Vitamin E Component Dramatically More Effective at Supporting Heart Health

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Vitamin E is often thought of as a single entity. However, it is a mixture of both tocotrienols and tocopherols, two forms of the same vitamin. Scientists have found that although both tocotrienols and tocopherols are similar, they work differently in the body. In fact, the newest research indicates that even though both forms possess antioxidant activity, tocotrienols are superior to tocopherols in ways essential to good health. Furthermore, evidence indicates that tocotrienols are absorbed better than tocopherols1 and that alpha-tocopherol (the most common form of Vitamin E supplementation worldwide) blocks absorption of tocotrienols,2 compromising tocotrienols' ability to maintain healthy cholesterol levels and sustain the integrity of nerves.

In this article, we will discuss the differences between tocopherols and tocotrienols and explain why a special form of delta-tocotrienol derived from the Annatto plant can play an important part in maintaining cardiovascular health

Supporting Healthy Cholesterol Levels

As mentioned above, tocopherols do not have tocotrienols' cholesterol-lowering ability. In fact, alpha-tocopherol lessens or interferes with the cholesterol-lowering action of tocotrienols.3 Most vitamin E supplements contain primarily tocopherols (especially alpha-tocopherol) and only traces of tocotrienols. This is counterproductive in light of what we know about tocopherols inhibiting tocotrienols' absorption and the fact that large clinical studies on alpha-tocopherol's benefits to cardiovascular health have been equivocal.

Effective cholesterol-lowering preparations consist of less than 15-20 percent alpha-tocopherol and more than 60 percent gamma- and delta-tocotrienol, whereas less effective or ineffective preparations consist of more than 30 percent alpha-tocopherol and less than 45 percent of gamma- and delta-tocotrienol. In clinical studies, high alpha-tocopherol supplements did not contribute to cholesterol lowering,4-5 whereas supplements containing low amounts of alpha-tocopherol and high amounts of gamma- and delta-tocotrienol led to a significant decrease in total and LDL cholesterol.6-7

Animals consuming diets supplemented with gamma- and delta-tocotrienol showed the greatest cholesterol decrease (32 percent total cholesterol and 66 percent LDL cholesterol), whereas alpha-tocopherol had no effect on cholesterol lowering. In this study, HDL/LDL cholesterol ratios improved by 123-150 percent.8

In humans, two open studies2 measured fasting blood lipids before and 2 months after supplementation with annatto tocotrienols (75 mg/day). In both groups, total cholesterol levels dropped 13 percent, whereas LDL cholesterol

dropped 9-15 percent and HDL cholesterol increased 4-7 percent. The LDL/HDL ratio was reduced by 12-21 percent. Amongst others, a study conducted by Bristol-Myers Squibb found that after 4-weeks' supplementation with gamma- and delta-tocotrienol (100 mg/day), total cholesterol dropped by 15-22 percent, and LDL cholesterol decreased by 10-20 percent.9

Knowing the difference between the molecular structure of tocopherols and tocotrienols is important to understanding why tocotrienols, but not tocopherols, can support healthy cholesterol levels. Tocotrienol and tocopherol molecules both have the same head, the site of their well-known antioxidant activities. However, tocotrienols and tocopherols differ in the molecule's tail. Tocotrienol has a shorter tail containing double bonds that reduce the activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the enzyme controlling cholesterol synthesis and the same enzyme targeted by statin drugs. Tocopherols, on the other hand, have a longer structural tail without these double bonds and are therefore unable to reduce cholesterol.

Another key difference between tocopherols and tocotrienols has to do with the various isomers. Alpha, beta, gamma, and delta are among the isomers of tocotrienols as well as tocopherols. For tocotrienols, delta has the strongest cholesterol inhibition potency followed by gamma, alpha and beta. Only delta and gamma isomers found in tocotrienols are effective at lowering cholesterol due to the substitution and location of methyl groups at the head region of the molecule. Methyl groups are the simple addition of a carbon to 3 hydrogen molecules–CH3. Tocotrienols with less methyl groups are called desmethyl tocotrienols and they are more active, tremendously affecting the health properties of this portion of vitamin E. Delta- and gamma-tocotrienols are desmethyl tocotrienols and are therefore the only two isomers that fit this cholesterol-reducing molecular formula. Tocopherols do not have the same advantageous molecular structure associated with lowering of cholesterol.

Mechanism of Action

Tocotrienols positively affect lipids in the body thanks to their ability to suppress the activity of HMG-CoA reductase.10-11 Recently, it was reported that only gamma- and delta-tocotrienol stimulate the degradation of the HMG-CoA reductase.12

In addition, gamma- and delta-tocotrienol block processing of a certain protein that helps control the LDL receptor and genes in charge of cholesterol-creating enzymes. This may influence triglyceride synthesis (or reduction) with importance in prediabetic and diabetic conditions. Other vitamin E forms (all four tocopherols and alpha- and beta-tocotrienol) do not degrade, downregulate, or block this cholesterol-controlling protein—only gamma- and delta-tocotrienol possesses this ability.12

Other Heart-Supporting Actions

Metabolic Syndrome and Triglycerides

An estimated 16 percent of people in the US, 47 million, have metabolic syndrome13 with defining hallmarks such as increased waist circumference, increased serum triglyceride levels, high blood pressure (hypertension), elevated serum glucose, and insulin resistance.14-15

Tocotrienols, especially gamma- and delta-tocotrienols, increase the heart's vascular and metabolic integrity, leading to improved management of metabolic syndrome. When blood sugar is high, it encourages the formation of advanced glycosylation end-products (AGEs). AGEs are formed when sugars react with proteins in the body, causing a process called cross-linking that is tied to premature aging. Cross-linking increases the stiffness of tissues, decreasing their function, such as during cataract formation, which is a classic example of cross-linking. Studies on rats in which diabetes was induced showed that gamma- and delta-tocotrienol prevented the increase of serum AGEs that occurred in animals not given tocotrienols. Administration of tocotrienols also resulted in a decrease in blood glucose and glycosylated hemoglobin (HbA1c). 16 Lower HbA1c levels indicate better blood sugar control, whereas higher levels indicate how severely diabetes is progressing and the rate at which AGEs are being formed.

Tocotrienols have an effect on another metabolic syndrome component—high triglyceride levels. Rice bran oil containing tocotrienols lowered plasma triglyceride levels, LDL cholesterol, and hepatic triglyceride concentration, suppressing unbalanced lipid levels in diabetic rats.17

In several clinical studies with metabolic syndrome patients or diabetic patients, even small amounts of rice bran tocotrienols were shown to reduce symptoms. An aqueous extract of water soluble compounds from rice bran reduced hyperglycemia, glycosylated hemoglobin and insulin levels, while rice bran fiber reduced high lipid levels in both type 1 and type 2 diabetics.18 In another large clinical study, vitamin E intake from diet was associated with reduced type 2 diabetes risk.19 In type 2 diabetic patients, atherosclerosis progression is more rapid, and 80 percent of patients die of atherosclerotic events. In addition, LDL-lowering therapies normally prescribed for diabetic patients have many side effects, creating a need for alternative approaches. Tocotrienols, which have no known side effects, were shown to decrease serum total lipids by 23 percent, total cholesterol by 30 percent and LDL-cholesterol by 42 percent (from 179 mg/dL to 104 mg/dL) within 60 days in type 2 diabetics.20 Supplementation of 75 mg/day delta-tocotrienol in a small open study was found to promote metabolic health, where triglyceride levels dropped 20-30 percent.2

Arterial Health

One of the first steps in atherosclerosis development is fatty streak formation in the arteries. This begins when circulating monocytes—white blood cells that

are the first line of defense in the inflammatory process—adhere to the endothelium (cells that line the blood vessels). Although the monocytes are operating with the best intentions—they are trying to fight the inflammatory process—their adhesion to the cells of the artery walls reduces blood flow. Tocotrienols reduce expression of cellular adhesion molecules, preventing monocytes from tethering to the artery walls.21

Delta-tocotrienol showed the most profound inhibitory effect on monocyte cell adherence as compared to tocopherols and other tocotrienol isomers.22 It has been suggested that this phenomenon occurs because delta-tocotrienol inhibits vascular cell adhesion molecules (VCAM-1), which play a key role in allowing monocytes to cling to the artery walls.23

Another step in atherosclerosis development is the formation of unstable plaques, which occurs when platelets aggregate at the inner, inflamed surfaces of blood vessel walls, forming clots and eventually blocking arterial blood flow. In a human double-blind crossover study, delta-tocotrienol was significantly more potent in the inhibition of platelet aggregation than the other tocotrienol isomers, giving an overall inhibition of 71 percent, as compared to 5-37 percent with other tocotrienols.24

Tocotrienols' effects on this inflammatory thickening of the walls of the larger arteries have also been compared in animals. Mice fed a diet designed to induce atherosclerosis were simultaneously given a diet rich in desmethyl tocotrienols. The mice receiving tocotrienols had a 60 percent lower plasma cholesterol level than the control group on the same diet without supplementation. Furthermore, atherosclerotic lesion size was reduced 10-fold in the tocotrienol group. Alpha-tocopherol, on the other hand, had no effect. This finding was further corroborated in a similar independent study where desmethyl tocotrienols inhibited atherosclerotic lesions in a mouse model of high cholesterol. Atherosclerotic lesion size in mice supplemented with desmethyl tocotrienols decreased 42 percent, whereas in the mice given alpha-tocopherol, mean lesion size decreased only 11 percent.25 In another study, after tocotrienols supplementation, atherosclerotic lesion size in mice was 92-98 percent smaller than in the alpha-tocopherol and control groups.26 The reason why desmethyl tocotrienols showed such promising effects is because, as previously mentioned, fully methylated tocotrienols and tocopherols do not have the cardiovascular benefits characteristic of desmethyl tocotrienols.27

Another study of patients with carotid artery arteriosclerosis, the blocking of the artery supplying oxygen to the brain, showed that tocotrienols supplementation caused regression of carotid atherosclerosis over four years. In 88 percent of patients who took the tocotrienols, carotid artery stenosis regressed or stabilized. Of the placebo group, 60 percent deteriorated, and only 8 percent improved.28-29 Interestingly, total cholesterol decreased 14 percent and LDL cholesterol fell 21 percent in the tocotrienol group during the third and fourth

year of the study.30

Antioxidant Activities

Antioxidants play an important role in slowing atherosclerosis, especially by preventing LDL cholesterol oxidation, a process where fats essentially turn rancid in the body after being subjected to free radical damage (also known as lipid peroxidation). In a study evaluating the antioxidant efficiency of tocotrienols in inhibiting lipid peroxidation, reactive oxygen species (ROS) production, and other oxidation markers, delta-tocotrienol was found to have the greatest antioxidant properties among the tocotrienol isomers,31 due to the molecule being more easily incorporated into cell membranes.2 A comparative *in vitro* study showed that a mixture of gamma- and delta-tocotrienol was 4-fold more efficient as scavenger of free radicals than other tocotrienol isomers.32

Blood Pressure

Hypertension can also damage arterial walls, making them more susceptible to plaque formation. In recent animal studies, tocotrienols were shown to lower blood pressure. When hypertensive rats were given gamma-tocotrienol, an example of a desmethyl tocotrienol, for three months plasma and blood vessel lipid peroxides were reduced, and total antioxidant status was improved.33 Gamma-tocotrienol reduced systolic blood pressure significantly, and improved nitric oxide synthase activity (NOS), both of which play a critical role in the pathogenesis of essential hypertension.34 Tocotrienols' impact on hypertension was confirmed in humans, where tocotrienol-rich vitamin E supplementation resulted in significant reductions in aortic systolic blood pressure and a 9.2 percent improvement in total antioxidant status.35

Annatto: Unique Source of Tocotrienols

As mentioned previously, tocopherols do not have tocotrienols' cholesterol-lowering ability. In fact, alpha-tocopherol has been shown to attenuate or interfere with gamma- and delta-tocotrienols' cholesterol-lowering action.3 Therefore, it is important to find a supplement with a high tocotrienols content (especially gamma- and delta-tocotrienol) and a low tocopherols content. “Rice tocotrienols” contain about 50 percent tocotrienols and 50 percent tocopherols. “Palm tocotrienols” contain approximately 75 percent tocotrienols and 25 percent tocopherols. However, a little known tropical-rainforest-derived plant called Annatto ranks highest in tocotrienol content. Annatto contains 100 percent tocotrienols, and is virtually tocopherol-free. A special patented, solvent-free extraction of Annatto seeds produces the two most effective tocotrienol isomers: 90 percent delta-tocotrienol and 10 percent gamma-tocotrienol. Annatto is the only source of tocotrienols that contains 100 percent desmethyl tocotrienols and virtually no tocopherols.

Annatto-derived tocotrienols should be consumed 6 or more hours away from a multivitamin or other vitamin E supplement, due to the tocotrienol-inhibiting

ability of tocopherols (the form used in most multivitamins and vitamin E supplements).

Conclusion

Tocotrienols possess powerful cholesterol-lowering and heart-supporting properties not exhibited by tocopherols.36 Tocotrienols can help with premature aging associated with AGEs and support healthy cholesterol and blood pressure levels, arterial health, blood sugar regulation, and antioxidant protection. Gamma- and delta-tocotrienols have been found to be the most effective forms of vitamin E and are powerful antioxidants working at the cells' surface. Annatto is a particularly rich source of gamma- and delta-tocotrienols. It is virtually tocopherol free, indicating it is a superior choice for a vitamin E supplement that produces documented support for the heart and entire vascular system.

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