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Tocotrienol

... and its potential against chronic illnesses

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Cardiovascular disease and stroke, though preventable, remain major causes of death and disability worldwide. According to the World Health Organisation (WHO), by 2030, an expected 23.6 million people per year will die from these diseases. Supplementation with nutraceuticals may help heart and blood vessel health, through reduction in the level of body lipids, such as cholesterol and triglyceride, and reducing oxidative stress and inflammation.

Tocotrienols: The Natural Solution

Tocotrienols are part of the vitamin E family, along with the common tocopherol form. Both forms of vitamin E are lipid soluble and are able to prevent lipid peroxidation, which results in cell damage. Increasingly, scientific research has shown that the tocotrienol form of vitamin E possesses unique biophysical properties that provide greater anti-oxidation and health benefits than the alpha-tocopherol form of vitamin E [1].

Structure

Like tocopherols, tocotrienols can support fertility and provide antioxidant protection for all living cells. These common attributes between tocotrienols and tocopherols reflect the similarity in their chemical structures. However, there is a major difference in the three unsaturated bonds in the tocotrienol side chain. 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, and only a few contain both compounds. Tocotrienols are found mainly in palm fruit, wheat, and rice bran in the hard outer layer beneath the husk.

Palm Fruit (*Elaeis guineensis*)



Properties

It is believed that tocopherols and tocotrienols are nature's way of protecting seeds and seedlings from the damaging effects of ultraviolet (UV) light and oxidation. In a research study, tocotrienol is shown to possess up to 60 times superior antioxidant activity in biological systems, as compared to the standard vitamin E tocopherol [2]. Another study showed that initial cellular uptake of tocotrienol was up to 70 times faster than tocopherol [3].

Tocotrienols: Action Beyond Antioxidation

Lipid-Lowering Effects

Although cholesterol is important and necessary for maintaining bodily functions, high levels of cholesterol damage arteries and potentially lead to heart disease and other metabolic disorders. One of the earliest health benefits exhibited by tocotrienol is its ability to reduce blood lipid levels. In preclinical studies, Qureshi, *et al* [4] and Pearce, *et al* [5], observed that tocotrienols reduce cholesterol levels, through suppression of HMG-CoA reductase, a major protein that regulates cholesterol production. It is believed that this high level HMG-CoA suppression by tocotrienol is largely delivered by the farnesyl side chain that comprises tocotrienol's tail [6].

In a clinical trial, tocotrienol reduced LDL cholesterol by up to 25% [7], and another clinical study showed that tocotrienol reversed atherosclerosis in major neck arteries by 28% [8]. These studies demonstrate that tocotrienol supplementation reduced cholesterol levels, as well as inhibited fatty plaque formation in main arteries, suggesting their role in promoting cardiovascular health.

Metabolic Syndrome

Like cholesterol, triglycerides are a type of lipid found in blood. While cholesterol helps maintain cell structures and hormonal functions, triglycerides, which are stored in fat cells, serve as an energy reserve. Metabolic syndrome, famously known as Syndrome X, is a cluster of medical disorders, including obesity, and elevated blood pressure, blood sugar and triglyceride levels. When brought together, this combination can increase the risk of heart disease and diabetes by several fold.

Compelling evidence from independent clinical studies has established hyper triglyceridemia as an independent risk factor for atherosclerotic heart disease. The risk of coronary heart disease and possibly stroke, can be reduced by reducing triglyceride levels in the blood.

Researchers from Davos Life Science (DavosLife) demonstrated through *in vitro* studies, animal models and a placebo-controlled clinical trial that tocotrienol reduced the production and transport of triglycerides in the body, thereby reducing triglyceride levels by 27% (Figure 1) [9].

Non-alcoholic Fatty Liver Disease

The liver is the body's main production site for blood lipids, like cholesterol and triglycerides. Expectedly, the presence of metabolic syndrome and related disorders can largely affect the liver's overall health and function. Such is the case in Non-alcoholic Fatty Liver Disease (NAFLD), a liver condition closely associated with metabolic syndrome. In NAFLD, persistently elevated blood sugar and triglyceride levels can lead to accumulation of fat in liver cells. NAFLD is the most prevalent chronic liver disease worldwide and is present in 20% to 40% of the general population, with most cases observed in obese individuals. When left unchecked, NAFLD can progress to liver cirrhosis.

To further investigate tocotrienol's potential in promoting metabolic health, a double-blind, placebo-controlled clinical trial was conducted on subjects with NAFLD. Results from the study showed that 69% of the patients on tocotrienols showed improvement in their fatty liver condition as compared to 33% in the placebo group [10].

Stroke Attenuation

According to WHO, stroke affects an estimated 15 million people worldwide each year, of which 87% suffer from ischemic stroke, the most common type of stroke. Ischemic stroke happens when blood flow in the brain is interrupted by a blood clot, a process similar to the blockage of heart vessels in a heart attack.

Scientists have investigated the neuroprotective properties of tocotrienol on the brain's blood circulation during ischemic stroke in a pre-clinical trial. 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 white matter fiber tract connectivity. Brain white matter tracts serve as nerve-rich pathways that maintain brain function, by connecting different areas of the brain [11].

Anti-Inflammatory Effects

Many medical conditions like cardiovascular disease, NAFLD and cancer share a common pathway in inflammation. Inflammation involves a cascade of molecular responses, bringing forth a stream of cellular signals that aggravate existing tissue damage and injury. In cardiovascular disease, inflammation plays a central role throughout the various stages of atherosclerosis from plaque deposition to blood clot formation.

Tocotrienol exhibits anti-inflammatory abilities, suggesting its potential role in addressing a wider range of medical

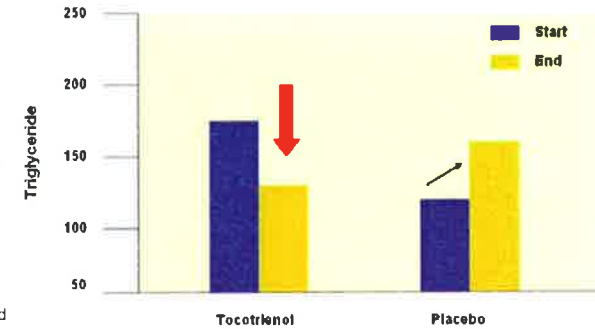


Fig 1. Triglyceride levels in tocotrienol and placebo groups after 8 weeks [9]

conditions, including diabetes and cancer [12]. Tocotrienol targets inflammatory molecules, such as phospholipase A2, 12-lipoxygenase, cyclooxygenase-2, and nuclear factor-KappaB (NF-KB) [13]. The NF-KB transcription factor is a central player in the regulation of inflammation and immune responses. Consequently, problems with NF-KB regulation have been implicated in the development of diverse forms of diseases, including autoimmune disorders and certain cancers.

Scientists have demonstrated that gamma-tocotrienol regulates NF-KB activation, while gamma-tocopherol has no effect. According to the scientists, their "results demonstrate that gamma-tocotrienol is a potent inhibitor of NF-KB activation, which may explain its anti-angiogenic, anti-proliferative, pro-apoptotic, anti-metastatic, anti-inflammatory, and immunomodulatory effects." Moreover, they 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." [14].

A Promising Future Ahead

For a multi-functional ingredient to work, safety and proven efficacy are essential. Tocotrienol is a 100% natural source ingredient, found in low concentrations in common edible plant seeds. In 2009, the US FDA granted tocotrienol the Generally Regarded as Safe (GRAS) status, supporting its use as an ingredient in functional food and beverages, as well as food supplements. It is non-irritant, non-mutagenic and non-toxic.

A growing awareness of tocotrienol's distinct health benefits has fueled an increasing number of research studies worldwide. In addition to its beneficial effects in cardiovascular and metabolic health, scientists are conducting research studies exploring tocotrienol's cancer-fighting properties as well. Tocotrienol is increasingly being incorporated in food and beverages, health supplements as well as cosmetics and personal care products. It is a rising star in the health and wellness industry that is worthy of further attention.

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