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Growing Evidence Suggests that Lutein, a Carotenoid, Plays Diverse Roles in Health

Few researchers are willing to come right out and say it, but growing evidence suggests that the carotenoid lutein is an essential nutrient. Currently, neither lutein nor any other carotenoid is officially recognized as essential for health.

Lutein and zeaxanthin, a closely related carotenoid, form the macular pigment, a yellowish deposit in the center of the eye's retina. As antioxidants, lutein and zeaxanthin limit free-radical damage to this crucial part of the eye and appear to reduce the risk of macular degeneration, the leading cause of blindness among the elderly. According to Billy R. Hammond, Jr., PhD, of the University of Georgia, Athens, the macular pigment also functions like polarizing sunglasses, absorbing stray light, reducing glare, and enabling the eye to see details.

In a recent study, Julie A. Mares-Perlman, PhD, of the University of Wisconsin, Madison, analyzed dietary and health data obtained in the third National Health and Nutrition Survey (NHANES III). She and her colleagues examined photographs of the subjects' eyes and dietary and blood levels of lutein and zeaxanthin among 8,222 men and women.

The highest dietary intake of lutein and zeaxanthin was associated with a 90 percent reduction in risk of pigmentary abnormalities in the retina, an early sign of age-related macular degeneration.

In another recent article, Hammond reviewed several studies showing that high intake or blood levels of lutein and zeaxanthin are associated with a low risk of macular degeneration and cataracts. He cited a study in which lutein supplements improved visual acuity in patients with retinitis pigmentosa and other forms of retinal degeneration.

"Lutein and zeaxanthin may help improve vision throughout life through direct effects on the optics of the eye," Hammond and his colleagues wrote. "These carotenoids may also help retard age-related visual loss by retarding the cumulative effects of oxidative damage to the retina and lens."

In a separate line of research, Elizabeth R. Bertone, ScD, of the Harvard Medical School, compared the dietary habits of 327 women with ovarian cancer and 3,129 healthy subjects. Women consuming the greatest amounts of lutein and zeaxanthin – more than 24 mg combined weekly – had a 40 percent lower risk of developing ovarian cancer, compared with women who consumed less than 3.8 mg weekly. The higher amount is equal to five servings of raw, or two to three servings of cooked, spinach weekly.

Other rich dietary sources of lutein and zeaxanthin include kale and broccoli. Lutein supplements, derived from marigold petals, are available as "free lutein" and "lutein esters," which are well absorbed. The body converts some lutein to zeaxanthin.

References: Mares-Perlman JA, Fisher AI, Klein R, et al. Lutein and zeaxanthin in the diet and serum and their relation to age-related maculopathy in the Third National Health and Nutrition Examination Survey. *American Journal of Epidemiology*, 2001;153:424-432. Hammond Jr BR, Wooten BR, Curran-Celentano J. Carotenoids in the retina and lens: possible acute and chronic effects on human visual performance. *Archives of Biochemistry and Biophysics*, 2001;385:41-46. Bertone ER, Hankinson SE, Newcomb PA. A population-based case-control study of carotenoid and vitamin A intake and ovarian cancer (United States). *Cancer Causes and Control*, 2001;12:83-90. □

Four Out of Five Recent Vitamin E Studies Support Heart Benefits

Human trials of vitamin E supplements have provided a mixed bag: some have found vitamin E is good for the heart, and others have found that supplements have no benefits.

But a new analysis of the five largest trials of vitamin E supplements has found that four support the use of vitamin E supplements in reducing the risk of heart attack.

Ishwalal "Kenny" Jialal, MD, of the University of Texas Southwestern Medical Center, analyzed data

Continues on next page

from: (1) the Alpha-Tocopherol Beta-Carotene (ATBC) study, (2) the Cambridge Heart Antioxidant Study (CHAOS), (3) the Gruppo Italiano per lo Studio della Supravivenza nell'Infarto Miocardico (GISSI) Study, (4) the Secondary Prevention with Antioxidants of Cardiovascular Disease in End-Stage Renal Disease (SPACE) study, and (5) the Heart Outcomes Prevention Evaluation (HOPE) Study.

Among people taking vitamin E supplements, the risk of nonfatal heart attack was reduced by 38 percent in the ATBC study, by 77 percent in the CHAOS study, and by 70 percent in the SPACE study. A slight increase in fatal heart attacks in the CHAOS study's vitamin E group was attributed to subjects who did not take their vitamin E.

When the GISSI study was published, researchers concluded that vitamin E had no effect on the risk of heart attack. However, Jialal's reanalysis found that vitamin E supplements reduced the risk of cardiovascular death by 20 percent.

Finally, the HOPE study showed no benefit from vitamin E supplements. However, Jialal criticized the study for its relatively short period of supplementation and for not measuring blood levels of vitamin E, which would have confirmed that subjects took their supplements.

"Thus, the totality of evidence…appears to support a benefit for α-tocopherol supplementation in patients with pre-existing cardiovascular disease," Jialal wrote.

Reference: Jialal I, Traber M, Deveraj S. Is there a vitamin E paradox? *Current Opinion in Lipidology*, 2001;12:49-53. ▯

Natural, But Not Synthetic, Vitamin E Prevents Blood Clots, Researchers Find

Abnormal clotting of blood cells – platelet aggregation – contributes to the risk of heart disease. Vitamin E is well-known for its anticoagulant properties, but a new study reveals that the vitamin's natural form may be superior to its synthetic version.

Jane E. Freedman, MD, and John F. Keaney, MD, obtained blood from healthy volunteers and filtered it to obtain platelet-rich plasma. Platelet cells are blood cells that promote clotting.

The researchers, who are affiliated with Georgetown University and Boston University, measured how well platelet cells absorbed d-alpha tocopherol and d-alpha tocopheryl acetate (both natural forms) and dl-alpha tocopherol (a synthetic form). They also investigated how well all three forms of vitamin E influenced platelet aggregation.

Platelet cells efficiently absorbed d-alpha tocopherol acetate and d-alpha tocopherol. However, almost none of the synthetic vitamin E was absorbed.

Perhaps most significantly, both forms of natural vitamin E reduced platelet aggregation by more than half. In contrast, there was virtually no change with synthetic vitamin E.

Freedman and Keaney also determined that vitamin E's anticoagulant effect was unrelated to its antioxidant properties. Instead, the vitamin's anticoagulant property appears to result from its inhibition of protein kinase C, an enzyme that promotes blood clotting and breakdown of collagen tissue.

In an analysis of recent human trials with vitamin E, Ishwarlal Jialal, MD, found that supplementation did not increase the risk of hemorrhagic stroke – an often-stated concern – even when taken by patients simultaneously taking anticoagulant drugs. (See previous story.)

Freedman JE, Keaney JF Jr. Vitamin E inhibition of platelet aggregation is independent of antioxidant activity. *Journal of Nutrition*, 2000;131:374S-377S. ▯

British Researchers Link High Vitamin C Levels to Lower Risk of Death

Men and women with high blood levels of vitamin C have about half the risk of dying at any given age, compared with people who have low blood levels of the vitamin.

High blood plasma levels of vitamin C were directly and inversely related to death from all causes and, specifically, death from cardiovascular disease and ischemic heart disease in both men and women. Vitamin C was also associated with a reduced risk of cancer in men.

Kay-Tee Khaw, MBBChir (British medical degrees), and her colleagues from Cambridge University, England, tracked the health of almost 20,000 people ages 45-79 over four years. They found that men and women consuming about 109-113 mg of vitamin C daily had about half the risk of death compared with people consuming only 51-57 mg of vitamin C daily.

The lower death rates were largely the result of substantially reduced risks of death for cardiovascular disease (61 percent lower in men and 41 percent lower in women) and ischemic heart disease (68 percent lower in men and more than 99 percent lower in women). Ischemic heart disease is characterized by a lack of oxygen in heart tissue, often resulting in pain.

The researchers also found that eating the equivalent of one extra serving of vitamin C-rich fruit or vegetables daily reduced the risk of death by 20 percent.

Khaw and her colleagues explained in the *Lancet* that vitamin C could reduce the risk of disease and

death for many reasons, including its antioxidant properties. However, she acknowledged that vitamin C levels might also reflect the consumption of foods rich in potassium, folic acid, magnesium, and other nutrients important to health.

In conclusion, Khaw wrote that very modest increases in fruit and vegetable intake could have a major impact in preventing disease.

Khaw KT, Bingham S, Welch A, et al. Relation between plasma ascorbic acid and mortality in men and women in EPIC-Norfolk prospective study: a prospective population study. *Lancet*, 2001;357: 657-663. ▯

Quercetin Shows Promise As a Natural Treatment for Prostate Cancer

Quercetin, an antioxidant flavonoid found in apples and onions, may block the hormone activity that fuels some types of prostate cancer, according to cell studies conducted at the Mayo Clinic in Rochester, Minn.

The study is the second one showing that quercetin may protect the prostate. In 1999, a separate team of researchers found that supplemental quercetin relieved prostate inflammation.

In the latest study, Nianzeng Xing, PhD, focused on a specialized cell receptor for male hormones in male androgen-responsive prostate cancer cells. This particular "androgen receptor" acts somewhat like a light switch, in that it turns on hormone-dependent cancer-causing genes.

Xing and his colleagues discovered that quercetin blocked the activation of the gene coding for the "androgen receptor" in prostate cancer cells. Quercetin also inhibited the secretion of several indicators of tumor growth, including prostate-specific antigen, or PSA.

Male hormones, such as testosterone, can stimulate the growth of prostate cancer, and pharmacological treatments often use the female hormone estrogen to suppress testosterone levels. If human trials show quercetin to be helpful, it would have the advantage of being a safe, nonhormonal treatment for prostate cancer.

Reference: Xing N, Chen Y, Mitchell SH, et al. Quercetin inhibits the expression and function of the androgen receptor in LNCap prostate cancer cells. *Carcinogenesis*, 2001;22:409-414. ▯

B-Vitamin Supplements Lower Three Risk Factors for Heart Disease

Supplements of B-complex vitamins are well-known for their ability to reduce blood levels of homocysteine, a byproduct of protein metabolism that increases the risk of heart disease and stroke. The same supplements can also lower levels of fibrinogen and lipoprotein(a), which are also cardiovascular risk factors.

Marek Naruszewicz, PhD, and his colleagues at the Pomeranian Academy of Medicine, Poland, treated 11 men and 10 women suffering from chronic kidney failure and undergoing kidney dialysis. Such patients commonly have elevated blood levels of homocysteine, fibrinogen, and Lp(a), and they are also known to have an increased risk of heart disease.

"It follows that pharmacological intervention should be aimed at reducing the concentrations of these risk factors," Naruszewicz wrote in the journal *Metabolism – Clinical and Experimental*.

He and his colleagues asked the patients to take 15,000 mcg of folic acid, 150 mg of vitamin B6, and 1,000 mcg of vitamin B12 daily for four weeks. The supplements decreased homocysteine levels by 33.6 percent, fibrinogen by 18.2 percent, and Lp(a) by 21 percent.

"The results suggest that vitamin supplementation has a favorable efect on risk factors of atherosclerosis in patients with renal failure…" Naruszewicz wrote.

Reference: Naruszewicz M, Klinke M, Dziewanowski K, et al. Homocysteine, fibrinogen, and lipoprotein(a) levels are simultaneously reduced in patients with chronic renal failure treated with folic acid, pyridoxine, and cyanocobalamin. *Metabolism – Clinical and Experimental*, 2001;50:131-134. ▯

Pycnogenol® Supplements Ease Sluggish Blood Flow in Legs

It may come as a surprise, but the lion's share of antioxidants in vegetables, fruits, and other plant foods are not vitamins. Rather, they are a large family of micronutrients called polyphenolic flavonoids.

A recent study demonstrated that a proprietary source of these "phytonutrients," called Pycnogenol®, can relieve the swelling and "heavy legs" feeling of venous insufficiency, a condition characterized by sluggish blood flow in the legs.

"Varicose veins, calf tenderness or heaviness, pain, ankle or leg edema, pigmentation of the skin, and ulceration are the most common complaints of patients with chronic venous insufficiency," explained Carla Petrassi, MD, of the University of L'Aquila, Italy.

Petrassi treated 40 people with chronic venous insufficiency. In the first part of the trial, he gave 20 subjects either placebos or 100 mg of Pycnogenol® three times daily for two months. In the second part, he gave the same amount of Pycnogenol® but no placebo to 20 more subjects.

Continues on next page

Quick Reviews of Recent Research

• Vitamin B12 supplements would save millions

Switching patients with pernicious anemia from intramuscular injections of vitamin B12 to oral supplements would save about $145 per person each year, according to a study by Canadian researchers. Based on a study of more than 34,000 seniors living in Ontario, the researchers estimated that the Canadian health care system could save as much as $17.6 million in Canadian dollars over five years if all patients currently receiving injections took daily vitamin B12 supplements. Most of the savings would be the result of fewer physician visits.

van Walraven C, et al. *Canadian Family Physician*, 2001;47:79-86.

• Antioxidants give hospitalized patients a boost

Belgian physicians treated 37 critically ill patients (hospitalized for head trauma, stroke, or respiratory failure) with either a standard intravenous nutritional formula or one with large amounts of vitamins A, C, E, and beta-carotene for one week. Although there were no differences in recovery or death, the group receiving the antioxidant supplements had lower levels of oxidized low-density lipoprotein (LDL) cholesterol, indicating lower free radical stress.

Preiser JC, et al. *Critical Care Medicine*, 2001;28:3828-3832.

• Genistein improve blood vessel function

Genistein, the principal antioxidant isoflavone in soybeans, also has very weak estrogen-like properties, which may explain some of the nutrient's health benefits. Researchers in England injected genistein into the forearms of healthy young and middle-age men and premenopausal women. The genistein increased blood vessel vasodilation – that is, flexibility – in the forearm by two to three times. The effect was almost identical to that of the hormone estrogen.

Walker HA, et al. *Circulation*, 2001;103:258-262.

• Ginkgo extract protects against stomach injury

In a study of laboratory rats and mice, Chinese researchers found that supplemental extracts of *Ginkgo biloba* significantly reduced levels of free radicals and the risk of damage to gastric mucosa.

Wang Q, et al. *Acta Pharmacologica Sinica*, 2000;21:1153-1156.

• Creatine supplements boost athletic performance

Creatine supplements can increase strength and duration of physical workouts, according to a double-blind Canadian study. Researchers gave 41 university athletes either 7.7 grams of creatine supplements or placebos daily for 21 days. They concluded that creatine supplements can greatly improve short-duration, high-intensity physical activity.

Burke DC, et al. *International Journal of Sport Nutrition*, 2000;10:235-244.

•Melatonin may benefit Alzheimer's patients

Researchers from Argentina administered very high doses of melatonin (9 mg before bedtime) to 14 elderly Alzheimer's patients for 22 to 35 months. All patients benefited from improvements in sleep quality. There was no progression in the patients' Alzheimer's disease while they were taking melatonin.

Brusco LI, et al. *Neuroendocrinology Letters*, 2000;21:39-42.

• Trans-fats boost heart attack risk

In a 10-year study of 667 elderly men, Dutch researchers found that a high intake of trans-fats was associated with a 28 percent increased risk of coronary heart disease. Trans fats are found in partially hydrogenated vegetable oils, which are processed to have characteristics of solid fats. Trans fats are used in commercial baked products (e.g., bread, doughnuts), hard margarine, and fast foods.

Oomen CM, et al. *Lancet*, 2001;357:746-751.

Pycnogenol® and Venous Insufficiency...

Continues from previous page

Pycnogenol® is an antioxidant herbal complex containing about 40 proanthocyanidins (a family of flavonoids) and organic acids extracted from the bark of French maritime pine trees.

Patients taking Pycnogenol® in the first part of the study benefited from a 60 percent reduction in their sense of leg "heaviness" and a 74 percent reduction in swelling. In the second part of the study, patients experienced a 44 percent decrease in leg heaviness and a 53 percent decrease in swelling.

Reference: Petrassi C, Mastromarino A, Spartera C. Pycnogenol(R) in chronic venous insufficiency. *Phytomedicine*, 2000;7:383-388.

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