

Tocotrienols in Nutrition and Health

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Tocotrienols Are Members of the Vitamin E Family

Mention vitamin E and most people will think alpha-tocopherol. Even most scientists will make the same connection. It is only recently that scientists and now consumers have been reminded that vitamin E is a family of compounds.

Tocotrienols are members of the vitamin E family.¹ Unlike some vitamins which consist of a single compound, vitamin E consists of eight different compounds: four tocopherols and four tocotrienols (designated as alpha, beta, gamma, and delta). Our food contains all eight compounds. Most vitamin E supplements, however, contain only alpha-tocopherol because it was thought that only this one was important. Emerging research proved this understanding wrong. To get the full spectrum of the many benefits of vitamin E, we must use products that contain the complete family of tocopherols plus tocotrienols.

Tocotrienols are most abundant in cereal grains including barley, rice, rye, and wheat, and the fruit of palm. Tocotrienols are extracted commercially from palm oil and rice bran oil. Unfortunately, the common commercial sources of natural vitamin E (soy, corn, cottonseed, canola, and sunflower oil distillates) contain little or no tocotrienols. Synthetic vitamin E contains only alpha-tocopherol and none of the other tocopherols and tocotrienols.

Tocopherols and Tocotrienols: Similarities and Differences

Tocopherols and tocotrienols have great similarities in their molecules, which consist of a head (chroman ring) and a tail (known as phytyl tail for tocopherols). The chroman ring carries the active antioxidant group. Each tocotrienol has an identical chroman ring as the corresponding tocopherol. For this reason, tocotrienols, like tocopherols, are excellent antioxidants.² Tocotrienols differ only on the tail; the tocotrienols have three unsaturated sites. Scientists are discovering important benefits of tocotrienols that are unique and different from those of alpha-tocopherol.

Underscoring the importance of taking the whole vitamin E family is the evidence that not only tocotrienols but also the other tocopherols have unique functions different from those of alpha-tocopherol. For example:

- Researchers at Berkeley reported that gamma-tocopherol has stronger anti-inflammatory properties than alpha-tocopherol. Specifically gamma-tocopherol reduced PGE2 synthesis in both macrophages and human epithelial cells. In addition, the major metabolite of dietary gamma-tocopherol gamma-CEHC (or LLU-alpha) also exhibited anti-inflammatory properties in these cells. In contrast, alpha-tocopherol slightly reduced PGE2 formation in macrophages but had no effect in epithelial cells.³
- Gamma-tocopherol appears to be more potent than alpha-tocopherol in increasing superoxide dismutase (SOD) activity in plasma and arterial tissues as well as Mn SOD and Cu/Zn SOD protein expression in arterial tissues. SOD is a major antioxidant enzyme.⁴
- Gamma-tocopherol, not alpha, is the effective form for fighting nitrogen radicals.⁵ These radicals are major culprits in arthritis, multiple sclerosis (MS), and diseases of the brain such as Alzheimer's.
- A metabolic product of gamma-tocopherol, code-named LLU-alpha, appeared to be a natriuretic factor which affects how much fluid and electrolytes pass through the kidney to the urine.⁶ The corresponding metabolite of alpha-tocopherol was not active.

The Science Behind the Unique Functions of Tocotrienols

Heart Disease

A number of studies produced evidence of the biochemical basis of the important and unique effects of tocotrienols.

Tocotrienols and, in particular, gamma-tocotrienol appear to act on a specific enzyme called 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA) involved in cholesterol production in the liver.⁷ Tocotrienols suppress the production of this enzyme, which may result in less cholesterol being manufactured by liver cells. This may in turn result in an overall reduction of plasma cholesterol levels. Unlike tocopherols, tocotrienols and particularly gamma-tocotrienol appear to reduce plasma apoB levels in hypercholesterolemic subjects. It has been suggested from preliminary data that gamma-tocotrienol stimulates apoB degradation possibly as the result of decreased apoB translocation into the endoplasmic reticulum lumen.⁸

A recent study evaluated the role of tocotrienol-rich extracts on atherosclerosis, using apolipoprotein ApoE +/- female mice, which develop atherosclerosis only when fed diets high in triglyceride and cholesterol. Mice fed a palm oil tocotrienol-rich extract had 60% lower plasma cholesterol than groups fed the atherogenic diets.⁹

Human studies have produced conflicting results.¹⁰⁻¹² In a recent clinical study in humans, a rice bran oil tocotrienol-rich extract supplying 312-mg tocotrienols and 360-mg tocopherols significantly reduced total cholesterol, LDL, and triglycerides. HDL was higher in the treated group than in the control.¹³ The conflicting results may be due in part to the levels used and the composition of the supplement especially as it relates to other components which may have an additive or synergistic effect. In the case of rice bran oil extract, there is significant literature suggesting a cholesterol-reducing effect. Sterols and other compounds present in palm oil may have similar effects. Beneficial effects on cardiovascular health may not necessarily be associated with reduction in cholesterol levels as discussed below.

Cancer

Laboratory studies indicate that tocotrienols may affect the growth and/or proliferation of some types of human cancer cells. A research group at the University of Texas at Austin, headed by Dr. Kimberly Kline, confirmed earlier results that tocotrienols slow down the growth of human breast cancer cells.^{14,15} This study showed that the naturally occurring tocotrienols and RRR-delta-tocopherol induced apoptosis (death) of these cancer cells. The gamma and delta-tocotrienols were the most effective. Alpha, beta, and gamma tocopherols were ineffective in this system. Another group reported that gamma-tocotrienol suppressed the growth of rat melanoma cells and, with greater potency, the growth of human breast adenocarcinoma and human leukemic cells.¹⁶ Another study indicated that tocotrienols reduced liver cancers in rats dosed with a potent liver carcinogen.¹⁷

Supporting the thesis that the other members of the vitamin E family may have an important role in cancer prevention is the evidence that gamma-tocopherol is superior to alpha in inhibiting prostate cancer cells *in vitro*.¹⁸ Our research indicated that gamma-tocopherol, added to a semipurified diet, was more effective than alpha-tocopherol in reducing *ras-p21* oncogenes in the colonocyte of rats.¹⁹

Benefits for Cardiovascular Health—Clinical Evidence

The strongest evidence yet for tocotrienols comes from a clinical study conducted by the Kenneth Jordan Heart Research Foundation in New Jersey. This 5-year study, evaluated 50 patients who had stenosis of the carotid artery.²⁰

The patients, ranging in age from 49 to 83 years, were divided in two groups. The narrowing of the carotid artery exceeded 49 percent in approximately half of them. One group of 25 received approximately 650 milligrams of tocotrienols plus tocopherols. The other group of 25 received a placebo. Tocotrienol-rich extract from palm oil was used in the first half of the study and from rice bran oil in the second half. All patients were examined every 6 months for the first year and every year after that with ultrasonography. This medical procedure measures the narrowing after 4 years:

- Placebo group: Fifteen patients showed worsening of the stenosis, 8 remained stable, and 2 showed some improvement.
- Tocotrienol (plus tocopherol) group: Three patients showed minor worsening and 12 remained stable. What is remarkable is that 10 patients showed regression of stenosis—their condition improved.

As discussed earlier,¹³ the researchers found a substantial drop in total cholesterol, triglycerides, and LDL and an increase in HDL with the tocotrienol-rich extract from rice bran oil.

Topical Use of Tocotrienols

Tocotrienols, like tocopherols, can protect the skin from the damaging effects of exposure to ultraviolet radiation, pollution, cigarette smoke, and other environmental and biological stress factors. Tocotrienols

applied topically appear to prevent the damaging effects of ultraviolet radiation.²² Topically applied tocotrienols and tocopherols penetrate the entire skin to the subcutaneous fat layer within 30 minutes and significantly increase the concentration of these antioxidants in the deeper subcutaneous layers.²³ Topical application of tocotrienols has been suggested to preserve the existing vitamin E level in skin cells.

Safe and Effective Use Levels

Research conducted in humans suggests that consumption of tocopherol plus tocotrienol blends containing up to 300 mg/day tocotrienols for more than 48 months results in no adverse effects. Vitamin E in general has an excellent safety record.

How much tocotrienols to take? Please remember that tocotrienols are available commercially as mixtures with tocopherols. If you are at high risk for heart disease, you may consider levels up to 300 mg/day of tocotrienols. For the great majority of consumers that want to get the benefit of the complete vitamin E family, much lower levels may still provide benefits.

It is extremely important to take products that contain natural tocopherols plus tocotrienols. While our individual needs differ, the following general guidelines might help you choose the right level for you.

- The adequate level—the 100/100 system: Take 100 IU plus 100 mg of mixed tocopherols and tocotrienols. For healthy young adults with no family history of chronic disease.
- The medium level—the 200/200 system: Take 200 IU plus 200 mg of mixed tocopherols and tocotrienols. For young adults with some risk factors and healthy people without risk factors up to 50 years old.
- The high, yet very safe dose—the 400/400 system: Take 400 IU plus 400 mg of mixed tocopherols and tocotrienols. For people who, because of their family history for chronic disease, age, level of stress, diet, and other factors, want to take a higher level.

Commercial Products

Tocotrienol rich products are extracts, which also contain tocopherols and other natural components present in raw materials. Commercial products are extracted from rice bran or palm oil. Eastman Chemical Company's *NuTriene*, the sole U.S.-manufactured product, is extracted from rice bran oil.

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