



BIOSA

Vitamins • Ingredients



ABOUT US

GRUPO COINSU

We are a company dedicated to the extraction and commercialization of palm oil and renewable energy.

Among the Biosa group is an integral part and is dedicated to the production and commercialization of vitamins and phytosustains of crude palm oil, which is Non GMO. With the objective of providing ethical health and nutrition solutions for its high potential for production and commercialization of renewable energy sources and by-products to use as raw material: vitamins, phytosubstances, biodiesel and high quality ingredients, derived from our enriched crude oil Non GMO palm with the objective of providing ethical health and nutrition solutions for its high potential to prevent degenerative and chronic diseases.



AIMED TO:

- Food Industry
- Vitamin Supplements
- Pharmaceuticals
- Cosmetics and Personal Care

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I BiosαTOCOTRIENOLS

BiosaTocotrienols from Honduran palm oil

Vitamin E is the term given to a group of fat-soluble compounds first discovered in 1922 by Evans and Bishop.¹

Chemically, these compounds have a chromanol ring (chroman-6-ols), termed tocopherols. They include two homologous series: tocopherols with a saturated side chain and tocotrienols with an unsaturated side chain (isoprenoid).

Tocopherols and tocotrienols have the same basic chemical structure, formed by a long side chain attached to the 2 position of a 6-chromanol ring.

Nomenclature of the homologs is dependent on the degree and position of methylation at C5 and C7 position at the chromanol head. Naturally occurring vitamin E includes eight fat-soluble isoforms: α-, β-, γ-, and δ-tocopherol and α-, β-, γ-, and δ-tocotrienol.²



Honduran palm oil

Bioactive Tocotrienols, the most effective tocotrienols from Honduran palm oil.

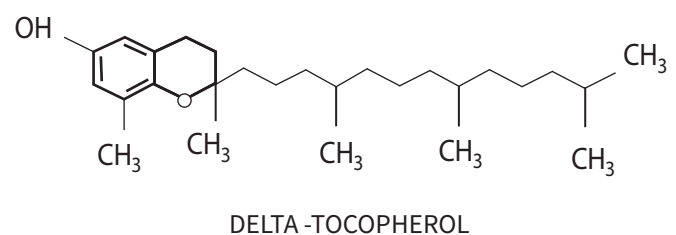
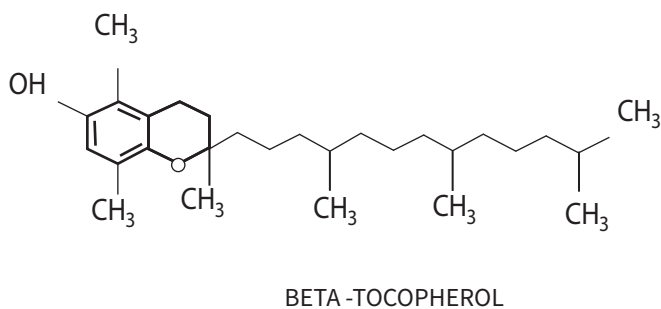
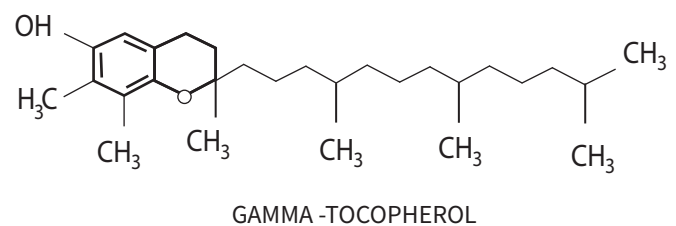
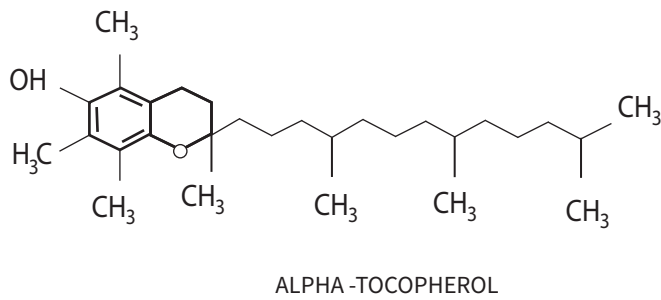
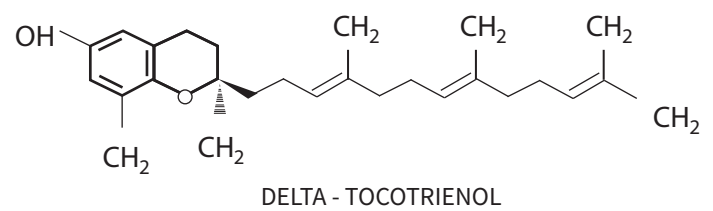
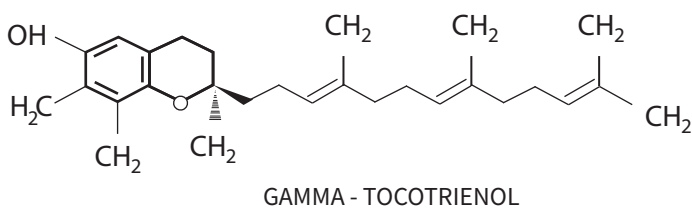
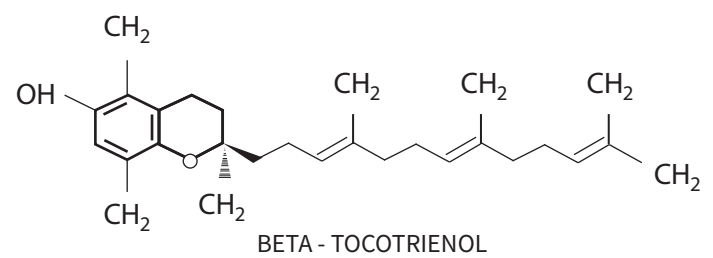
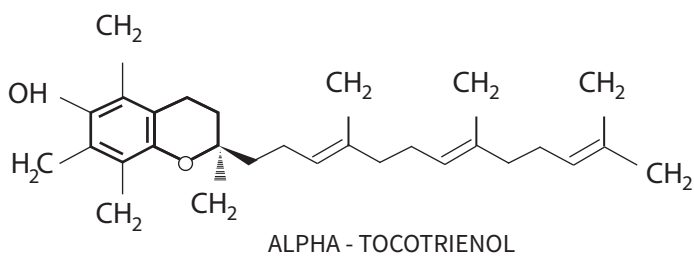


Figure 1. Chemical structures of tocotrienol and tocopherol subfamilies.

VITAMIN E

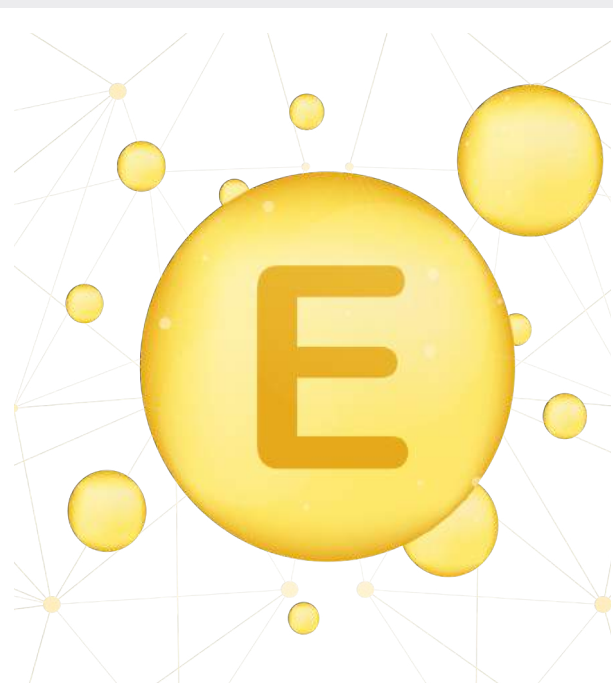
Vitamin E cannot be synthesized in humans and animals, and therefore, must be obtained from the diet.

The biological activity of vitamin E has been associated with its proven antioxidant property, specifically against lipid peroxidation in biological membranes and preventing oxidative stress. Oxidation to linked several diseases and conditions, including aging, cancer, cataracts, and arthritis. ⁴⁰

Vitamin E has been related to preventive effects against Alzheimer's disease, diabetes, and cancer among others. The platelet hyper-aggregation and atherosclerosis may be prevented with vitamin E supplementation. Also, vitamin E helps reducing the production of prostaglandins such as thromboxane, which originates platelet clumping.

Vitamin E is essential for the formation of red blood cells and structural and functional maintenance of skeletal, cardiac, smooth muscle. Also, vitamin E helps maintaining vitamin storage and immune health, protecting against oxidative damage that can lead to heart disease. Likewise, vitamin E promotes membrane repair by preventing the formation of oxidized phospholipids.²

Recent studies have shown that tocotrienols, from natural sources, are responsible for specific properties to make the body function properly and to prevent several diseases.





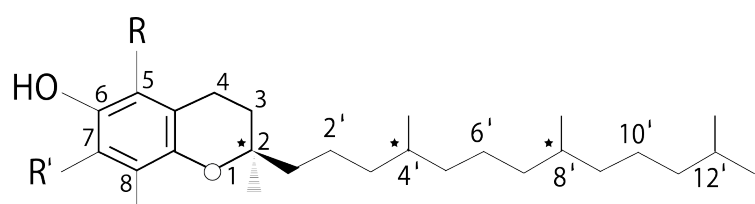
THE BENEFITS OF TOCOTRIENOLS

Tocotrienols possess novel hypocholesterolemic effects along with the capability to reduce the atherogenic apolipoprotein B and lipoprotein (a) plasma levels. Moreover, tocotrienols have been proposed to have anti-thrombotic and anti-tumor effects.

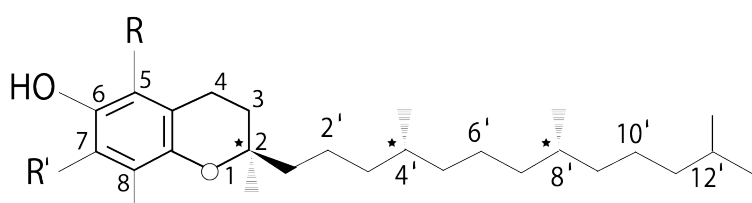
Tocotrienols scientific research continues, and the latest discovered properties had proven the importance of these vitamin E constituents.



“Tocotrienols represent the most potent forms of natural vitamin E.”



(R) - TOCOTRIENOL (α TE, γ TE, δ TE, β TE)

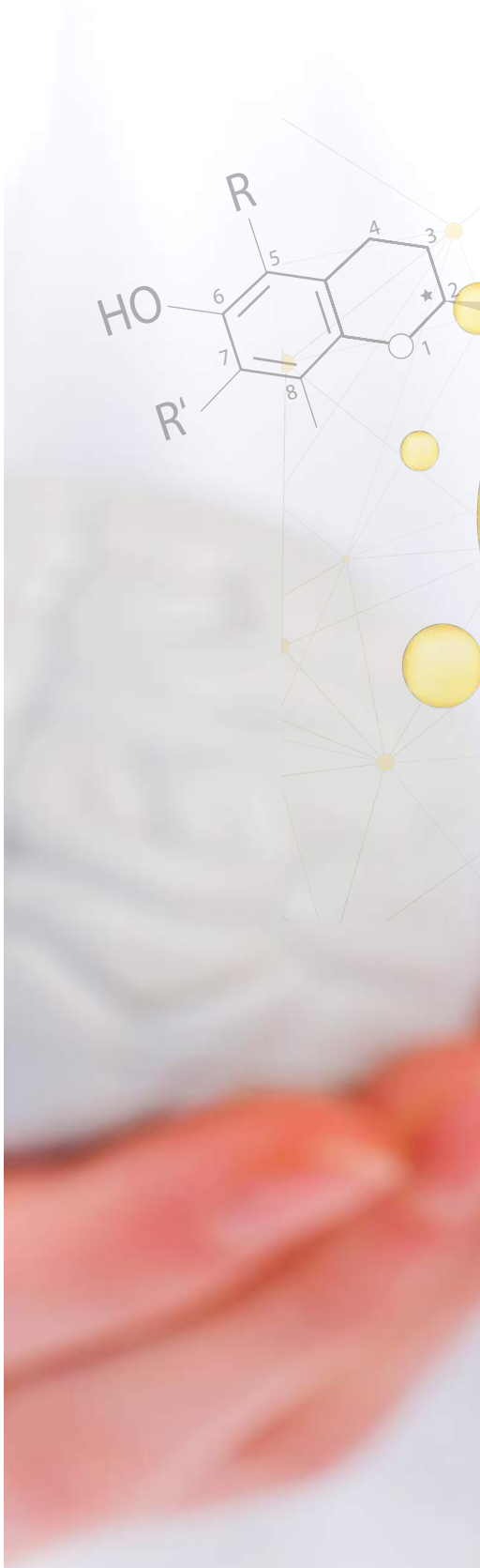


(2R,4'R,8'R) - TOCOPHEROL (α T, γ T, δ T, β T)





TOCOTRIENOLS
suppress
cancer-cell
proliferation,
induces
apoptosis in
cancer cells
thanks to
specific
mechanisms.



NEURO PROTECTION

The normal human body aerobic cellular metabolism constantly generates free radicals and other reactive oxygen species (ROS) as by-products of several physiological and biochemical processes. However, recent studies have demonstrated the neuroprotective properties of tocotrienols, particularly α -tocotrienol at nanomolar concentrations, to prevent stroke-associated neurodegeneration. Also, the neuroprotective property of tocotrienols defends against glutamate, homocysteic acid toxicities, glutathione deficiency, and linoleic acid -induced oxidative stress. Alpha-tocotrienol can prevent cell death due to prolonged excitatory stimulation by the neurotransmitter glutamate.^{3,4}



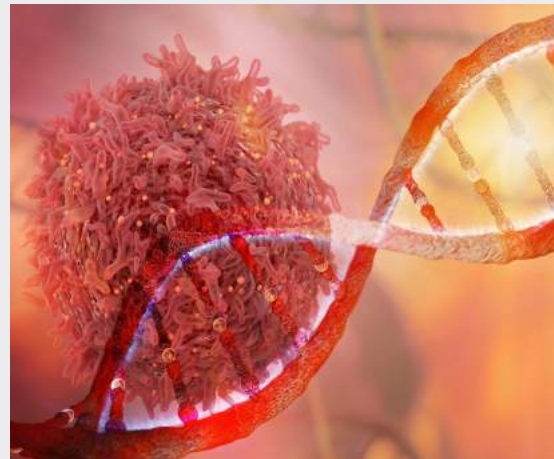
PROPERTIES OF TOCOTRIENOLS TO PREVENT THE RISK OF CANCER

The anticancer activity of tocotrienols has been shown in vitro and in vivo studies. Tocotrienols suppress cancer-cell proliferation, induces apoptosis in cancer cells thanks to specific mechanisms.^{3,4}

Studies have shown the anticarcinogenic action of isoprenoid constituents of plant-based diets on the tumor growth-suppressive action.⁵

Currently, it has been suggested the potential effects of tocotrienols in prevention and to control the progression of cancer. Mechanisms of action of tocotrienols in cancer prevention include decreasing of expression of cancer-causing genes and increasing the expression of genes that suppress cancer cells. On the other hand, the effective contribution of tocotrienols in cancer therapies has also been recognized due to effects such as apoptosis, angiogenesis, cell cycle arrest, inhibiting HMG- CoA reductase enzyme.^{6,7}

A clinical trial of tocotrienols in breast cancer patients has shown that γ - and δ -tocotrienol are potent inhibitors of breast cancer cell growth, also against colon carcinoma.^{8,9}





2.3

CARDIOVASCULAR HEALTH AND TOCOTRIENOLS

Since the 80's the properties α -tocotrienol isoform of the natural vitamin is known due to significant cholesterol-lowering ability.¹⁰ The positive effects of tocotrienols on cholesterol levels result from their ability to inhibit HMG-CoA reductase activity, a liver enzyme involved in the cholesterol synthesis. It has been suggested that the isoprenoid side-chain of tocotrienol is responsible for the observed cholesterol lowering levels.¹¹



The ability of tocotrienol-rich fraction (TRF) derived from palm oil to protect cardiovascular health and reverse metabolic syndrome has been proposed in recent research. Also, TRF reversed systolic and diastolic hypertension, hypercholesterolemia, hepatic steatosis, impaired antioxidant defense, myeloperoxidase hyperactivity triggered by the high-fat diet and reduce glycated hemoglobin A1c.¹² Ischemia occurs when your heart muscle doesn't get enough oxygen. Ischemia usually is produced due to a shortage of blood and oxygen caused by a blockage of one or more of the coronary arteries which supply blood to the heart muscle. Ischemia is linked to the progress of heart attack or stroke. An in vivo study showed that the supplementation of alpha- and gamma-tocotrienol lowered lipid levels and protected the heart muscle from damage by ischemia-induced.¹³





“

Vitamin E is an antioxidant. That means it protects body tissue from damage caused by substances called free radicals, which can damage cells, tissues and organs. It is believed that they play a role in certain conditions related to aging.

2.4



METABOLIC SYNDROME

Another condition associated with certain metabolic disorders and cardiovascular disease is the Metabolic Syndrome (MS). MS is characterized by insulin resistance, hypertension, abnormalities in cholesterol levels, and an increased risk for blood clotting.

Studies show that delta - tocotrienol and gamma-tocotrienol prevent accumulation of triglycerides in mouse adipose cells and suggest that tocotrienols may be useful to treat MS.¹⁴



CONTRIBUTOR TO THE PROTECTION

Vitamin E (VE) has a recognized leading role as a contributor to the protection of cell constituents from oxidative damage. However, evidence suggests that the health benefits of VE go far beyond that of an antioxidant acting in lipophilic environments. In humans, VE is channeled toward pathways dealing with lipoproteins and cholesterol, underlining its relevance in lipid handling and metabolism.





ANTI-INFLAMMATORY ACTIVITY OF TOCOTRIENOLS

Inflammation is the response of the immune system to foreign invaders such as viruses and bacteria. In response to infection or injury, various classes of white blood cells are transported through the bloodstream to the site of infection. The immune system recognizes damaged cells, irritants, and pathogens, and it begins the healing process. When infection or injury disappears, the inflammation usually subsides.

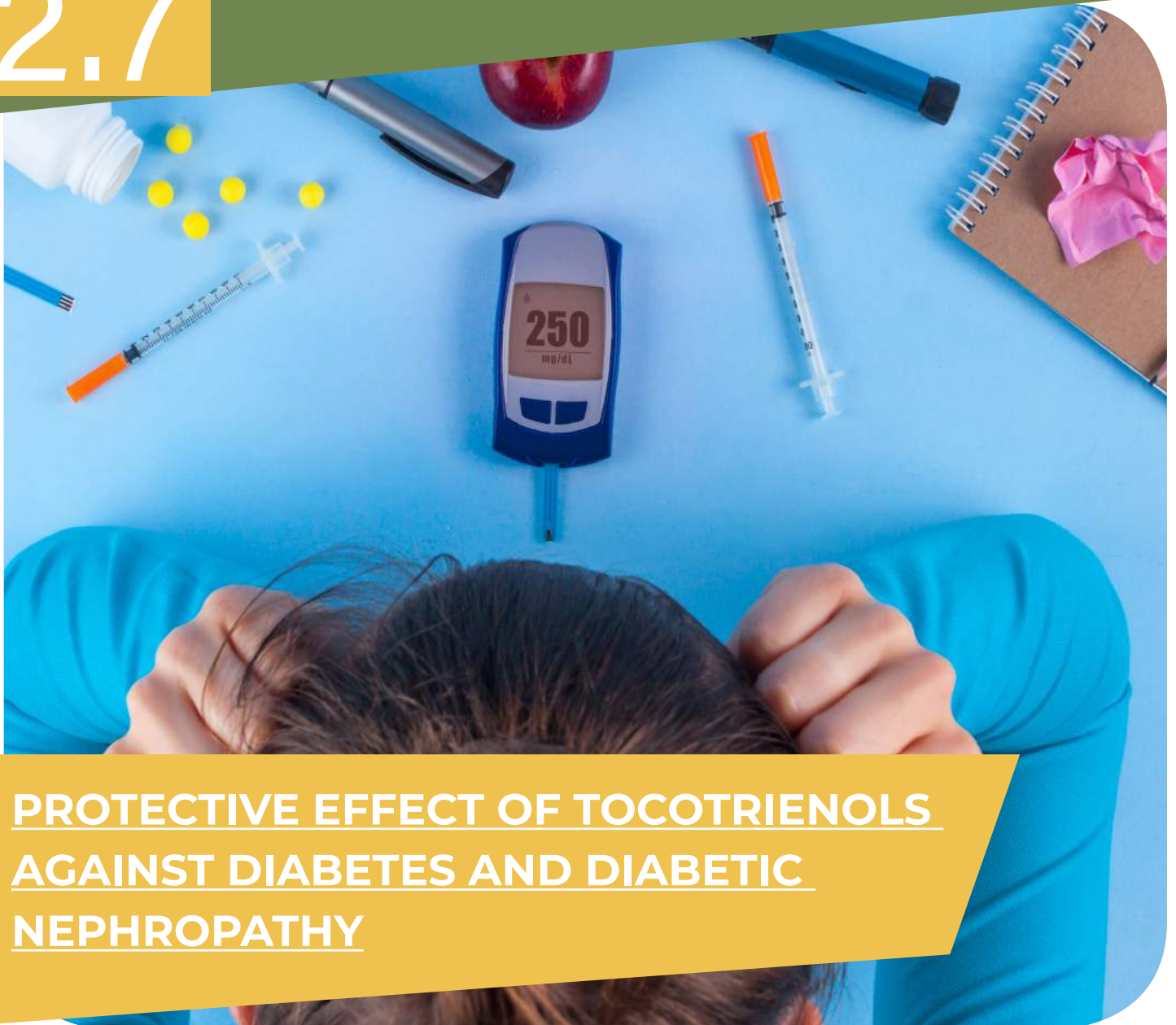
Various diseases have their origin in chronic inflammatory processes. They include arthritis, rheumatoid arthritis, cancer, Alzheimer's disease, cardiovascular diseases, asthma, peptic ulcer, ulcerative colitis and Crohn's disease among others.

Various studies have shown that specific isoforms of vitamin E such as γ -tocopherol, δ -tocopherol, tocotrienols, and particularly γ -tocotrienol are potent anti-inflammatory agents.



ANTI-OXIDANT ACTIVITY OF TOCOTRIENOLS

All tocopherols and tocotrienols are potent antioxidants with lipoperoxyl radical scavenging activities due to their phenolic group (-OH) in the chromanol ring, which stabilizes free radicals by donating a hydrogen atom.



PROTECTIVE EFFECT OF TOCOTRIENOLS AGAINST DIABETES AND DIABETIC NEPHROPATHY

Diabetes, a silent disease, occurs when the pancreas is no longer able to make insulin, or when the body cannot make good use of the insulin it produces.

Diabetes is associated with atherosclerosis, high risk of heart attack or a stroke. Also, diabetes produces accelerated ageing, damage to the body, neuropathy, and failure of various organs and tissues.

Dietary tocotrienols have effective lipid-lowering property in addition to their potent antioxidant activity and improve the damage to the nerves that lead to neuropathy and pain.¹⁵

Diabetic nephropathy (DN) is a serious complication associated with hyperglycemia. Tocotrienol-rich fraction (TRF) from palm oil (PO) have shown to lower the blood glucose level in patients¹⁶



ALZHEIMER'S DISEASE AND TOCOTRIENOLS

Alzheimer's disease (AD) has reached epidemic proportions in the United States and worldwide.¹⁷

In 1992, the World Health Organization (WHO) defined it as "a primary cerebral degenerative disease of unknown cause with characteristic neuropathological and neurochemical features." It is the first cause of dementia among the population between the ages of 60 and 90 in the most developed countries. Its clinical manifestation presents a loss of memory and mental faculties, anguish, depression, and generalized deterioration that ends with death.

Epidemiological evidence suggests the importance of adequate vitamin E intake in support of healthy brain function in the elderly.¹⁸

Tocotrienols and formulations with enhanced bioavailability may offer a novel approach to AD prevention and treatment.



TOCOTRIENOLS AND LIVER PROTECTION

A study with liver transplant patients, shown that oral tocotrienol supplementation significantly delayed progression of the end-stage liver disease.

The prevalence of the disease is expected to increase by 50% by 2030. NAFLD is a chronic liver disease, often asymptomatic, due to the accumulation of fat in the liver cells of people who do not drink alcohol excessively.¹⁹

NAFLD is associated with several diseases that include obesity, insulin resistance, diabetes, high blood pressure, liver failure, cancer, lipid peroxidation, oxidative stress, and elevated blood fats, among others.²⁰

Also, a randomized clinical trial of adults with high cholesterol and NAFLD showed that supplementation with tocotrienols significantly normalized the liver tissue.²¹



TOCOTRIENOL AND BONE HEALTH

Osteoporosis is a silent disease that thins and weakens the bones become fragile and break easily, especially the bones in the hip, spine, and wrist. Osteoporosis is a major health concern in postmenopausal women, and oxidative stress contributes to the development of bone loss. Tocotrienols, may be useful to bone health by improving bone mineral density and bone microstructure. It has been suggested that the beneficial effects of tocotrienols on bone health may be mediated via antioxidant and anti-inflammatory pathways and 3-hydroxy-3-methylglutaryl coenzyme. Tocotrienol demonstrates great potential as an antiosteoporotic agent and is also a potent antioxidant.²²



GASTRO PROTECTIVE EFFECTS

Several studies have proved the gastroprotective effects of tocotrienols. Tocotrienols possess antioxidant properties and anti-inflammatory effects which could be beneficial to reduce stress-induced gastric damages.²³

In comparison to omeprazole, tocotrienols have similar effectiveness in reducing stress-induced gastric lesions formation.²⁴





TOCOTRIENOLS AND HAIR GROWTH

The effect of tocotrienols on hair growth was investigated. The study carried out with patients with alopecia showed that supplementation with tocotrienols capsules (100 mg/day) increases hair number in volunteers suffering from hair loss as compared to the placebo group.²⁵





ANTICATARACT EFFECT OF TOCOTRIENOLS

A concern in diabetics is the blindness due to cataract that occurs at earlier onset. Tocotrienols have shown to reduce lens oxidative stress and inhibit cataractogenesis in streptozotocin-induced diabetic rats.²⁶



TOCOTRIENOLS AND SKIN

Tocotrienols have protective skin properties. Tocotrienols have anti-aging properties, greater skin penetration, moisturizing capacity and greater skin protection among others. Also, tocotrienols help in skin depigmentation, skin repair, and skin hydration. Tocotrienols are superior to protect the skin from prolonged exposure to ultraviolet rays that cause skin aging problems, ultimately leading to skin cancer. An in vitro study demonstrated the topic anti-inflammatory effect of tocotrienol-rich fractions (TRF) on UV-induced inflammation of the human skin.²⁷



II CLINICAL TRIALS OF TOCOTRIENOLS

1 Delta-tocotrienol has demonstrated chemopreventive and antineoplastic activity in preclinical models. A study to determine the safety and pharmacokinetics of delta-tocotrienol and its metabolites after single- and multiple-dose administrations in healthy subjects suggested that δ -tocotrienol can be safely administered at doses up to 1600 mg twice daily. Also, δ -tocotrienol achieves bioactive levels, supporting the investigation of δ -tocotrienol for chemoprevention.²⁸

A preoperative clinical trial of phase I investigated δ -tocotrienol in patients with pancreatic ductal neoplasia to assess its safety, tolerability, pharmacokinetics, and apoptotic activity. The results showed that δ -tocotrienol from 200 to 1600 mg daily taken orally for two weeks before pancreatic surgery was well tolerated, reached bioactive levels in the blood, and significantly induced apoptosis in the neoplastic cells of patients.²⁹

NEUROPROTECTIVE EFFECT OF TOCOTRIENOLS

2 White matter lesions (WMLs) are regarded as manifestations of cerebral small vessel disease, reflecting varying degrees of neurodegeneration and tissue damage.

The neuroprotective effect of mixed tocotrienols was proved in 121 volunteers with cardiovascular risk factors and confirmed WMLs through a 2-year intervention period. The supplementation of tocotrienols 200 mg or matching placebo twice daily showed that tocotrienols attenuate the progression of WMLs.³⁰





3 TOCOTRIENOLS AND LIVER PROTECTION

A randomized placebo-controlled clinical trial was carried out to determine the effects of mixed palm tocotrienols, in normalizing the hepatic echogenic response in eighty-seven untreated hypercholesterolemic patients with ultrasound-proven nonalcoholic fatty liver disease (NAFLD). The treatment, either mixed tocotrienols 200 mg twice daily or placebo, had a 1-year duration. The normalization of hepatic echogenic response was significantly higher for the tocotrienols treated group compared to the placebo group.²¹



4

PREGNANCY INDUCED HYPERTENSION (PIH)

A randomized, double-blind placebo-controlled clinical trial explored the effect the tocotrienol-rich fraction (TRF) of palm oil in preventing pregnancy induced hypertension (PIH). Healthy primigravidae were randomized to receive either oral TRF 100 mg daily or placebo, from early second trimester until delivery. The results showed substantial reduction in incidence of PIH.³¹



5

SUPPLEMENTATION EFFECT IN HEMODIALYSIS PATIENTS.

The anti-inflammatory and antioxidant properties of tocotrienol-rich fraction (TRF) were demonstrated in a randomized, double-blind, placebo-controlled, parallel trial conducted in 81 patients undergoing chronic hemodialysis. Subjects received daily capsules containing either tocotrienol-rich fraction (TRF) (180 mg tocotrienols, 40 mg tocopherols) or placebo (0.48 mg tocotrienols, 0.88 mg tocopherols). The TRF supplemented group showed improvement in lipid profiles after 12 and 16 weeks of intervention when compared with placebo at the respective time points.³²



III TOXICITY AND DOSAGE

In the regular diet, tocotrienols have been regarded as safe natural products. The long-term randomized clinical trials of tocotrienol-rich fractions (TRF) until now have shown that dosage regimens are safe and have therapeutic action. However, the treatment efficacy will depend on an array of variables including dose, formulation, and study populations.



In the regular diet, tocotrienols have been regarded as safe natural products.

• A dose of 42 mg/day	TRF decreased total, HDL, LDL cholesterol and TAG levels. ³³
• Dosage above 160 mg/day	Produced significant changes in aortic systolic blood pressure (ASBP) and augmentation index (AI). ³⁴
• 50 mg, 100 mg and 200 mg / day	self- emulsifying TRF can lower the AI. ³⁵
• Doses at 100 mg and 200 mg/day	Produced in a significant reduction of carotid- femoral pulse wave velocity (PWV). ³⁵
• Supplementation at 100 mg/day	demonstrated maximum decrease in AI with a reduction of 8.72% from baseline. ³⁵
• 25, 50, 100, and 200 mg tocotrienols/day	A study done on 90 volunteers show significant reduction in lipid profile. ³⁶
• 25 mg TRF/ day	LDL cholesterol and apolipoprotein B-100 levels coupled with elevated HDL cholesterol and apolipoprotein A1 levels. ³⁶
• Supplementation of 200 mg / day	TRF significantly reduced total, LDL cholesterol, and apolipoprotein B-100 levels while HDL cholesterol, TAG, and apolipoprotein A1 levels remained unchanged. ³⁷
• Supplementation of 400 mg / day	A double-blinded, placebo-controlled clinical trial to assess the effects of tocotrienol-rich fraction (TRF) supplementation on immune response following tetanus toxoid (TT) vaccine challenge in healthy female volunteers, Show that intake of TRF during two months had immunostimulatory effects.





TROCOTRIENOLS ARE GRAS

Tocotrienols are generally recognized as safe (GRAS) substance and can be used as an additive in dietary supplements.³⁹

MARKET AND APPLICATIONS OF BIOSA TROCOTRIENOLS

BiosaTocotrienols is obtained from natural sources through a proprietary process that guarantees the highest quality and purity. Market demand for tocotrienols is increasing; it is expected to reach about USD 350 million by 2024. This great development is thanks to the Nutraceutical market expansion and a large variety of market applications.



1 NUTRACEUTICAL MARKET



Tocotrienol exhibits antioxidant properties that further help reducing heart-related diseases, metabolic syndrome, Alzheimer's disease, among other health related problems, even associated preventing the risk of cancer. In the nutraceutical market, tocotrienols have extremely wide opportunities and a very large volume of applications to dietary supplements, formulations, such as tocotrienols gelatin, capsules, tocotrienol tablets, polyvitamin, capsules, tocotrienol emulsions, poly- component formulations, and as an ingredient for multi-vitamin products.



2 NUTRICOSMETIC COSMECEUTICAL COSMETICS INDUSTRIES

In the global beauty supply sector tocotrienols are extensively used in cosmetic applications, as skin conditioning agents since they help preventing the harmful effects of oxidation. Tocotrienols are superior to protect the skin from prolonged exposure to ultraviolet rays that cause skin aging problems, ultimately leading to skin cancer. The superiority of tocotrienols in this field include anti-aging properties, greater skin penetration, moisturizing capacity and greater skin protection among others. Also, tocotrienols help in skin depigmentation, skin repair, and skin hydration.



3 PHARMACEUTICAL INDUSTRY

Also, tocotrienols have a space in clinical applications. The new advances in clinical research have shown the pharmacological functions of tocotrienols extensively used to prevent and to treat several diseases. Tocotrienols have a lot of potential in this industry and may gain traction on multiple applications for new R&D medicinal projects.





THE FOOD AND BEVERAGE INDUSTRY

The important discoveries about the therapeutic superiority of the tocotrienols offer immense potential for the development of foods with effective properties.

4

An increasing population segment which is consciously caring about their wellbeing through healthy, natural and organic food consumption is growing overwhelmingly, demanding food manufacturers functional foods with preventive long term benefits to protect them from various diseases. Food companies that already began to include tocotrienols in their products are currently enjoying a competitive advantage over competitors that have not been able to read this growing market trend. Food developing leaders who capitalize the opportunities from recent scientific discoveries in terms health benefits through food functionality will prevail in a tight competitive marketplace.



TOCOTRIENOLS APPLICATIONS INCLUDE

Mayonnaise, salad dressing, spread, margarine, bakery products, snacks, sauces, juice drinks, processed fruits, functional beverages, yogurt, gelatin products, desserts, chocolate products, soy and vegetable milk, sweets, beverages, confectionery, chewing gum, candy, among others



NATURAL SOURCES OF TOCOTRIENOLS

1

The genus *Elaeis* is a genus of palms including three species of oil palm: *Elaeis guineensis*, *Elaeis oleifera*, and *Elaeis odora*. In general, the mature palms belonging to this botanical genus are single-stemmed and can grow well over 20 m tall.



VI

OIL PALM CULTIVATION IN HONDURAS

1

A National commitment to environment preservation.

The Biosa`s supplier develops environmental management plans for oil palm cultivation that includes prevention or mitigation measures to minimize the production process impact on the environment. Likewise, training programs are developed for all the personnel involved in the different activities, monitoring and evaluation system.

Biological control of pest management and diseases of oil palm cultivation to reduce chemical treatments and promote the recovery of natural populations, mainly insects that serve to control pests.

The oil palm cultivation of Biosa`s supplier is carried out under Good Agricultural Practices. These constitute a set of principles and technical recommendations applicable to the production, processing, and transport of food aimed to preserve the human health and the environment, through ecologically safe, hygienically acceptable and economically feasible methods.

VII

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