled trials. BMJ. 2013 Jan 18;346(jan18 1):f10–f10.
36. Ye Y, Li J, Yuan Z. Effect of Antioxidant Vitamin Supplementation on Cardiovascular Outcomes: A Meta-Analysis of Randomized Controlled Trials. Hernandez AV, editor. PLoS ONE. 2013 Feb 20;8(2):e56803.
37. Vrolijk MF, Opperhuizen A, Jansen EHJM, Godschalk RW, Van Schooten FJ, Bast A, et al. The shifting perception on antioxidants: The case of vitamin E and β-carotene. Redox Biol. 2015 Apr;4:272–8.
38. Cohen PA. The Supplement Paradox: Negligible Benefits, Robust Consumption. JAMA. 2016 Oct 11;316(14):1453.
39. Bast A, Haenen GRMM. Ten misconceptions about antioxidants. Trends Pharmacol Sci. 2013 Aug;34(8):430–6.
40. Halliwell B. Free radicals and antioxidants – quo vadis? Trends Pharmacol Sci. 2011 Mar;32(3):125–30.
41. Podmore ID, Griffiths HR, Herbert KE, Mistry N, Mistry P, Lunec J. Vitamin C exhibits pro-oxidant properties. Nature. 1998 Apr;392(6676):559–559.
42. Panel on Dietary Antioxidants and Related Compounds, Subcommittee on Upper Reference Levels of Nutrients, Subcommittee on Interpretation and Uses of Dietary Reference Intakes, Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids [Internet]. Washington, D.C.: National Academies Press; 2000 [cited 2023 Jun 16]. Available from: https://www.nap.edu/catalog/9810
43. Shahidi F, De Camargo A. Tocopherols and Tocotrienols in Common and Emerging Dietary Sources: Occurrence, Applications, and Health Benefits. Int J Mol Sci. 2016 Oct 20;17(10):1745.
44. de la Lastra CA, Villegas I. Resveratrol as an antioxidant and pro-oxidant agent: mechanisms and clinical implications. Biochem Soc Trans. 2007 Nov 1;35(5):1156–60.
45. Poljsak B, Milisav I. The Neglected Significance of “Antioxidative Stress.” Oxid Med Cell Longev. 2012;2012:1–12.

Dijetarne intervencije suplementacijom antioksidativnim jedinjenjima

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Kratak sadržaj

Dijetetski suplementi (DS) ili dodaci ishrani su proizvodi koji sadrže jedan ili više sastojaka i primenjuju se kao dopuna ishrani, odnosno imaju posebnu nutritivnu namenu. Brojni su naučni dokazi koji sugerišu da DS koji sadrže antioksidativna jedinjenja imaju blagotvorno dejstvo u različitim (pato)fiziološkim procesima, odnosno bilo kom stanju koje u osnovi ima narušenu redoks ravnotežu (kardiovaskularne bolesti, rak, starenje, intenzivno vežbanje). Najčešći antioksidansi u dodacima ishrani su antioksidativni mikronutrijenti kao što su vitamin C, vitamin E, selen, i cink, ali i različiti sekundarni biljni metaboliti, uključujući polifenole i karotenoide. Posebna pažnja mora biti usmerena na doze i dužinu suplementacije. Neadekvatna primena antioksidanasa putem dijetetskih suplemenata često ishoduje time da dijetarne intervencije suplementacijom antioksidativnim jedinjenjima imaju ograničen efekat ili on kompletno izostane. Stoga ove ali i sve druge dijetarne suplementacije treba sprovoditi isključivo u skladu sa uputstvima zdravstvenih radnika kako bi se osigurali njihova efikasnost i bezbednost, ali i prikladnost za stanje i potrebe pojedinca.

Ključne reči: dijetarna intervencija, dijetetski suplementi, antioksidativna aktivnost, bolesti, starenje, sportisti