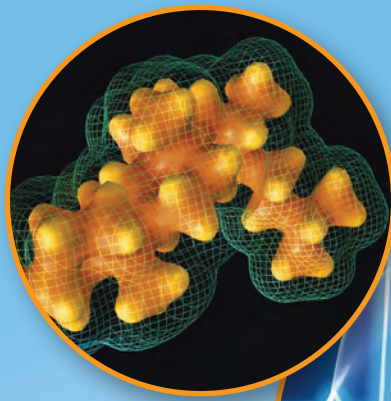




Matters Of The Heart

Tocotrienol And Cardiovascular Health



Every year, an estimated 16.7 million people succumb to heart disease, which now accounts for 29.2% of total global deaths. Many who survive continue to suffer painful symptoms or disabilities, in addition to reduced life expectancy.

Medical science has made much progress in reducing heart disease globally. But other than the sound advice of "eat right and exercise", many people obtain little information from their doctors on ways to prevent heart disease. Therefore, it is not surprising why many are now making an effort to learn how to ward off heart disease by monitoring new breakthroughs in medicine and natural remedies. Instead of focusing on treating the symptoms of heart disease, people are now seeking strategies to prevent heart disease from developing in the first place.



Natural e³
DAVOS Tocotrienols

Natural e³ – A 'Super Vitamin E'

Tocotrienol enjoys a growing status as a 'Super-Vitamin E', given the increasing volume of data confirming its superiority compared to the common Vitamin E 'd- α -tocopherol'. Derived from palm oil, Natural e³ is Davos Life Science's solution for food and supplement manufacturers who seek to offer the health benefits of Tocotrienol along with the assurance of a product high in quality and made without solvents. Backed by a growing library of research on its ability to maintain a healthy cardiovascular system, Natural e³ is your natural choice and partner to create a new generation of products that address the concerns of people who truly care for their heart.

REFERENCES

1. Schaffer, S., W.E. Muller, and G.P. Eckert, Tocotrienols: constitutional effects in aging and disease. *J Nutr*, 2005. 135(2): p. 151-4.
2. Hosomi, A., et al., Affinity for alpha-tocopherol transfer protein as a determinant of the biological activities of vitamin E analogs. *FEBS Lett*, 1997. 409(1): p. 105-8.
3. Ikeda, S., et al., Dietary alpha-tocopherol decreases alpha-tocotrienol but not gamma-tocotrienol concentration in rats. *J Nutr*, 2003. 133(2): p. 428-34.
4. Watkins, T., et al., gamma-Tocotrienol as a hypo-cholesterolemic and antioxidant agent in rats fed atherogenic diets. *Lipids*, 1993. 28(12): p. 1113-8.
5. Pearce, B.C., et al., Inhibitors of cholesterol biosynthesis. 2. Hypocholesterolemic and antioxidant activities of benzopyran and tetrahydronaphthalene analogues of the tocotrienols. *J Med Chem*, 1994. 37(4): p. 526-41.
6. Khor, H.T. and D.Y. Chieng, Effect of dietary supplementation of Tocotrienols and Tocopherols on serum lipids in the hamster. *Nut&ion Research*, 1996. 16(8): p. 1393-401.
7. Kamat, J.P. and T.P. Devasagayam, Tocotrienols from palm oil as potent inhibitors of lipid peroxidation and protein oxidation in rat brain mitochondria. *Neurosci Lett*, 1995. 195(3): p. 179-82.
8. Yu, S.G., et al., Dose-response impact of various tocotrienols on serum lipid parameters in 5-week-old female chickens. *Lipids*, 2006. 41(5): p. 453-61.
9. Tomeo, A.C., et al., Antioxidant effects of tocotrienols in patients with hyperlipidemia and carotid stenosis. *Lipids*, 1995. 30(12): p. 1179-83.
10. Rasool, A.H., et al., Arterial compliance and vitamin E blood levels with a self emulsifying preparation of tocotrienol rich vitamin E. *Arch Pharm Res*, 2008. 31(9): p. 1212-7.
11. Qureshi, A.A., et al., Response of hypercholesterolemic subjects to administration of tocotrienols. *Lipids*, 1995. 30(12): p. 1171-7.
12. Qureshi, A.A., et al., Novel tocotrienols of rice bran modulate cardiovascular disease risk parameters of hypercholesterolemic humans. *J. Nutr. Biochem*, 1997. 8: p. 290-8.
13. Rapola, J.M., et al., Randomised trial of alpha-tocopherol and beta-carotene supplements on incidence of major coronary events in men with previous myocardial infarction. *Lancet*, 1997. 349(9067): p. 1715-20.
14. Ness, A.R., Fruits and vegetables and cardiovascular disease: a review. *Int. J. Epidemiol.*, 1977. 26: p. 1-13.
15. de Gaetano, G., Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. *Lancet*, 2001. 357(9250): p. 89-95.
16. Davos Life Science unpublished clinical data.
17. Ultra Trienols Plus. Available from: <http://www.rockwellnutrition.com/assets/images/docs/utratrienolsplus.pdf>
18. Newaz, M.A. and N.N. Nawal, Effect of gamma-tocotrienol on blood pressure, lipid peroxidation and total antioxidant status in spontaneously hypertensive rats (SHR). *Clin Exp Hypertens*, 1999. 21(8): p. 1297-313.
19. Rasool, A.H., et al., Dose dependent elevation of plasma tocotrienol levels and its effect on arterial compliance, plasma total antioxidant status, and lipid profile in healthy humans supplemented with tocotrienol rich vitamin E. *J Nutr Sci Vitaminol (Tokyo)*, 2006. 52(6): p. 473-8.
20. Kuhad, A., et al., Suppression of NF-kappaB signaling pathway by tocotrienol can prevent diabetes associated cognitive deficits. *Pharmacol Biochem Behav*, 2009. 92(2): p. 251-9.
21. Wan Nazaimoon, W.M. and B.A. Khalid, Tocotrienols-rich diet decreases advanced glycosylation end-products in non-diabetic rats and improves glycemic control in streptozotocin-induced diabetic rats. *Malays J Pathol*, 2002. 24(2): p. 77-82.
22. Chao, J.T., A. Gapor, and A. Theriault, Inhibitory effect of delta-tocotrienol, a HMG CoA reductase inhibitor, on monocyte-endothelial cell adhesion. *J Nutr Sci Vitaminol (Tokyo)*, 2002. 48(5): p. 332-7.
23. Naito, Y., et al., Tocotrienols reduce 25-hydroxycholesterol-induced monocyte-endothelial cell interaction by inhibiting the surface expression of adhesion molecules. *Atherosclerosis*, 2005. 180(1): p. 19-25.

Heart Disease: Tackling It From The Top

Tocotrienol – More Than A Powerful Antioxidant

Tocotrienol and tocopherol are members of the Vitamin E family commonly accepted as powerful fat-soluble antioxidants. In the last decade, Tocotrienol has become increasingly recognized as a natural compound that plays a number of roles in supporting a healthy cardiovascular system, reducing the likelihood of heart disease and maintaining healthy cholesterol levels.

The basis of these beneficial properties is thought to be via Tocotrienol's down-regulation of the enzyme 3-Hydroxy-

3-methylglutaryl Coenzyme A (HMG-CoA) reductase, which in turn limits cholesterol synthesis in the liver. Recent research indicates that isomeric Tocotrienol displays a more varied tissue distribution and response pattern compared to tocopherol [1].

Further studies [2] demonstrate that alpha-tocopherol present in mixed Vitamin E preparations may actually compete with Tocotrienol for binding sites on the alpha-T transfer protein, a protein that transports Vitamin E around the human body. As a result, alpha-tocopherol may interfere with and reduce the bioavailability of Tocotrienol

by limiting the distribution of Tocotrienol to the body's tissues [3], thus compromising its ability to help support healthy cholesterol levels.

It is important to recognize that Tocotrienol preparations that are high in alpha-tocopherol (>30%) and low in gamma and delta-tocotrienol, such as those derived from rice bran, may be inferior in maintaining healthy cholesterol levels compared to preparations derived from palm oil that are naturally low in alpha-tocopherol while containing higher amounts of both gamma and delta-tocotrienol.

Tocotrienol And Cardiovascular Disease Management

Animal studies [4-7] through oral administration of Tocotrienol have shown an extraordinary impact on cholesterol levels, with total cholesterol levels falling by over 30% and a reduction in LDL cholesterol of almost 70%. In contrast, standard vitamin E (alpha-tocopherol) has little or no effect on cholesterol levels. In one study [8], HDL/LDL cholesterol ratios improved by up to 150% following administration of Tocotrienol.

Numerous clinical studies on the oral administration of Tocotrienol have shown an extraordinary impact on known cardiovascular disease factors, including reduction of cholesterol levels, cardiovascular inflammation, arterial hardening and triglyceride levels [9-12]. In contrast, the most commonly used vitamin E (alpha-tocopherol) has through various clinical studies been shown to have little or no beneficial effect towards reducing cardiovascular disease [13-15].

Clinical studies have generated strong evidence of the benefits that Tocotrienol can bring to the human cardiovascular system. In one study, after supplementation with Tocotrienol at 100mg per day, trial subjects' saw their

total cholesterol drop by up to 22% together with a 20% reduction in their LDL cholesterol levels. Furthermore, another study found a significant improvement in arterial compliance, a factor that may have promising implications on reducing arterial hardening and hypertension. Triglyceride levels, which are also strongly associated with heart disease, have also been shown to be reduced, falling by almost 20% [16, 17].

Other Benefits Of Tocotrienol

There is additional evidence that Tocotrienol may assist in reducing premature aging associated with advanced glycosylation end-products (AGEs) as well as support healthy blood pressure levels [18], arterial health [10, 19] and blood sugar regulation [20]. AGEs are formed when high blood sugar levels react with proteins, resulting in a cross-linking process linked to premature aging, tissue stiffness and decreased cellular function. Studies on diabetic rats demonstrate that Tocotrienol is able to reduce serum AGEs, blood glucose and glycosylated hemoglobin (HbA1c) [21].



Why Delta- And Gamma-Tocotrienol?

Compared to tocopherol and alpha-tocotrienol isomers, delta-tocotrienol has shown a strong inhibitory effect on monocyte cell adherence [22], due to its ability to inhibit vascular cell adhesion molecules (VCAM-1) that play a key role in helping monocytes bind to artery walls [23] and causing inflammation and arterial hardening. When hypertensive rats were given gamma-tocotrienol for three months, plasma and blood vessel lipid peroxides were reduced and the overall antioxidant status of the subjects improved [18]. The impact of Tocotrienol on hypertension has also been confirmed in human clinical studies, where Tocotrienol-rich vitamin E resulted in significant reductions in aortic systolic blood pressure and an improvement in total antioxidant status of almost 10% [19].

Tocotrienol

At A Glance



- ◆ Superior antioxidant properties (x60) in biological system compared to Vitamin E tocopherol
- ◆ Protects the body from damage by free radicals
- ◆ Supports cardiovascular and circulatory health
- ◆ Lowers LDL cholesterol
- ◆ Reduces the severity of atherosclerosis
- ◆ Lowers the risk of a second heart attack
- ◆ Inhibits cancer cells
- ◆ Highly bioavailable and safe when administered orally

Davos Life Science: A World Leader In Tocotrienol Research And Applications

The world's leader in Tocotrienol, Davos Life Science owns and operates a state-of-the-art manufacturing facility in Singapore to produce top-grade natural Tocotrienol. Under the Natural e³ brand, we offer both active single ingredients as well as signature formulations premixed for market-ready applications.

Our parent company, KLK Berhad, is a Malaysian conglomerate with 150,000 hectares of sustainable palm plantations managed to the highest quality and environmental standards. This assures Davos Life Science of a continuous supply of feedstock to support our clients worldwide.

Supporting Our Customers With Science

We also operate the world's largest R&D centre for Tocotrienol, located near the Tuas Biomedical Park in Singapore. Manned by a team of senior scientists, this custom-build laboratory is equipped for advanced work in analytical chemistry, organic chemistry, biochemistry and cell biology. There is also a pilot lab to isolate and purify natural ingredients for bioactivity testing.

Our laboratory reviews, archives and offers access to the most current journals in chemical, biochemical and medical research on Tocotrienol and other valuable plant lipid extracts. We also provide technical support to help you communicate the latest science and benefits of natural Tocotrienol to your consumers.

To learn about the functional properties of Natural e³ Tocotrienol and its use in food and nutraceutical products, please contact us at:

Davos Life Science Pte Ltd (A subsidiary of KLK)
16 Tuas South Street 5, Singapore 637795
Tel: 65 6513 9370 Fax: 65 6873 7106
Email: info@davoslife.com

