Tocotrienols – The Missing Vitamin E

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Tocotrienols

Natural vitamin E comprises 8 different analogues, the alpha-, beta-, gamma-, and delta-tocopherols and the alpha-, beta-, gamma-, and delta-tocotrienols. However, only alpha-tocopherol is selectively enriched by the liver; the other vitamin E analogues and also excess alpha-tocopherol are converted to several metabolites and eliminated. (Zingg 2007) (Sen, Khanna et al. 2007) (Sen, Khanna et al. 2006)

Sources

Palm oil and rice bran oil represent two major nutritional sources of natural tocotrienol. (Sen, Khanna et al. 2007) Amaranth grain contains tocotrienols and squalene compounds, which are known to affect cholesterol biosynthesis. (Martirosyan, Miroshnichenko et al. 2007)

One study showed that intestinal epithelial cells absorb gamma-tocotrienol faster than alpha-tocopherol. (Tsuzuki, Yunoki et al. 2007)

Therapeutic Effects

Symptoms caused by alpha-tocopherol deficiency can be alleviated by tocotrienols. The tocotrienol forms of natural vitamin E possess powerful properties that are often not exhibited by tocopherols, including:

- Lowering cholesterol and cardioprotection
- anti-cancer, and
- neuroprotection.

Cardioprotection

Tocotrienols may have potent cardioprotective properties. (Das, Nesaretnam et al. 2007)

Tocotrienols may help prevent atherosclerosis:

One study showed that delta-tocotrienol inhibited monocyte cell adherence to human aortic endothelial cells, whereas 25-hydroxycholesterol enhanced it. An earlier study found the same mechanism for alpha-tocopherol. (Naito, Shimozawa et al. 2005) (Theriault, Chao et al. 2002)

Tocotrienols lower cholesterol and improves the lipid profile:

A randomized, double blind, placebo-controlled study involving 19 type 2 diabetic subjects with hyperlipidemia examined the effects of vitamin E and tocotrienols. After 60 days of tocotrienol rich fraction treatment, subjects showed an average decline of 23, 30, and 42% in serum total lipids, total cholesterol, and LDL-C, respectively. Tocotrienols
mediated a reduction of LDL-C from an average of 179 mg/dl to 104 mg/dl. (Baliarsingh, Beg et al. 2005)

**Neuroprotection**

Several studies have found that alpha-tocotrienol is much more potent than alpha-tocopherol in protecting neuronal cells against toxicity induced by glutamate and other toxins. (Sen, Khanna et al. 2004) (Osakada, Hashino et al. 2004)

- Alpha-tocotrienol may be neuroprotective by antioxidant-independent as well as antioxidant-dependent mechanisms. (Khanna, Roy et al. 2006)
- Alpha-tocotrienol protects against glutamate- and stroke-induced neurodegeneration. (Khanna, Roy et al. 2005)

**Cancer**

Several studies have found that tocotrienols, especially delta-tocotrienol, have anti-cancer properties, primarily by inhibiting angiogenesis.

- Oral administration of tocotrienols resulted in significant suppression of liver and lung carcinogenesis in mice. Delta-tocotrienol exerted the most significant antiproliferative effect. (Wada, Satomi et al. 2005)
- One study found that tocotrienol inhibited the proliferation of bovine aortic endothelial cells, which may make it useful in preventing tumor angiogenesis. (Miyazawa, Inokuchi et al. 2004)
- A detailed study of the anti-cancer properties of tocotrienol found that apoptosis in colon carcinoma cells is mediated by p53 signaling network which appears to be independent of cell cycle association. The mechanisms included induction of WAF1/p21 and alteration in Bax/Bcl2 ratio in favor of apoptosis. (Agarwal, Agarwal et al. 2004)
- One study found that tocotrienol inhibited both the proliferation and tube formation of bovine aortic endothelial cells, with delta-tocotrienol having the highest activity. Also, delta-tocotrienol reduced the vascular endothelial growth factor-stimulated tube formation by human umbilical vein endothelial cells. (Inokuchi, Hirokane et al. 2003)

**Breast Cancer**

Tocotrienols are potent antioxidants that have significant anti-tumor activity and may provide significant health benefits in lowering the risk of breast cancer in women. (Sylvestre and Shah 2005) (Kline, Yu et al. 2004) (Schwenke 2002)

Several studies have examined the anti-tumor mechanisms of tocotrienols:

- Initial research found that tocotrienols induce programmed cell death (apoptosis). (Shah and Sylvester 2005)
- Alpha-tocopherol was found to increase in caspase-8 activity, which initiates apoptosis; and increase capase-3 activity, which induces apoptosis. (Sylvestre and Shah 2005)
- Gamma-tocotrienol was found to inhibit neoplastic mammary epithelial cell proliferation by decreasing Akt and nuclear factor kappaB activity. (Shah and Sylvester 2005)
One study examined the effects of tocotrienols from palm oil on estrogen-dependent (MCF-7) and estrogen-independent (MDA-MB-231) human breast cancer cells. Tocotrienol supplementation modulated significantly 46 out of 1200 genes in MDA-MB-231 cells. In MCF-7 cells, tocotrienol administration was associated with a lower number of affected genes. (Nesaretnam, Ambra et al. 2004)

Researchers at the Palm Oil Research Institute of Malaysia found that tocotrienols inhibited growth of ZR-75-1 breast cancer cells. The authors concluded that there might be clinical advantage in using tocotrienols along with anti-estrogen therapy for breast cancer. (Nesaretnam, Dorasamy et al. 2000)

**Prostate Cancer**

Early research has found that tocotrienols may inhibit prostate cancer. (Conte, Floridi et al. 2004)

Tocotrienols extracted from palm oil resulted in G0/G1 phase arrest and sub G1 accumulation in three prostate cancer cell lines. (Srivastava and Gupta 2006)

**Sodium Secretion**

One study found that gamma-tocotrienol stimulates sodium excretion in vivo, suggesting that gamma-tocotrienol possesses a hormone-like natriuretic function. (Saito, Kiyose et al. 2003)

**Osteoporosis**

Obesity and osteoporosis are known side effects of long-term glucocorticoid treatment. One study found that palm gamma-tocotrienols resulted in weight-loss and an increase in the fourth lumbar vertebra bone calcium content of adrenalectomized rats replaced with two doses of dexamethasone, 120 microg/kg and 240 microg/kg daily. (Ima-Nirwana and Suhaniza 2004)
References


