Vitamin E

Nutrition Information Briefs

Nutrient

Vitamin E.

Vitamin E is a lipid-soluble antioxidant. Specifically, vitamin E acts as an antioxidant by intercepting peroxyl radicals, which are formed instantaneously when a lipid radical reacts with oxygen. During lipid peroxidation, vitamin E reacts with the peroxyl radical before it can attack the PUFA but generates a tocopheroxyl radical that must be reduced by other antioxidants, such as ascorbic acid (1).

Plants synthesize 8 different lipid-soluble molecules with "vitamin E antioxidant" activity. These are α-, β-, γ-, δ-tocopherols and α-, β-, γ-, δ-tocotrienols, which differ in the number of methyl groups on the chromanol head and whether the tail is a phytyl tail or an unsaturated tail. Plants synthesize a specific stereochemical form, *RRR*, where the 3 chiral carbons are in the *R*-conformation at positions 2, 4′, and 8′. Chemically synthesized *all-racemic (all rac)*-α-tocopherol has an approximately equal mixture of 8 different stereoisomers (*RRR*, *RSR*, *RRS*, *RSS*, *SRR*, *SSR*, *SRS*, *SSS*). The α-tocopherol 2 position, the junction of the ring and phytyl tail, is critical for in vivo vitamin E biologic activity. Specifically, only 2*R*-α-tocopherol forms meet human vitamin E requirements.

Vitamin E biologic activity is different from its antioxidant activity. The biological preference for 2*R*-α-tocopherol is mediated by the α-tocopherol transfer protein (α-TTP) (2). Hepatic α-TTP facilitates the selective incorporation of 2*R*-α-tocopherol into circulating lipoproteins that distribute the vitamin to nonhepatic tissues. Additionally, other vitamin E (non-α-tocopherol natural) forms and 2*S*-α-tocopherol are preferentially catabolized and excreted.

Deficiencies

Vitamin E deficiency symptoms include failure of placentation, neuromuscular impairments, hemolytic anemia, retinopathy, reduced immunity, and enhanced inflammation. Human vitamin E deficiency results from genetic abnormalities in α-TTP or in lipoprotein synthesis, or occurs secondary to fat malabsorption syndromes (3). Genetic α-TTP defects are associated with a characteristic syndrome, ataxia with vitamin E deficiency, AVED.

Vitamin E deficiency as a result of inadequate intakes is difficult to assess. Circulating α-tocopherol concentrations can be elevated in the presence of hyperlipidemia. Thus, evaluation of circulating lipids or cholesterol should also be undertaken. Adipose tissue measurements have been used to assess status but have not been widely used. Vitamin E deficiency based on circulating α-tocopherol concentrations (<12 μmol/L serum or plasma) has been observed in large population studies in Africa, southeast Asia, and the west Pacific (4). Prevalence may be increasing because of the increased intake of vegetable oils that may have become rancid by exposure to sunlight and prolonged heat through multiple uses.

Diet recommendations

The vitamin E DRI for adult men and women (and individuals 14–18 y) was set in 2000 at a daily estimated average requirement (EAR) of 12 mg α-tocopherol and an RDA of 15 mg (5). There are no increases for pregnancy, but for lactation the RDA is 19 mg/d. The adequate intake (AI) for infants (0 through 6 mo) was estimated to be 4 mg and for 7 through 12 mo to be 5 mg. The RDA for children 1–3 y is 6 mg, for those 4–8 y is 7 mg, and those 9–13 y is 11 mg.

Food sources

Major dietary vitamin E sources are vegetable oils, nuts and seeds, and green/leafy vegetables (5). Foods with a percent daily value (DV) for α-tocopherol greater than 10% are, for example in descending order: wheat germ oil; sunflower seeds; almonds, hazelnuts, and peanuts; sunflower, safflower, olive oils; spinach and broccoli.

Clinical uses

Humans with defects in the *TTPA* gene (encoding α-TTP) have extraordinarily low (1/100 of normal) plasma vitamin E concentrations, but if they are given large vitamin E supplements, plasma concentrations normalize within hours (3). If supplementation is halted, plasma vitamin E concentrations fall within days to deficient concentrations. A daily α-tocopherol dose (800 to 1200 mg) is usually sufficient to prevent further deterioration of neurologic function and in some cases improvements have been noted. Postmortem analysis of a brain from a vitamin E-supplemented AVED patient demonstrated α-tocopherol accumulation and prevention of Purkinje cell loss.

Vitamin E deficiency due to impaired lipoprotein synthesis or fat malabsorption syndromes (e.g. abetalipoproteinemia, cystic fibrosis, short bowl disorder, cholestasis, and inherited defects in bile acid synthesis) is also treated with daily vitamin E supplements (100 mg/kg body weight). This enormous amount is necessary to promote absorption.

Vitamin E supplementation is controversial for subjects who are not clinically vitamin E deficient (3). In the elderly, impaired immune function was improved with vitamin E supplementation. Macular degeneration in the retina was slowed in patients given a supplement cocktail that included vitamin E. Vitamin E supplements have decreased heart attack risk in subjects with haptoglobin 2–2 genotype, which results in a dysfunctional protein and causes increased oxidation by

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free heme. Vitamin E supplements have also been studied in Alzheimer's disease with mixed success.

Toxicity

The upper limit of tolerable intakes (UL) is 1000 mg/d, equivalent to 1100 IU synthetic or 1500 IU natural vitamin E (3). The UL was based on the adverse effect of an increased bleeding tendency observed in rat studies. This tendency to bleed was found to have beneficial effects in preventing venous thrombosis in a trial of vitamin E supplements in women.

Subsequent to the publication of the DRIs, there have been several meta-analyses evaluating the outcomes of human vitamin E supplementation trials. Thus far, there have been no uniform mechanisms identified for the claim in meta-analyses of increased mortality associated with vitamin E supplements.

Recent research

Vitamin E in the central nervous system.

Vitamin E deficiency in humans manifests primarily as cerebellar ataxia with loss of Purkinje cells, underscoring the unique sensitivity of the central nervous system to oxidative stress (6). Interestingly, α-TTP is expressed in the cerebellum and is expressed in the embryonic zebrafish developing nervous system. α-Tocopherol supplementation of α-TTP knockout mice normalizes its status in all tissues *except* the brain. Thus, a unique relation exists between *localized* vitamin E concentrations, expression of α-TTP, oxidative stress, and optimal cerebellar function. The detailed description of this relation, and the molecular mechanisms that underlie it, are critical research questions.

Fertility

Vitamin E was discovered as an essential dietary factor for reproductive health in female rodents. Surprisingly, very little is known regarding human vitamin E status and reproductive health. α-TTP is expressed in the uterine wall of pregnant female mice and in the human yolksac and placenta. α-TTP is required for zebrafish embryonic survival (7). Research in this field is of high importance because 96% of US women do not meet vitamin E EARs.

Interactions with other nutrients

The untoward effects of vitamin E supplements on blood clotting may result from vitamin E and K interactions because these supplements increase undercarboxylation of prothrombin, suggesting lower vitamin K activity. Possible mechanisms for the vitamin E and K interaction have been proposed, but none have been proven.

The interactions of vitamins E and C are likely dependent upon their roles as antioxidants; vitamin C can regenerate tocopherol from the tocopheroxyl radical, as discussed above.

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Maret G Traber

Linus Pauling Institute, College of Public Health and Human Sciences, Oregon State University, Corvallis, OR, USA

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Address correspondence to MGT (e-mail: maret.traber@oregonstate.edu).

Abbreviations used: AVED, ataxia with vitamin E deficiency; EAR, estimated average requirement; UL, upper limit of tolerable intake.

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