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NATURE'S BEST PHYTONUTRIENT

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Abstract:
Tocotrienols are chemicals in the vitamin E family. Vitamin E is a substance necessary for proper body and brain function.As with the other Vitamin E chemicals, tocopherols, there are four types of tocotrienols found in nature: alpha, beta, gamma, and delta. Tocotrienols occur in the oils of rice bran, palm fruit, barley, and wheat germ. Tocopherols, on the other hand, are found mostly in vegetable oils such as olive, sunflower and safflower oils, whole grains, and green leafy vegetables. These substances are also available in supplement form as capsules or pills. Although tocotrienols are structurally similar to tocopherols, each has slightly different health properties. Experts believe that tocotrienols have many health benefits — some that are more powerful . review is based on the pharmacological properties of tocotrienols

Keywords: *Tocotrienols, Tocopherols. safflower,rice barn*

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INTRODUCTION:

Thus, vitamin E was scientifically named as tocopherol from the Greek word tokos meaning childbirth, phero meaning to bring forth, and ol ending to indicate the alcohol properties(1). Since its discovery, vitamin E has been extensively studied to better understand their roles in different pathophysiological conditions [2–4] Tocotrienols are members of the vitamin E family. An essential nutrient for the body, vitamin E is made up of four tocopherols (alpha, beta, gamma, delta) and four tocotrienols (alpha, beta, gamma, delta). The slight difference between tocotrienols and tocopherols lies in the unsaturated side chain of tocotrienols, having three double bonds in its farnesyl isoprenoid tail.Tocotrienols are natural compounds found in certain vegetable oils, including rice bran oil and palm oil, wheat germ, barley, saw palmetto, anatto, and certain other types of seeds, nuts, grains, and the oils derived from them.Tocotrienol and Tocopherol isomers have this antioxidant activity due to the ability to donate a hydrogen atom (a proton plus electron) from the hydroxyl group on the chromanol ring, to a free radical in the body. This process inactivates ("quenches") the free radical by effectively donating a single unpaired electron (which comes with the hydrogen atom) to the radical. Tocotrienols have only a single chiral center, which exists at the 2' chromanol ring carbon, at the point where the isoprenoid tail joins the ring. Tocotrienols extracted from natural sources always consist of the dextrorotatory enantiomers only. These naturally occurring, dextrorotatory stereoisomers are generally abbreviated as the "d-" forms, for example, "d-tocotrienol" or "d-alpha-tocotrienol". Synthetic mixed stereoisomer ("dl-tocotrienol") or synthetic single stereoisomer ("l-tocotrienol") are marketed as dietry supplements.The biological significance of tocotrienols was clearly delineated in the early 1980s, when its ability to lower cholesterol was first reported by Qureshi and Elson in the Journal of Medicinal Chemistry. During the 1990s, the anti-cancer properties of tocopherols and tocotrienols was reported.The current commercial sources of tocotrienol are rice, palm, and annatto.. nnatto naturally contains only δ- and γ-tocotrienols and is essentially tocopherol-free. Annatto tocotrienol has the highest tocotrienol concentrations, and is tocopherol-free. Tocotrienols are safe and human studies show no adverse effects with consumption of 240mg/day for 48 months.

Tocotrienols are only available from selected plant sources. Tocotrienols are minor components in plants, mainly concentrated in cereals like rice bran, barley, rye and wheat germ. Unlike tocopherols that occur naturally in most common vegetable oils, tocotrienols are found only in selected oils such as palm oil and rice branoil (seeTable1).

Source	Tocotrienols				Toco-pherol
	α	β	γ	δ	α
	mg				
Palm oil	14.6	3.2	29.7	8.0	15.0
Rice bran	23.6	NA	34.9	–	32.4
Wheat germ	2.6	18.1	NA	NA	133.0
Coconut	0.5	0.1	–	–	0.5
Soybean	0.2	0.1	0	0	7.5
Olive	0	0	0	0	11.9

Sources: Sheppard A. J., Pennington J.A.T., Weihrauch J. L. Analysis and distribution of vitamin E in vegetable oils and foods. Packer L. Fuchs J. eds. Vitamin E in Health and Disease 1993:9-31 Marcel Dekker, Inc New York, NY. Ong A.S.H. Natural sources of tocotrienols. Packer L. Fuchs J. eds. Vitamin E in Health and Disease 1993:3-8 Marcel Dekker, Inc New York, NY.

NA: Not available

Table 1. Vitamin E content (mg per 100g product) of selected oils.

Tocotrienols have an unsaturated side tail which differs from tocopherols and this may account for significant difference in the biological activities of these isomers (see Figure 1).

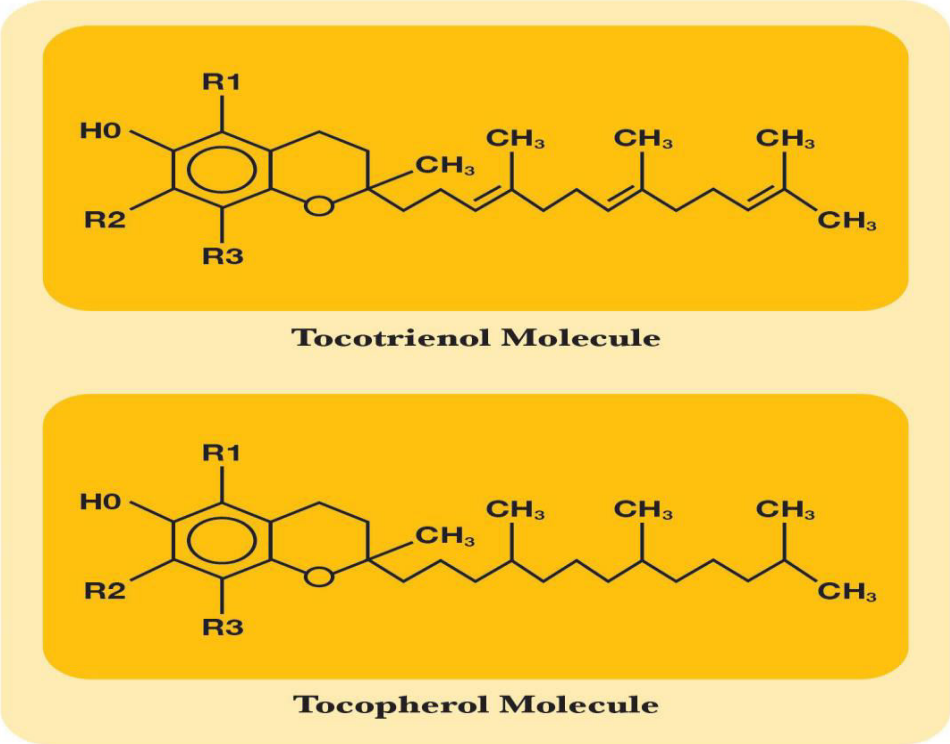

Figure 1. Molecular structure of Vitamin E – Tocotrienol and Tocopherol

FUNCTIONS & HEALTH EFFECTS OF TOCOTRIENOLS

- Tocotrienol is more effective antioxidant than tocopherol because its unsaturated side chain facilitates better penetration into saturated fatty layers of the brain and liver.
- Tocotrienols can lower tumor formation, DNA damage and cell damage. Micromolar amounts of tocotrienol suppress the activity of 3-Hydroxy-3- Methyl Glutaryl coenzyme A (HMG-CoA) reductase, the hepatic enzyme responsible for cholesterol synthesis.
- Tocotrienol but not tocopherol, suppresses growth of human breast cancer cells. The oral supplementation of the palm tocotrienol complex acts on key molecular checkpoints (c-Src and 12-Lipoxygenase) to protect against glutamate- and stroke-induced neurodegeneration and ultimately protect against stroke in vivo.
- In a 2009 in vitro study, scientists at department of nutrition and food sciences, Texas Woman's University evaluated the impact of d-delta-tocotrienol, on human MIA PaCa-2 and PANC-1 pancreatic carcinoma cells and BxPC-3 pancreatic ductal adenocarcinoma cells. They concluded suppression of mevalonate pathway activities, be it by modulators of HMG CoA reductase, farnesyltransferase (farnesyltransferase inhibitors), and/or mevalonate pyrophosphate decarboxylase (phenylacetate) activity, have a potential in pancreatic cancer chemotherapy. In a 2009 study at the Li KaShing Faculty of Medicine, The University of Hong Kong, scientists found reduction in skin cancer cells when treated with gamma-tocotrienol with chemotherapy drugs.

PHARMACOLOGICAL PROPERTIES OF TOCOTRIENOLS

Tocotrienols have a very broad range of medicinal properties and are used as antioxidant, analgesic, anti-inflammatory, antibacterial, antipyretic, antithrombotic, anticancer, cardioprotective, hepatoprotective, hypoglycemic, and nephroprotective

ANTI-CANCER EFFECTS

Tocotrienols not only suppress cancer-cell proliferation, but also induces apoptosis in cancer cells. It has been reported that γ- and δ-tocotrienols exhibit greater anticancer activity than α- or β-tocotrienols . They exert anti-cancer activity on cancer cells by cell cycle arrest through induction of cell cycle inhibitory protein and decreased expression of cyclin dependent kinase . Tocotrienols also work as an anti-cancer agent by inhibiting angiogenesis or

by enhancing immunity and inhibiting tumor cell migration . Tocotrienol induces cell-cycle arrest and mitochondria-mediated apoptosis in human pancreatic cancer cells . It has also been shown to inhibit the tumor cell growth by suppressing HMG-CoA reductase activity . It has been shown to induce apoptosis in stomach cancer cells through down-regulation of the Raf-ERK signaling pathway . γ- and δ-tocotrienols derived from palm oil exhibited strong activity against tumor promotion by inhibiting Epstein–Barr virus (EBV) early antigen expression in EBV-genome-carrying human lymphoblastoid cells induced by phorbol ester . Gamma-Tocotrienol induced poly (ADP-ribose) polymerase (PARP) cleavage and stimulated a rise in caspase-3, caspase-8 and caspase-9 activities in human hepatoma Hep3B cells. The antiproliferative activity of tocotrienols are mediated through modulation of growth factors such as vascular endothelial growth factor (VEGF) , basic fibroblast growth factor (bFGF) and transforming growth factor-beta (TGF-β) , HER2/neu , and interleukin-6 (IL-6) . Cyclin-dependent kinases (CDK2, CDK4, CDK6) and their inhibitors, such as p21, p27 and p53 and downregulation of Rb phosphorylation also mediate the growth-suppressive effects of this agent. Downregulation of the telomerase, c-myc, and raf–ERK signaling pathways has been linked to tocotrienol's ability to inhibit cell survival .

ANTI-OXIDANT ACTIVITY

The antioxidant activities of tocotrienols are mediated through induction of antioxidant enzymes such as superoxide dismutase NADPH: quinoneoxidoreductase , and glutathione peroxidase , which quench free radicals such as superoxide radicals. Effects of tocotrienols on antioxidant defense system in various animal models have been studied from time to time. lntragastric administration of tocotrienol for 30 days caused a significant elevation in different components of hepatic antioxidant defence and reduction in serum enzymes of hepatic damage in animals fed with 2-acetylaminofluorene (AAF).

ANTI-INFLAMMATORY ACTIVITY

The activation of the transcription factor NF-κB has been closely linked with inflammation. Tocotrienols have been shown to suppress the expression of TNF-α , IL-1 , IL-6 , IL-8 , inducible nitric oxide synthase , and cyclo-oxygenase 2 , all of which mediate inflammation. Tocotrienols have also been shown to suppress STAT3 cell-signaling pathway, also involved in inflammation . Hypoxia-induced factor-1 is another pathway that has been linked with inflammation and is modulated by tocotrienols.

ANTI-DIABETIC ACTIVITY

Tocotrienol from palm oil (200 mg/kg) significantly reduced the blood glucose level, oxidative stress markers and improved dyslipidemia in diabetics. Co-administration of tocotrienol significantly prevented behavioural, biochemical and molecular changes associated with diabetes. Tocotrienol also prevented diabetic neuropathy in rat models . Oral administration of tocotrienol also significantly reduced the fasting serum glucose level in streptozotocin induced diabetic rats by increased glucose metabolism and partly by hypotriglyceridemic effect of the plant extract. The tocotrienol from palm oil and rice bran oil was able to cause a significant reduction of elevated glucose-insulin index, signifying a potential insulin sensitizing effect in streptozotocin induced diabetic rats . Oral administration of tocotrienol decreased the HbA1c, plasma glucose, lipids, peroxylipid (malonedialdehyde, MDA), albuminuria, proteinemia and uremia, and also improved the insulin sensitivity in various animal models . It also prevents the incidence of long term complication in diabetic nephropathy.

ANTI-HYPERLIPIDEMIC ACTIVITY

Hyperlipidaemia is a group of disorders in which a person has increased levels of lipids in the bloodstream. These lipids consist of cholesterol, phospholipids, triglycerides and cholestryl esters. Since lipids are insoluble in aqueous medium, they are usually carried in body fluids as soluble protein complexes called as lipoproteins. Hyperlipidaemia can lead to a number of metabolic diseases like cardiovascular dysfunction and atherosclerosis. Hyperlipidemia may also result from diseases such as diabetes, thyroid disease, renal disorders, obesity, alcohol consumption and liver disorders Tocotrienols, because of their antioxidant activity, have long been used for reducing blood lipid levels. Tocotrienols from barley, oats, palm and rice bran have been demonstrated to lower cholesterol levels in animals and humans , and that this effect has been reported to be mediated by suppressing HMG-CoA reductase activity through a post-translational mechanism. Furthermore, the study showed that tocotrienols significantly reduced serum levels of total cholesterol (TC), low density lipoproteins (LDL) and triglycerides (TG). . In patients with hyperlipidemia and carotid stenosis, long term treatment with palm oil (a rich source of tocotrienols) resulted in attenuation of oxidative modification of LDL and significantly prevented the initiation and propagation of atherosclerosis. Tocotrienol (75 mg/day) supplementation for 2 months significantly reduced fasting blood lipid levels.

IMMUNOMODULATORY ACTIVITY

Tocotrienol enhanced both antigen specific (observed against humoral as well as Cell-mediated immune response) and nonspecific responses. Tocotrienols have been shown to induce favourable effects on the human immune system.Tocotrienols have immunostimulatory effects and potential clinical benefits to enhance immune response .Tocotrienol enhance T cell proliferation. Oral administration of tocopherol and tocotrienol affected the proliferation and function of spleen and MLN lymphocytes .

PROTECTION AGAINST CARDIOVASCULAR DISEASE

Out of four different isoforms of tocotrienols,alpha tocotrienols are considered as the effective isoforms which possess the cardioprotective abilities.Tocotrienol has been suggested to have an antioxidant, anti-thrombotic, and antitumor effect indicating that tocotrienol may serve as an effective agent in the prevention and/or treatment of cardiovascular disease and cancer. The bioactivity exhibited is due to the structural characteristics of tocotrienols. Rich sources of tocotrienols which include rice bran, palm oil, and other edible oils exhibit protective effect against cardiovascular disorders.

Coronary heart disease, cardiomyopathy, ischemic heart disease, heart failure, hypertensive heart disease, inflammatory heart disease and valvular heart disease are some of cardiovascular complications. Tocotrienol has long been used for various cardiac complications. Tocotrienols' cardioprotective effects are mediated through their antioxidant mechanisms and their ability to suppress inflammation, and inhibit HMG-CoA reductase, a rate-limiting enzyme in cholesterol biosynthesis, and reduce the expression of adhesion molecules and monocyte–endothelial cell adhesion . Tocotrienols were found to be more effective than α-tocopherol.

The tocotrienols also significantly reduce the ischemia-reperfusion injury, and reduced infarct size in the ischemic region of myocardial tissue, through the downmodulation of c-Src and upregulation of phosphorylation of Akt, thus generating a survival signal. The tocotrienols also lowered the hepatic HMG-CoA reductase activity and cholesterol and fatty acid levels in various tissues. The γ-tocotrienol exhibited a dose dependent hypotensive effect on the systolic blood pressure. It also caused a significant drop in the mean arterial pressure, decreased lipid peroxidation and increased the activity of antioxidant enzymes , γ-tocotrienol significantly reduced coronary perfusion pressure and heart rate. It exerted protection against myocardial injury by mitigating cardiac dysfunction and oxidative injury

NEUROPROTECTIVE EFFECTS

Current developments in α-tocotrienol research demonstrate neuroprotective properties for the lipid-soluble vitamin in brain tissue rich in polyunsaturated fatty acids (PUFAs). Arachidonic acid (AA), one of the most abundant PUFAs of the central nervous system, is highly susceptible to oxidative metabolism under pathologic conditions. Cleaved from the membrane phospholipid bilayer by cytosolic phospholipase A2, AA is metabolized by both enzymatic and nonenzymatic pathways. A number of neurodegenerative conditions in the human brain are associated with disturbed PUFA metabolism of AA, including acute ischemic stroke. Palm oil–derived α-tocotrienol at nanomolar concentrations has been shown to attenuate both enzymatic and nonenzymatic mediators of AA metabolism and neurodegeneration. Alpha tocotrienol in neurodegenerative disorders of the CNS are well characterized, with specific molecular targets (cPLA2, 12-LOX, and c-Src) and mechanisms of action identified.

a-Tocotrienol (TCT) represents the most potent neuroprotective form of natural vitamin E that is generally recognized as a safe certified by the U.S. Food and Drug Administration.

HEPATOPROTECTIVE ACTIVITY

Liver the largest glandular organ of the body and the key organ of metabolism has a pivotal and immense task of detoxification of xenobiotics, environmental pollutants and chemotherapeutic agents. Hence this organ is subjected to a variety of diseases and disorders.

Tocotrienol has been extensively studied for its efficacy against hepatic toxicity. Oral administration of tocotrienols offered a significant protection against 2-acetylaminofluorene (AAF) induced hepatotoxicity as assessed in terms of biochemical and histological parameters. Tocotrienols completely normalized the 2-acetylaminofluorene (AAF) induced increase in the levels of plasma and liver microsomal gamma-glutamyltranspeptidase (GGT) and liver microsomal UDP-glucuronyltransferase (UDP-GT) confirming in vivo hepatoprotective activity of tocotrienols against AAF induced toxicity. In addition to their antioxidant activity, tocotrienols are found to increase the expression of drug metabolising enzymes such as cytochrome P450 enzyme (CYP450), UDP-glucuronosyltransferase 1A1 (UGT1A1) and multidrug resistance protein-1 (MDR1) via the activation of the pregnane-X-receptor (PXR) and steroid and xenobiotic receptor (SXR), which are the

nuclear receptors that regulate drug clearance in the liver and intestine via induction of genes involved in drug and xenobiotic metabolism, thus increasing the activity of liver to metabolize the xenobiotics.

GASTROPROTECTIVE EFFECTS

Both tocopherols and tocotrienols had gastroprotective effects against damage by free radicals generated in stress conditions, but only tocotrienols had the ability to block stress induced changes in gastric acidity and gastrin level. Another group showed that tocotrienols can prevent aspirin-induced gastric lesions through their ability to limit lipid peroxidation.

NEPHROPROTECTIVE ACTIVITY

The kidneys are organs that serve several essential regulatory roles in vertebrate animals. They are essential in the urinary system and also serve homeostatic functions such as the regulation of electrolytes, maintenance of acid–base balance, and regulation of blood pressure (via maintaining salt and water balance). They serve the body as a natural filter of the blood, and remove wastes produced by metabolism in the form of urine. Just like liver, kidneys are also susceptible to a variety of diseases and disorders. Tocotrienols have been reported to possess significant nephroprotective activity. Tocotrienol (100 mg/kg) as well as TRF (200 mg/kg) from palm oil and rice bran oil prevents the kidneys from diabetic nephropathy. Tocotrienols modulated the release of profibrotic cytokines, oxidative stress, ongoing chronic inflammation and apoptosis and thus exerts a marked renoprotective effect .Tocotrienol also prevents the kidneys from ferric nitrilotriacetate (Fe-NTA) toxicity, a well-established nephrotoxic agent.

RADIOPROTECTIVE EFFECTS

Following exposure to gamma radiation,hamato poietic stem cells(HSCs) in the bone marrow,which are important for producing cells ,rapidly undergoe apoptosis(cell death).There are no known treatment for the acute effect of radiation.Two studies conducted by researchers at U.S Radiology Research Institute found that treatment with gamma tocotrienol or delta tocotrienol significantly enhanced survival of hematopoietic stem cells,which are essential for the body's supply of blood cells.

POSITIVE EFFECTS ON BONE METABOLISM

Bone is a specialised connective tissue hardened by mineralisation with calcium phosphate in the form hydroxyapatite ([Ca3(PO4)2]Ca(OH)2). Bone has well recognised mechanical functions: it provides rigidity and shape, protection and support for body structures, and aids locomotion. The rate of bone turnover, collagen matrix, size, structure, geometry and density all combine to determine the bone's overall mechanical properties. Defects in these parameters will result in diseases such as osteoporosis, Paget's disease of bone, osteoporosis and osteogenesis imperfecta. In order for the strength of the bone to be maintained, the process of bone turnover must be carefully regulated. Vitamin E and its various forms have been reported to help in the maintenance of bone metabolism . Vitamin E supplements reversed nicotine-induced bone loss and stimulated bone formation. Tocotrienols are slightly effective than tocopherols in attenuating the effects of tobacco; γ-tocotrienol especially may have therapeutic potential to repair bone damage caused by chronic smoking. Other studies have shown that tocotrienols can reverse glucocorticoid-induced or free radical-induced bone loss in adrenalectomized rats and improve normal bone structure possibly through its antioxidant activity in bone . Therefore, palm-oil derived γ-tocotrienol has the potential to be utilized as a prophylactic agent in prevention of the skeletal side effects of long-term glucocorticoid and tobacco use.

MECHANISTIC ACTION OF TOCOTRIENOLS IN BONE PROTECTION

Tocotrienols prevent the increase in expression of TNF-α and nitric oxide (NO) due to nicotine administration, oxidative stress and inflammation and thus prevent osteoclast formation. Tocotrienols also downregulate the expression of Receptor activator of nuclear factor kappa-B (RANK) and Receptor activator of nuclear factor kappa-B ligand (RANKL). Osteoporosis and glucocorticoids also decrease the calcium ion concentration in bone leading to bone desorption. Tocotrienols prevent the desorption of calcium ions from bone, thus increasing the bone strength. Tocotrienols also increase the expression of interleukin-8 (IL-8), IL-17, granulocyte colony stimulating factor (G-CSF) which in turn lead to the formation of bone osteoblasts.

ANTI-AGING AGENT

Tocotrienol preferentially accumulates at the stratum corneum of the skin. Being a more potent antioxidant, the tocotrienols neutralizes free radicals at a faster rate and hence protect tocopherols.Tocotrienols topically applied onto the skin was found to penetrate rapidly through the skin and the highest concentrations are found in the uppermost 5 microns.Tocotrienol-treated skin contained Vitamin E at concentration 7-30 fold higher than control values.

TABLE SHOWING THE PHARMACOLOGICAL POTIENT OF DIFFERENT TYPES OF TOCOTRIENOLS
Figure 1:

S.No.	Protective activity	Tocotrienol type	Proposed mechanism of action
1.	Anti-cancer	γ-T_3	Inhibition of NF-κB, TGF-β and P38 signalling pathways
		γ-T_3, δ-T_3	Induction and potentiation of apoptosis
		α-T_3, γ-T_3, δ-T_3	Activation of caspases
		γ-T_3, δ-T_3	Down-regulation of Bcl-2 and cyclin D
		α-T_3, γ-T_3	Suppression of HMGR activity
		TRF from palm oil	Induction of DNA fragmentation
		α-T_3, δ-T_3	Inhibition of angiogenesis
		γ-T_3, δ-T_3	Inhibition of cell proliferation through cell cycle arrest
		γ-T_3, δ-T_3	Down-regulation of Raf/Erk pathway
2.	Anti-diabetic	TRF from palm oil and rice bran oil	Prevents the formation of advanced glycationendproducts in diabetic rats
		α-T_3, γ-T_3, δ-T_3	Reduces hyperglycemia and hyperlipidemia in diabetic rats
		α-T_3, γ-T_3, δ-T_3	Inhibition of NF-κB signalling pathway
		α-T_3, γ-T_3, δ-T_3	Inhibition of oxidative-nitrosative stress
		α-T_3, γ-T_3, δ-T_3	Inhibition of TNF-α, IL-1β, TGF-β1 and caspase-3 activity
		TRF from palm oil and rice bran oil	Reduction of glucose-insulin index
		α-T_3, γ-T_3, δ-T_3	Increase in insulin sensitivity
3.	Anti-inflammatory	α-T_3, γ-T_3, δ-T_3	Suppression of NF-κB, TNF-α, IL-1, IL-6, IL-8 and iNOS
		α-T_3, γ-T_3, δ-T_3	Suppression of cyclooxygenase-2 activity
		α-T_3, γ-T_3, δ-T_3	Suppression of STAT-3 signalling pathway
4.	Antioxidant	α-T_3, γ-T_3, δ-T_3	Increase in the activity of antioxidant enzymes
		TRF from palm oil and rice bran oil, α-T_3, γ-T_3, δ-T_3	Quenching and scavenging of free radicals
		α-T_3, γ-T_3, δ-T_3	Inhibition of lipid peroxidation
5.	Immuno-stimulatory	α-T_3, δ-T_3	Induction of antibody production
		α-T_3, γ-T_3, δ-T_3	Induction of IFN-γ, IL-4, IL-1β production
		δ-T_3	Suppression of TNF-α

S.No.	Protective activity	Tocotrienol type	Proposed mechanism of action
6.	Cardio-protective	α-T_3, γ-T_3	Inhibition of HMG-CoA reductase activity
		α-T_3, γ-T_3	Inhibition of expression of cell adhesion molecules
		α-T_3, γ-T_3	Reduction in the levels of blood cholesterol
		TRF from palm oil and rice bran oil, δ-T_3	Inhibition of lipid peroxidation
		γ-T_3, δ-T_3	Downregulation of c-Src expression
		γ-T_3, δ-T_3	Upregulation of phosphorylation of Akt
		TRF from palm oil	Reduction in the production of apolipoprotein B, platelet derived factor-4, thromboxane B2
		TRF from palm oil and rice bran oil	Downregulation of TGF-β
7.	Neuro-protective	α-T_3	Inhibition of PP 60 (c-Src) kinase activity and phosphorylation of Erk
		α-T_3, γ-T_3	Inhibition of 12-lipoxygenase activity
		α-T_3, γ-T_3, δ-T_3	Reduction of oxidative stress
8.	Hepato-protective	α-T_3, γ-T_3	Inhibition of lipid peroxidation and oxidative damage
		γ-T_3, δ-T_3	Induction of the expression of CYP450, UGT1A1 nad MDR-protein 1
		TRF from palm oil and rice bran oil, α-T_3, γ-T_3, δ-T_3	Induction of hepatic antioxidant status
9.	Nephro-protective	TRF from rice bran oil, α-T_3, γ-T_3	Inhibition of oxidative-nitrosative stress
		TRF from palm oil and rice bran oil, α-T_3, γ-T_3	Downregulating the expression of NF-κB, TGF-β, TNF-α and caspase-3

NATURAL SOURCES OF TOCOTRIENOLS

Tocotrienols are the primary form of vitamin E in the seed endosperm of most monocots, including agronomically important cereal grains such as wheat, rice and barley. Palm oil contains significant quantities of tocotrienol. Crude palm oil extracted from the fruits of Elaeis guineesis particularly contains a high amount of tocotrienols (upto 800 mg/kg) mainly consisting of γ- tocotrienol and α-tocotrienol. Compared to tocopherols, tocotrienols are considerably less widespread in the plant kingdom. The identification of α-tocotrienol as a cholesterogenesis inhibitory factor derived from barley (Hordeum vulgare L.) Palm oil represents one of the most abundant natural sources of tocotrienols. The distribution of vitamin E in palm oil is 30% tocopherols and 70% tocotrienols. α-tocotrienol is the predominant form of tocotrienol in oat (Avena sativa L.) and barley (56 and 40 mg/kg of dry weight, respectively) . β-Tocotrienol is the major form of tocotrienol found in hulled and dehulled wheats (from 33 to 43 mg/kg of dry weight).

Palm

Rice

Wheat

Barley

Tocotrienols From Normal Diet Alone

Since tocotrienols only occur at very low levels in nature, with the highest concentration found in palm oil, it is virtually impossible to attain the amount of tocotrienols that show beneficial effects from the normal diet alone.

TOCOTRIENOL PRODUCTS AVAILABLE IN MARKET

Tocotrienols are members of vitamin family with unique biological activities.

Tocotrienols are powerfull radial scavengers that may help to promote normal arterial function,health cholesterol metabolism and liver health.The patented self emulsifying oral delivery system utilized help in improving the absorption of tocotrienol with a bioavailability up to 300%

1.Red Palm Tocotrienol -50mg Soft Gels
2.Delta Gold Tocotrienol -50mg Soft Gels
3.Tocomin Supra Bio -100mg

TOCOTRIENOL TOXICITY

ACUTE AND SUBCHRONIC TOXICITY

Oo et.al (1992) administerd a palm oil extract containing 80% tocotrienol to rats and mice by intubation up to a dose of 25,000 mg/kg bw in an acute toxicology studty.No mortality or adverse effect were observed in animals at any dose .Ima-Nirwanaet.al(2011) perfomed 14 day acute and 42 day subchronic toxicity studies in mice given a palm oil extract by intubation that contained 18.43% alpha tocopherol ,14.62 % alpha tocotrienol ,32.45% gamma tocotrienol and 23.93% delta tocotrienols.Doses of the extract administered were 200,500 and 1000mg/kg.The controlled group received vitamin E free palm oil.no deaths were reported in the acute toxicity study.

CHRONIC TOXICITY

Tasaki.et al(2008) evaluated tha toxicological effects of a 52 weeks exposure to tocotrienol concentrate from palm oil extract(21.4% alpha tocotrienol ,3.5% beta tocotrienol,36.5% gamma tocotrienol,8.6% delta tocotrienol) in wistar Hannover rats of both sexes . Four groups (10 rats /sex /group) where fed daily doses of 0%,0.08%, 0.4% or 2% of a preparation in powdered diet .By week 50 six male rats had died at the 2% dose .At necropsy, this rats were found to have hemorrhaging observed at the cerebral base and in the thoracic cavity, testis,prostate,and/or bladder because of this for the last 2 weeks of the study, the 2% dose was decreased to 1% in both sexes. The final body weights of male and female rats werw significantly decreased in the initially 2% treated group. Relativr but not absolute weights of brain,heart,lungs and kidneys were significantly increased in male rats receaving the initial 2% dose.absolute weights were significantly increased for heart,liver and kidney at 0.4% and decreased for lungs at 2% dose for female rats.

TOCOTRIENOL DOSAGE

50mg/d – Antioxidant
100 to 400mg/d – Heart and Cellular health
200 to 3200mg/d – Used in Cancer studies without sideeffects

CONCLUSION:

In recent years, the basic research on vitamin E has expanded from primarily focusing on αTocotrienol and its antioxidant effects to investigation of different tocopherols and tocotrienols, their metabolism, and their non-antioxidant activities including anti-inflammatory properties. Despite well-documented beneficial effects, as well as negative association between αT intake and chronic diseases, supplementation with αTocotrienol has failed to offer consistent benefits for the prevention of chronic diseases, including cancer and cardiovascular diseases, in many large clinical intervention studies . αTocotrienol may be beneficial to individuals with deficiency of αTocotrienol and/or other micronutrients , that can be caused by low dietary intake of this vitamin E or depletion of αTocotrienol due to pathological condition or malnutrition associated with smoking, alcoholism, and malabsorption. Under these subclinical conditions, αTocotrienol supplementation is likely to be beneficial, as indicated in the Linxian study in a population with deficiencies of micronutrients and the ATBC study including heavy smokers. On the other hand, αTocotrienol supplementation did not show beneficial effects in people with adequate nutrient status. In contrast to αTocotrienol, despite no evidence that deficiency of other vitamin E forms would result in obvious clinical symptoms, accumulating evidence suggests that γT, δT, and tocotrienols seem to have unique properties that are superior to αTocotrienol and relevant to prevention and therapy against chronic diseases even under conditions with adequate αTocotrienol status. It is noteworthy that these bioactivities of tocopherols and tocotrienols including anti-inflammatory properties have been identified by mechanistic studies and subsequently substantiated in some preclinical models as well as clinical studies. Hence, tocotrienols possess neuroprotective, antioxidant, anti-cancer and cholesterol lowering properties. Tocotrienols are thought to have more potent antioxidant and free radical scavenging properties due to their better distribution in the lipid layers of the cell membrane. In spite of the promising potential, the experimental analysis of tocotrienols accounts for only a small portion of vitamin E research.

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