

Tocotrienol research: past into present

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The vitamin E family consists of eight isomers known as alpha-, beta-, gamma-, and delta-tocopherols and alpha-, beta-, gamma-, and delta-tocotrienols. Numerous studies focused on the health benefits of these isomers have been performed since the discovery of vitamin E in 1922. Recent discoveries on the potential therapeutic applications of tocotrienols have revolutionized vitamin E research. Nevertheless, despite the abundance of literature, only 1% of vitamin E research has been conducted on tocotrienols. Many new advances suggest that the use of tocotrienols for health improvement or therapeutic purposes is promising. Although the mechanisms of action of tocotrienols in certain disease conditions have been explored, more detailed investigations into the fundamentals of the health-promoting effects of these molecules must be elucidated before they can be recommended for health improvement or for the treatment or prevention of disease. Furthermore, many of the studies on the effects of tocotrienols have been carried out using cell lines and animal models. The effects in humans must be well established before tocotrienols are used as therapeutic agents in various disease conditions, hence the need for more evidence-based human clinical trials.

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INTRODUCTION

Vitamin E is an important nutrient in the human diet and is a well-known antioxidant that is readily available in lipid-rich plant products. Historically, drug discovery research has focused on natural products, some of which are huge reservoirs of biological compounds with pharmacologic properties.¹ Since the discovery of vitamin E in 1922, many studies have focused on the potential health benefits and therapeutic use of the two main forms of vitamin E, namely, tocopherols and tocotrienols. Tocotrienols represent a very important part of the vitamin E family. However, most of the vitamin E research has focused on alpha-tocopherols, and only 1% of vitamin E studies have investigated tocotrienols.² Several studies have

reported that tocotrienols may have more potent antioxidation³ and anticancer effects^{4,5} than tocopherols. Studies have also reported that tocotrienols possess lipid-lowering,^{6–10} antiatherogenic,^{11,12} blood-pressure-lowering,^{13,14} antidiabetic,^{15–17} neuroprotective,^{18–20} and anti-inflammatory²¹ effects. The abundance of literature suggests that the use of tocotrienols for therapeutic purposes is very promising. The health benefits of tocotrienols have been reviewed previously,^{2,22} but the rapid expansion of the literature on tocotrienol research and the more recent discoveries pertaining to the benefits of tocotrienols necessitate frequent updates on this topic. This review, therefore, aims to provide an overview that includes the major discoveries of the past as well as the more recent advances in tocotrienol-related health benefits.

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TOCOTRIENOLS

Historical background

Tocotrienols belong to the vitamin E family. Together with the tocopherols, there are eight isomers of vitamin E, namely, alpha-, beta-, gamma-, and delta tocopherols and alpha-, beta-, gamma-, and delta tocotrienols.²² Vitamin E was first discovered in green leafy vegetables,²³ and at that point, this micronutrient was thought to be important for human reproduction.²³ It was later scientifically named “tocopherol.” The word “tocopherol” has a Greek origin, with “tokos” referring to “childbirth,” “phero” meaning “to bring-forth,” and “ol” indicating the alcohol properties of this molecule. The chemical structure of vitamin E was elucidated in 1938, and the vitamin E molecule was first synthesized chemically in the same year.²⁴

Natural sources

The main sources of vitamin E are lipid-rich plant products and vegetable oils. Tocotrienols are found in palm oil and rice bran,²⁵ whereas sunflower, peanut, walnut, sesame, and olive oils contain only tocopherols.²⁶ Other natural sources of tocotrienols include coconut oil, cocoa butter, soybeans, barley, and wheat germ. In 1965, tocotrienols were first reported to be present in latex.²⁷ Among the natural sources of tocotrienols, palm oil is one of the most abundant.²⁸ The oil palm tree, *Elaeis guineensis* Jacq., is native to many West African countries, and large-scale plantations have been established in tropical regions of Asia, Africa, and Latin America, aiming mainly at the production of palm oil.²⁹ Tocopherols make up 30% of the vitamin E in palm oil, with the remaining 70% being tocotrienols.³⁰ The US Food and Drug Administration's final ruling on trans-fatty acid labeling in 2003 transformed the fat and oil industries.³¹ As palm oil is free of trans-fatty acids, palm oil has since gained wide acceptance by the food industry in the United States as well as in other parts of the world.

Intake of tocotrienols from food and supplements

Isomers of vitamin E are widely available in many types of food consumed daily. A study undertaken to assess the tocopherol and tocotrienol levels of 79 food items consumed in Hawaii found that the average content of tocotrienols in all food was ≤ 432 mg/kg. Some common foods found to be rich in tocotrienols include cereals and breads, while other items were found to contain mainly tocopherols.³² The daily tocotrienol intake of the Japanese population was estimated to be between 1.9 mg and 2.1 mg/day/person, which was lower than tocopherol

intake (8–10 mg/day/person).³³ In food supplements, tocotrienols are usually incorporated into softgel capsules. A 1,000-mg daily dose is equivalent to a daily intake of 16.7 mg tocotrienols/kg/day for a 60-kg person, a dosage that is seven times below the level at which no adverse effects were observed in rats but higher than the level at which adverse effects were absent in human studies, which is 5 mg/kg/day.³⁴

Both tocotrienols and tocopherols are bioavailable, with the former having shorter plasma half-lives. The tissue distribution of tocotrienols is also different from that of alpha-tocopherol.³⁴ The bioavailability of tocotrienols can be affected by many factors. For example, it was shown that dietary alpha-tocopherol decreases alpha-tocotrienol but not gamma-tocotrienol concentrations in rats.³⁵ In addition, food status may also contribute to the bioavailability. It has been reported that the mean apparent volume of distribution values in the fed state were significantly smaller than those in the fasted state, which could be due to an increased absorption of tocotrienols in the fed state.³⁶ On the other hand, food processing may affect the availability of tocotrienols in food. For example, the seeds of buckwheat, after being subjected to an extrusion cooking process, were found to contain 62% less tocotrienols,³⁷ while sourdough fermentation was reported to reduce the levels of tocopherols and tocotrienols in whole-grain rye.³⁸

Chemical structure and properties of tocotrienols and tocopherols

Structurally, tocopherols and tocotrienols are very similar. The main difference is that tocopherols have a long saturated carbon side chain with chiral centers, while tocotrienols have three unsaturated bonds in the carbon side chain with one chiral center.³⁹ This unique property promotes the efficient metabolic function of tocotrienols, which allows tocotrienols to penetrate tissues with saturated fatty layers more readily when compared with tocopherols. Figure 1 illustrates the structures of tocopherols and tocotrienols.

ANTIOXIDANT EFFECTS OF TOCOTRIENOLS

Vitamin E is a well-known antioxidant. The antioxidant effects of vitamin E result from the incorporation of vitamin E into cellular membranes, where it inhibits peroxidation of lipids.²⁴ As important members of the vitamin E family, tocotrienols exhibit antioxidant effects by scavenging the chain-propagating peroxy radical.²⁴ It has been reported that alpha-tocotrienol possesses a more potent antioxidant activity than alpha-tocopherol in terms of scavenging peroxy radicals in liposomes.³ The

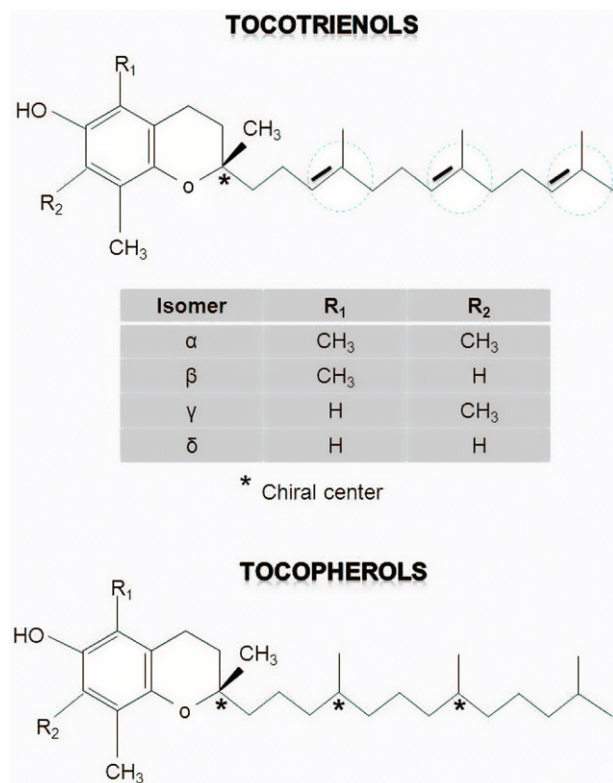


Figure 1 The structures of tocotrienols and tocopherols. Tocotrienols have only one chiral center and an unsaturated side chain containing three double bonds (in circles), while tocopherols have three chiral centers and a saturated side chain.

more even distribution of alpha-tocotrienol in the phospholipid bilayer of the plasma membrane and the more efficient collision of alpha-tocotrienol with radicals are among the many reasons why alpha-tocotrienol is a better antioxidant than alpha-tocopherol.²⁴ Many health-promoting effects of tocotrienols are attributed to their antioxidant effects, especially in cardiovascular diseases. For instance, Tomeo et al.¹² reported that tocotrienols were beneficial in patients with hyperlipidemia and carotid stenosis by demonstrating a significant reduction in thiobarbituric-acid-reactive substances in serum (indicator of maximal platelet peroxidation) in the treatment group. In animal models, tocotrienols have been shown to exert antiatherogenic effects via antioxidant-dependent and -independent mechanisms.⁴⁰ In addition, the ability of tocotrienols to scavenge free radicals has also been shown to reduce DNA damage. Chin et al.⁴¹ demonstrated that tocotrienol supplementation might benefit older healthy adults by providing DNA protection, as evidenced by decreases in DNA damage, sister chromatid exchange frequency, and urinary 8-hydroxy-2'-deoxyguanosine levels.

ANTICANCER EFFECTS OF TOCOTRIENOLS

Since the late 1980s, there has been extensive research into the anticancer effects of tocotrienols. As a result, there has been a rapid expansion of literature in this area, giving rise to an exhaustive list of publications, with the majority of work conducted on breast cancer. Other cancers that have been investigated include liver, prostate, pancreatic, cervical, colorectal, and skin cancers.

Breast cancer

As early as 1989, tocotrienol-rich palm oil was reported to prevent chemically induced mammary tumorigenesis.⁴² The mechanism of tocotrienol-induced cell death in breast cancer cells was gradually elucidated in the 1990s, with aggressive research carrying forward into the 21st century. In one study, the mechanism of tumor growth inhibition was shown to be via estrogen-independent mechanisms.⁴³ In contrast, Yu et al.⁴⁴ showed that tocotrienols are effective inducers of apoptosis in human breast cancer cells. Further studies demonstrated that tocotrienols induced apoptosis in mammary cancer cells via activation of the caspase-8 signaling pathway⁴⁵ or disruption of mitochondrial function.⁴⁶ When treated with tocotrienol-rich fraction (TRF) from palm oil, MDA-MB-231 and MCF-7 breast cancer cells were shown to be associated with c-Myc binding protein MM-1, 23-kDa highly basic protein, and interferon-inducible protein 9-27, which are proteins involved in the cell cycle that have inhibitory effects on cell growth and differentiation.⁴⁷ In a more recent study, gamma-tocotrienol-induced cell death in breast cancer cells was associated with suppression of Id1, a key cancer-promoting protein, further substantiating the antiproliferative and chemosensitization effects of gamma-tocotrienol.⁴⁸ In a pilot clinical trial, the effectiveness of TRF combined with tamoxifen in the management of early breast cancer was investigated. While evidence showed that tamoxifen and tocotrienol exhibit synergism *in vitro*, the study reported an insignificant 60% lower mortality in the intervention group and concluded that a larger randomized trial is warranted.⁴⁹

Other cancers

There is increasing evidence of the anticancer effects of tocotrienols in malignancies other than breast cancer. For instance, tocotrienols have been reported to suppress hepatocarcinogenesis in rats.^{50,51} Tocotrienols have also been demonstrated to inhibit cell growth in PC3 and LNCaP prostate cancer cells.⁵² Gamma-tocotrienol has been reported to be the most potent isomer that induced apoptosis in prostate cancer cells, and this effect was

found to be associated with the suppression of nuclear factor kappa B, epidermal growth factor receptor (EGFR), and Id family proteins (Id1 and Id3).⁵³ In addition, it was reported that TRF from palm oil activated p53, modulated the Bax-Bcl2 ratio, and induced cell-cycle-independent apoptosis in RKO colorectal cancer cells.⁵⁴ The first report on the anti-invasion and chemosensitization effects of gamma-tocotrienol against human malignant melanoma cells showed that chemotherapy using gamma-tocotrienol reduced skin cancer cells.⁵⁵ The anti-cancer effects of tocotrienols have also been demonstrated in pancreatic cancer, when it was shown that delta-tocotrienol induced suppression of cell proliferation in PANC-1 and 35 BxPC-3 pancreatic cancer cells.⁵⁶ These effects were attributable to cell cycle arrest at the G1 phase and induction of apoptosis. It was further shown that the inhibitory effect was attenuated by mevalonate, while delta-tocotrienol and lovastatin synergistically suppressed the proliferation of MIA PaCa-2 cells. In a recent report, tocotrienols were shown to exert anticancer effects in HeLa cervical cancer cells. These findings suggested that alpha- and gamma-tocotrienols were more effective in inhibiting HeLa cell proliferation, possibly through a pathway that upregulated IL-6 expression and downregulated cyclin D3, p16, and CDK6 expression.⁵⁷

CARDIOPROTECTIVE EFFECTS OF TOCOTRIENOLS

According to the World Health Organization,⁵⁸ an estimated 17.1 million people die of cardiovascular diseases each year. A large number of these deaths can be attributed to smoking, which increases the risk of coronary heart disease.⁵⁸ The high mortality rates as a result of coronary heart disease implies a need for urgent global attention. Among the many causes of coronary heart disease, coronary atherosclerosis accounts for more than 90% of cases. Therefore, the risk factors of coronary heart disease are those of atherosclerosis, which include hyperlipidemia, hypertension, diabetes mellitus, increasing age, smoking, a positive family history, and male sex.⁵⁹ Hence, many groups have investigated the cardioprotective effects of tocotrienols, which may be attributed to the antioxidant, lipid-lowering, blood-pressure-lowering, antiatherogenic, and antidiabetic effects of this form of vitamin E.

Lipid-lowering effects

For the past 30 years, investigations on the lipid-lowering effects have been carried out in cell lines, animal models, and humans. Study of the hypocholesterolemic effects of tocotrienols dates back to the 1980s, when it was shown that the addition of tocotrienols in chick diets signifi-

cantly lowered hepatic cholesterogenesis and serum low-density lipoprotein while concomitantly increasing lipogenic activity.⁶⁰ This finding resulted in an increase in tocotrienol-based research in the 1990s^{8–10,61–63} and the early 21st century.⁶⁴ From these studies, the mechanism by which tocotrienols exert their hypocholesterolemic effects was elucidated: it was shown that tocotrienols acted on the mevalonate pathway in mammalian cells by post-transcriptional suppression of 3-hydroxy-3-methyl-glutaryl CoA (HMG-CoA) reductase.^{7,9} More recently, Zaiden et al.⁶ examined the lipid-lowering effects of tocotrienols in HepG2 (liver) cells, hypercholesterolemic mice, and humans and concluded that ingestion of delta- and gamma-tocotrienols may lead to a reduction in triglyceride synthesis and transport.

Antiatherogenic effects

Studies on the antiatherogenic effects of tocotrienols date back to the 1990s. In 1993, a double-blind placebo-controlled study showed that patients with high cholesterol experienced a reversal of arterial blockage of the carotid artery after tocotrienol consumption, suggesting that tocotrienols may exert antiatherogenic effects.¹² Later, it was reported that tocotrienols from palm oil reduced lesion formation in atherosclerosis-prone mice, which was possibly achieved via both antioxidant-dependent and antioxidant-independent mechanisms.⁴⁰ In another study, it was shown that rice bran tocotrienols significantly reduced the size of atherosclerotic lesions in mice.¹¹

Other cardioprotective effects

Palm tocotrienols have been reported to have the ability to stabilize proteasomes.⁶⁵ This is an important finding, as it has been postulated that inactivation of proteasomes during myocardial infarction may play a role in cardiac cell survival or death.⁶⁶ This could be the pathway through which tocotrienols exert their cardioprotective effects. Other reported cardioprotective properties of tocotrienols include the ability to lower blood pressure,^{13,14} to protect against endothelial dysfunction and platelet aggregation,¹⁰ and to improve arterial compliance.⁶⁷ The antidiabetic effects of tocotrienols, which may also contribute to cardioprotection, are discussed separately in the next section.

ANTIDIABETIC EFFECTS OF TOCOTRIENOLS

Diabetes mellitus is a group of metabolic diseases that have hyperglycemia as a hallmark feature. It is due to defects in insulin secretion or action, or both. Chronic

Table 1 Summary of health-promoting effects of tocotrienols.

Health-promoting effects	Remarks and references
Antioxidant effects	Reduction in serum-thiobarbituric-acid-reactive substances (indicator of maximal platelet peroxidation) in patients with hyperlipidemia and carotid stenosis ¹² Demonstration of antiatherogenic effects via antioxidant-dependent and -independent mechanisms ⁴⁰ DNA protection as evidenced by a decrease in DNA damage, sister chromatid exchange frequency, and urinary 8-hydroxy-2'-deoxyguanosine levels in older healthy adults ⁴¹
Anticancer effects	Breast cancer Tocotrienol-rich palm oil prevented chemically induced mammary tumorigenesis ⁴² Mechanism of tumor-growth inhibition was shown to be via estrogen-independent mechanisms ⁴³ Tocotrienols were shown to be effective apoptotic inducers in human breast cancer cells ⁴⁴ Tocotrienols induced apoptosis in mammary cancer cells via activation of the caspase-8 signaling pathway ⁴⁵ Tocotrienols induced apoptosis in mammary cancer cells by disrupting mitochondrial function ⁴⁶ Tocotrienols induced cell death in breast cancer cells via proteins that have inhibitory effects on cell growth and differentiation (MM-1, 23-kDa highly basic protein, and interferon-inducible protein 9–27) ⁴⁷ Gamma-tocotrienol-induced cell death in breast cancer cells was associated with Id1, a key cancer-promoting protein, contributing to its antiproliferative and chemosensitization effects ⁴⁸ Tamoxifen and tocotrienol exhibited synergism in vitro ⁴⁹ Liver cancer Tocotrienols suppressed hepatocarcinogenesis in rats ^{50,51} Prostate cancer Tocotrienols shown to inhibit cell growth in PC3 and LNCaP prostate cancer cells ⁵² Gamma-tocotrienol-induced apoptosis in prostate cancer cells was associated with suppression of NF-κB, EGFR, and Id family proteins (Id1 and Id3) ⁵³ Colorectal cancer Tocotrienol-rich fraction of palm oil activated p53, modulated Bax-Bcl2 ratio, and induced cell-cycle-independent apoptosis in RKO colorectal cancer cells ⁵⁴ Skin cancer Gamma-tocotrienol shown to have anti-invasion and chemosensitization effects against human malignant melanoma cells ⁵⁵ Pancreatic cancer d-delta-tocotrienol-induced suppression of cell proliferation in PANC-1 and 35 BxPC-3 pancreatic cancer cells was attributed to cell-cycle arrest at the G1 phase and apoptosis. The inhibitory effect was attenuated by mevalonate, while d-delta-tocotrienol and lovastatin synergistically suppressed the proliferation of MIA PaCa-2 cells ⁵⁶ Cervical cancer Inhibition of HeLa cell proliferation by alpha- and gamma-tocotrienols was due to upregulation of IL-6 and downregulation of cyclin D3, p16, and CDK6 expression in the cell-cycle signaling pathway ⁵⁷
Cardioprotective effects	Lipid-lowering effects Ingestion of delta and gamma tocotrienols may lead to reduction in triglyceride synthesis and transport ⁶ Tocotrienols resulted in reduced synthesis and increased degradation of HMG-CoA reductase ⁷ Tocotrienols influenced the mevalonate pathway in mammalian cells by post-transcriptional suppression of HMG-CoA reductase ⁹ Tocotrienols in chick diet significantly lowered hepatic cholesterogenesis, serum total cholesterol, and low-density lipoprotein cholesterol with a concomitant increase in lipogenic activity ⁶⁰ Antiatherogenic effects Rice bran tocotrienols significantly reduced the size of atherosclerotic lesions in mice ¹¹ Patients with high cholesterol experienced a reversal of arterial blockage of the carotid artery after tocotrienol consumption ¹² Palm oil tocotrienols reduced lesion formation in atherosclerosis-prone mice via both antioxidant-dependent and antioxidant-independent mechanisms ⁴⁰ Other cardioprotective effects Protection against endothelial dysfunction and platelet aggregation ¹⁰ Blood-pressure-lowering effects ^{13,14} Palm tocotrienols demonstrated cardioprotection by stabilization of proteasomes ⁶⁵ Improvement of arterial compliance ⁶⁷
Antidiabetic effects	Tocotrienol-rich fraction improved blood glucose, dyslipidemia, and oxidative stress in diabetic rats and was shown to possibly have protective effects in the structure of thoracic aortas in diabetic rats ¹⁵ Total vitamin E and beta-tocotrienol intakes were associated with a significantly reduced risk of type 2 diabetes mellitus, with an inverse association between serum levels of total vitamin E and the incidence of type 2 diabetes ¹⁶ Tocotrienol-rich diet decreased advanced glycosylation end products in nondiabetic rats and improved glycemic control in rats with streptozotocin-induced diabetes ¹⁷
Antiosteoporotic effects	Tocotrienols protected the bone from damage by free radicals generated by ferric nitrilotriacetate in rats ⁸⁰ Gamma-tocotrienol increased bone calcium content in adrenalectomized rats given dexamethasone ⁸¹
Other effects	Neuroprotective effects Palm oil alpha-tocotrienol attenuated both enzymatic and nonenzymatic mediators of arachidonic acid metabolism and neurodegeneration ¹⁸ Alpha-tocotrienol decreased the size of cerebral infarcts in mice ¹⁹ Tocotrienols potentially inhibited glutamate-induced pp60c-Src kinase activation and death of HT4 neuronal cells ²⁰ Anti-inflammatory effects Tocotrienol-rich fraction of palm oil demonstrated anti-inflammatory properties through the inhibition of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) production and nuclear factor-κB (NF-κB) expression ²¹

Abbreviations: EGFR, epidermal growth factor receptor; HMG-CoA, 3-hydroxyl-3-methyl-glutaryl CoA.

hyperglycemia is associated with many debilitating complications involving multiple organs such as the eyes, kidneys, heart, nerves, and blood vessels.⁶⁸ The worldwide prevalence of diabetes mellitus for all ages was estimated to be 2.8% in 2000 and was predicted to be 4.4% in 2030.⁶⁹ In addition, the total number of people with diabetes mellitus is estimated to increase from 171 million in 2000 to 366 million in 2030.⁶⁹

Studies on the antidiabetic effects of vitamin E started in the early 1990s. Several researchers have tried to find an association between dietary vitamin E and the risk of diabetes^{70–72} as well as a relationship between vitamin E dietary intake and the action of insulin.^{73,74} In rats with streptozotocin-induced diabetes, it was reported that diets rich in tocotrienols can decrease advanced glycosylation end products, which in turn resulted in improved glycemic control.¹⁷ Total vitamin E and beta-tocotrienol intake was found to be associated with a significant reduction in the risk of type 2 diabetes mellitus, and there appeared to be an inverse association between serum levels of total vitamin E and the incidence of type 2 diabetes.¹⁶ More recently, the effects of palm oil TRF supplementation on biochemical parameters, oxidative stress, and the vascular wall of streptozotocin-induced diabetic rats showed that TRF supplementation improved blood glucose, dyslipidemia, and oxidative stress and that TRF may have protective effects on the structure of thoracic aortas in diabetic rats.¹⁵

ANTIOSTEOPOROTIC EFFECTS OF TOCOTRIENOLS

Osteoporosis is a metabolic bone disease characterized by decreased bone mineral density. The World Health Organization defines osteoporosis as bone mineral density 2.5 standard deviations or more below the mean peak bone mass as measured by dual-energy X-ray absorptiometry.⁷⁵ A common problem among postmenopausal women and the elderly, osteoporosis has been related to an increased risk of fracture.⁷⁶

The pathogenesis of osteoporosis has been associated with oxidative stress, and those with the disease have been demonstrated to have a low levels of antioxidants⁷⁷ and high levels of reactive oxygen species.⁷⁸ In many studies, tocotrienols have been found to exert protective effects on the bones in osteoporotic animal models.⁷⁹ For example, in one study in rats in which the effects of palm tocotrienols on bone damage induced by free radicals generated by ferric nitrilotriacetate were investigated, it was reported that tocotrienols protected the bone from such damage and that the effect was better than that of alpha-tocopherol.⁸⁰ In another study, gamma-tocotrienol was demonstrated to increase bone calcium content in adrenalectomized rats given dexamethasone, and the study concluded that palm gamma-tocotrienol could be a

potential prophylactic agent for the prevention of long-term glucocorticoid-induced side effects.⁸¹

OTHER HEALTH-PROMOTING EFFECTS OF TOCOTRIENOLS

In addition to their antioxidant, anticancer, cardioprotective, and antiosteoporotic effects, tocotrienols have been demonstrated to have other health-promoting effects. For instance, several studies have looked into the neuroprotective effects of tocotrienols. It is now known that glutamate toxicity plays an important role in neurodegeneration. Tocotrienols were shown to have a potent effect in inhibiting glutamate-induced pp60c-Src kinase activation and death of HT4 neuronal cells.²⁰ Alpha-tocotrienol was reported to decrease the size of cerebral infarcts in mice.¹⁹

Arachidonic acid, one of the most abundant polyunsaturated fatty acids of the central nervous system, is highly susceptible to oxidative metabolism under pathological conditions. Palm oil alpha-tocotrienol was shown to attenuate the activity of both enzymatic and nonenzymatic mediators of arachidonic acid metabolism and neurodegeneration.¹⁸ In addition, TRF has also been reported to possess anti-inflammatory properties, with the proposed mechanism of action being inhibition of the expression of inducible nitric oxide synthase, cyclooxygenase-2, and nuclear factor kappa B genes.²¹

The health-promoting effects of tocotrienols are summarized in Table 1.

CONCLUSION

Current developments and new advances suggest that tocotrienols have promising therapeutic potential. A growing body of research supports the health-promoting benefits of tocotrienols, with increasing evidence that they may be indicated in the prevention and/or treatment of various disease conditions. While the effects of tocotrienols in some diseases have been well explored, research into their effects in other diseases, especially relatively newer ones, is limited and further exploration is thus warranted. Many studies have been carried out in cell lines and animals, and more evidence-based human trials are necessary. Tocotrienols should be used for disease prevention and therapy only when the effects of tocotrienols in humans are well established.

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