

# The Nutrition Reporter™

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## Two Carotenoids, Lutein and Lycopene, May Reduce the Risk of Cardiovascular Diseases

Two new medical journal reports strongly suggest that lutein and lycopene, both antioxidant carotenoids, can help reduce the risk of cardiovascular diseases.

In the journal *Circulation*, James H. Dwyer, PhD, of the University of Southern California, Los Angeles, and his colleagues described three related studies. In the first, Dwyer compared blood levels of lutein in a group of 480 middle-age men and women and the thickening of their carotid arteries, an important indicator of overall cardiovascular health. Over 18 months, people with the highest lutein levels had virtually no thickening of their carotid arteries. However, subjects with the lowest lutein levels had a significant thickening of their carotid arteries – more than five times greater than in the other group.

In the next experiment, Dwyer and his colleagues grew several batches of human artery cells, some with different amounts of lutein and one without any lutein at all. They then measured free radical oxidation of cholesterol in the artery cells and how quickly white blood cells migrated toward the artery cells. Both oxidation of cholesterol and infiltration of white blood cells between artery cells are early steps in the development of heart disease. Lutein reduced cholesterol oxidation and also inhibited the movement of white blood cells, and larger amounts of lutein were more effective than the smaller doses.

In the third experiment, Dwyer gave large amounts of lutein supplements to one of two groups of mice bred to develop heart disease. Mice receiving the lutein developed heart vessel lesions about half the size of untreated mice.

“These epidemiological, in vitro, and mouse model findings support the hypothesis that increased dietary intake of lutein is protective against the development of early atherosclerosis,” wrote Dwyer and his colleagues.

In the second report, Jukka T. Salonen, PhD, of the University of Kuopio, Finland, tracked the relationship between blood levels of lycopene and

health among 725 men ages 46-64 years. Forty-one of the men had a heart attack or stroke four to six years after the researchers measured their lycopene levels.

In analyzing the data, Salonen found that men with the lowest lycopene levels were 3.3 times more likely to have a heart attack or stroke, compared with those who had the highest blood levels of lycopene.

Spinach and broccoli are rich in lutein, and tomatoes are the principal food source of lycopene.

References: Dwyer JH, Navab M, Dwyer KM, et al. Oxygenated carotenoid lutein and progression of early atherosclerosis. The Los Angeles atherosclerosis study. *Circulation*, 2001;103:2922-2927. Rissanen TH, Voutilainen S, Nyyssonen K, et al. Low serum lycopene concentration is associated with an excess incidence of acute coronary events and stroke: the Kuopio ischaemic heart disease risk factor study. *British Journal of Nutrition*, 2001;85:749-754. □

### “Oxidized” Vitamin C May Reduce Brain Damage and Death from Strokes

Researchers have found that dehydroascorbic acid, the oxidized form of vitamin C, can greatly reduce brain damage and neurological impairment after a stroke. In contrast, regular vitamin C does not appear to offer such benefits, according to the results of a recent animal study.

Normally, vitamin C is a powerful antioxidant that quenches hazardous molecules known as free radicals. After quenching these radicals, vitamin C becomes oxidized – in effect, a weak free radical. But the body is capable of regenerating dehydroascorbic acid back to full-strength vitamin C.

That ability to make vitamin C from dehydroascorbic acid may be crucial in antioxidant-starved stroke victims. The reason is that dehydroascorbic acid readily passes through a membrane called the blood-brain barrier, but vitamin C does not, reports E. Sander Connolly Jr, PhD, of Columbia University, New York.

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Connolly and his colleagues induced ischemic strokes in laboratory mice, but also gave them a placebo, vitamin C, or two different amounts of dehydroascorbic acid. They found that regular vitamin C had little effect on the amount of tissue damaged by the stroke or on subsequent brain function.

However, dehydroascorbic acid significantly reduced the amount of stroke-damaged tissue and brain impairment in the mice – regardless of whether it was administered before or after a stroke.

The highest dosages of dehydroascorbic acid resulted in 95 percent less stroke damage, compared with untreated mice. In addition, dehydroascorbic acid resulted in fewer neurological changes and about half of the incidence of stroke-induced death. “Overall mortality was decreased in a dose-dependent manner with dehydroascorbic acid treatment,” Connolly reported.

This study clearly undermines the belief that vitamin C radicals are dangerous, an idea that has been proposed in the medical literature.

Although Connolly suggested that dehydroascorbic acid might be useful as a drug for stroke patients, it is not available commercially. However, it appears that the brain converts dehydroascorbic acid to vitamin C and back again. Brain concentrations of vitamin C are 25 times greater than in the blood.

Reference: Huang J, Agus DB, Winfree CJ, et al. Dehydroascorbic acid, a blood-brain barrier transportable form of vitamin C, mediates potent cerebroprotection in experimental stroke. *Proceedings of the National Academy of Sciences*, 2001;98:11720-11724. □

## **Vitamins E and A Reduce Haze, Improve Healing After Laser Eye Surgery**

Laser eye surgery has become a popular means of correcting vision, but the procedure generates harmful free radicals, which could slow recovery, cause complications, and harm vision. A recent study, however, has found that supplements of vitamins E and A can reduce the risk of problems and speed recovery.

Michele Vetrugno, MD, and her colleagues at the University of Bari, Italy, asked 20 patients to take 230 mg (342 IU) of vitamin E and 25,000 IU of vitamin A daily for 30 days after undergoing photoreactive keratectomy (PRK), a procedure that corrects near-sightedness by shaving cells from the cornea. (In contrast, LASIK eye surgery cuts the cornea to change its shape.) Vetrugno gave 20 other patients an identical-appearing placebo.

Patients taking vitamins E and C healed faster than did those taking placebos. In addition, the vitamin takers had substantially less visual haze after surgery. And significantly, people who were the most

near-sighted and also took the vitamins had much better visual acuity after PRK.

Reference: Vetrugno M, Maino A, Cardia G, et al. A randomised, double masked, clinical trial of high dose vitamin A and vitamin E supplementation after photoreactive keratectomy. *British Journal of Ophthalmology*, 2001;85:537-539. □

## **Lutein Supplements Improve Vision in Patients with Eye Disorders**

Lutein, an antioxidant found in spinach and broccoli, has in recent years been recognized for its likely role in maintaining vision and reducing the risk of age-related macular degeneration and cataracts. It appears to work, in part, by reducing free radical damage to cells in the eye.

Other research, however, suggests that lutein functions somewhat like polarizing sunglasses. In this way, it filters out stray or disorganized particles of light and improves visual acuity, or sharpness.

In a recent study, Begona Olmedilla, PharmD, and her colleagues in Madrid, Spain, used supplements containing 15 mg of “lutein esters” and 3.3 mg of vitamin E to treat patients with macular degeneration or cataracts. The lutein esters, like other forms of the supplement, were extracted from the petals of marigold flowers.

Five patients with macular degeneration took the supplements three times weekly for an average of 25 months, and they were periodically monitored for changes in visual acuity. Five other patients with cataracts took the supplements for an average of 13 months, and they were monitored for visual acuity and sensitivity to glare and contrast.

One of the patients with macular degeneration dropped out of the study, but exams showed that four patients benefited from various improvements in vision, such as less fuzziness, or better color definition. Among the cataract patients, visual acuity improved significantly, as did tolerance of glare.

Reference: Olmedilla B, Granado F, Blaco I, et al. Lutein in patients with cataracts and age-related macular degeneration: a long-term supplementation study. *Journal of the Science of Food and Agriculture*, 2001;81:904-909. □

## **Two New Studies Support Benefits of St. John’s Wort in Depression**

Two more studies – one with children – have found the herb St. John’s wort to be an effective and safe treatment for depression.

In the first study, a team of German researchers treated 72 adult patients with mild-to-moderate depression, giving them either a placebo or 300 mg of a St. John’s wort extract three times daily for 42 days.

The doctors used several clinical tests, including the Hamilton Depression Scale and the Clinical Global Impression test, to assess the degree of depression among the patients. They also used an “adaptive interim analysis” to determine how quickly patients responded to treatment.

Patients started to show improvements just seven days after starting the herbal treatment, and they had major reductions in depression after 28 and 42 days of supplementation. Patient scores on the Hamilton Depression Scale were reduced by an average of 55 percent among those taking St. John’s wort, and no one reported any side effects.

In the other study, Wolf-Dietrich Hübner, MD, and Tilman Kirste, MD, oversaw a study of 101 children at 35 pediatric clinics in Germany. The children had depression or at least one of several other disorders, including anxiety, restlessness, irritability, poor concentration, sleep disturbances, feelings of dejection, or lack of drive. The children, who ranged from one to 12 years in age, were given 300-1,800 mg of St. John’s wort extract daily for four to six weeks.

The researchers were able to obtain complete treatment data on 74 of the children. Seventy-two percent of the children were “good” or “excellent” responders after two weeks of supplementation, with the number growing to 97 percent after four weeks and 100 percent after six weeks, according to the data from the children’s physicians. The parents’ evaluations of their children were almost identical.

Although no side effects were noted, Hübner and Kirste did report that one child initially worsened after taking the herb, but improved over the subsequent two weeks. St. John’s wort reduced most symptoms in the children, but it had no effect on their ability to concentrate.

References: Kalb R, Troutman-Sponsel RD, Kieser M. Efficacy and tolerability of *Hypericum* extract WS 5572 versus placebo in mildly to moderately depressed patients. *Pharmacopsychiatry*, 2001;34:96-103. Hübner WD, Kirste T. Experience with St John’s wort (*Hypericum perforatum*) in children under 12 years with symptoms of depression and psychovegetative disturbances. *Phytotherapy Research*, 2001;15:367-370. □

## Vitamin B1 May Either Stimulate or Slow Cancer Growth, Depending on Dosage

A study with laboratory mice has found that modest amounts of vitamin B1 (thiamin) can stimulate the growth of an existing cancer, but that massive doses of the vitamin can significantly slow the tumor’s growth.

Begona Comin-Andiux, PhD, of the University

of Barcelona, Spain, and colleagues from the United States and Belarus injected laboratory mice with vitamin B1 before and after being inoculated with tumor cells.

After being injected with the tumor cells, different groups of mice were given eight different dosages of vitamin B1, ranging from 12.5 times the mouse RDA (recommended dietary allowance) for the vitamin to 2,500 times the RDA. In mice given vitamin B1 *before* tumor inoculation, the dosages were limited to only 25 and 2,500 times the RDA.

In both experiments, all but the highest dosages of vitamin B1 stimulated tumor growth above that in untreated mice. However, the highest dosage of vitamin B1, given after the tumor inoculation, reduced the cancer growth by 10 percent. The dosage was 2,500 times the mouse RDA, equivalent to about 3,500 mg in a person.

When the same high dosage of vitamin B1 was given starting seven days *before* tumor inoculation, the vitamin slowed the cancer growth by 36 percent.

“These results indicate that when thiamin supplementation is necessary for the cancer patients, it is advised to supply it in high doses to avoid the tumor promoting effect of low doses,” wrote the researchers.

Vitamin B1 is a cofactor for cellular production of transketolase, which plays a key role in DNA synthesis and cell replication.

Reference: Comin-Andiux B, Boren J, Martinez, et al. The effect of thiamine supplementation on tumour proliferation. A metabolic control analysis study. *European Journal of Biochemistry*, 2001;268:4177-4182. □

## Antioxidant Combination Significantly Reduces Leg Cramps in Dialysis Patients

A combination of vitamins E and C do a better job of relieving leg cramps in kidney dialysis patients than either vitamin does by itself.

Patients undergoing dialysis often experience painful muscular contractions in the leg, which often force them to get up in the middle of the night. Previous research has shown that carnitine supplements reduce such cramps.

In the latest study, Parviz Khajehdehi, MD, and his colleagues at the Shiraz University of Medical Sciences, Iran, gave 60 dialysis patients 400 mg (600 IU) of vitamin E, 250 mg of vitamin C, both supplements, or placebos daily for eight weeks.

Patients taking only vitamin E had a 54 percent reduction in cramps, and those taking vitamin C had a 61 percent reduction. Those taking both vitamins had a 97 percent reduction in cramps. In contrast,

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# Quick Reviews of Recent Research

**• Devil's claw blocks inflammation**

The herb known as devil's claw (*Harpagophytum procumbens*) has been shown useful in reducing pain associated with acute low-back pain and osteoarthritis. In a recent study with healthy human subjects, researchers found that a standardized extract of the herb inhibited leukotriene and thromboxane B2, two of the pro-inflammatory substances produced by the body. The effect of devil's claw was related to blood levels of harpagoside, regarded as the marker of the herb's potency.

Loew D, et al. *Clinical Pharmacological Therapeutics*, 2001;69:356-364.

**• Vitamin B6 found helpful in tardive dyskinesia**

Researchers used vitamin B6 to treat 15 patients with tardive dyskinesia, characterized by severe tremors, in a four-week crossover study. By the third week of the study, patients taking the vitamin experienced significant improvements.

Lerner V, et al. *American Journal of Psychiatry*, 2001;158:1511-1514.

**• Supplements boost intelligence in some children**

In a recent review of published studies, 10 of 13 recent trials found that vitamin supplements improved non-verbal abilities in children. The greatest benefits occurred in children who had been eating diets low in micronutrients.

Benton D. *Neuroscience and Biobehavioral Reviews*, 2001;25:297-309.

**• Nutritional supplement reduces post-surgical risk**

Researchers gave 50 elderly coronary artery bypass patients either a placebo or a proprietary supplement containing arginine, omega-3 fatty acids, and yeast RNA (ribonucleic acid) for at least five days. Only 17 percent of the patients taking the nutritional supplement developed an infection after

## Antioxidants and Dialysis

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patients taking placebos had only a 7 percent reduction.

"We showed for the first time that combined vitamin E and C supplementation was conclusively effect against them. Combination therapy was significantly more effective than treatment with either vitamin E or C given alone," wrote Khajehdehi.

Reference: Khajehdehi P, Moverlou M, Behzahi S, et al. A randomized, double-blind, placebo-controlled trial of supplementary vitamins E, C and their combination for treatment of haemodialysis cramps. *Nephrology Dialysis Transplantation*, 2001;16:1448-1451.□

surgery, compared with 55 percent of those taking the placebo. In addition, those taking the supplement had better kidney function and recovered quickly enough to be discharged earlier from the hospital. Levels of pro-inflammatory interleukin-6 were lower in the group taking the supplement.

Tepaske R, et al. *Lancet*, 2001;358:696-701.

**• Lack of antioxidants may increase preeclampsia risk**

Researchers analyzed carotenoid levels in the blood of 19 women with preeclampsia and 22 healthy pregnant women. Preeclampsia is a toxemia of pregnancy characterized by high blood pressure, headaches, and water retention. Levels of beta-carotene, lycopene, and canthaxanthin were significantly lower in the placentas of women with preeclampsia. This finding is consistent with other studies that have found low antioxidant levels in women with preeclampsia, as well as research that has found antioxidants to reduce the risk of this disorder.

Palan PR, et al. *Obstetrics and Gynecology*, 2001;98:459-462.

**• Hawthorn found helpful in heart failure**

The herb hawthorn, a potent antioxidant, has long been used to treat heart disorders. In a study of men and women with Class II heart failure, treatment with a standardized extract of the herb resulted in a significant improvement, based on almost a 27 percent reduction in heart rate and systolic blood pressure. Patients taking the placebo had only a 2.7 percent reduction.

Zapfe G Jr. *Phytomedicine*, 2001;8:262-266.

**• Supplements boost cognitive function in elderly**

Researchers found that a multivitamin/trace-mineral supplement, compared with a placebo, significantly improved cognitive function in 96 seniors over the course of a year. "Such a nutritional approach may delay the onset of Alzheimer's disease," concluded the researcher.

Chandra RK. *Nutrition*, 2001;17:709-712.

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