

IMPACT OF VITAMIN E ON DIFFERENT ORGAN SYSTEMS

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Abstract: Vitamin E, present in both plant and animal-based foods, is a lipophilic compound with multifaceted biochemical functions. Its deficiency can lead to severe health consequences, while excessive intake may result in hypervitaminosis. Among tocopherols, Alpha-tocopherol stands out for its pharmacokinetic properties and potent antioxidant effects. It exerts significant influence on the immune, nervous, and cardiovascular systems, as well as on skin health. Notably, it plays a crucial role in preventing carcinogenesis. While Alpha-tocopherol garners attention, other tocopherol group members should not be overlooked, as advancements in science uncover their diverse biological impacts. In recent years, tocotrienols have emerged with distinct biochemical properties that profoundly affect human health.

Keywords: vitamin E, alpha-tocopherol, immune system.

INTRODUCTION

Vitamin E was first found in green vegetables (1). Isolated in 1922, its numerous roles in biological functions have since become the focal point of study for many scientists. It serves as a powerful antioxidant and plays a crucial role in preventing lipid peroxidation and removing free radicals. The vitamin E family consists of two major groups: tocopherols and tocotrienols, both of which are fat-soluble. These groups can be further divided into four subgroups. All tocopherols share an aromatic chromanol head, leading to several isomers such as alpha, beta, gamma, and delta isomers. In contrast, tocotrienols, the other group, possess hydrocarbon chains of unsaturated fatty acids, differing from tocopherols, which have saturated fatty acids in their tail comprised of 16 carbons. Tocotrienols demonstrate higher solubility in lipid membranes compared to tocopherols (2).

Vitamin E, particularly α -tocopherol, is abundant in rice bran, palm oil, olives, soybeans, and various grains (1). Its antioxidant properties play a crucial role in neutralizing free radicals generated by lipid oxidation. Consequently, an inadequate diet leads to decreased vitamin E levels, increasing the risk of cardiovascular diseases. Certain nutrients exhibit the ability to reduce free radicals and offer protective effects against oxidative stress (3), with α -tocopherol being the most potent and prevalent vitamin in this group. Various studies provide adequate recommendations for this vitamin (4).

A year-long study conducted in India on two groups of subjects evaluated the influence of antioxidants, specifically vitamins A and E. Subjects with well-controlled diabetes exhibited significantly higher serum vitamin levels compared to those with uncontrolled disease (5). Tocotrienols possess a molecular structure distinct from tocopherols, featuring a farnesyl group (6). Tocopherol serves as a ubiquitous antioxidant in nature and plays a pivotal role in neutralizing free radicals. Consequently, it is predominantly found in mitochondria and the sarcoplasmic reticulum within cells (7).

Vitamin E encompasses eight different compounds. Like other fat-soluble vitamins, they are absorbed into the bloodstream via the small intestine. Metabolic processing in the liver primarily occurs for α -tocopherol, while other forms are excreted unchanged (8). Common causes of deficiency often stem from irregularities in dietary fat absorption or inadequate metabolism. The optimal serum tocopherol level for adults should not exceed 5 mcg/ml (8)

Impact on the immune system

Vitamin E exerts its effects on the immune system by influencing certain inflammatory mediators, including eicosanoids and cyclooxygenase-2 (1). Studies primarily focusing on α -tocopherol have elucidated its immunomodulatory effects through various mechanisms. α -Tocopherol directly affects T lymphocytes by stabilizing their membranes and also contributes to the generation of intercellular signals that influence inflammatory factors (9). Hypovitaminosis of vitamin E adversely affects both cellular and humoral immunity. Furthermore, vitamin E enhances the phagocytic capacity of macrophages (10) and increases the production of interleukin-2 (IL-2). Tocopherols have also been shown to protect respiratory tract cells during viral infections, including SARS-CoV-2 infection (11).

Supplementation, sources, and recommendations of Vitamin E

Some studies suggest that tocopherol supplementation reduces erythrocyte deformities, although the evidence remains inconclusive, warranting further research. A dosage of 1600 IU of vitamin E for several weeks has been shown to reduce oxidative stress, thereby decreasing the susceptibility to diseases associated with this issue (7). However, data from randomized trials indicate that routine supplementation does not reduce the risk of preeclampsia and poor fetal growth (12). For adolescents of both sexes, the recommended daily intake is 9 mg for ages 10 to 13 and 12 mg for ages 14 to 19 (4). The safe and optimal intake of tocopherol for adults is up to 15 mg per day (13).

Vitamin E is exclusively obtained through dietary sources and is not synthesized by intestinal flora bacteria or within the organism itself (14). Breastfeeding mothers may need to supplement

their vitamin E intake to achieve the recommended daily dose of 19 mg. Daily vitamin E supplementation from prenatal multivitamins for the mother can be safe and modestly increase vitamin E levels in breast milk, thereby improving the baby's vitamin E status. Additionally, women with higher polyunsaturated fatty acid intake tend to have higher levels of alpha-tocopherol in breast milk (15). However, it's essential to prioritize a healthy diet over vitamin E supplementation, and any supplementation should be recommended by a healthcare professional (16).

In practice, vitamin E has not demonstrated toxicity within recommended doses for humans (17). Results from a randomized study conducted in Pakistan suggest that delta-tocotrienol supplementation, when added to other glycemic control agents, may prevent long-term diabetic complications in patients with type 2 diabetes mellitus (18).

Vitamin E hypervitaminosis

Hemorrhage can occur as a result of excessive doses of vitamin E. Toxic doses ranging from 100 mg to 1 gram can lead to cerebral hemorrhage (13). While vitamin E deficiency is uncommon, routine supplementation is not recommended. Instead, patients should be encouraged to maintain a balanced and varied diet to obtain adequate levels of alpha-tocopherols. If supplementation is deemed necessary, it's crucial to monitor for common adverse reactions, potential drug interactions, and the risk of bleeding, particularly in patients receiving anticoagulant therapy (16).

Vitamin E and carcinogenesis

Recent studies have examined the impact of tocopherols and its isomers on cancer prevention. Vitamin E has been found to have a preventive effect against certain types of cancer. For instance, a meta-analysis demonstrated an inverse relationship between increased vitamin E intake and the risk of uterine cancer (19). However, comparisons between tocopherol and tocotrienol have shown that while alpha-tocopherol exhibits higher systemic bioavailability, gamma and delta forms have a stronger protective effect against cancer (19). Additionally, research investigating the combined effect of vitamin E and doxorubicin on breast cancer cells in vitro revealed significant cytotoxicity with high doses of vitamin E (20). Certain members of the vitamin E group have also shown preventive effects against mechanisms leading to prostate cancer (21).

Genetic factors and the influence of Vitamin E on the nervous system

Vitamin E supplementation has been associated with reductions in certain neurological symptoms (22, 23). Moreover, vitamin E plays a role in gene expression regulation (24). Nutrigenomics, as a complex field, must consider the polymorphic properties of different genetic groups involved in vitamin E metabolism (25). Mutations in the alpha-tocopherol transfer protein gene can lead to familial vitamin E deficiency, oxidative stress, and progressive neurological diseases such as spinocerebellar ataxia (26). Current research indicates that vitamin E and its metabolites have neuroprotective effects (27).

Alzheimer's disease, mitochondrial dysfunction, and Vitamin E

Alzheimer's disease, characterized by memory loss and cognitive decline, is associated with mitochondrial dysfunction and increased oxidative stress. Vitamin E's potent antioxidant properties make it effective in combating free radicals, which play a role in neuronal damage. Walnuts, rich in vitamin E, are linked to Alzheimer's prevention (28, 29). Studies have also shown that ascorbic acid and high doses of vitamin E can positively impact cognitive function (30). Furthermore, several meta-analyses have found correlations between serum antioxidant levels, particularly vitamin E, and depression (29).

Impact on the skin

The skin serves as a crucial barrier, safeguarding the body's integrity against various external factors. Research conducted by the World Health Organization reveals that nearly a third of the global population suffers from skin issues, attributable to deficiencies in specific vitamins and minerals (31). Among these, Vitamin E stands out for its profound impact on skin health. Its primary function is to protect the skin from oxidative damage induced by sunlight through neutralizing free radicals (32).

Studies indicate that pre-exposure application of alpha-tocopherol can shield the skin from various types of damage caused by ultraviolet radiation (33). For example, a regimen of 1000 IU of Vitamin E daily for six months has been effective in treating yellow nail syndrome. Additionally, it plays a role in managing other skin disorders. In cases of skin amyloidosis, Vitamin E, when combined with other active ingredients, significantly contributes to the disease's treatment (34,35).

CONCLUSION

Vitamin E, found in both plant and animal foods, holds significant importance for overall health. While alpha tocopherol has traditionally received the most attention, recent research has highlighted the biological significance of other tocopherol forms and tocotrienols. The powerful antioxidant properties of these compounds play a crucial role in preventing various diseases discussed in this paper, emphasizing the importance of maintaining optimal levels of vitamin E in the body.

The impact of vitamin E on skin health is particularly notable, with its antioxidant properties offering protection against photooxidant damage. Studies on photoprotection demonstrate its effectiveness in reducing acute skin reactions, while its therapeutic potential is evident in dermatological disorders such as yellow nail syndrome and subcorneal pustular dermatoses.

Special attention should be given to pregnant and breastfeeding women, as well as individuals with diets deficient in vitamin E. Prevention remains key in avoiding pathology associated with vitamin E deficiency, underscoring the importance of ensuring adequate intake of this essential vitamin.

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Sažetak

UTICAJ VITAMINA E NA RAZLIČITE ORGANSKE SISTEME

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Vitamin E se nalazi u hrani biljnog i životinjskog porekla. Vitamin E je lipofilno jedinjenje koje ima brojne biohemijske funkcije. Nedostatak vitamina E može imati ozbiljne zdravstvene posledice kao i hipervitaminoza sa datim vitaminom. Među svim jedinjenjima koja pripadaju grupi tokoferola, alfa-tokoferol se posebno ističe po svojim farmakokinetičkim svojstvima i funkciji. Alfa tokoferol je veoma jak antioksidans. Njegovo dejstvo na ljudski organizam ogleda se u brojnim antioksidativnim reakcijama, posebno na imuni, nervni sistem i kardiovaskularni sistem, kao i na kožu. Od posebnog značaja u proučavanju ovog vitamina je prevencija kancerogeneze. Međutim, ne treba zanemariti ni druge predstavnike ove grupe, jer su njihovi biološki uticaji postali sve očigledniji sa napretkom nauke. Poslednjih decenija otkrivena su različita biohemijska svojstva tokotrienola koja značajno utiču na ljudski organizam.

Ključne reči: vitamin E, alfa tokoferol, imuni sistem.

REFERENCES

1. Mohd Zaffarin AS, Ng SF, Ng MH, Hassan H, Alias E. Pharmacology and pharmacokinetics of Vitamin E: nanoformulations to enhance bioavailability. *Int J Nanomedicine*. 2020;15:9961-74. doi:10.2147/IJN.S276355.
2. Aykin-Burns N, Pathak R, Boerma M, Kim T, Hauer-Jensen M. Utilization of vitamin E analogs to protect normal tissues while enhancing antitumor effects. *Semin Radiat Oncol*. 2019;29(1):55–61. doi:10.1016/j.semradonc.2018.10.008.
3. Keshawarz A, Joehanes R, Ma J, Lee GY, Costeira R, Tsai PC, et al. Dietary and supplemental intake of vitamins C and E is associated with altered DNA methylation in an

epigenome-wide association study meta-analysis. *Epigenetics*. 2023;18(1):2211361. doi:10.1080/15592294.2023.2211361.

4. Jordão KSLU, Assumpção D, Barros MBA, Barros Filho AA. Vitamin E intake and food sources in adolescent diet: a cross-sectional population-based study. *Rev Paul Pediatr*. 2020;39:e2019295. doi:10.1590/1984-0462/2021/39/2019295

5. Thakur RK, Ambiger S, Shindhe VM. Assessment of vitamin A and vitamin E levels in patients with controlled and uncontrolled type 2 diabetes mellitus: a case-control study. *JCDR*. 2022;16(6):23–7. doi:10.7860/JCDR/2022/53424.16517.

6. Radović J, Leković A, Tačić A, Dodevska M, Stanojković T, Marinković T et al. Black trumpet, *Craterellus cornucopioides* (L.) Pers.: culinary mushroom with angiotensin converting enzyme inhibitory and cytotoxic activity. *Polish Journal of Food and Nutrition Sciences*. 2022;72(2):171-81. doi:10.31883/pjfn/149914.

7. Higgins MR, Izadi A, Kaviani M. Antioxidants and exercise performance: with a focus on vitamin E and C supplementation. *Int J Environ Res Public Health*. 2020;17(22):8452. doi:10.3390/ijerph17228452

8. Kemnic TR, Coleman M. Vitamin E Deficiency. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2024 .

9. Lee GY, Han SN. The role of vitamin E in immunity. *Nutrients*. 2018;10(11):1614. doi:10.3390/nu10111614.

10. Lewis ED, Meydani SN, Wu D. Regulatory role of vitamin E in the immune system and inflammation. *IUBMB Life*. 2019;71(4):487-94. doi:10.1002/iub.1976.

11. Ristic-Medic D, Petrovic S, Arsic A, Vucic V. Liver disease and COVID-19: The link with oxidative stress, antioxidants and nutrition. *World J Gastroenterol*. 2021;27(34):5682-99. doi:10.3748/wjg.v27.i34.5682.

12. Md Amin NA, Sheikh Abdul Kadir SH, Arshad AH, Abdul Aziz N, Abdul Nasir NA, Ab Latip N. Are vitamin E supplementation beneficial for female gynaecology health and diseases? *Molecules*. 2022;27(6):1896. doi: 10.3390/molecules27061896.

13. Owen KN, Dewald O. Vitamin E toxicity. In: *StatPearls* . Treasure Island (FL): StatPearls Publishing; 2024.

14. Zaaboul F, Liu Y. Vitamin E in foodstuff: Nutritional, analytical, and food technology aspects. *Compr Rev Food Sci Food Saf*. 2022;21(2):964-98. doi: 10.1111/1541-4337.12924.

15. Drugs and Lactation Database (LactMed®). Bethesda (MD): National Institute of Child Health and Human Development; 2006-. Vitamin E. [Updated 2023 Dec 15]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK500951/>
16. Medina J, Gupta V. Vitamin E. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK557737/>
17. Teo CWL, Tay SHY, Tey HL, Ung YW, Yap WN. Vitamin E in atopic dermatitis: from preclinical to clinical studies. *Dermatology*. 2021;237(4):553-64. doi:10.1159/000510653.
18. Suleman F, Khan DA, Pervez MA, Aamir M. Effects of delta-tocotrienol supplementation on glycaemic control in individuals with prediabetes: A randomized controlled study. *J Pak Med Assoc*. 2022;72(1):4-7. doi:10.47391/JPMA.966.
19. Yang CS, Luo P, Zeng Z, Wang H, Malafa M, Suh N. Vitamin E and cancer prevention: Studies with different forms of tocopherols and tocotrienols. *Mol Carcinog*. 2020;59(4):365-89. doi:10.1002/mc.23160.
20. Ahmadi M, Hedayatizadeh-Omran A, Alizadeh-Navaei R, Saeedi M, Zaboli E, Amjadi O, et al. Effects of vitamin E on doxorubicin cytotoxicity in human breast cancer cells in vitro. *Asian Pac J Cancer Prev*. 2022;23(1):201-5. doi: 10.31557/APJCP.2022.23.1.201.
21. Wang Hong, Yan W, Sun YuHai, Yang CS. δ -Tocotrienol is the most potent vitamin E form in inhibiting prostate cancer cell growth and inhibits prostate carcinogenesis in Ptenp^{-/-} mice. *Cancer Prev Res (Phila)*. 2022;15(4):233–45. doi: 10.1158/1940-6207.CAPR-21-0508.
22. Zhao R, Han X, Zhang H, Liu J, Zhang M, Zhao W, et al. Association of vitamin E intake in diet and supplements with risk of dementia: A meta-analysis. *Front Aging Neurosci*. 2022;14:955878. doi: 10.3389/fnagi.2022.955878.
23. Chen J, Shan H, Yang W, Zhang J, Dai H, Ye Z. Vitamin E for the prevention of chemotherapy-induced peripheral neuropathy: a meta-analysis. *Front Pharmacol*. 2021;12:684550. doi:10.3389/fphar.2021.684550.
24. Sozen E, Demirel T, Ozer NK. Vitamin E: Regulatory role in the cardiovascular system. *IUBMB Life*. 2019;71(4):507-15. doi:10.1002/iub.2020.
25. Bartolini D, Marinelli R, Giusepponi D, Galarini R, Barola C, Stabile AM, et al. Alpha-Tocopherol metabolites (the vitamin E metabolome) and their interindividual variability during supplementation. *Antioxidants (Basel)*. 2021;10(2):173. doi: 10.3390/antiox10020173.
26. Ulatowski L, Ghelfi M, West R, Atkinson J, Finno CJ, Manor D. The tocopherol transfer protein mediates vitamin E trafficking between cerebellar astrocytes and neurons. *J Biol Chem*. 2022;298(3):101712. doi: 10.1016/j.jbc.2022.101712.

27. Ismail M, Alsalahi A, Imam MU, Ooi J, Khaza'ai H, Aljaberi MA, et al. Safety and neuroprotective efficacy of palm oil and tocotrienol-rich fraction from palm oil: a systematic review. *Nutrients*. 2020;12(2):521. doi: 10.3390/nu12020521.
28. Alam J. Vitamins: a nutritional intervention to modulate the Alzheimer's disease progression. *Nutr Neurosci*. 2022;25(5):945–62. doi: 10.1080/1028415X.2020.1826762.
29. Esselun C, Dieter F, Sus N, Frank J, Eckert GP. Walnut oil reduces A β levels and increases neurite length in a cellular model of early Alzheimer disease. *Nutrients*. 2022;14(9):1694. doi:10.1080/1028415X.2020.1826762.
30. Gil Martínez V, Avedillo Salas A, Santander Ballestín S. Vitamin supplementation and dementia: a systematic review. *Nutrients*. 2022;14(5):1033. doi: 10.3390/nu14051033.
31. Dattola A, Silvestri M, Bennardo L, Passante M, Scali E, Patruno C, et al. Role of vitamins in skin health: a systematic review. *Curr Nutr Rep*. 2020;9(3):226-35. doi: 10.1007/s13668-020-00322-4.
32. Kagan V, Witt E, Goldman R, Scita G, Packer L. Ultraviolet light-induced generation of vitamin E radicals and their recycling. a possible photosensitizing effect of vitamin E in skin. *Free Radic Res Commun*. 1992;16(1):51-64. doi: 10.3109/10715769209049159.
33. Thiele JJ, Ekanayake-Mudiyanselage S. Vitamin E in human skin: organ-specific physiology and considerations for its use in dermatology. *Mol Aspects Med*. 2007;28(5-6):646-67. doi: 10.1016/j.mam.2007.06.001.
34. Keen MA, Hassan I. Vitamin E in dermatology. *Indian Dermatol Online J*. 2016;7(4):311-5. doi: 10.4103/2229-5178.185494.
35. Shaikh PA, Shaikh PN, Nakashidze I. Vitamin D levels and VDR rs2228570 genetic variant in Autoimmune Thyroiditis. *Sanamed*. 2023;18(3):217-22. doi: 10.5937/sanamed0-46407.

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