Complete E SAP

Science-based synergistic combination of mixed tocopherols and tocotrienols

Vitamin E, a peroxyl radical scavenger, is the major lipid-soluble component in the cell antioxidant defense system and is exclusively obtained from the diet. Plants synthesize eight forms of vitamin E from homogentisic acid, namely the *alpha*, *beta*, *gamma*, and *delta* classes of tocopherol and tocotrienol. Although each of these molecules is a peroxyl radical scavenger, the human body seems to have a particular affinity for *alpha*-tocopherol. Vitamin E, in general, has been shown for its potential benefits for cardiovascular health and its role in the development of different types of cancer. Vitamin E's ability to inhibit protein kinase C protects against inflammation, lipid buildup in the aorta, diabetic vascular complications, and platelet aggregation. Tocotrienols are equally superior in their antioxidant capacity and have a strong neuroprotection capability. NFH **Complete E SAP** provides a high-quality synergistic combination of mixed tocopherols and tocotrienols for optimal health.

ACTIVE INGREDIENTS

Each softgel contains:

Natural vitamin E (d-*alpha*-tocopherol) (from non-GMO sunflower)	268 mg AT (400 IU)
Mixed tocopherols (from non-GMO soy)	53 mg
d-*alpha*-Tocopherol	7–14%
beta-Tocopherols	0.5–2%
delta-Tocopherols	13–25%
gamma-Tocopherols	45–60%
Squalene (from olive [*Olea europaea*] fruit)	45 mg
Free plant sterols (from non-GMO soy) (8 mg *beta*-sitosterol, 4 mg campesterol, 4 mg stigmasterol)	20 mg
Tocotrienols (from non-GMO palm fruit)	3.16 mg
d-*alpha*-Tocotrienols	24–30%
beta-Tocotrienols	2–4%
gamma-Tocotrienols	30–46%
delta-Tocotrienols	10–20%

NON-MEDICINAL INGREDIENTS: Beeswax, organic sunflower oil, and sunflower lecithin in a softgel composed of annatto extract (in sunflower oil), gelatin, glycerin, and purified water.

This product is non-GMO.

Contains no: Gluten, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavour or colour, starch, or sugar.

Complete E SAP contains 60 softgels per bottle.

DIRECTIONS FOR USE

Adults: Take 2 softgels daily with food or as directed by your healthcare practitioner.

INDICATIONS

Complete E SAP can help:

- Promote cardiovascular and metabolic health
- Improve bone metabolism and turnover in postmenopausal women
- Enhance vascular and endothelial function

SAFETY, CAUTIONS, AND WARNINGS

Consult a healthcare practitioner prior to use if you are pregnant or breastfeeding; if you have cancer; if you have cardiovascular disease or diabetes; or if you are taking blood thinners. Colour, size, and smell may vary from one lot to another. Do not use if seal is broken. Keep out of reach of children.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for each **Complete E SAP** lot number have been tested by an ISO 17025– accredited third-party laboratory for identity, potency, and purity.

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

NFH

351, Rue Joseph-Carrier, Vaudreuil-Dorion, Quebec, J7V 5V5
T 1 866 510 3123 • F 1 866 510 3130 • nfh.ca

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Plants produce eight distinct vitamin E-related molecules in a human's daily diet. [1] In several animal-based and clinical studies, vitamin E, in general, has been proven to possess peroxyl radical-scavenging properties and inhibit lipid peroxidation. [2] Although each of these molecules is a peroxyl radical scavenger, the human body seems to have a particular affinity for alpha-tocopherol. [3] Alpha-tocopherol's unique benefits include its potential to act against health issues, including atherosclerosis, ischemic heart disease, and the development of different types of cancer. [4] Vitamin E's ability to inhibit protein kinase C protects against inflammation, lipid buildup in the aorta, diabetic vascular complications, and platelet aggregation. [5] Tocotrienols are equally superior in their antioxidant capacity and have a strong neuroprotection capability. [6]

SOURCES AND CHEMISTRY OF TOCOPHEROLS AND TOCOTRIENOLS

Alpha-tocopherol is widely found in oils extracted from almonds, peanuts, olives, and sunflowers. Similarly, *gamma*-tocopherol is rich in edible oils from canola, corn, camelina, linseed, soybean, and walnut. [7] Likewise, palm oil is a rich source of tocotrienols; other sources include coconut oil, cocoa butter, soybeans, barley, and wheat germ. [8] Both tocopherol and tocotrienol hold a common chroman head in their chemical structure; while the former exists as free phenols, the latter is present as an esterified form. [9] Intestinal uptake of vitamin E and its isomers occurs in a free alcohol form, 6-hydroxyl. [10]

CARDIOVASCULAR AND METABOLIC HEALTH BENEFITS OF MIXED TOCOPHEROLS

Vitamin E helps maintain vascular health by breaking the lipid peroxidation chain reaction via the free radical scavenging process; thus, uptake of supplemental of 100–250 IU/day of vitamin E can reduce the risk of major coronary diseases such as CAD, non-fatal myocardial infarction (MI), and cardiovascular death by 35–40%. [11] A preclinical study on nephrectomized mice receiving a 1000 mg/kg diet of α-tocopherol supplementation or a 1000 mg/kg diet of mixed-tocopherol (60% γ-tocopherol) showed an enhancement in aortic contraction and a substantial decrease in the levels of IL-6, IL-10, and TNF levels. [12] A study on the effect of mixed tocopherols on hydrogen peroxide-induced lipid peroxidation in human erythrocytes revealed that the mixture had higher potential in inhibiting lipid peroxidation induced in human erythrocytes than alpha-tocopherol alone. [13] A clinical study by Wang et al. showed a significant reduction in the plasma F2-isoprostanes. [14]

When diabetes-affected individuals were supplemented with mixed tocopherols, it helped stimulate neutrophil leukotriene levels in the mixed tocopherol group, resulting in a beneficial effect against oxidative stress and inflammation. [15] It helped improve the cardiovascular health of diabetic individuals by significantly decreasing the postprandial brachial artery flow-mediated dilation (30 to 44%) after glucose ingestion. [16] Similarly, 800 mg of alpha- or gamma-tocopherol in combination helped in the noteworthy decline of hs-CRP levels and a substantial decrease in tumour necrosis factor (TNF) levels. [17]

MIXED TOCOPHEROLS IN POSTMENOPAUSAL HEALTH

Several proinflammatory factors, including interleukin-1 alpha and TNF-alpha, are found to be responsible for bone resorption. [18] A preclinical study on vitamin E's effect on bone health using ovariectomized rats can improve bone quality and reduce bone resorption while promoting bone formation. [19] A human trial showed that 400 units of mixed tocopherols per day can significantly improve the serum C-terminal telopeptide of type I collagen (CTX), indicating an improvement in the mean bone resorption. [20] A similar study also noted that postmenopausal insomnia can be resolved by mixed tocopherol supplementation. [21]

MIXED TOCOPHEROL AND INFLAMMATORY BIOMARKERS

As indicated above, receiving 500 to 800 mg of mixed tocopherols per day for six weeks helped in the significant decrease of TNF levels, which indicates that it has the potential to control the expression of inflammatory biomarkers. [22]

CARDIOVASCULAR AND METABOLIC HEALTH BENEFITS OF MIXED TOCOTRIENOLS

Diabetic peripheral neuropathy is one of the significant morbidities caused by the inappropriate activation of protein kinase C (PKC) isoforms and accumulation of advanced glycation end products. [23] When diabetic rats were treated with 25, 50, and 100 mg/kg body weight of mixed tocotrienol, it helped attenuate behavioural, biochemical, and molecular changes associated with diabetic neuropathy. [24] A clinical intervention showed that 400 mg of mixed tocotrienols per day led to a substantial reduction in lancinating pain among patients with hemoglobin A1C levels greater than 8% in the mixed tocotrienols group. [25] Similarly, 400 mg TOCOVID enhanced nerve conduction velocities and significantly improved tibial motor nerve conduction velocity. [26, 27]

A study on hamsters showed that tocotrienol can effectively help treat dyslipidemia-related infection and inflammation. [28] Two other clinical studies elucidated that mixed tocotrienols helped in a substantial decrease of the serum total cholesterol, low-density lipoprotein (LDL) cholesterol, diastolic blood pressure, total cholesterol, LDL and HDL-cholesterol, IL-6 and tumour necrosis factor. [29, 30] Receiving a supplement of 400 mg of mixed tocotrienols per day for a year aided in normalizing hepatic echogenic response. [31]

MIXED TOCOTRIENOLS IN POSTMENOPAUSAL HEALTH

Postmenopausal women treated with 430 or 860 mg of mixed tocotrienols (annatto-extracted) per day for 12 weeks showed a noticeable decrease in bone resorption, and there was a substantial improvement in bone turnover rate via suppressing bone remodelling regulators. [32]

SYNERGISTIC EFFECT OF COMBINATION OF TOCOPHEROLS AND TOCOTRIENOLS

A clinical trial by Stonehouse et al. showed that receiving 1020 mg per day of tocotrienols and tocopherols as a combination led to a substantial increase in serum levels of tocotrienols. [33] An increase in fasting plasma tocotrienol concentration was noted in a similar study. [34] Osman et al. studied the effectiveness of this combination on hypercholesterolemia and found that it had a neutral effect on inflammatory biomarkers, including hs-CRP and interleukin-6. [35]

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INDICATION SPECIFIC DOSAGE SUMMARY BASED ON HUMAN CLINICAL RESEARCH#

#Please note these suggestions are guidelines based on the clinical studies. Evidence for efficacy and safety have been qualitatively (study quality in terms of study design, sample size, appropriate methods of analysis, use of appropriate placebo/control, bias etc) assessed and have been rated using a 5 star ★ rating classification.

Indication	Suggested dosage	Supporting evidence and study outcome	Study design	Outcome measures	Safety	Evidence quality rating
MIXED TOCOPHEROLS: Cardiovascular and Metabolic Health						
Diabetes[1, 2, 3]	2 softgels/day	A significant decrease in the plasma F2-isoprostanes and stimulated neutrophil leukotriene levels in the mixed tocopherol group resulting in beneficial effect against oxidative stress and inflammation	Randomized, double-blind, placebo-controlled study. (n=55), 500 mg of mixed tocopherols or *alpha*-tocopherols per day for 6 weeks	Cellular tocopherols, plasma and urine F2-isoprostanes, erythrocyte antioxidant enzyme activities, plasma inflammatory markers, ex vivo assessment of eicosanoid synthesis	No severe adverse effects were reported	★★★
	2 softgels/day	A significant decrease (30%–44%) in the postprandial Brachial artery flow-mediated dilation (FMD) following glucose ingestion thereby helped in improvement of vascular endothelial function	Randomized, crossover, single-blind study. (n=15), 500 mg γ-tocopherol-rich mixture of tocopherols (γ-TmT) per day for 5 days. 500 mg γ-tocopherol, 60 mg α- tocopherol, 170 mg δ- tocopherol and 9 mg β-tocopherol	Brachial artery flow-mediated dilation (FMD), plasma glucose, insulin, antioxidants, malondialdehyde (MDA), inflammatory proteins, arginine, asymmetric dimethylarginine (ADMA)	No severe adverse effects were reported	★★★
	2 softgels/day	A significant increase in the excretion of *gamma*-carboxyethyl-hydroxychroman indicating the displacement of *gamma*-tocopherol by *alpha*-tocopherol due to incorporation of the latter into lipoproteins in the liver	Randomized, placebo-controlled study. (n=55), 500 mg of mixed tocopherols or *alpha*-tocopherols per day for 6 weeks	Serum, erythrocyte, and platelet tocopherol and urinary metabolite concentrations such as soluble CD40 ligand, urinary 11-dehydro-thromboxane B2, serum thromboxane B2, soluble P-selectin, von Willebrand factor	No severe adverse effects were reported	★★★
Blood Pressure[4,5]	2 softgels/day	A significant decrease in the plasma F2-isoprostanes, and an increase in systolic and diastolic BP, heart rate and pulse pressure	Randomized, double-blind, placebo-controlled study. (n=58), 500 mg of mixed tocopherols or RRR *alpha*-tocopherols per day for 6 weeks. 60% *gamma*, 25% *delta* and 15% *alpha*-tocopherol	24-hour ambulatory BP, heart rate, endothelium- dependent and independent vasodilation and plasma and urinary F2-isoprostanes	No severe adverse effects were reported	★★★
	2 softgels/day	A significant increase in the serum level of *gamma*-tocopherol but there was no significant difference in 24-hour systolic or diastolic BP	2 Randomized, double-blind, placebo-controlled studies. (n=58 for the first study and n=69 for the second) 500 mg of mixed tocopherols or RRR *alpha*-tocopherols per day for 6 weeks 60% *gamma*	24-hour ambulatory BP, rate of measurement-to-measurement BP variation	No severe adverse effects were reported	★★★
MIXED TOCOPHEROLS: Women's Health						
Postmenopausal insomnia[6]	1 softgel/day	A significant improvement in sleep quality corresponding to the decrease in the PSQI scores, also a significant decrease in the percentage of patients using sedative drugs in vitamin E group	Randomized, double-blind, placebo-controlled study. (n=160), 400 IU of mixed tocopherols per day for 3 weeks. 20% *delta*-tocopherol, 1% *beta*-tocopherol, 62% *gamma*-tocopherol, and 10% *alpha*-tocopherol	Post-intervention sleep quality by PSQI, the reduction of sedative drugs used	No severe adverse effects were reported	★★★
Postmenopausal bone turnover[7]	1 softgel/day	A significant improvement in the serum C-terminal telopeptide of type I collagen (CTX) indicating an improvement in the mean bone resorption	Randomized, double-blind, placebo-controlled study. (n=160), 400 IU of mixed tocopherols per day for 12 weeks 20% *delta*-tocopherol, 1% *beta*-tocopherol, 62% *gamma*-tocopherol, and 10% *alpha*-tocopherol. 600 mg of calcium carbonate twice per day (total of 1200 mg per day) and 20,000 IU of vitamin D2 one time per week	A comparison of the bone turnover markers, C-terminal telopeptide of type I collagen (CTX) and N-terminal propeptide of type I collagen (PINP)	No severe adverse effects were reported	★★★

Indication	Suggested dosage	Supporting evidence	Study design	Outcome measures/ selection criteria for studies	Safety	Evidence quality rating
MIXED TOCOPHEROLS: Immune Health						
Inflammatory biomarkers[8]	2 to 3 softgels/day	A significant decrease in the tumor necrosis factor-α (TNF-α) concentrations	33 Randomized, controlled studies. (n=2102), 500 to 800 mg of mixed tocopherols per day for 6 weeks	Serum CRP concentrations, serum concentrations of tumor necrosis factor-α (TNF-α), inflammatory cytokines including IL-1, IL-2, IL-4, IL1β	No severe adverse effects were reported	★★★★
MIXED TOCOTRIENOLS: Cardiovascular and Metabolic Health						
Diabetic peripheral neuropathy[9, 10, 11]	NA	A significant reduction in lancinating pain among patients with hemoglobin A1C levels greater than 8% in the mixed tocotrienols group	Randomized, double-blind, placebo-controlled, parallel study. (n=391), 400 mg of mixed tocotrienols per day for 12 months oral folic acid, 5 mg once daily, and 500 µg methylcobalamin thrice daily	Patient-reported neuropathy Total Symptom Score (TSS) (lancinating pain, burning pain, paresthesia, and asleep numbness) changes, Neuropathy Impairment Score (NIS), sensory nerve conduction test result	No severe adverse effects reported (more infections were observed in the tocotrienols group)	★★★
	NA	A significant improvement in nerve conduction velocities corresponding to the increase in levels of serum nerve growth factor (NGF)	Randomized, double-blind, placebo-controlled, multi-center, prospective study. (n=80), 400 mg of TOCOVID per day for 8 weeks d-α-Tocotrienol: 61.52 mg d-γ-Tocotrienol: 112.80 mg d-δ-Tocotrienol: 25.68 mg d-α-Tocopherol: 91.60 IU Plant Squalene: 51.28 mg Phytosterol Complex: 20.48 mg	Nerve conduction study, serum biomarkers including nerve growth factor (NGF), malondialdehyde, vascular cell adhesion molecule 1, tumor necrosis factor receptor 1, thromboxane B2	No severe adverse effects were reported	★★★
	NA	A significant improvement of tibial motor nerve conduction velocity	Randomized, double-blind, placebo-controlled study. (n=90), 400 mg of TOCOVID per day for 8 weeks	HbA1c, renal profile, lipid profile, nerve conduction study (NCS)	No severe adverse effects reported (Gastrointestinal issues)	★★★
Hypercholestero-lemia[13]	NA	A significant decrease in the serum total cholesterol and low density lipoprotein (LDL) cholesterol	Randomized, double-blind, parallel group study. (n=32), 300 mg of mixed tocotrienols per day for 6 months	Total cholesterol, high density lipoprotein (HDL) cholesterol, LDL cholesterol, triacylglycerol, *alpha*-tocotrienol, *gamma*-tocotrienol, *delta*-tocotrienol, *alpha*-tocopherol	No severe adverse effects were reported	★★★
	NA	A decrease in the diastolic blood pressure, total cholesterol, LDL and HDL-cholesterol, interleukin-6 and tumour necrosis factor-a from baseline	Randomized, double-blind, placebo-controlled study. (n=70), 400 mg of mixed tocotrienols per day for 16 weeks	Serum levels of TC, HDL-cholesterol, plasma levels of fasting plasma glucose (FPG), interleukin-6 (IL-6), tumour necrosis factor- a (TNF-a), leptin, adiponectin, high sensitivity C-reactive protein	No severe adverse effects were reported	★★★
Fatty liver[14]	NA	A significant normalisation of hepatic echogenic response, and also a substantial rate of remission	Randomized, double-blind, placebo-controlled, parallel study. (n=87), 400 mg of mixed tocotrienols per day for a year 61.5 mg, 112.8 mg, and 25.7 mg for *alpha*, *gamma* and *delta*-tocotrienol	Normalisation of hepatic echogenic response	No severe adverse effects were reported	★★★
MIXED TOCOTRIENOLS: Women's Health						
Postmenopausal bone resorption[15]	NA	A significant increase in the serum levels of tocotrienols but no changes in vascular functions	Randomized, double-blind, placebo-controlled study. (n=70), 430 or 860 mg of mixed tocotrienols per day for 12 weeks. An extract from annatto seed with 70% purity, consisted of 90% *delta*-TT and 10% *gamma*-TT	Bone markers (serum bone-specific alkaline phosphatase (BALP), urine N-terminal telopeptide (NTX), serum soluble receptor activator of nuclear factor- kappaB ligand (sRANKL), and serum osteoprotegerin (OPG)), urine calcium, and an oxidative stress biomarker (8-hydroxy-2'-deoxyguanosine (8-OHdG))	No severe adverse effects were reported	★★★
COMBINATION OF TOCOPHEROLS AND TOCOTRIENOLS: Cardiovascular and Metabolic Health						
Vascular function[16]	3-4 softgels/day	A significant normalisation of hepatic echogenic response, and also a substantial rate of remission	Randomized, double-blind, placebo-controlled study. (n=90), 1020 mg of combination of tocotrienols and tocopherols per day for 8 weeks 420 mg tocotrienols and 132 mg tocopherols	FMD, other physiological and circulatory markers of vascular function, lipid profiles, glucose, insulin, and inflammatory markers	No severe adverse effects were reported	★★★

Indication	Suggested dosage	Supporting evidence	Study design	Outcome measures/ selection criteria for studies	Safety	Evidence quality rating
COMBINATION OF TOCOPHEROLS AND TOCOTRIENOLS: Cardiovascular and Metabolic Health						
Metabolic syndrome[17]	2 softgels/day	A significant increase in fasting plasma tocotrienol concentration, but no significant effect on the fasting platelet aggregation reactivity	Randomized, double-blind, crossover, placebo-controlled study. (n=32), 400 mg of combination of tocotrienols and tocopherols per day for 2 weeks 69% tocotrienols and 31% α-tocopherol	Fasting platelet aggregation reactivity	No severe adverse effects were reported	★★★★
Hypercholestero-lemia[18]	1-2 softgels/day	A neutral effect on the inflammatory biomarkers including high sensitivity C-reactive protein (hsCRP) and interleukin-6 (IL6)	Prospective study. (n=35), 320 mg of combination of tocotrienols and tocopherols per day for 12 months (+ 500 mg vitamin C) *alpha*-tocopherol (44mg), *alpha*-tocotrienol (118.48%), *beta*-tocotrienol (9.04%), *gamma*-tocotrienol (117.28%), *delta*-tocotrienol (75.20%) and palm super olein (128mg)	Inflammatory biomarkers including high sensitivity C-reactive protein (hsCRP) and interleukin-6 (IL6)	No severe adverse effects were reported	★★
TWO TOCOPHEROLS (GAMMA AND ALPHA): Metabolic Health						
Metabolic syndrome[19]	3 to 4 softgels/day	Significant decline in hsCRP levels in the combination group, also a substantial decrease in TNF levels in the combination and alpha- alone group	Randomized, double-blind, placebo-controlled study. (n=90), 800 mg of *alpha* or *gamma*-tocopherol or in combination per day for 6 weeks	Measurement of indices of oxidative stress and inflammation, including whole blood cytokines (IL-1b, TNF-α, IL-6), hsCRP, and urinary nitrotyrosine, a complete blood count, plasma lipid profile, kidney (creatinine) and liver function (AST, ALT) test, blood glucose test, and TSH	No severe adverse effects were reported	★★★

NA- Studies related to supplementing with only mixed tocotrienols where the dosages used are much higher compared to the amounts present in Complete E SAP to suggest a reusable dosage. The studies are included to provide an review on the available research.

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