

LE Magazine October 2000

In The **News**

Combining alpha- and gamma-tocopherol for maximum antioxidant effect

A growing body of research has applauded vitamin E's antioxidant ability, specifically with regards to preventing lipid peroxidation, a process that's been linked to many degenerative disorders, including heart disease, cancer and Alzheimer's disease. However, recent research is now delineating the unique functions of different vitamin E forms, namely alpha-tocopherol and gamma-tocopherol, as well as explaining how they might work together or against one another. For example, studies have suggested that alpha-tocopherol may not yield the much purported health benefits (i.e. prevention of coronary heart disease) unless it's combined with the gamma-tocopherol form. Moreover, some research has demonstrated that too much alpha-tocopherol opposes the antioxidant effects of gamma-tocopherol by displacing it. The new research, combined with other emerging findings regarding gamma-tocopherol's antioxidant functions, underlines Life Extension's own reports that alpha-tocopherol should always be paired up with gamma-tocopherol, and that the latter should constitute about 20% of a vitamin E supplement, or be taken in conjunction with an alpha-tocopherol supplement.



For example, the latest research from Italian researchers (*Pharmacol Res* 2000 Jan;41[1]:65-72), which examined the distribution of fat-soluble antioxidants in lipoproteins, reveals that supplementing with 600 mg of alpha-tocopherol (about 600-800 IU of vitamin E) for just two weeks depleted gamma-tocopherol by a significant 22%. Meanwhile, plasma concentrations of alpha-tocopherol rose by almost 96%, and levels of lycopene and beta-carotene remained largely unaffected. Previous research, such as a study published in the *Proceedings of the National Academy of Sciences* (Vol. 94, pp. 3217-3222, April 1997), support the theory that gamma-tocopherol's antioxidant role goes above and beyond that of alpha-tocopherol by effectively entrapping and removing mutagenic oxidants and nitrating species. Meanwhile, a Swedish study (*J Am Coll Cardiol* 1999 Oct;34[4]:1208-15) showed that, while both forms of vitamin E decreased platelet aggregation, delayed thrombus formation, inhibited arterial lipid peroxidation and LDL oxidation while increasing endogenous SOD activity, gamma-tocopherol was much more potent in all of these effects.

Similarly, a University of Michigan in vitro study (*Semin Urol Oncol* 1999 May;17[2]:85-90), which compared the effects of alpha- and gamma-tocopherol supplementation on prostate cancer, found that the gamma form was superior for inhibiting cancer cell growth. While gamma-tocopherol is the most abundant form of vitamin E and largely available through diet, research has found that much of it gets excreted through urine after being metabolized by the liver (*J Lipid Res* 1999 April;40[4]:665-71). In addition, a special protein mechanism in the liver, called the alpha-tocopherol transfer protein, shows preferential treatment for alpha-tocopherol. The protein is believed to identify and selectively choose alpha-tocopherol over other forms of vitamin E, thus distributing much larger concentrations of the alpha- form in lipids, blood and tissues throughout the body. Both factors basically mean that there's more alpha-tocopherol in the body and less gamma-tocopherol. Unfortunately, it's the gamma-form that seems to disband free radicals and force them into submission. While alpha-tocopherol's vital role is to inhibit free radical production, it's gamma-tocopherol that sequesters and effectively removes existing free radicals, meaning that those who take vitamin E supplements should also take gamma tocopherol. —Angela Pirisi

Artichoke extract lowers cholesterol safely

Artichoke has long been held in esteem for its effects as a natural digestive aid. Stemming from that long-known function, research has unearthed a number of other vital benefits that artichoke compounds can perform with regards not only to the gastrointestinal system but also to the liver and heart. The connection is that artichokes contain some powerful compounds, a combination of flavonoids and caffeoylquinic acids, which are being increasingly recognized for their anti-lipid and choleric (increasing bile production and flow) effects. As such, artichoke extract derived from these important byproducts has a dual benefit for cholesterol metabolism, first by decreasing cholesterol output within the liver and, secondarily, by increasing the conversion of cholesterol into bile acids. The latter action basically helps to mobilize toxins and cholesterol out of the liver through the more efficient excretion of bile.

One of the most recent studies to look at the effects of dried artichoke extract for lowering cholesterol (*Arzneimittelforschung* 2000

Mar;50[3]:260-5) confirmed the significant potency of one of the plant's natural compounds, cynarin. Cynarin is a type of caffeoylquinic acid. Researchers asked 143 patients with elevated cholesterol levels to take 1800 mg of dry artichoke extract (using 450-mg tablets) or a placebo, for six weeks. At the beginning of the study, participants had total cholesterol levels that were over 7.3 mmol/l (over 280 mg/dl). By the end of the study period, the subjects taking the artichoke extract showed a significant drop in their total cholesterol, which fell by 18.5% compared to 8.6% in the placebo group. LDL cholesterol decreased by 22.9% for the treated group compared to 6.3% for the controls. Meanwhile the LDL/HDL ratio showed a decrease of 20.2% in the extract group and 7.2% for the non-treated individuals. The authors conclude that artichoke extract may be useful for the treatment of high cholesterol and, subsequently, effective for the prevention of atherosclerosis and coronary heart disease.

Other research has already pointed to a potential role for artichoke extract as an adjuvant therapy for cholesterol reduction, in addition to its merits as an effective digestive aid. A study involving 553 patients with various chronic digestive disorders had subjects take 320 mg capsules of artichoke extract 1-2 times per day for six weeks (J Gen Med 1996;2:3-19). Results showed a decrease in symptoms by 70.5% in general, while vomiting decreased by 88.3%, nausea 82.4%, abdominal pain 7.2%, loss of appetite 72.3%, constipation 71.0%, flatulence 68.2% and fat intolerance 58.8%. What was even more interesting was that results also showed that the artichoke extract caused blood cholesterol levels to decrease significantly. The subjects' average serum cholesterol fell from about 264 mg/dL to 233 mg/dL. Likewise, their triglyceride levels also fell by 12.5% from 214.97 mg/dL at the beginning of the study to 188.07 mg/dL by the end of it.

In addition to its touted benefits, researchers have found that artichoke extract boasts a very low toxicity profile. In fact, one study revealed that only 1 out of 100 subjects reported mild side effects (e.g. increased flatulence) (Curr Ther Res 1993;53[1]:98-102). Many currently available lipid-lowering drugs carry the threat of hepatotoxicity, which casts artichoke extract in an even more favorable light. —AP

COX-2 inhibitors and cancer treatment

A new study published in The Journal of Clinical Investigation (2000 [June]; 105 [11]:1589-1599) bolsters the already strong case that a class of aspirin-like drugs may represent an effective adjunctive approach to cancer treatment. In this new animal study conducted at Vanderbilt University, a COX-2-inhibiting drug dramatically slowed the growth of cancerous lung tumors. This finding supports an impressive body of evidence, which suggests that COX-2 inhibitors may successfully treat cancers of the colon, pancreas, breast, prostate, bladder, head and neck, among others. COX-2 block an enzyme implicated in the development of malignant tumors. This enzyme, called cyclooxygenase-2 (COX-2), promotes tumor growth via several mechanisms, one of which is to promote the development of blood vessels into the tumor. As the tumor receives nourishment by an expanding vascular (blood vessel) network, it grows in the uncontrollable fashion that characterizes malignant disease.

Researchers believe that blocking the action of the COX-2 enzyme is a crucial variable in cancer therapy. In this particular study, Raymond DuBois, MD, PhD showed how effective COX-2 inhibition was in several ways. First, he implanted cells altered so as to eliminate the gene that produces the COX-2 enzyme. In this population of test animals, "tumor growth was markedly attenuated," said Dr. DuBois. In fact, COX-2-free mice developed about 30% fewer blood vessels than animals that had the active COX-2 gene. Then, DuBois induced cancer growth in laboratory mice by implanting them with Lewis lung carcinoma (LLC) cells, which grow rapidly into solid tumors. DuBois' intent was to treat the animals with the relatively new arthritis drug Celebrex. This drug selectively targets the COX-2 enzyme. "Treatment of wild-type C57BL/6 mice bearing LLC tumors with the selective COX-2 inhibitor Celecoxib (brand name: Celebrex) reduced tumor growth," said Dr. DuBois. Specifically, Celebrex dried up the blood supply for established tumors. As a result, they grew more slowly and remained smaller than in untreated animals. Dr. DuBois also treated animals possessing the active COX-2 gene with Celebrex—it again markedly suppressed levels of the enzyme and, in turn, stunted tumor growth. "It appears that the inhibition of tumor growth is due to lack of tumor-associated angiogenesis (blood vessel formation)," said Dr. DuBois. "We are now examining how that is controlled." What's so intriguing about this link is that it suggests any substance capable of disrupting the blood supply to tumors could have tremendous value as a way to prevent tumor growth and treat already established cancers with fewer adverse side effects.

In collaboration with researchers at the University of Kansas, in Kansas City, and at Osaka University in Osaka, Japan, Dr. DuBois also made another key observation. The team determined that as levels of COX-2 fell through treatment, so too did levels of VEGF, or vascular endothelial growth factor—this is a protein released by tumor cells that also triggers formation of new blood vessels. In fact, the reduction in VEGF was dramatic. When working in tandem, COX-2 and VEGF represent a double whammy that paves the way for invasive tumor growth. They combine to enable tumors in the lung or elsewhere to take over the normal body mechanism used to form new blood vessels. "It seems like [tumors] have taken over this machinery to make sure they get the right blood supply they need to survive," added Dr. DuBois.

Scientists have been searching for ways to disable this rogue machinery. When tumors capture the body's ability to produce blood vessels, they subvert it to their feed malignant growth—and, as frustrating experience has shown, that is a very difficult process to stop. Shark cartilage raised hopes over a decade ago through its ability to block angiogenesis. But research has not confirmed any practical value in this compound. Aspirin and other aspirin-like non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen do knock out the COX-2 enzyme. But at the same time, they suppress the closely related COX-1 enzyme, and that's not a good thing. The digestive tract needs COX-1 to maintain its proper structure and function, and putting the lid on it can cause severe

gastrointestinal upsets.

Aspirin-like COX-2 inhibitors are shaping up as the most promising option yet. Celebrex, in particular, is looking good. Each new study that comes out indicates there may be genuinely practical value to this therapy. "I don't know how important [the effect of Celebrex and other COX-2 inhibitors] will play out in the long run. But it could have an effect on any solid tumor," said DuBois, who several years ago observed the important link between elevated levels of COX-2 and the development of colon tumors. NSAID drugs such as Celebrex and Vioxx primarily affect COX-2, which cancer cells use to multiply. The original purpose of Celebrex was to treat arthritis, because it also suppresses an inflammation-causing chemical in the body known as prostaglandin E2. Life Extension magazine has reported extensively on the use of COX-2 inhibitors as an adjunctive cancer therapy for many years. A wide range of background information on this topic is available at www.lef.org. —Jim O'Brien

[Back to the Magazine Forum](#)

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

LifeExtension®

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.