Tocotrienol: Emerging ingredient in cardiovascular health

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HO report states that cardiovascular disease (CVD) remains a leading cause of death and disability worldwide. Though preventable, an expected 23.6 million people will die mainly from CVD by 2030¹. To help support cardiovascular health, the majority of nutraceuticals are directed towards promoting heart and blood vessel health through reduction in the level of body lipids such as cholesterol and triglyceride.

Novel, safe and effective vitamin E ingredient

Tocotrienol is a natural form of vitamin E derived from certain plant seeds. Scientific research has shown that tocotrienol possesses unique biophysical properties that provide greater antioxidation and health benefits than the alpha-tocopherol form of vitamin E. Being an essential vitamin, vitamin E is not synthesized by the body; thus, it has to be obtained from the diet. Lack of vitamin E can cause nerve damage, blood disorders and infertility. In 2009, the FDA granted tocotrienols Generally Recognized as Safe (GRAS) status making these safe to incorporate in foods and beverages. Suggested food applications for tocotrienols include fats or oils, such as salad dressing, mayonnaise and margarine, bakery products, cereals, soup mix, sauces, meal replacement and functional beverages.

Structure

Common attributes between tocotrienols and tocopherols reflect the similarity in their chemical structures, with the difference being in their side chains. Both tocotrienols and tocopherols have four isomeric forms: alpha (α), beta (β), gamma (γ), and delta (δ)—making up the eight members of the vitamin E family.

Sources

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 forms. Tocotrienols are found mainly in palm fruit, wheat, and rice bran in the hard outer layer beneath the husk.

Properties

It is believed that tocopherols and tocotrienols are protective seeds and seedlings from the damaging effects of ultraviolet (UV) light and oxidation. Tocotrienol and tocopherol are closely related yet vary widely in their effectiveness in lipid systems. In studies, tocotrienol is shown to possess up to 60 times more superior antioxidation activity compared to the standard vitamin E tocopherol². Moreover, tocotrienol’s distinct chemical structure gives it more fluidity, enabling its cellular uptake in biological systems to be up to 70 times higher than tocopherol³. Tocotrienol, when applied topically, enhances vitamin E levels on the skin’s outer surface, as it is more easily absorbed in the skin with its affinity for certain skin layers.

Tocotrienol: Cardiovascular and metabolic health

“Tocotrienols” lipid-lowering properties and significant effects on cholesterol reduction are believed to be due to its distinct farnesyl tails, a structural property absent in standard tocopherol form of vitamin E. This may explain the wide range of cardiometabolic benefits associated with tocotrienols.

Targeting the HMG-CoA reductase pathway

“Tocotrienols,” particularly the gamma and delta isoforms, inhibit cholesterol synthesis through the suppression of HMG-CoA reductase, the key protein essential for cholesterol production. Cholesterol reduction is achieved through the increased breakdown and reduced translation of reductase protein to active proteins necessary for HMG-CoA activity. Presently, statins remain the primary pharmacologic standard for the treatment of dyslipidemia (loss of lipid balance). While, readily available and effective, statins at higher doses come with unfavourable side effects such as abnormal liver function tests, nerve dysfunction and muscle disease. Being naturally derived with a stellar safety profile, tocotrienol’s ability to suppress HMG-CoA activity is suggestive of its potential as a valid statin alternative and an emerging functional ingredient for cardiovascular and metabolic health.

Cardiovascular and metabolic health promoting properties

Results from studies conducted in various areas of cardiovascular and metabolic health including dyslipidemia and non-alcoholic fatty liver have shown tocotrienol’s effective lipid-lowering properties with beneficial effects for heart and blood vessel health.

- Dyslipidemia

“Tocotrienols” help maintain cardiovascular and metabolic health by promoting lipid balance through triglyceride and LDL cholesterol
In 2001, Qureshi et al. showed that the combination of tocotrienol-rich formulation and the standard anti-cholesterol lovastatin plus a controlled diet significantly reduced lipid parameters by up to 25% in hypercholesterolemic human subjects. In the same study, a significant increase in the HDL/LDL ratio by up to 46% was noted in these subjects. HDL cholesterol because of its ability to carry cholesterol away from blood vessels and back to the liver where cholesterol is metabolized is called the good cholesterol. High levels of HDL appear to provide cardio-protective benefits.

**Triglyceride-Lowering Effects**

![Figure 1: Triglyceride levels in tocotrienol and placebo groups after 8 weeks](image)

*Figure 1: Triglyceride levels in tocotrienol and placebo groups after 8 weeks*  

In a study involving human subjects, tocotrienols reduce triglyceride levels by 28% as compared to an increase in triglyceride levels in the placebo group. In addition, tocotrienol-treated subjects showed decreasing trends in average weight, body fat mass, body fat percentage and waist measurement.

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**Heart Health**

When a blood clot impedes blood flow to the heart, local oxygen supply to the heart tissue is cut off leading to a cascade of molecular events with damaging consequences. In many cases, removing the blood clot and re-establishing blood flow into the dead tissue (infarct), may cause further harm. In these so-called perfusion-reperfusion injuries, key proteins such as c-Src are activated and protein particles (proteasome) necessary for “cleaning” affected tissues are reduced. In a pre-clinical study conducted in isolated rat hearts, Das et al. showed that tocotrienols possess direct cardio-protective mechanisms through inhibition of c-Src activation and maintaining proteasome integrity.

While all tocotrienol isoforms provide a certain degree of heart protection, gamma-tocotrienol is shown to be the most protective.

**Blood Vessel Health**

In a study involving human subjects, tocotrienols reduced the production and transport of apoB and triglycerides by 20%, 25%, 69% of the patients with NAFLD on tocotrienols. In a clinical trial, DavosLife Science (Singapore) showed that tocotrienol improved blood vessel function when administered to hypertensive animal models. Tocotrienol is shown to be the most protective.

**Liver Health**

Metabolic syndrome also contributes to the development of non-alcoholic fatty liver disease (NAFLD), a common medical condition that can eventually lead to inflammation (hepatitis) and scarring (cirrhosis) of the liver. While reversible during the early stages, NAFLD when left unchecked may lead to liver inflammation and fibrosis. A study showed that men and women with metabolic syndrome have 4 to 11 times higher risk of developing NAFLD compared to those without the condition.

Presently, there is no known cure for late stage NAFLD also known as non-alcoholic steatohepatitis (NASH). Recently, in a trial conducted by Sanyal et al. in adults with diabetes, vitamin E at 800 IU daily was superior to placebo for the treatment of NASH in adults without diabetes. In addition, in a recent double-blind, placebo-controlled human study, 69% of the patients with NAFLD on tocotrienols showed improvement in their fatty liver conditions as compared to 33% in the placebo group.

**Brain and Nerve Health**

Canines were given tocotrienol supplements at 200 mg twice daily for 10 weeks before a stroke was induced in the transient middle cerebral artery, one of the major blood vessels in the brain. Results showed that tocotrienol supplementation significantly reduced ischemic stroke-induced lesion volume and prevented loss of nerve tissue connectivity.

**Skin Care**

As published in the leading Pigment Cell & Melanoma Research, DavosLife research showed tocotrienols’ ability to promote skin depigmentation through inhibition of the key protein tyrosinase in melanin synthesis. In the study, tocotrienols reduce melanin production by 55% through tyrosinase inhibition that is up to 150 times more effective as compared to other skin depigmenting agents.

**Novel health promoting properties for overall wellness**

- **Anti-Inflammation and Cancer**
  
  NF-κB is a key transcription factor regulating the body’s inflammatory systems and which has been found to be over-expressed in diverse forms of diseases including autoimmune diseases and certain cancers. As reported by scientists from the MD Anderson Cancer Center, “gamma-tocotrienol is a potent inhibitor of NF-κB activation, which may explain its anti-angiogenic, anti-proliferative, pro-apoptotic, anti-metastatic, anti-inflammatory, and immunomodulatory effects.”

  A study by Davos (Singapore) published in the International Journal of Cancer (July 2010) showed that tocotrienols prevented prostate cancer from forming in 75% of the mice pre-treated with tocotrienols compared to 100% cancer tumour formation in the control group.

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**A rising star in functional ingredients**

For a multi-functional ingredient to work, safety, in addition to proven efficacy, is essential. Tocotrienol is a 100% natural source ingredient found in low concentrations in common plant seeds used for food. With its GRAS status, it can be used as an ingredient in functional food and beverages, as well as in food supplements. Besides oral application, tocotrienol is also safe
New study suggests soy protein consumption may reduce body and liver fat accumulation and support colon health

While much research on soy protein has focused on its cholesterol lowering properties, exciting recent research suggests that consuming soy protein may have benefit in weight management, liver and colon health, which are of specific concern for obese individuals. The new study published in PLOS One in September 2012 was conducted in mice and aimed to explore the effects of dietary soy protein or casein on serum hormones implicated in colon health and body fat deposition. The authors had previously shown that inclusion of soy protein in the diets of mice resulted in lower body fat and promoted normal cell growth in the colors of rats.

Results of this study showed that mice fed the soy protein versus casein based diets had significantly reduced body fat, blood insulin levels, fat cell size and expression of genes associated with abnormal colonic cell growth. There was also a trend for lower fat accumulation in the livers of normal mice fed a high fat diet containing soy protein compared to a high fat diet containing casein.

The research led by Dr. Frank A. Simmen in collaboration with Dr. Robert C. M. Simmen and their lab groups also gleaned some insights into the possible way that soy protein consumption leads to these benefits by comparing the normal mice fed a high fat diet containing soy protein to a naturally occurring strain of mice that do not express an enzyme important for fat accumulation in the body. These mice are healthy and tend to be smaller and have less body fat than mice without this mutation. Since soy protein had less of an effect in these mice, it suggests that the gene that is mutated may be in a pathway that is affected when normal mice consume soy protein.

“Our findings support an increasing body of evidence linking healthy diets with altered metabolic states and biomarkers potentially favourable for prevention of chronic diseases” said Frank Simmen, professor in the Department of Physiology and Biophysics at the University of Arkansas for Medical Sciences in Little Rock.

“We are excited by these findings as they continue to support and extend the observations of other researchers that have shown a benefit of soy protein in maintaining healthy fat levels in the livers of other animal models,” commented Elaine Knul, Science Fellow and Lead, Nutrition Discovery at Soera LLC. “We are eager to confirm these observations in human studies.”

The study was funded by the National Institutes of Health and the Arkansas Biosciences Institute-Arkansas Children’s Hospital Research Institute and Soera LLC provided the soy protein used in the animal diets. The article is available online at the following link: http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0046716.

DavosLife Science (Singapore) will be at the SupplySide West 2012, The Venetian and Sands Expo Center, Las Vegas (Nov 5-9, 2012). Visit us at Booth No. 23064.

References


DSM FloraGLO® lutein in a starch based matrix is more bioavailable than alginate-based matrix Lyc-O-Lutein

DSM Nutritional Products is pleased to report that a revealing new study was published online in the European Journal of Nutrition that clearly demonstrates that not all sources of lutein are equivalent. This study adds to the body of scientific evidencemonstrating the importance of choosing a lutein source with proven absorption that will assure users they are in fact getting lutein’s important health benefits.

In this randomized, double-blind, cross-over study conducted by lead author Dr. Maikananthi Evans and co-authors, the effect of formulation differences on the bioavailability of lutein was evaluated using a starch-matrix FloraGLO Lutein 5% and a alginate-matrix Lyc-O-Lutein 20%.

Forty-eight healthy subjects were given a single dose of 20 mg lutein from either of the two formulations and lutein was measured in the plasma at several time intervals. After a wash out period of 28 days the study was repeated with the alternative formulation. The findings were highly significant. After 14 hours, total plasma lutein increased by 126% with the starch matrix FloraGLO Lutein 5% compared to only 7% with the alginate matrix Lyc-O-Lutein 20%. After 672 hours the drop of plasma lutein was of 5-fold higher for the starch-matrix FloraGLO Lutein 5% compared to the alginate-based Lyc-O-Lutein 20%.

The practical application of this study is highly relevant. Although lutein has demonstrated benefits in eye health it can only impart those benefits if this bioactive compound is efficiently absorbed by the body. This study shows that not all lutein sources are equivalent. Their bioavailability clearly depends on the formulation and in this study the starch matrix formulation was much more bioavailable than the alginate matrix utilized in the Lyc-O-Lutein 20% product. The benefits associated with FloraGLO lutein are based on a suite of high quality clinical studies. The above result is a further demonstration that not all brands can deliver these benefits. FloraGLO Lutein has proven high bioavailability.

Link to the study: http://rd.springer.com/article/10.1007%2Fs00394-012-0447-9

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