*Dr. Jonathan V. Wright's*

# NUTRITION & HEALING

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# Learn the WHOLE TRUTH about vitamin E
# The little-known healing potential of tocotrienols is finally revealed

*By Jonathan V. Wright, M.D.*

It was just five months ago (*Nutrition & Healing*, August 2013) that you read that the growth of pancreatic cancer cells—remember, pancreatic cancer has a 5% five-year survival rate—can be significantly slowed by two of the four forms of the tocotrienol family of the E vitamins, specifically the delta- and gamma-tocotrienol varieties. This month, we'll review other uses and potential uses for tocotrienols. But a little background first.

Tocotrienols are the "second family" of E vitamins. (The "first family" are the more familiar "tocopherols".) Both exist in alpha, beta, delta, and gamma forms. The tocopherol form of vitamin E has been studied (and frequently mis-studied) since 1922, when it was first isolated from green leafy vegetables by two Berkeley researchers. It was called "fertility factor" at that time because a deficiency of it led to infertility (in animal studies) and spontaneous abortion. When tocopherols are deficient in the diet, difficulty with voluntary movement, (technically, ataxia), can develop. Another form of deficiency seen with low vitamin E is a muscle degeneration that resembles Duchenne muscular dystrophy.[1]

Tocotrienol research is much more recent. Tocotrienols are more reactive (for the technically inclined, they have more "double bonds") than tocopherols. "Delta" and "gamma" forms in each of the two vitamin E families are smaller than the "alpha" and "beta" forms, which also allows them to be metabolically more active.

The various forms of vitamin E are found in a wide variety of foods, particularly oils, including wheat bran, oat, coconut, grape seed, and in meats, eggs, and avocados, as well as foods we don't normally associate with vitamin E, including carrots, cauliflower, blueberries, almonds, and grapes.[2]

In Nature, no one member of either vitamin E family is found all by itself, without another of the family members (for the technically inclined, "isoforms" of its family). Most often, all four of the tocopherols or all four of the tocotrienols are found together in varying concentrations, although in a few instances—delta combined with gamma tocotrienols are currently the best known—there are fewer than four in a particular group. But **never** just one!

This is why when alpha-tocopherol (misidentified as "vitamin E," which actually includes all eight forms listed above) when used alone in research has led to several negative, and well-publicized, reports.[3] Some researchers have even used a synthetic, non-bioidentical and un-Natural form of "vitamin E," dl-alpha-tocopherol, (still sold in discount warehouse stores) and when they got the very predictable poor results they proclaimed that "vitamin E is bad for you." Finally, after much "vitamin E is bad for you" fuss, researchers have figured out that those bad effects they had observed didn't occur if the "vitamin E" is used as Nature provides it, as a group of two or more vitamin E family members. (Duh!) But let's get back to the positive effects of tocotrienols.

## Curb cancer with tocotrienols?

In part, the anti-cancer properties of most forms of vitamin E are due

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to their well-known antioxidant capability.[4] But the anti-cancer potential of *tocotrienols* goes well beyond antioxidation, and beats the anticancer properties of tocopherols by a mile. Tocotrienols have been shown to have the ability to inhibit many different cancer cell types, including colon, skin, lung, liver, breast,[5] pancreatic, and prostate cancers.

The delta and gamma forms of tocotrienols and tococopherols are considered to be the most anti-carcinogenic.[6] According to one research report, alpha tocopherol doesn't have any cancer preventive properties at all.[7] In fact, the SELECT study (the one that actually studied alpha tocopherol, selenium and prostate cancer risk, but was misused to "prove" that omega-3 fatty acids raise prostate cancer risk) reported that alpha tocopherol actually increased the risk of prostate cancer.[8] But gamma tocopherol has protective benefits in prostate cancer[9,10] so if this research had been done with Nature's full pattern of tocopherols, the outcome would have been very different!

## Starve and kill cancer cells

The tocotrienols, as compared to the tocopherols, may be much more effective at reducing the spread of many types of cancers by encouraging apoptosis (in English, cell death). For the technically inclined, the way tocotrienols accomplish apoptosis is by activating a protein important to the pathway responsible for cell death in cancer cells known as caspase-3.[11]

Tocotrienols are also showing much promise in their ability to reduce "neo-angiogenesis," the formation of brand-new blood vessels that provide nourishment to cancer cells and tumors.[12] Tocotrienols inhibit neo-angiogenesis (for the technically inclined, by down-regulating receptors for vascular endothelial growth factor or "VEGF"), causing cancer cells to die through starvation.[13] Tocotrienols also reduce inflammation *within* cancer cells! (For the technically inclined, the mechanisms have been found to include reducing inflammatory cytokines, such as NF-KB, COX-2, and STAT3.[14])

Tocotrienols are protective for our hearts because of their ability to lower cholesterol and triglycerides.[15,16] Like the recently introduced, entirely natural supplement bergamot (more details in *Nutrition & Healing*, August 2013), tocotrienols lower cholesterol by inhibiting HMG CoA reductase, the final enzyme in cholesterol production, which is also the enzyme target for the much more dangerous patent statin medicines.

## Better brain support with vitamin E

In a study of adults over the age of 65 involving 168 with Alzheimer's disease, 166 with mild cognitive impairment, and 187 who were cognitively normal, lower levels of both tocopherols and tocotrienols were associated with an increased risk of cognitive changes. Those with mild cognitive impairment had plasma vitamin E (both tocopherol and tocotrienol) levels 15% lower than those with normal cognitive function. Those with Alzheimer's disease had levels 8% lower.[17] The development of cognitive decline in the individuals studied may be linked to increased oxidative damage, as evidenced by increased plasma level markers associated with low vitamin E and oxidative stress. The antioxidant properties of the tocopherols and tocotrienols might be helpful in reducing oxidative damage in the brain.

The association between tocotrienols and cognitive impairment was also demonstrated in a Finnish study

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in which 140 adults who were cognitively normal were followed for 8 years to detect the development of any cognitive changes. Researchers confirmed that those with the highest levels of beta and gamma tocotrienols and total tocotrienols had a lower risk of cognitive impairment.[18] Other studies suggest that the tocotrienols may have potential in the treatment of cognitive impairment.[19]

The potential neuroprotective benefits of alpha-tocotrienol on cerebrovascular circulation after ischemic (lack of blood flow) stroke were recently demonstrated in an animal study. Over the course of a 10-week study, animals were treated with either 200 mg of alpha-tocotrienol given twice daily or a placebo. At the end of the trial, analysis showed that there was reduced brain injury following stroke and increased cerebrovascular circulation, suggesting it could have benefit in the prevention of transient ischemic attack ("TIA," lack of blood flow for a short time) and stroke incidence in patients at risk.[20]

## Could help reverse diabetes and obesity

One research report using delta-tocotrienol from annatto beans in animals found that metabolic syndrome and obesity were improved after eight weeks of supplementation. Abdominal adipose tissue and waist circumference were reduced. The researchers also reported that there was improvement in glucose levels, symptoms of insulin resistance, and blood pressure along with reduction in ventricular stiffness.[21, 22]

Diabetic neuropathy and pain was induced in experimental animals that were then treated with 25, 50 or 100 mg/kg of tocotrienols over a 4 week period. At the end of the study, researchers reported a reversal of diabetic neuropathy when tocotrienol was combined with insulin. They also reported a reduction in oxidative stress and less release of inflammatory cytokines.[23]

## Tame tummy troubles with vitamins

As noted earlier, tocotrienols have shown anti-inflammatory properties, and tocopherols do also. Switching just for a moment to the alpha tocopherol form of vitamin E leads us to a potentially useful reseach study which found it to be significantly helpful in reducing ulcerative colitis inflammation in experimental animals (For the technically inclined, alpha-tocopherol reduced levels of tumor necrosis factor alpha and other inflammatory cytokines.) The researchers suggested vitamin E might be a potent therapy in the treatment of human ulcerative colitis.[24] But back to tocotrienols: Research is identifying the enzymes that the tocotrienols inhibit and the cell signaling pathways that are targeted to reduce inflammation.[25,26]In an animal study involving rats made deficient in vitamin E, the addition of either tocopherols or tocotrienols protected the gastrointestinal tract from oxidative damage and stress. Not only that, the tocotrienols also blocked changes in stomach acidity and gastrin (a hormone which stimulates stomach acid production).[27]

## Better bones with tocotrienols

While the importance of tocopherols in bone mineralization and osteoporosis protection has long been established, only a few studies have examined the effects of *tocotrienols* in this process. One animal study compared the effects of alpha tocopherol and gamma and delta tocotrienols on specific bone parameters. One control group of male rats wasn't given any tocopherols or tocotrienols at all. The other three groups were given the same amounts of alpha tocopherol or delta or gamma tocotrienol. After four months, their bone structure was evaluated. The researchers reported that all the animals receiving either tocotrienol did better than the any of animals on alpha tocopherol. Gamma tocotrienol helped the most.[28]

### Foods that contain forms of vitamin E

- wheat bran
- oat oil
- coconut oil
- grapeseed oil
- meats
- eggs
- avocados
- carrots
- cauliflower
- blueberries
- almonds
- grapes

## Reduce age spots naturally

In a very small study of facial age spots in 13 women, some were asked to use a delta and gamma tocotrienol containing skin cream, and some used the same cream but without any tocotrienols. After one month, the age spots in those women receiving tocotrienol-containing skin cream showed "observable skin lightening." The women using the same skin cream without tocotrienols had no change in their age spots.[29]

Facial age spots are in part caused by a local excess in production of melanin, the natural biochemical that (among other things) gives pigment to our skins. Studies have reported that gamma and delta tocotrienols decrease the activity of the enzymes responsible for melanin synthesis without showing any signs of toxicity over time.[30,31]

## Rapid recovery from radiation exposure; anti-bacterial action

Delta and gamma tocotrienols have been studied for their ability to protect the body from radiation

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damage.[32,33] Gamma tocotrienol was found to offer the most potent protection. One of the effects of radiation exposure is failure of the body to produce many types of blood cells ("pancytopenia"). There was a more rapid recovery of the levels of many blood cells, including white cells, platelets, monocytes and reticulocytes in mice given gamma tocotrienol than mice not given it. The researchers concluded that gamma tocotrienol offers great promise in as a protector from radiation for humans.[34] Other researchers reported that delta and gamma tocotrienols restored blood cell levels to normal in animals receiving them while the animals who received none had no recovery.[35,36]

Tocotrienols have shown some antibacterial activity against chlamydia, most likely because of its cholesterol reducing effect covered earlier. Chlamydia is dependent on cholesterol to reproduce in the cells it infects and evidence suggests that tocotrienols may inhibit chlamydia growth by interfering with this process.[37]

## Should tocotrienols be supplemented?

Should we supplement with tocotrienols to support health? While we should always turn to food sources to obtain nutrients first, tocotrienols are not found in very many foods. The best known source is palm oil, which also contains naturally occurring saturated fats. Other food sources include rice bran and oats. Supplements appear to be necessary if we're not using these food sources, or if we have any of health problems that tocotrienols may help.

## How to determine dosages

Studies are underway to determine the effective dosing of tocotrienols for a variety of health conditions. One of these is a phase 1 dosing study of surgically treatable pancreatic cancer using delta-tocotrienol. Evidence to date shows effectiveness in treatment ranging from a low of 200 mg a day to as high as 3,200 mg a day, without adverse effects.[38] To lower cholesterol and triglycerides, one clinical study found that 100 mg a day was the best dose to achieve results.[39] Another study of cholesterol-lowering doses conducted in an animal model showed the likely safe ranges of dosing of tocotrienols (in humans) from 200 to 1000 mg a day.[40]

Absorption of the alpha, gamma and delta tocotrienols appears to be best when taken with food.[41] However, leading tocotrienol researcher Barrie Tan Ph.D. tells us to avoid taking tocotrienols at the same time as alpha tocopherol, or they won't be absorbed as well. If you want to get the full advantages of all the forms of vitamin E supplementation, take tocopherols and tocotrienols separately, at least a few hours apart. JVW