Cellular Health
Beyond Antioxidation

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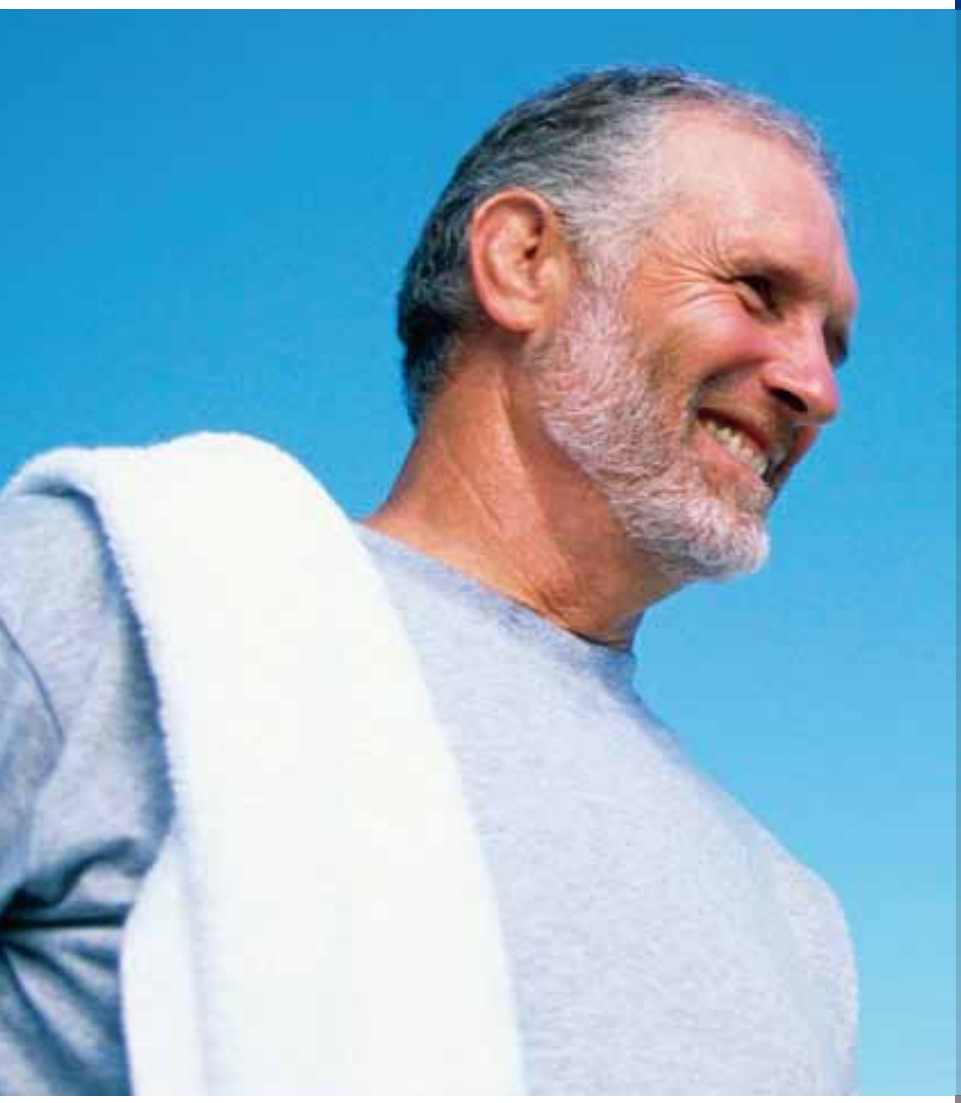
Merging Science with Nature



Natural e3™
DavosLife Tocotrienols

Cancer:
A Preventable Modern Day Epidemic

Despite the enormous amount of research during the past many decades, cancer remains the second leading cause of death globally. According to the World Health Organisation, it is one of the most preventable non-communicable chronic disease with up to 40% of all cancer deaths avoidable[1]. Certain cancers can be prevented through changes in nutrition and lifestyle modifications[2]. For example, habitual consumption of foods high in ingredients that protect against cancer is one of the important ways to prevent cancer risk[3].

Antioxidation

Antioxidants play a role in keeping our bodies healthy and reducing cancer risk by protecting our cells from the adverse effects of free radicals[4].

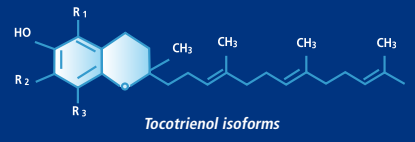
Free radicals are normally produced in the body as by-products of bodily functions and metabolic processes. When free radicals are generated excessively by stress, cigarette smoke and certain diets, they may damage cell DNA, proteins and lipids. Cells are covered by a lipid membrane layer which are prone to free radical damage through lipid peroxidation that can cause adverse cellular effects[5]. Cellular damage lays the groundwork for cancer and other illnesses[4].

Tocotrienol and tocopherol (the more common form of vitamin E) are well-known lipid antioxidants that constitute the Vitamin E family. Tocopherols and tocotrienols are found naturally in various types of plant seeds, ranging from wheat, rice, soybean, palm and grape seed to peanut, walnut and pecan. Most of these seeds contain only tocopherols; only a few contain both compounds. Tocotrienols are found mainly in palm fruit and from wheat and rice bran which form the hard outer layer covering the seed beneath the husk. It is believed that tocopherols and tocotrienols are nature's way of protecting seeds and seedlings from the damaging effects of ultraviolet light and oxidation[6]. Unfortunately for modern man, wheat and rice bran are removed during the processing of grains into white wheat flour and polished white rice, hence removing the natural full spectrum vitamin E from his diet.

Tocotrienol Delivers Excellent Antioxidation in Lipid Systems

As compared to tocopherols, tocotrienols have up to 60 times more powerful antioxidation properties in the body due to its more uniform distribution in cell membranes, stronger effect on membrane lipids and its higher recycling efficiency by the body[7]. Another study showed that cellular uptake of tocotrienols is up to 70 times faster initially than tocopherol[8]. It is tocotrienol's distinct chemical structure in the unsaturated double bonds in its tail as compared to saturated bonds of tocopherols that gives it health properties not seen in tocopherols.

A randomized, double-blind, placebo-controlled study of 64 subjects aged 37-78 years old showed a significant reduction of DNA damage in their blood samples after 3 months of 160 mg daily dose of tocotrienols and the positive effects continued to the end of the trial at 6 months[9].



Tocotrienol isoforms

α: R_1=CH_3 R_2=CH_3 R_3=CH_3 β: R_1=CH_3 R_2=H R_3=CH_3
γ: R_1=H R_2=CH_3 R_3=CH_3 δ: R_1=H R_2=H R_3=CH_3

Natural e³

DavosLife Tocotrienols

Davos Life Science (DavosLife) was established in 2004 as the world's largest tocotrienol manufacturer and research company. Currently, DavosLife Tocotrienols are sold to leading international nutraceutical and cosmeceutical finished product manufacturers under the brand name, Natural e³.

Cellular Wellness Beyond Antioxidation

Most antioxidants that are available in the market are simply different types of antioxidants that do not have much bioactivity beyond antioxidation. Keeping cells healthy through anti-oxidation alone may not be enough. Cancers develop through a variety of causes not only from free radical attack, but also from natural mutations in DNA, viruses and carcinogens in our diet and environment.

Although tocotrienols are powerful anti-oxidants, research has shown that they provide excellent bioactivity beyond antioxidation, including its well-studied cholesterol- and triglyceride- lowering[10,11] neuroprotective[12] and anti-tumor properties[13] that are not found in other antioxidants.

Over 200 research studies have shown that tocotrienols have powerful anti-cancer properties not found in alpha-tocopherol. These studies show that tocotrienols can induce apoptosis or cell death in prostate, breast, skin, pancreas, liver and colon cancer cells, while leaving normal cells healthy[13]. For cancer to develop, it requires an environment that will support its growth. This entails sufficient blood supply that will carry oxygen and nutrients to the cancer cells. Tocotrienols has been shown to be able to inhibit the formation of new blood vessels (angiogenesis) which can inhibit cancer growth and tumour development[14]. It has also been shown to reduce the propensity of cancer cells to spread (metastasis)[15].

Anti-inflammation

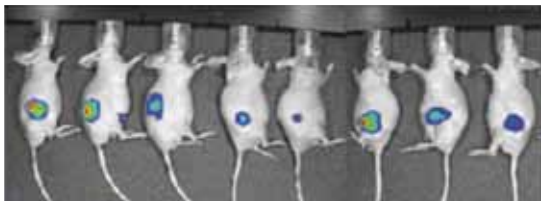
The NF-kappaB transcription factor plays a central role in the regulation of inflammation and immune responses. Consequently, NF-kappaB dysregulation has been implicated in the development of diverse forms of diseases including certain cancers. Researchers from a leading cancer center in the United States found that gamma-tocotrienol suppresses NF-kappaB activation while gamma-tocopherol has no effect. They reported that "Overall, our results demonstrate that gamma-tocotrienol is a potent inhibitor of NF-kappaB activation, which may explain its anti-angiogenic, anti-proliferative, pro-apoptotic, anti-metastatic, anti-inflammatory, and immunomodulatory effects". They further pointed out that their "data are in agreement with other published reports that tocotrienol is a superior molecule among the members of the family of Vitamin E"[16].

Research by DavosLife

A research study by DavosLife showed that tocotrienols could kill prostate cancer stem cells unaffected by docetaxel, an anti-cancer drug. Cancer stem cells are believed to be involved in the initiation and recurrence of cancer. In the study, DavosLife also showed that tocotrienols prevented prostate cancer formation in 75% of mice pre-treated with tocotrienols as compared to the control group[17].

Natural e³ prevents prostate cancer formation in mice models through prostate cancer stem cell-targeting mechanisms

Control



Tocotrienol

Fig 1.Tocotrienol inhibits prostate tumor development in mice[17]

Natural e³ increases cancer cell death in pancreatic tumours

A phase I clinical trial of Natural e³ delta-tocotrienol was carried out in patients with pancreatic cancer by researchers at the Moffitt Cancer Center & Research Institute in Florida, United States. For a period of 2 weeks prior to surgery, subjects received Natural e³ at various dose levels. This oral treatment occurred pre-surgery to examine the effect of Natural e³ on the resected pancreatic cancer tumours. Initial results revealed that Natural e³ was able to increase apoptosis (cell death) in pancreatic cancer tumours with no toxicity. They also found increased expression of p27, an important kinase inhibitor involved in the regulation of the cell cycle. Reduced levels of p27 have been found in some types of cancers[18].

DavosLife Natural e³

DavosLife produces Natural e³, containing the full-spectrum of tocotrienols (alpha, beta, delta and gamma isomers) extracted from non-GMO palm fruit. It is rich in gamma-tocotrienol, the tocotrienol isomer known for its potent cancer-fighting properties. DavosLife's tocotrienols are entirely natural, extracted only through proprietary purification processes that maintain the tocotrienols' original chemical forms while ensuring the production of high purity tocotrienols. Being FDA GRAS certified, Natural e³ is available in oil, powder and water-soluble forms that can be readily incorporated in food supplements, functional food and beverages.

Safety and Toxicity

Natural e^3 is granted Generally Recognised as Safe (GRAS) status by the US FDA. In a toxicology study conducted in rats, the no-observed-adverse-effect-level (NOAEL) for tocotrienols was at 303mg/kg/day, which is equivalent to over 2,000mg/day in humans[19].

DavosLife Patents

- *Use Of Tocotrienol Composition For The Prevention Of Cancer –PCT/SG2009/000390*

  Patent Granted: Singapore (2010)

  Patent Pending: US, Japan, EU, China, Malaysia

- *Delta Tocotrienol for the treatment of pancreatic cancer –PCT/SG2007/014912*

  Patent Pending: US, Japan, Singapore, EU, China, Malaysia

DavosLife Publications

Gamma-tocotrienol suppresses prostate cancer cell proliferation and invasion through multiple-signalling pathways. Br J Cancer. 2008 Dec 2;99(11):1832-41

Evidence of gamma-tocotrienol as an apoptosis-inducing, invasion-suppressing, and chemotherapy drug-sensitizing agent in human melanoma cells. Nutr Cancer. 2009;61(3):357-66

Id1, inhibitor of differentiation, is a key protein mediating anti-tumor responses of gamma-tocotrienol in breast cancer cells. Cancer Lett. 2010 May 28;291(2):187-99

In vivo evidence of gamma-tocotrienol as a chemosensitizer in the treatment of hormone-refractory prostate cancer. Pharmacology. 2010;85(4):248-58

Gamma tocotrienol as an effective agent in targeting prostate cancer stem cell-like population. International Journal of Cancer 2010 July 8

Reference:

1. WHO. The World Health Organization's Fight Against Cancer Strategies that Prevent Cure and Care. 2007. **2.** Desmond S. Diet and cancer--should we change what we eat? *West J Med* 1987;146(1):73–8. **3.** Glade MJ. Food, nutrition, and the prevention of cancer: a global perspective. American Institute for Cancer Research/World Cancer Research Fund. *Nutrition* 1999;15(6):523–6. **4.** Khan N, Afaq F & Mukhtar H. Cancer chemoprevention through dietary antioxidants: progress and promise. *Antioxid Redox Signal* 2008;10(3):475–510. **5.** Devasagayam TP, Tilak JC, Boloor KK, Sane KS, Ghaskadbi SS & Lele RD. Free radicals and antioxidants in human health: current status and future prospects. *J Assoc Physicians India* 2004;52:794-804. **6.** Krause GH, *et al*. Photoprotection, photosynthesis and growth of tropical tree seedlings under near-ambient and strongly reduced solar ultraviolet-B radiation. *J Plant Physiol* 2007; 164 (10):1311–22. **7.** Serbinova E, Kagan V, Han D & Packer L. Free radical recycling and intramembrane mobility in the antioxidant properties of alpha-tocopherol and alpha-tocotrienol. *Free Radic Biol Med* 1991;10(5):263–75. **8.** Saito Y, Yoshida Y, Nishio K, Hayakawa M & Niki E. Characterization of cellular uptake and distribution of vitamin E. *Ann N Y Acad Sci* 2004;1031:368–75. **9.** Chin SF, Hamid NA, Latiff AA, *et al*. Reduction of DNA damage in older healthy adults by Tri E Tocotrienol supplementation. *Nutrition* 2008; 24(1):1–10. **10.** Qureshi AA, Qureshi N, Wright JJ, *et al.* Lowering of serum cholesterol in hypercholesterolemic humans by tocotrienols (Palmvitee). *Am J Clin Nutr* 1991;53(4 Suppl):1021S–1026S. **11.** Zaiden N, Yap W, Ong S, Xu C, *et al.* Gamma Delta Tocotrienols Reduce Hepatic Triglyceride Synthesis and VLDL Secretion. *J Atheroscler Thromb* 2010. **12.** Rink C, Christoforidis G, Khanna S, *et al.* Tocotrienol vitamin E protects against preclinical canine ischemic stroke by inducing arteriogenesis. *J Cereb Blood Flow Metab* 2011. doi: 10.1038/jcbfm.2011.85. [Epub ahead of print] **13.** Aggarwal BB, Sundaram C, Prasad S & Kannappan R. Tocotrienols, the vitamin E of the 21st century: its potential against cancer and other chronic diseases. *Biochem Pharmacol* 2010;80(11):1613–31. **14.** Miyazawa T, Inokuchi H, Hirokane H, *et al.* Anti-angiogenic potential of tocotrienol in vitro. *Biochemistry* (Mosc) 2004; 69(1): 67–9. **15.** Yap WN, Chang PN, Han HY, *et al.* Gamma-tocotrienol suppresses prostate cancer cell proliferation and invasion through multiple-signalling pathways. *Br J Cancer* 2008; 99(11):1832–41. **16.** Aggarwal BB & Ahn KS. M.D. Anderson Cancer Center. Targeting Inflammation for Prevention and Treatment of Cancer by Tocotrienols: Food for Thought. PIPOC. 2007. **17.** Luk SU, Yap WN, Chiu YT, *et al.* Gamma-tocotrienol as an effective agent in targeting prostate cancer stem cell-like population. *Int J Cancer* 2011;128(9):2182-91. doi: 10.1002/ijc.25546. **18.** Springett G NA, Centeno B, Helm J, *et al.* A phase I dose escalation study of the safety, PK, and PD of vitamin E-tocotrienol administered to subjects with resectable pancreatic exocrine neoplasia. Poster presented at The Annual Meeting of the American Association of Cancer Research (AACR).2011. **19.** Tasaki M, Umemura T, Inoue T, *et al.* Induction of characteristic hepatocyte proliferative lesion with dietary exposure of Wistar Hannover rats to tocotrienol for 1 year. *Toxicology* 2008;250(2-3):143–50.

Derived from Nature
Driven by Science

World Leader in
High Quality, High Purity Palm Tocotrienols

DavosLife - No.1 Supplier Of High Purity Palm Tocotrienols

Stable Supply
DavosLife produces a 100% natural tocotrienol-rich complex extracted using standards of the highest quality from GMO-free palm fruit fully traceable to the plantations of its parent Company, the Kuala Lumpur Kepong Berhad Group. Natural e^3 contains a balanced blend of all tocotrienol isoforms (alpha, beta, delta, gamma) at high concentration levels for maximum health benefits.

Science Driven
DavosLife has established the world's largest tocotrienol R&D center to spearhead cutting-edge tocotrienol research and innovation in chronic diseases and skin care. It was awarded the 2010 Asia Pacific Excellence in Research Award in the Natural Vitamin E Market by Frost and Sullivan.

Unrivaled Technical Support
Our team of experienced in-house scientists is available to support your technical needs ensuring that you meet the demands of today's market.

Custom Formulations
We offer custom formulations for higher potencies to meet your needs.

Natural e^3™
DavosLife Tocotrienols

Available Products:

High Purity Palm Tocotrienol Oil
Up to 95% (total vitamin E)

Palm Tocotrienol Powder
Up to 30% (total vitamin E)

T3Boost™ - Water Soluble Tocotrienol
Up to 1.5% (total vitamin E)

Tocotrienol Isomers
up to 97% (alpha, beta, gamma, delta)

Palm Tocotrienol Analytical Test and Cell Culture Kits

GRAS Affirmed

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