

EASTMAN

**Eastman
NuTriene™
tocotrienols**

frequently
asked
questions

Eastman NuTriene™ tocotrienols

FAQs

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1

What is the product Eastman NuTriene™ tocotrienols?

The product Eastman's NuTriene™ tocotrienols is a natural blend of tocotrienols and tocopherols extracted and concentrated from rice bran oil distillate. Recent research shows that tocotrienols may be the most important members of the vitamin E family.¹

Eastman NuTriene™:

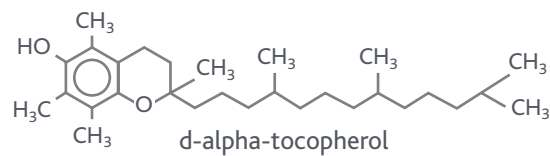
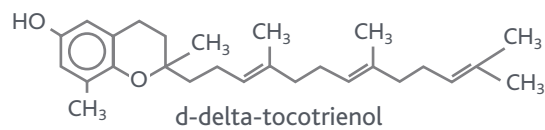
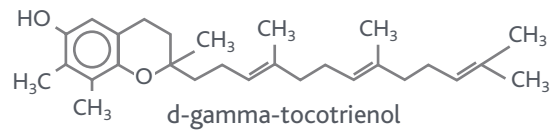
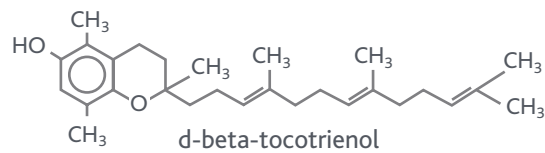
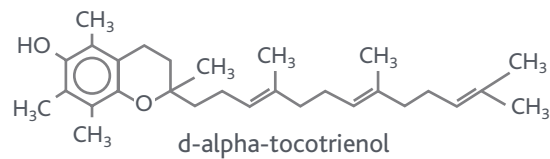
- Contains a mixture of tocotrienols and tocopherols (vitamin E) and other nutrients such as phytosterols and phytosqualene.
- Contains tocotrienols, a family of dietary supplements related to vitamin E, which are considered to be more powerful antioxidants with important health benefits.¹
- Has distinct functional differences compared to vitamin E.

¹Packer, L., Weber, S. U. & Rimbach, G. (2001). Molecular aspects of alpha-tocotrienol antioxidant action and cell signaling. *J Nutr.* 131, 369S–373S.

2 What are tocotrienols?

Tocotrienols:

- Are members of the vitamin E family along with tocopherols.
- Exist as four isomers — alpha, beta, gamma and delta.
- Are structurally similar to tocopherols except with three double bonds on the side chain.
- Have benefits not provided by alpha-tocopherol, otherwise known as vitamin E.



3

Are tocotrienols considered vitamins?

Tocotrienols belong to the family of vitamin E compounds and alpha-tocotrienol has some vitamin E activity;¹ however, the United States Food and Drug Administration assigns vitamin E activity only to the alpha-tocopherol contained in commercial vitamin products. The other beneficial tocopherols and the tocotrienols in Eastman NuTriene™ tocotrienols are considered natural-source dietary supplements.

¹Machlin, L. J., (ed.). (1980). In *Vitamin E: A Comprehensive Treatise*, New York: Marcel Dekker Inc.

4

What is the difference between Eastman NuTriene™ tocotrienols and other vitamin E products?

The difference is that Eastman NuTriene™ tocotrienols is a combination of all 8 members of the vitamin E family. Many vitamin E products contain only alpha-tocopherol which can be either natural or synthetic. In most natural-source vitamin E products, the other 7 compounds are removed. Synthetic vitamin E products can contain synthetic alpha-tocopherol or stabilized forms of this molecule.

5

Can tocotrienols take the place of vitamins in the diet?

No, tocotrienols themselves cannot replace vitamin E in the diet. While tocotrienols are similar in their chemical structure to vitamin E, they do not appear to function in exactly the same way as vitamin E in the body. Tocotrienols cannot be taken to fulfill the suggested RDI, reference daily intake, for vitamin E. Only alpha-tocopherol or compounds containing alpha-tocopherol can be used to fulfill the requirement for vitamin E.¹ The natural, rice-based product, Eastman NuTriene™, contains a mixture of tocotrienols and tocopherols with an alpha-tocopherol content of at least 100 IU/gram.

¹United States Pharmacopeial Convention, Inc., *The United States Pharmacopeial 23 — The National Formulary 18*. (1995). Rockville, MD.

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Is there any difference between synthetic vitamin E and the natural vitamin E in Eastman NuTriene™ tocotrienols?

Natural vitamin Es are biologically similar to synthetic vitamin E but are not identical since natural vitamin E can contain alpha, beta, gamma and delta (referring to the number and position of methyl groups on the aromatic ring) isomers. The material is synthesized by plants and the isomers are often extracted and sold as a mixture. Natural vitamin E contains the molecule humans assimilate most effectively.¹ Alpha-tocopherol can be synthetic and has some very distinctive properties.

- Synthetic vitamin E, referred to as dl-alpha-tocopherol on a supplement label, contains both active and inactive forms of alpha-tocopherol.
- Recent studies using different groups of people indicated that natural vitamin E is utilized twice as efficiently as the synthetic form.
- Blood levels of natural vitamin E were consistently twice those of the synthetic form.
- In one experiment, Japanese researchers alternately gave natural and synthetic vitamin E to healthy young women. It took 300 mg of synthetic vitamin E to equal the blood levels achieved by a 100 mg dose of natural vitamin E.²
- Researchers at Oregon State University, Covallis, found the human body excretes synthetic vitamin E three times faster than the natural form.³
- Dietary Reference Intakes (DRI) labeling offers this strength relationship between natural and synthetic vitamin E: "Historical vitamin E conversion factors were amended in the DRI report, so that 15 mg is defined as the equivalent of 22 IU of natural vitamin E or 33 IU of synthetic vitamin E."⁴

¹Challem, J. (2001). Natural vs. Synthetic Vitamin E. *Nutrition Science News*.

²Kiyose, C., Muramatsu, R., Kameyama, Y., Ueda, T. & Igarashi, O. (1997). Biodiscrimination of alpha-tocopherol stereoisomers in humans after oral administration, *Am J Clin Nutr*, 65(3), 785–789.

³Traber, M. G., Elsner, A. & Brigelius-Flohe, R. (1998). Synthetic as compared with natural vitamin E is preferentially excreted as alpha-CEHC in human urine: studies using deuterated alpha-tocopheryl acetate, *FEBS Letters*, 437, 145–148.

⁴The Dietary Reference Intakes (DRI) are the most recent set of dietary recommendations established by the Food and Nutrition Board of the Institute of Medicine, 1997–2001. They replace previous RDAs and may be the basis for eventually updating the RDIs according to the Council for Responsible Nutrition.

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How can synthetic alpha tocopherol be distinguished from natural alpha tocopherol on labels of vitamin E supplements?

The origin of the alpha tocopherol can be determined by the name on the label.

Form	Label Name
Natural vitamin E	d-alpha tocopherol, d-alpha tocopherol acetate, d-alpha tocopherol succinate
Synthetic version	dl-alpha-tocopherol, dl-alpha tocopherol acetate, dl-alpha tocopherol succinate

Note: Current FDA labeling regulations allow supplements that contain a mixture of both natural and synthetic vitamin E to be labeled as “natural.”

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What other nutrients are in Eastman NuTriene™ and what benefits may be related to them?

Other components in Eastman NuTriene™ tocotrienols with nutritional value are plant derived squalene, phytosterols and rice bran waxes:

- **Squalene:** In humans, about 60% of dietary squalene is absorbed. It is transported in blood and found in the greatest concentration in the skin.¹ Squalene is a natural moisturizer and accounts for 12% of the lipid content of human sebum. As a skin surface lipid, squalene functions to protect against exposure to UV radiation.² Squalene has been shown to reduce cholesterol and triglyceride levels in animal studies and might be useful in humans in conjunction with some cholesterol-lowering drugs. The primary clinical use of squalene currently is as an adjunctive therapy in a variety of cancers.^{3,4}
- **Phytosterols:** More than 30% of the composition of Eastman NuTriene™ is a mixture of valuable phytosterols, including alpha- and beta-sitosterol and their esters, campesterol and others. There is much published literature dating back to the 1950s documenting the cholesterol lowering effects of phytosterols.⁵ Recent studies continue to show phytosterols provide several health benefits, including reduction of serum cholesterol and low-density lipoproteins.⁶
- **Rice Bran Waxes:** Eastman NuTriene™ contains the essential fatty acids — linoleic and alpha-linolenic acids; as well as palmitic, stearic and oleic acids and long chain saturated hydrocarbons. Essential fatty acids are important because the body does not contain enzymes to synthesize these compounds that are necessary for human metabolism.

¹Stuchlik, M. & Stanislav, Z. (2002). Vegetable lipids as components of functional foods. *Biomed Papers*, 146(2), 3–10.

²Storm, H. M., Oh, S. Y. & Kimler, B. F. (1993). Radioprotection of mice by dietary squalene. *Lipids*, 28, 555–559.

³Newmark, H. L. (1997). Squalene, olive oil, and cancer risk: a review and hypothesis. *Cancer Epidemiol Biomarkers Prev*, 6, 1101–1103.

⁴Rao, C. V., Newmark, H. L. & Reddy, B. S. (1998). Chemopreventive effect of squalene on colon cancer. *Carcinogenesis*, 19, 287–290.

⁵Ling, W. H. & Jones, P. J. H. (1995). Dietary phytosterols: a review of metabolism, benefits and side effects. *Life Sciences*, 57(3), 195–206.

⁶Moghadasian, M. H. (2000). Pharmacological properties of plant sterols – *In vivo* and *in vitro* observations. *Life Sciences*, 67, 605–615.

9 What is the INCI name for Eastman NuTriene™ tocotrienols?

The INCI name is: Phytosterols (and) Tocopherols (and) Tocotrienols (and) Squalene (and) Oryza Sativa (Rice) Bran Wax.

10 Can I get these nutrients from food?

A healthy diet does meet many of the needs of the body and provides in most cases a natural source of nutrients. Vitamin E is found in green leafy vegetables, vegetable oils, nuts and fortified cereals. Supplements help ensure that the body has an adequate supply. Supplements such as vitamin E provide antioxidant levels that are “virtually impossible” to come by through food alone.¹

¹Huang, H., Appel, L. J., Croft, K. D., Miller, E. R., Mori, T. A. & Puddey, I. B. (2002). Effects of vitamin C and vitamin E on *in vivo* peroxidation: results of a randomized controlled trial. *Amer J of Clin Nutr*, 76, 549–555.

11 How should tocotrienol supplements be taken?

Tocotrienols and tocopherols are fat soluble molecules, so it is important to take supplements containing these with food to aid in absorption.

12 What are the symptoms of vitamin E deficiency?

Vitamin E deficiency is relatively rare in humans. It is characterized by neurological problems typically showing up first in the extremities — hand and feet.

13 What are the reported benefits of tocotrienols?

- **Cardiovascular:** Tocotrienols help reduce the risk of cardiovascular disease (CVD) by inhibiting the enzyme regulating the rate-limiting step in cholesterol biosynthesis (HGM Co-A reductase). The effect is a cholesterol-lowering action or hypocholesterolemic property.¹ Tocotrienols' antioxidant properties help prevent oxidation of low-density lipoproteins which in turn helps to keep the arterial walls free from materials that will develop over time into plaque. The plaque can reduce blood flow and eventually cause blockage leading to strokes or progressive atherosclerotic plaques.²
- **Skin:** Researchers believe that antioxidants such as tocotrienols may help counter the effects of exposure to the sun's ultraviolet radiation.^{3,4}
- **Cancer:** The material has value in lowering the risk or helping to prevent cancer. Tocotrienols showed growth inhibition of several tumor cell lines.^{5,6}
- **Neuroprotective:** Tocotrienols are currently being studied to see if dementia and Alzheimers can be slowed or prevented.^{7,8} Several recent studies have shown positive neuroprotective properties of alpha-tocotrienol.^{9,10}

¹Watkins, T. R., Geller, M., Kooyenga, D. K. & Bierenbaum, M. (1999). Hypocholesterolemic and antioxidant effect of rice bran oil non-saponifiables in hypercholesterolemic subjects. *Env & Nutr Int*, 3, 115–122.

²Therhault, A., Chao, J., Wang, Q., Gapor, A. & Adeli, K. (1999). Tocotrienol: A review of its therapeutic potential. *Clinical Biochemistry*, 32, 309–319.

³Weber, C., Podda, M., Rallis, M., Thiele, J. J., Traber, M. G. & Packer, L. (1997). Efficacy of topically applied tocopherols and tocotrienols in protection of murine skin from oxidative damage induced by UV-irradiation. *Free Radic Biol Med*, 22, 761–769.

⁴Traber, M. G., Rallis, M., Podda, M., Weber C., Maibach, H. I. & Packer, L. (1998). Penetration and distribution of α -tocopherol, α - or γ -tocotrienols applied individually onto murine skin. *Lipids*, 33(1), 87–91.

⁵McIntyre, B. S., Briski, K. P., Gapor, A. & Sylvester, P. W. (2000). Antiproliferative and apoptotic effects of tocopherols and tocotrienols on preneoplastic and neoplastic mouse mammary epithelial cells. *Proc Soc Exp Biol Med*, 224, 292–301.

⁶Nesaretnam, K., Stephen, R., Dils, R. & Barbre, P. (1998). Tocotrienols inhibit the growth of human breast cancer cells irrespectively of estrogen receptor status. *Lipids*, 33, 461–469.

⁷Masaki, K. H., Losonczy, K. G., Izmirlan, G., Foley, D. J., Ross, G. W., Petrovitch, H., Havlik, R. & White, L. R. (2000). Association of vitamin E and C supplement use with cognitive function and dementia in elderly men, *Neurology*, 54, 1265–1272.

⁸Chandan, S., The Ohio State University Medical Center, Neuro, Protection by Vitamin E α -Tocotrienol, paper presented at 2nd Rayson Huang Foundation Lecture (July 16, 2003).

⁹Osakada, R., Hashino, A., Kume, T., Katsuke, H., Kaneko, S. & Akaike, A. (2004). α -tocotrienol provides the most potent neuroprotection among vitamin D analogs on cultured striatal neurons, *Neuropharm*, 47, 904–915.

¹⁰Khanna, S., Sashwati, R., Slivka, A., Craft, T. K. S., Chaki, S., Rink, C., Notestine, M. A., DeVries, A. C., Parinandi, N. L. & Sen, C. K. (2005). Neuroprotective properties of the natural vitamin E alpha-tocopherol. *Stroke*, 36(10), 2258–2264.

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What is the advantage of having gamma tocopherol and alpha tocopherol in Eastman NuTriene™ tocotrienols?

These different isomers or forms of vitamin E may have individual and complementary health benefits.

- **Fighting cancer:** More studies are suggesting that different isomers of vitamin E protect against different forms of cancer. For example, alpha-tocopherol reduced the risk of developing bladder cancer by 44% while gamma-tocopherol offered no protection.¹ Several studies point to a benefit from gamma-tocopherol in reducing the risk of developing or treating prostate cancer.²⁻⁴
- **Tissue builder:** Gamma-tocopherol may contribute to human health in ways not previously recognized. This naturally occurring form of vitamin E represents approximately 70% of the vitamin E in a typical American diet. Human plasma concentrations of alpha-tocopherol are generally 410 times higher than those of gamma-tocopherol; while as much as 30–50% of the total vitamin E in human skin, muscle, vein and adipose tissue is in the form of gamma-tocopherol. Ingesting alpha-tocopherol has been shown to decrease the amount of gamma-tocopherol in the body, while ingesting gamma-tocopherol increases the amount of both gamma- and alpha-tocopherol.⁵
- **Biological action:** Gamma-tocopherol has certain biological actions that alpha-tocopherol does not, including decreasing inflammation⁶ and blocking the adverse effects of nitrogen oxide radicals that are formed from nitrous oxide which the body produces to fight various conditions, such as bacterial infection, atherosclerosis, cancer, etc.⁷ In addition, gamma-tocopherol has a greater anti-inflammatory activity than does alpha-tocopherol. Alpha-tocopherol and gamma-tocopherol both improve atherosclerotic plaque stability and vasomotor function and decrease platelet aggregation and tendency to thrombus formation.⁸ Gamma-tocopherol has a greater anti-inflammatory activity than alpha-tocopherol, and it also inhibits platelet aggregation to a greater degree.⁹
- **Maintaining gamma tocopherol levels:** Alpha-tocopherol has been found to decrease the levels of gamma-tocopherol in human plasma and tissue, while supplementing with gamma-tocopherol increases the level of both alpha-tocopherol and gamma-tocopherol.⁵

- ¹Anderson, M. D., Cancer Center, One form of vitamin E appears beneficial in reducing bladder cancer risk, news release (March 30, 2004).
- ²Weinstein, S. J., Wright, M. E., Pietinen, P., King, I., Tan, C., Taylor, P. R., Virtamo, J. & Albanes, D. (2005). Serum alpha-tocopherol and gamma tocopherol in relation to prostate cancer risk in a prospective study. *J Natl Cancer Inst*, 97, 396–399.
- ³Jiang, Q., Wong, J. & Ames, B. N. (2004). Gamma-tocopherol induces apoptosis in androgen-responsive LNCaP prostate cancer cells via caspase dependent and independent mechanism. *Ann NY Acad Sci*, 1031, 399–400.
- ⁴Jiang, Q., Wong, J., Fyrst, H., Saba, J. D. & Ames, B. N. (2004). Gamma-tocopherol, or combinations of vitamin E forms, induce cell death in human prostate cancer cells by interrupting sphingolipid synthesis. *Proc Natl Acad Sci USA*, 101, 17825–17830.
- ⁵Jiang, Q., Christen, S., Shigenaga, M. K. & Ames, B. N. (2001). Gamma-tocopherol, the major form of vitamin E in the U. S. diet, deserves more attention, *Am J Clin Nutr*, 74(6), 714–722.
- ⁶Jiang, Q. & Ames, B. N. (2003). Gamma-tocopherol, but not alpha-tocopherol, decreases proinflammatory eicosanoids and inflammation damage in rats. *J Fed Amer Soc Experimental Biology*, 17, 816–822.
- ⁷Papas, A. (1999). The Vitamin E. Factor, *Harper Perennial*, 36–37.
- ⁸Saldeen, T., Dayuan, L. & Mahta, J. (1999). Differential effects of alpha and gamma-tocopherol on low-density lipoprotein oxidation, superoxide activity, platelet aggregation and arterial thrombogenesis. *J Am Col Cardiol*, 34, 1205–1215.
- ⁹Jiang, Q., Elson-Schwab, I., Courtemanche, C. & Ames, B. N. (2000) Gamma-tocopherol and its major metabolite, in contrast to α -tocopherol, inhibit cyclooxygenase activity in macrophages and epithelial cells. *Proc Natl Acad Sci USA*, 97, 11494–11499.

15 What are antioxidants and why do I need them?

We breathe in air and our bodies use the oxygen in various metabolic processes. A normal by-product of some of these metabolic processes are free radicals — highly reactive species. Free radicals can be harmful resulting in cellular damage that can, among other things, result in premature aging. The human body can deal with a certain level of free radicals; however, exposure to the sun, pollution, cigarette smoke, etc. can overload our natural defense mechanisms. Antioxidants are manufactured by the body as a defense system and also come from the food we eat, but sometimes this is not enough. Tocopherols and tocotrienols are excellent antioxidants and can help keep free radicals from doing harm.

16 How do tocotrienols act as antioxidants?

Vitamin E compounds are well known for their antioxidant properties.¹ Antioxidants are compounds that scientists believe counteract cell damage caused by excess oxygen or the activity of free radicals. Free radicals are reactive compounds generated by our normal biological processes, and their induction is accelerated by exposure to ultraviolet radiation, pollution, cigarette smoke and other environmental and biological stress factors. If high levels of free radicals remain active in our bodies, they can break down cell membranes and damage cellular DNA. Free radical activity has been implicated in a number of chronic diseases. Antioxidants are one of the body's natural defenses against the damage that may be caused by free radicals. Vitamin E has long been known as an important antioxidant nutrient. Tocotrienols also have antioxidant activity.^{2,3} Some studies suggest that the antioxidant potential of tocotrienols is even greater than that of vitamin E in certain types of fatty cell membranes and in parts of brain cells.⁴ Tocotrienols have also been found to be effective antioxidants when applied topically to help counteract the effects of ultraviolet radiation.^{5,6} Topical application of tocotrienols helps to fight oxidative damage to the skin while preserving the existing vitamin E level in skin cells.

¹Kamal-Eldin, A. & Appelqvist, L. A. (1996). The chemistry and antioxidant properties of tocopherols and tocotrienols. *Lipids*, 31(7), 671–701.

²Therault, A., Chao, J., Wang, Q., Gapor, A. & Adeli, K. (1999). Tocotrienol: A review of its therapeutic potential. *Clin Biochem*, 32(5), 309–319.

³Surana, C., Hood, R. L., Dean, R. T. & Stocker, R. (1993). Comparative antioxidant activity of tocotrienols and other natural lipid-soluble antioxidants in a homogeneous system, and in rat and human lipoproteins. *Biochem Biophys Acta*, 1166, 163–170.

⁴Suzuki, Y. J., Tsuchiya, M., Wassall, S. R., Choo, Y. M., Govil, G., Kagan, V. E. & Packer, L. (1993). Structural and dynamic membrane properties of alpha-tocopherol and alpha-tocotrienol; implication to the molecular mechanism of their antioxidant potency. *Biochem*, 32, 10692–10699.

⁵Weber, C., Podda, M., Rallis, M., Thiele, J. J., Traber, M. G. & Packer, L. (1997). Efficacy of topically applied tocopherols and tocotrienols in protection of murine skin from oxidative damage induced by UV-irradiation. *Free Radic Biol Med*, 22, 761–769.

⁶Traber, M. G., Rallis, M., Podda, M., Weber, C., Maibach, H. I. & Packer, L. (1998). Penetration and distribution of α -tocopherol, α - or γ -tocotrienols applied individually onto murine skin. *Lipids*, 33(1), 87–91.

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What are the potential benefits of tocotrienols in topical products?

Tocotrienols offer multiple benefits to a topical product. The antioxidant and free radical scavenging properties of tocotrienols and tocopherols are highly desirable in skin care products as oxidative processes are believed to increase the signs of aging.¹

Squalene, a natural component of NuTriene™, is a highly penetrative natural emollient. The main source for this oil has traditionally been the livers of deep sea sharks and it has been very desirable in skin care products for many years in Asia. Human sebum which provides the normal lubricity in the skin is composed of up to 12% squalene. It is useful in specialty skin care products for its emolliency and for moisture protection.

¹Darvin, M., Zastrow, L., Sterry, W. & Lademann, J. (2006). Effect of supplemented and topically applied antioxidant substances on human tissue. *Skin Pharm Physiology*, 19, 238–247.

18 What is the role of vitamin E in aging?

The free radical theory of aging holds that through a gradual accumulation of microscopic damage to the cellular structure of our skin, antioxidants prevent excessive oxidative damage to these important structures. Vitamin E is believed to play an important role during times of oxidative stress.

19 Can taking antioxidants help us stay healthy?

Free radicals are believed to play a part in the aging process and without antioxidants protecting us from relentless attack; the body could be subject to disease. These free radicals can destroy living tissue and fluids, hinder the immune system and accelerate the aging process. Supplements can provide additional antioxidants to combat these adverse effects, but will not enable us to live forever. Antioxidants may, however, increase the chances for living longer and maintaining a healthy life.

Recent studies using roundworms indicate that tocotrienols extended their life span by 19% while reducing protein carbonylation — a particularly toxic process indicative of aging. Exposure to solar radiation shortened the life span of untreated worms, while worms dosed with tocotrienols prior to exposure retain the life span of unexposed roundworms.¹

¹Adachi, H. & Ishii, N. (2000). Effects of tocotrienols on life span and protein carbonylation in *Caenorhabditis elegans*. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 55, B280–285.

20 What benefits do nutritional supplements offer the elderly?

Scientific research has confirmed the importance of nutritional supplements for the elderly. Antioxidants can have a substantial positive impact on the immune systems of elderly people and can also play a key role in protecting eye and brain function. Research has found that consistent use of multivitamins and other supplements can boost resistance to infectious disease. This is a valuable insight that may offer tremendous improvement in quality of life for older people.¹

¹CRN (Council for Responsible Nutrition), Scientific Research Confirms Importance of Nutritional Supplements for Elderly. News release, Washington, D.C. (June 24, 2002).

21 Can vitamin E antioxidants aid the elderly with a cold or with the risk of having a cold?

A new study suggests taking a daily vitamin E supplement may protect the elderly from getting colds. The research found nursing home residents supplemented with vitamin E were 20% less likely to get a cold and also had fewer colds over the study period than a placebo group. Common colds are frequent and associated with increased morbidity in this age group, and these findings suggest important implications for the well-being of the elderly.¹ These results confirm a previous study conducted in 1997 regarding infections.

The number of elderly living in such facilities is increasing with an estimated 43% who will be admitted to a nursing home, with more than 85% of them admitted to long-term care facilities. Infections in the elderly can result in decreased daily activity, prolonged recovery times, increased health care service use, and more frequent complications, including death.

¹Meydani, S. N., Leka, L. S., Fine, B. C., Dallal, G. E., Keusch, G. T., Singh, M. F. & Hamer, D. H. (2004). Vitamin E and respiratory tract infections in elderly nursing home residents: a randomized controlled trial. *J of the Amer Med Assoc*, 292, 828–836.

22 Can antioxidants protect against vascular dementia?

Vascular dementia is a disease with symptoms including memory loss and a decline in thinking skills that affects everyday life. Vascular dementia may be treatable and early detection and an accurate diagnosis is important. Researchers at Johns Hopkins Medical Institution, Baltimore, have studied whether antioxidant supplements can protect against vascular dementia according to a June 14, 2001 news release.¹ Taking supplements may indeed protect against the disease. In the study, those who took vitamins C and E had an 88% lower risk for vascular dementia than those who did not and their cognitive function was significantly better than that of people taking only one of the vitamins.

¹Johns Hopkins Reports, Vitamin C and Vitamin E Can Protect Against Type of Memory Loss, news release, *Baltimore: Foods for the Future* (June 14, 2001).

23 What does research show concerning dietary tocotrienols and cardiovascular health?

Listed below are studies with tocotrienols:

- Researchers at the University Kebangsaan Malaysia stated that alpha-tocotrienol as a “more potent antioxidant,” may be a superior means of protecting heart health.¹
- Several studies have shown benefits linked to taking mixed tocotrienols as well as some of the isomers singularly. In an animal model, researchers from Advanced Medical Research in Madison, Wisconsin, showed the tocotrienol-rich fraction of rice bran induced a 42% reduction in atherosclerotic lesion size while alpha-tocopherol only induced an 11% decrease.²
- Additional animal research from Texas Southern University in Houston showed gamma-tocotrienol increased nitric oxide (NO) activity, which was correlated with a decrease in blood pressure.³

¹Yusoff, K. (2002). Vitamin E in cardiovascular disease: has the die been cast? *Asia Pac J Clin Nutr* 11 (Suppl 7), S443–447.

²Qureshi, A. A., Salser, W. A., Parmar, R. & Emeson, E. E. (2001). Novel tocotrienols of rice bran inhibit atherosclerotic lesions in C57BL/6 ApoE-deficient mice. *J Nutr*, 131(10), 2606–2618.

³Newaz, M. A., Yousefipour, Z., Nawal, N. & Adeeb, N. (2003). Nitric oxide synthase activity in blood vessels of spontaneously hypertensive rats: antioxidant protection by gamma-tocotrienol. *J Physiol Pharmacol*, 54(3), 319–327.

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If a person is at moderate to high risk for heart disease, can tocotrienols lower LDL cholesterol?

For people at the highest risk, the latest recommendations by federal authorities (July 12, 2004) are suggesting that LDL should be lowered to less than 70.¹ If modifications to diet and exercise don't work, statin drugs are the first medication that doctors usually prescribe to lower LDL. Studies indicate that Eastman NuTriene™ tocotrienols could offer additional reduction.² Tocotrienols are reported to work synergistically with statin drugs thus enhancing their effectiveness.³ Tocotrienols also act as an anticoagulant and can be used in the same way as aspirin but do not pose GI bleeding problems.

¹Kolata, G. (July 13, 2004). Experts set a lower low for cholesterol levels, *New York Times*.

²Watkins, T. R., Kooyenga, D. K. & Bierenbaum, M. L. (1999). Hypocholesterolemic and antioxidant effect of rice bran oil nonsaponifiables in hypercholesterolemic subjects, oxidants and antioxidants in biology, Oxygen Club of California. *World Congress*.

³Leonard, S. W., Joss, J. D., Bustacich, D. J., Blatt, D. H., Lee, Y. S. & Traber, M. G. (2007). Effects of vitamin E on cholesterol levels of hypercholesterolemic patients receiving statins. *Am J Health-Syst Pharm*, 64, 2257–2266.

25 Can antioxidants reduce the risk of heart disease?

In vitro studies have shown vitamin E to have several potentially cardioprotective effects, including antagonizing the oxidation of low-density lipoproteins, inhibiting platelet aggregation and adhesion, preventing smooth muscle proliferation and preserving normal coronary dilation. Several prospective studies¹ include:

- The U.S. Nurses' Health Study and the U.S. Health Professionals' Follow-up Study, found a 34% and 39% reduction, respectively, in the risk of having a cardiac event for those taking vitamin E supplements.
- The Iowa Women's Health Study found a 47% reduction in cardiac mortality.

Results of randomized, controlled clinical trials have not found consistent benefit, however, possibly due to their shorter duration. The best known of these trials, the Cambridge Heart Antioxidant Study, found a 47% reduction in fatal and non-fatal myocardial infarction in patients with proven coronary atherosclerosis who were given 400 or 800 IU of vitamin E daily. The effect is statistically significant only after 200 days. There was, however, no effect on mortality.

¹Emmert, D. H. & Kirchner J. T. (1999). The role of vitamin E in the prevention of heart disease. *Arch Fam Med*, 8, 537–542.

26 What has been done regarding tocotrienols and breast cancer cell research?

Some studies indicate that vitamin E did not have a protective effect against breast cancer, but more recent studies are finding that it is the form of vitamin E that makes the difference.¹ The more common form of vitamin E in supplements and in most food sources is alpha-tocopherol and it apparently is not protective although it certainly is a very powerful antioxidant and needed nutrient. Women consuming other forms of vitamin E, called tocotrienols, have been found to have dramatically lower risk of contracting breast cancer — 50% less risk for women without family history and as much as 90% for premenopausal women with family history.

Tocotrienols have been shown to inhibit growth of estrogen receptor positive breast cancer cells by as much as 50% in culture.²⁻⁵ The objective of any cancer therapy is to induce the cancer cells to differentiate in a way that promotes programmed cell death (apoptosis). Several studies indicate that tocotrienols induce breast cancer cell apoptosis.

When different kinds of live breast cancer cells were injected into the mammary tissue of female mice, tocotrienols were found to be growth inhibitory on each breast cancer cell line tested.⁶

¹Does vitamin E prevent breast cancer? In-depth coverage based on reviewing the scientific studies made about vitamin E and breast cancer. Evidence points to the form of vitamin E called tocotrienols as effective in preventing breast cancer — and not alpha-tocopherol (the one commonly available as a supplement). (May 2002). *Life Extension Magazine*.

²Nesaretnam, K., Stephen, R., Dils, R. & Darbre, P. (1998). Tocotrienols inhibit the growth of human breast cancer cells irrespective of estrogen receptor status. *Lipids*, 33:461–469.

³Gunthrie, N., Gapor, A., Chambers, A. F. & Carroll K. K. (1997). Inhibition of proliferation of estrogen receptor — negative MDA-MB-435 and positive MCF-7 human breast cancer cells by palm oil tocotrienols and tamoxifen, alone and in combination, *J Nutr*, 127, S544–S548.

⁴Nesaretnam, K., Dorasamy, S. & Darber P. D. (2000). Tocotrienols inhibit growth of ZR-75-J breast cancer cells. *Int. J Food Sci Nutr*, 51(Suppl), S95–S103.

⁵Nesaretnam, K., Guthrie, N., Chambers, A. F. & Carroll, K. K. (1995). Effect of tocotrienols on the growth of a human breast cancer cell line in culture. *Lipids*, 30(12), 1139–1143.

⁶McIntyre, B. S., Bridski, K. P., Gapor, A. & Sylvester, P. W. (2000). Antiproliferative and apoptotic effects of tocopherols and tocotrienols on preneoplastic and neoplastic mouse mammary epithelial cells, *Soc Exptl Biol Med*, 224, 292–301.

27 Are tocotrienols useful in new strategies to curtail cancer growth and tumors?

A cancer can only grow if it has a means of nourishing itself. It develops this means by surrounding itself with capillaries and larger blood vessels so that oxygen rich blood can reach its cells. The medical term for this process is angiogenesis. Excess angiogenesis is involved in many diseases such as: macular degeneration, diabetic blindness, rheumatoid arthritis, psoriasis, rosacea and many more.

Anti-angiogenesis slows or stops the process and could effectively “starve” tumors. This would stop them from growing and metastasizing (spreading to other parts of the body) and possibly even cause them to disappear. Tocotrienols, but not tocopherols, curtail angiogenesis in laboratory assays of bovine aortic endothelial cells.¹ According to a study from Japan, “modulation of angiogenesis is now a recognized strategy for the prevention of various angiogenesis-mediated disorders.” In a more recent study, these results were confirmed in human umbilical vein endothelial cells, mouse corneal air sac assay and the chick embryo chorioallantoic membrane assays.²

Tocotrienols have been found to work synergistically with statin drugs and offer a novel approach to cancer chemo-prevention and/or therapy. Statin drugs and tocotrienols inhibit cellular growth by different mechanisms. Statins at high doses can cause muscular weakness, ulcers, nausea and other dose-limiting toxicities. Combined tocotrienols and statin drugs provide more effective tumor growth reduction than is obtained when either is dosed alone.³

¹Miyazawa, T., Inokuchi, H., Hirokane, H., Tsuzuki, T., Nakagawa, K. & Igarashi, M. (2004). Anti-angiogenic potential of tocotrienol *in vitro*. *Biochemistry (Moscow)*, 69(1), 67–69.

²Nakagawa, K., Shibata, A., Yamashita, S., Tsuzuki, T., Kariya, J., Oikawa, S. & Miyazawa, T. (2007). *In vivo* angiogenesis is suppressed by unsaturated vitamin E, tocotrienol. *Amer Soc Nutr*, 137, 1938–1943.

³McAnally, J. A., Gupta, J., Sodhani, S., Bravo, L. & Mo, H. (2007). Tocotrienols potentiate lovastatin mediated growth suppression *in vitro* and *in vivo*. *Soc Exptl Bio Med*, 232, 523–531.

28 Are there risks associated with taking tocotrienols/tocopherols?

As with anything, excessively high doses are not desirable though there are few, if any, long term studies on the safety of vitamin E, not to mention tocotrienols or tocopherols. Other studies, investigating, for instance, the effect on cancer or cardiovascular issues, have not identified risks from taking tocotrienols or tocopherols unless the levels used in the study were very high. The tolerable upper intake levels of vitamin E in milligrams of alpha-tocopherol is 1,000 mg/day or 1,500 IU/day for adults.¹

¹Institute of Medicine, Food and Nutrition board. Dietary Reference Intakes: Vitamin C, Vitamin E, Selenium, and Carotenoids. *National Academy Press*, Washington, D.C., (2000).

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