7.2C: Vitamin E

Vitamin E refers to a group of compounds that include both tocopherols and tocotrienols. Of the many different forms of vitamin E, γ-tocopherol is the most common form found in the North American diet. γ-Tocopherol can be found in corn oil, soybean oil, margarine, and dressings. α-tocopherol, the most biologically active form of vitamin E, is the second-most common form of vitamin E in the diet. This variant can be found most abundantly in wheat germ oil, sunflower, and safflower oils. As a fat-soluble antioxidant, it interrupts the propagation of reactive oxygen species that spread through biological membranes or through a fat when its lipid content undergoes oxidation by reacting with more-reactive lipid radicals to form more stable products. Regular consumption of more than 1,000 mg (1,500 IU) of tocopherols per day may be expected to cause hypervitaminosis E, with an associated risk of vitamin K deficiency and consequently of bleeding problems.

Sample of α-tocopherol, one of the various forms of vitamin E

Functions

Vitamin E has many biological functions, including its role as a fat-soluble antioxidant.
• As an antioxidant, vitamin E acts as a peroxyl radical scavenger, disabling the production of damaging free radicals in tissues, by reacting with them to form a tocopheryl radical, which will then be reduced by a hydrogen donor (such as vitamin C) and thus return to its reduced state.[16] As it is fat-soluble, it is incorporated into cell membranes, which protects them from oxidative damage. Vitamin E has also found use as a commercial antioxidant in ultra high molecular weight polyethylene (UHMWPE) used in hip and knee implants by resisting oxidation.

• As an enzymatic activity regulator, for instance, protein kinase C (PKC), which plays a role in smooth muscle growth, can be inhibited by α-tocopherol. α-Tocopherol has a stimulatory effect on the dephosphorylation enzyme, protein phosphatase 2A, which in turn, cleaves phosphate groups from PKC, leading to its deactivation, bringing the smooth muscle growth to a halt.

• Vitamin E also has an effect on gene expression. Macrophages rich in cholesterol are found in atherosclerotic tissue. Scavenger receptor CD36 is a class B scavenger receptor found to be up-regulated by oxidized low density lipoprotein (LDL) and binds it. Treatment with α-tocopherol was found to downregulate the expression of the CD36 scavenger receptor gene and the scavenger receptor class A (SR-A) and modulates expression of the connective tissue growth factor (CTGF). The CTGF gene, when expressed, is responsible for the repair of wounds and regeneration of the extracellular tissue lost or damaged during atherosclerosis.

• Vitamin E also plays a role in eye and neurological functions, and inhibition of platelet coagulation.

• Vitamin E also protects lipids and prevents the oxidation of polyunsaturated fatty acids.

Although most vitamin E supplementation studies used α-tocopherol individually, this design of studying only one isoform of vitamin E may introduce errors in interpreting overall vitamin E effects; for example, using only α-tocopherol in studies of inflammation can reduce serum γ- and δ-tocopherol concentrations. Moreover, a 2013 review involving single long-term supplementation with α-tocopherol showed that many clinical studies revealed an inverse relationship between supplementation and cardiovascular disease risk or mortality, but other studies showed no effect.

### Deficiency

Vitamin E deficiency can cause:

• spinocerebellar ataxia
• myopathies
• peripheral neuropathy
• ataxia
• skeletal myopathy
• retinopathy
• impairment of the immune response
• red blood cell destruction

### Supplementation

Vitamin E supplementation has not been shown to have significant benefit for people who are healthy, and appears to be harmful. It does not improve blood sugar control in an unselected group of people with diabetes mellitus[35] or decrease the risk of stroke.[36] Daily supplementation of vitamin E does not decrease the risk of prostate cancer, and may increase it. Studies on its role in age-related macular degeneration are ongoing, though if it is of a combination of dietary antioxidants used to treat the condition it may increase the risk. Routine supplementation with vitamin E during pregnancy has been shown to offer no benefit to the mother or the child. Vitamin E has been reported to cause more side effects.
effects, such as abdominal pain in pregnant women, and also the increased risk of having early rupture of membranes at term.

Vitamin E, along with β-carotene and vitamin C, has no protective effect on reducing the risk of cataract, cataract extraction, progression of cataract, and slowing the loss of visual acuity.

Toxicity

The LD$_{50}$, or the toxic dose required to kill 50% of group of rats and mice, respectively is 4000 mg of Vitamin E/kg of rat and 4000 mg of Vitamin E/kg of mouse.[43] Comparatively speaking, and at lethal doses, Vitamin E is less toxic than table salt and acetaminophen and it is more toxic than ethanol and Vitamin C. Vitamin E can act as an anticoagulant, increasing the risk of bleeding problems. As a result, many agencies have set a tolerable upper intake levels (UL) at 1,000 mg (1,500 IU) per day.[1] In combination with certain other drugs such as aspirin, hypervitaminosis E can be life-threatening. Hypervitaminosis E may also counteract vitamin K, leading to a vitamin K deficiency.

Dietary Reference Intake

The Food and Nutrition Board (FNB) of the U.S. Institute of Medicine updated Estimated Average Requirements (EARs) and Recommended Dietary Allowances (RDAs) for vitamin E in 2000. The current EAR for vitamin E for women and men ages 14 and up is 12 mg/day. The RDA is 15 mg/day. RDAs are higher than EARs so as to identify amounts that will cover people with higher than average requirements. RDA for pregnancy equals 15 mg/day. RDA for lactation equals 19 mg/day. For infants up to 12 months the Adequate Intake (AI) is 4–5 mg/day and for children ages 1–13 years the RDA increases with age from 6 to 11 mg/day. The FNB also sets Tolerable Upper Intake Levels (ULs) for vitamins and minerals when evidence is sufficient. In the case of vitamin E the UL is 1,000 mg/day.

For U.S. food and dietary supplement labeling purposes the amount in a serving is expressed as a percent of Daily Value (%DV). For vitamin E labeling purposes 100% of the Daily Value was 30 mg, but as of May 2016 it has been revised to 15 mg. A table of the pre-change adult Daily Values is provided at Reference Daily Intake. Food and supplement companies have until July 28, 2018 to comply with the change.

Vitamin E and atherosclerosis

Atherosclerosis is a disease condition that refers to the buildup of plaque, which is a substance containing lipid and cholesterol (mainly the low-density lipoprotein or LDL cholesterol) on the inner layer of the arterial lumen. With the existing plaque, instead of being smooth and elastic, the layers become thickened and irregular and the lumen of the artery become narrower. This vessel-narrowing effect lead to a reduction of blood circulation and can lead to or worsen the condition of hypertension.

There are currently multiple theories explaining factors causing and affecting the cholesterol plaque build up within arteries with the most popular theory indicating that the rate of build up is affected by the oxidation of the LDL cholesterol. LDL cholesterol is one of the five major groups of lipoproteins with one of the physiological roles being lipid transportation. A typical LDL particle contain 2,700 fatty acid molecules and half of them are poly-unsaturated fatty acids, which are very oxidation sensitive. Once the oxidation of LDL occur, it will start a series of undesirable effects starting from the
increase production of inflammatory cytokines by stimulating the endothelial cells and monocytes, followed by increased production of tissue factors, production of macrophages and monocytes, which eventually lead to the formation of foam cells and accelerated development of atherosclerosis. With the presence of adequate concentration of vitamin E, which is a very potent fat-soluble antioxidant, it can inhibit the oxidation of LDL, and this inhibition contributes protection against the development of atherosclerosis and can stabilize the existing plaque.

According to one meta-analysis, nine cohort studies showed that high intake of tocopherol was associated with a lower risk of cardiovascular diseases compared with lower intake. In this study, higher dietary, supplementation and combined vitamin E intake was also associated with lower disease incidents. In 1993, a study of 39,919 male health professionals aged 40 to 75 showed that consumption of more than 60 IU of vitamin E (any form) per day was associated with a lower incidence of coronary heart disease compared with less than 7.5 IU/day intake. This study also showed an inverse association between vitamin E supplementation and the incidence of heart disease.

A 2015 systematic review of clinical trials concluded that vitamin E supplementation alone improved endothelial function as determined by measurements of forearm blood flow, but when combined with vitamin C supplementation, it did not.[63] A meta-analysis of clinical trials showed no significant association between vitamin E supplementation and cardiovascular mortality.

Contributors

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