INE INSTITUTE OF NUTRITIONAL ENDOCRINOLOGY

Micronutrients: Vitamin E

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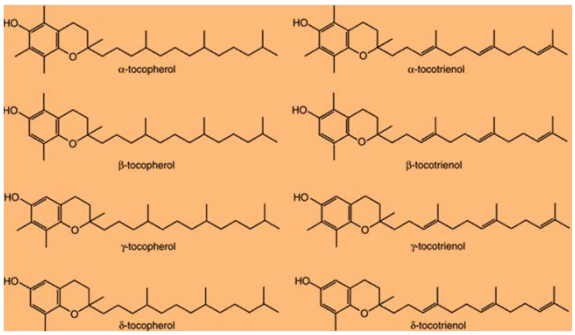
Vitamin E Basics

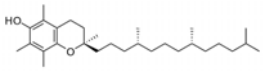
- ✓Vitamin E is a fat-soluble antioxidant
- ✓The term describes a family of 8 antioxidants
  - ➢4 tocopherols –
    - α- alpha
    - β- beta
    - γ- gamma
    - δ- delta
  - ➢4 tocotrienols
    - α- alpha
    - β- beta
    - γ- gamma
    - δ- delta

Tocopherols and Tocotrienols



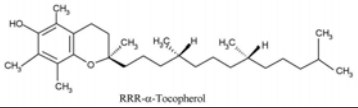
α-Tocopherol

- ✓ Main function is as an anti-oxidant
- ✓ Intercepts free radicals and prevents lipid destruction
- ✓ Maintains integrity of cell membranes throughout the body
- ✓ Protects the fats in low-density lipoproteins (LDL) from oxidation
- ✓ Inhibits the activity of protein kinase C, a cell-signaling molecule
- ✓ Inhibits platelet aggregation to enhance vasodilation



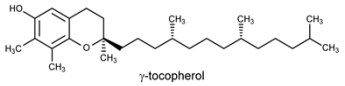
RRR-α-tocopherol

- ✓ The isomeric form of α-tocopherol found in foods is RRR-α-tocopherol (also referred to as "natural" or d-α-tocopherol).
- ✓ Synthetic α-tocopherol, which is labeled all-rac- or dl-α-tocopherol, has only one-half the biological activity of RRR-α-tocopherol.
- ✓ Often vitamin E-fortified foods contain synthetic α-tocopherol, and the amounts are given as a percentage of the daily value of 30 IU.



γ-Tocopherol

- ✓ Gamma tocopherol is the most common form of vitamin E in the American diet.
- ✓ Blood levels are 10 times lower than α-tocopherol.

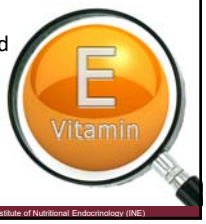


γ-tocopherol

- ✓ α-Tocopherol is preferentially retained in the body by the action of the α-tocopherol transfer protein (a-TTP) in the liver, which preferentially incorporates α-tocopherol into lipoproteins that are circulated in the blood.
  - ➢ Delivers α-tocopherol to different tissues in the body

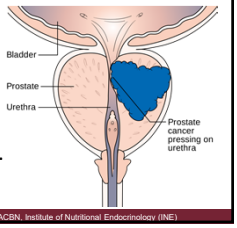
γ-Tocopherol vs α-Tocopherol

- ✓ Forms of vitamin E other than α-tocopherol are actively metabolized.
- ✓ Because γ-tocopherol is initially absorbed in the same manner as α-tocopherol, small amounts of γ-tocopherol are detectable in blood and tissue.
- ✓ Breakdown products of tocopherols, known as metabolites, can be detected in urine. More γ-tocopherol metabolites are excreted in urine than α-tocopherol metabolites, suggesting less γ-tocopherol is needed for use by the body.



γ-Tocopherol and Metabolites

- ✓ Limited research in the test tube and in animals indicates that γ-tocopherol or its metabolites may play a role in protecting the body from free radical-induced damage.
- ✓ In one study, increased levels of plasma γ-tocopherol were associated with a significantly reduced risk of developing prostate cancer.
- ✓ Increased levels of plasma α-tocopherol and toenail selenium were protective against prostate cancer development only when γ-tocopherol levels were also high.



Deficiency of Vitamin E

- ✓ Neurological symptoms, including impaired balance and coordination (ataxia)
- ✓ Injury to the sensory nerves (peripheral neuropathy)
- ✓ Muscle weakness (myopathy)
- ✓ Damage to the retina of the eye (pigmented retinopathy)

Observed in individuals with severe malnutrition, genetic defects affecting the α-tocopherol transfer protein, and fat malabsorption syndromes

Nervous System and E Deficiency

- ✓ The developing nervous system appears to be especially vulnerable to vitamin E deficiency.
  - ➢ Children with severe vitamin E deficiency at birth rapidly develop neurological symptoms if not treated with vitamin E.
  - ➢ Individuals who develop malabsorption of vitamin E in adulthood may not develop neurological symptoms for 10-20 years.

- ✓ Symptomatic vitamin E deficiency in healthy individuals who consume diets low in vitamin E has never been reported.

Recommended Dietary Allowance

- ✓ The RDA for vitamin E was previously 8 mg/day for women and 10 mg/day for men.
- ✓ The RDA was revised by the Food and Nutrition Board of the Institute of Medicine in 2000.
- ✓ This new recommendation was based largely on the results of studies done in the 1950s in men fed vitamin E deficient diets.

Recommended Daily Allowance

Life Stage	Age	Males		Females	
		mg/day	IU/day	mg/day	IU/day
Infants (AI)	0-6 months	4	6	4	6
Infants (AI)	7-12 months	5	7.5	5	7.5
Children	1-3 years	6	9	6	9
Children	4-8 years	7	10.5	7.5	10.5
Children	9-13 years	11	16.5	11	16.5
Adolescents	14-18 years	15	22.5	15	22.5
Adults	19 years and older	15	22.5	15	22.5
Pregnancy	all ages	-	-	15	22.5
Breast-feeding	all ages	-	-	19	28.5

Source: http://ods.od.nih.gov/factsheets/VitaminE-Consumer/

World's Healthiest Foods ranked as quality sources of vitamin E						
Food	Serving Size	Cals	Amount (mg (ATE))	DRI/DV (%)	Nutrient Density	World's Healthiest Foods Rating
Sunflower Seeds	0.25 cup	204.4	12.31	82.07	7.2	excellent
Spinach	1 cup	41.4	3.74	24.93	10.8	excellent
Swiss Chard	1 cup	35.0	3.31	22.07	11.3	excellent
Turnip Greens	1 cup	28.8	2.71	18.07	11.3	excellent
Asparagus	1 cup	39.6	2.70	18.00	8.2	excellent
Mustard Greens	1 cup	36.4	2.49	16.60	8.2	excellent
Chili Peppers	2 tsp	15.2	2.06	13.73	16.2	excellent
Almonds	0.25 cup	132.2	6.03	40.20	5.5	very good
Broccoli	1 cup	54.6	2.26	15.07	5.0	very good
Bell Peppers	1 cup	28.5	1.45	9.67	6.1	very good
Kale	1 cup	36.4	1.11	7.40	3.7	very good
Cayenne Pepper	2 tsp	11.4	1.07	7.13	11.2	very good
Tomatoes	1 cup	32.4	0.97	6.47	3.6	very good

RDA Study

- ✓In a test-tube analysis, hydrogen peroxide was added to blood samples and hemolysis was used to indicate vitamin E deficiency.
- ✓Because hemolysis has also been reported in children with severe vitamin E deficiency, this analysis was considered to be a clinically relevant test of vitamin E status.
- ✓Latest RDA for vitamin E is based on the prevention of deficiency symptoms rather than on health promotion and prevention of chronic disease.

Cardiovascular Disease

- ✓ Results of at least five large observational studies suggest that increased vitamin E consumption is associated with decreased risk of myocardial infarction or death from heart disease in both men and women.
- ✓ Each study was a prospective study that measured vitamin E consumption in presumably healthy people and followed them for a number of years to determine how many were diagnosed with or died as a result of heart disease.

Bypass and Vitamin E

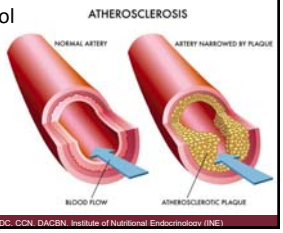
- ✓ Small observational study of men
- ✓ History of coronary artery bypass surgery
- ✓ Those who took at least 100 IU of supplemental α-tocopherol (67 mg of RRR-α-tocopherol) daily had a reduction in the progression of coronary artery atherosclerosis measured by angiography compared to those who took less than 100 IU/day of α-tocopherol.

Cardiovascular Disease Studies

- ✓ In two of the studies, individuals who consumed more than 7 mg/day of α-tocopherol in food were only approximately 35% as likely to die from heart disease as those who consumed less than 3-5 mg/day of α-tocopherol.
- ✓ Two other large studies observed a significantly reduced risk of heart disease only in women and men who consumed at least 100 IU of supplemental RRR-α-tocopherol (67 mg of RRR-α-tocopherol) daily.

Atherosclerosis

- ✓ Several studies have observed plasma or red blood cell levels of α-tocopherol to be inversely associated with severity of carotid atherosclerosis, detected using ultrasonography.
- ✓ A randomized, placebo-controlled, intervention trial in 39,876 women participating in the Women's Health Study found that supplementation with 600 IU of RRR-α-tocopherol (400 mg of RRR-α-tocopherol) every other day for ten years had no effect on the incidence myocardial infarction and stroke, but the vitamin E intervention decreased cardiovascular-related deaths by 24%.

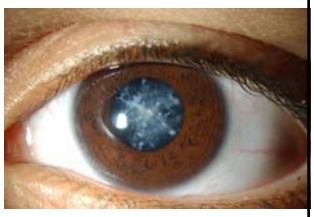


More Studies

- ✓ Analysis of data from the Women's Health Study also showed that women receiving the vitamin E intervention experienced a 21% reduction in risk of venous thromboembolism.
- ✓ A large randomized control trial conducted in healthy middle-aged men (trial name: PHS II) observed that supplementation with 400 IU of synthetic α-tocopherol every other day for eight years had no significant effect on the risk of major cardiovascular events.

Cataracts and Vitamin E

- ✓ Cataracts formed by protein oxidation in the lens of the eye may be prevented by α-tocopherol.
- ✓ Mixed results of observational studies: some report increased vitamin E intake protects against cataract development, while others report no association.

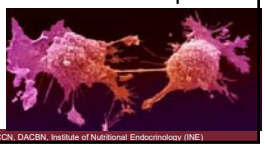


Immune Function and Vitamin E

- ✓α-Tocopherol has been shown to enhance specific aspects of the immune response that appear to decline as people age.
- ✓A randomized, placebo-controlled trial in elderly nursing home residents reported that daily supplementation with 200 IU of synthetic α-tocopherol (equivalent to 90 mg of RRR-α-tocopherol) for one year significantly lowered the risk of upper respiratory tract infections, especially the common cold, but had no effect on lung infections.

Cancer and Vitamin E

- ✓Many types of cancer are thought to result from oxidative damage to DNA caused by free radicals.
- ✓The ability of α-tocopherol to neutralize free radicals has made it the subject of a number of cancer prevention studies.
- ✓Several large prospective studies have failed to find significant associations between α-tocopherol intake and the incidence of lung or breast cancer.



Vitamin E and Prostate Cancer

- ✓The effect of vitamin E supplementation on prostate cancer risk has received particular attention in randomized control trials.
- ✓A placebo-controlled intervention (trial name: ATBC) reported a 34% reduction in the incidence of prostate cancer in smokers given daily supplements of 50 mg of synthetic α-tocopherol (equivalent to 25 mg of RRR-α-tocopherol) daily.

Using Vitamin E with Cancer

- ✓ Cancer cells proliferate rapidly and are resistant to death by apoptosis (programmed cell death).
- ✓ Cell culture studies indicate that the vitamin E ester, α-tocopheryl succinate, can inhibit proliferation and induce apoptosis in a number of cancer cell lines.
- ✓ The ester form, α-tocopheryl succinate, not α-tocopherol, is required to effectively inhibit proliferation or induce cancer cell death.

Diabetes and Vitamin E

- ✓ One study found urinary excretion of F2-isoprostanes, a biochemical marker of oxidative stress, was elevated in type 2 diabetic individuals.
- ✓ Supplementation with 600 mg of synthetic α-tocopherol (equivalent to 300 mg of RRR-α-tocopherol) for 14 days reduced levels of the biomarker.

Dementia and Alzheimer's

- ✓ The brain is particularly vulnerable to oxidative stress, and low vitamin E is considered a contributory factor in Alzheimer's disease.
- ✓ Low vitamin E has been found in cerebrospinal fluid of patients with Alzheimer's disease.
- ✓ A large placebo-controlled intervention trial in individuals with moderate neurological impairment found that supplementation with 2,000 IU of synthetic α-tocopherol daily for two years (equivalent to 900 mg/day of RRR-α-tocopherol) significantly slowed progression of Alzheimer's dementia.

Toxicity

- ✓ Few side effects have been noted in adults taking supplements of less than 2,000 mg of α-tocopherol daily (RRR- or all-rac-α-tocopherol).
- ✓ Most studies of toxicity or side effects of α-tocopherol supplementation have lasted only a few weeks to a few months.
- ✓ Side effects as a result of long-term α-tocopherol supplementation have not been adequately studied.
- ✓ It's possible that excess vitamin E may increase the likelihood of hemorrhage in some individuals.

Drug Interactions

- ✓ Use of vitamin E supplements may increase the risk of bleeding in individuals taking anticoagulant drugs, such as warfarin (Coumadin); antiplatelet drugs, such as clopidogrel (Plavix) and dipyridamole (Persantine); and non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin, ibuprofen, and others.
- ✓ Also, individuals on anticoagulant therapy (blood thinners) or individuals who are vitamin K deficient should not take α-tocopherol supplements without close medical supervision because of the increased risk of hemorrhage.

Food Sources

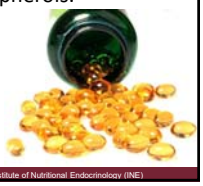
- ✓ Major sources of α-tocopherol in the American diet include vegetable oils (olive, sunflower, and safflower oils), nuts, whole grains, and green leafy vegetables.
- ✓ All eight forms of vitamin E (α-, β-, γ-, and δ-tocopherols and tocotrienols) occur naturally in foods but in varying amounts.

Supplements: α-Tocopherol

- ✓ In the US, the average intake of α-tocopherol from food (including enriched and fortified sources) for individuals 2 years and older is 6.9 mg/day; this level is well below the RDA of 15 mg/day of RRR-α-tocopherol.
- ✓ Many scientists believe it is difficult for an individual to consume more than 15 mg/day of α-tocopherol from food alone without increasing fat intake above recommended levels.

α-Tocopheryl succinate and α-tocopheryl acetate (α-tocopheryl esters)

- ✓ α-Tocopherol supplements are available in the ester forms: α-tocopheryl succinate and α-tocopheryl acetate.
- ✓ Tocopherol esters are more resistant to oxidation during storage than unesterified tocopherols.
- ✓ When taken orally, the succinate or acetate moiety is removed from α-tocopherol in the intestine.



γ-Tocopherol Supplements

- ✓ γ-Tocopherol supplements and mixed tocopherol supplements are also commercially available.
- ✓ The amounts of α- and γ-tocopherol in mixed tocopherol supplements vary, so it is important to read the label to determine the amount of each tocopherol present in supplements.