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Alpha-Lipoic Acid May Be of Particular Benefit in Stroke, Other Brain Disorders

The antioxidant alpha-lipoic acid may protect against a variety of brain and nervous system diseases.

In a paper published in *Free Radical Biology & Medicine* (Jan/Feb 1997;22:359-78) Lester Packer, PhD, a leading antioxidant researcher at the University of California, Berkeley, described how supplemental alpha-lipoic acid can guard brain cells against free radical damage.

"Very few neuropharmacological intervention strategies are currently available for the treatment of stroke and numerous other brain disorders involving free radical injury," Packer wrote.

Alpha-lipoic acid and its dihydrolipoic acid form (to which some alpha-lipoic acid is converted in the body) neutralize a variety of oxygen and nitrogen free radicals, including superoxide, hydroxyl, singlet oxygen, hypochlorous, and peroxynitrite radicals. It also promotes the metabolism of glucose into energy. (See THE NUTRITION REPORTER, July 1996.)

Alpha-lipoic acid looks particularly promising because it passes through the blood-brain barrier and can protect neurons from free radical damage. It works partly by recycling and increasing levels of glutathione and other antioxidants, including vitamins C and E and coenzyme Q10, and it has a particular advantage over glutathione in that it is readily absorbed.

Dihydrolipoic acid appears to stem the production of free radicals in the cell's mitochondria, which is where most free radicals are formed in the body. It can also inhibit the transport of calcium in the mitochondria, which would prevent calcium contamination of many metabolic pathways.

According to Packer, alpha-lipoic acid might play a beneficial role in a number of brain and nervous system disorders, including stroke, Alzheimer's, amyotrophic lateral sclerosis (Lou Gehrig's disease), multiple sclerosis, head injury, and spinal cord damage.

"In vitro, animal, and preliminary human studies indicate that α-lipoate [another name for alpha-lipoic acid] may be effective in numerous neurodegenerative disorders," Packer wrote.

In other recent research...

• Stephan Jacob, MD, confirmed that alpha-lipoic acid stimulates insulin activity and the metabolism of glucose in insulin-resistant laboratory rats. (*Diabetes*, 1996;45:1024-9.) At an American Diabetes Association scientific symposium on antioxidants and diabetic complications, in Orlando, Fla., Nov 15-17, Jacob described a similar human clinical trial with alpha-lipoic acid. Blood glucose levels fell, insulin resistance decreased, and glucose tolerance improved in patients receiving 600 mg or more of alpha-lipoic acid daily.

• Alpha-lipoic acid improves the cellular uptake and burning of glucose, according to an animal study by Phillip A. Low, MD, of the Mayo Clinic Foundation. It could prevent insulin neuritis, the worsening of nerve pain when glucose control is induced therapeutically. (*Diabetologia*, 1996;39, suppl 1; abstr 120.)

• Changes in blood flow to the brain increase production of free radicals. German researchers reported that alpha-lipoic acid protects brain cells against the ischemic damage that occurs when blood flow is interrupted. (Wolz P and Krieglstein, *Neuropharmacology*, 1996;35:369-75.)

• Alpha-lipoic acid might also be useful in protecting the skin against free radical damage, such as during exposure to sunlight. In an animal study, researchers found that alpha-lipoic acid was readily absorbed by the skin and converted to dihydrolipoic acid. (Podda M, et al., *Biochemical Pharmacology*, 1996;52:627-33.) □

Garlic Supplements Lower Cholesterol, Blood Pressure

The Chinese, Egyptians, and Greeks used garlic medicinally thousands of years ago. Today, with more than 1,800 scientific studies published on garlic, a lot of people take it very seriously—and rightfully so—as a therapeutic food.

Late last year, Manfred Steiner, MD, PhD, of East Carolina University, Greenville, N.C., added to the evidence. He and his colleagues reported that supplements of "aged garlic extract" reduced total cholesterol, low-density lipoprotein (LDL) form of cholesterol, and blood pressure in a group of 41 men with moderate hypercholesterolemia (220-290 mg/dl).

In a double-blind crossover study, Steiner gave the men either 7.2 grams (9 capsules) of aged garlic extract daily or a placebo for six months. Among the men taking garlic, total blood cholesterol levels dropped by an average of 7 percent, or 15-20 mg/dl, LDL cholesterol

Continues on next page

decreased by about 4.6 percent, according to Steiner's article in the *American Journal of Clinical Nutrition* (Dec 1996;64:866-70).

Systolic blood pressure (the higher number, as in 120/70) went down by an impressive 5.5 percent among men taking the garlic supplements, which were manufactured by Wakunaga of America Co. The maximum effect in terms of both cholesterol and blood pressure reductions occurred after three months.

Commenting on other recent research, Steiner wrote that "two recent meta-analyses evaluated the published trials on the basis of objective criteria for comparison. The authors of both studies concluded that garlic supplementation produced a reduction in cholesterol concentrations ranging from 9% to 12%."

In a separate study, a team of researchers at the University of Queensland, Australia, also found that garlic can protect against coronary heart disease. The researchers fed rabbits either a normal diet or one containing a small amount of cholesterol, with or without Kyolic® brand aged garlic extract from Wakunaga.

The cholesterol diet resulted in fatty deposits over about 70 percent of the thoracic aorta's surface area. In contrast, animals eating the cholesterol diet but taking garlic had fatty deposits over only 25 percent of their thoracic aortas, according to an abstract in the *Journal of Vascular Research* (Efendy J, et al., Sept 1996;33 [S1]:23 [abst 90]). □

Yogurt Can Cure Vaginal Infections

Eating live-culture *Lactobacillus acidophilus* yogurt works better than pasteurized yogurt in treating recurrent bacterial vaginosis (BV), but both types of products work equally well in controlling vaginal *Candida albicans* infections.

That's the conclusion of Elizer Shalev, MD, of the Central Emek Hospital, Afula, Israel, who conducted a crossover study with 46 women suffering from BV or *Candida* infections, or both.

The women were instructed to consume either a serving of either the live-culture or pasteurized yogurt daily for two months. After that time, the type of yogurt was switched.

L. acidophilus produces large amounts of hydrogen peroxide and acidifies the vagina, creating an environment that discourages the growth of many pathogenic bacteria and *Candida*.

Women consuming the live-culture *L. acidophilus* had fewer than half the episodes of BV compared with those taking pasteurized yogurt, according to Shalev's article in *Archives of Family Medicine* (Nov/Dec 1996;5:593-6). The pasteurized yogurt decreased BV only slightly.

Among women with *Candida* infections, both types of yogurt reduced the incidence by more than half. The live-culture *L. acidophilus* was slightly more effective, but Shalev did not consider the difference statistically significant. □

Vitamin E: At Least 500 IU Daily Needed to Protect the Heart

You can prevent oxidative damage to your low-density lipoprotein (LDL) form of cholesterol with 500 IU or more natural vitamin E daily, according to a recent study by Australian researchers.

LDL is generally considered the "bad" cholesterol because high levels of it are strongly associated with risk of coronary heart disease. A number of researchers have shown that oxidized LDL—that is, damaged by free radicals—is a more precise risk factor.

Leon A. Simons, MD, of St. Vincent's Hospital, Darlinghurst, gave 42 healthy subjects either a placebo or supplements of 500 IU, 1,000 IU, or 1,500 IU of vitamin E daily for six weeks. At all doses of vitamin E, LDL took significantly longer than normal to oxidize. Oxidation took about 25 percent longer to occur at the lower doses and 35 percent longer at the higher dose.

Furthermore, less of the LDL ultimately did oxidize. At 500 IU, 14 percent less LDL oxidized. At 1,000 IU, 19 percent less LDL oxidized. And at 1,500 IU, 25 percent less LDL oxidized, according to Simons' article in the *Australian and New Zealand Journal of Medicine* (Aug 1996;26:496-503).

Other studies, such as those by Ishwarlal Jialal, MD, of the University of Texas Southwestern Medical Center, have also reported that dosages between 400 IU and 1,200 IU of natural vitamin E daily significantly lowered LDL oxidation. LDL is essential for transporting fat-soluble vitamins through the bloodstream.

In another study, Howard N. Hodis, MD, of the University of Southern California School of Medicine, found that patients taking at least 100 IU of vitamin E daily had less thickening of their carotid artery wall than did people taking less of the vitamin. The benefit would be a lower risk of stroke and heart disease.

Vitamin C had no effect on the thickening of the carotid artery wall. Furthermore, vitamin E failed to provide benefits among patients taking a combination of the cholesterol-lowering drug colestipol and niacin, according to an article in *Circulation* (Nov 15, 1996;94:2369-72). □

Low Vitamin E May Lead to Spasms

Insufficient vitamin E might lead to variant angina, a type of resting heart pain and coronary artery spasm, according to a study by Kunihisa Miwa, MD, of Toyama Medical and Pharmaceutical University, Japan.

Miwa studied patients with active variant angina, inactive variant angina, or with either condition. The

patients with active variant angina had low blood levels of the alpha and gamma fractions of vitamin E, according to Miwa's article in *Circulation* (1996;94:14-18). However, their vitamin E levels were significantly higher after a symptom-free six-month period.

The cause of variant angina is not clear. However, Miwa noted that oxidized low-density lipoprotein (LDL) might be related to arterial spasm. Vitamin E is needed to relax blood vessel walls, and it is possible that free radicals caused "exaggerated coronary vasoconstriction." □

Folic Acid Benefits Outweigh Risks

Many physicians are concerned that folic acid supplementation or food fortification will mask some cases of vitamin B12 deficiency. But the benefits will far outweigh the risks, according to a paper published in the *Journal of the American Medical Association*.

Katherine L. Tucker, PhD, of the USDA Human Nutrition Research Center on Aging at Tufts University, Boston, noted that folic acid reduces blood levels of homocysteine, a substance that damages arteries and is a major risk factor for coronary heart disease.

According to Tucker's calculations, the risk of coronary artery disease will decrease with increasingly higher amounts of folic acid added to bread and other bakery foods. However, the risk of masking a B12 deficiency will also increase.

But the risk of a B12 deficiency may not be a significant issue because, as Tucker noted, "Most subjects with high folate intakes after fortification will be supplement users." That means they will probably be getting supplemental B12.

Not long ago, a team of researchers suggested that people take both folic acid and vitamin B12 together, since both vitamins are safe and beneficial. (See Beresford SAA, *JAMA*, 1995;274:1049-57). The advice is sound, since large numbers of people are deficient in both vitamins.

Note: Editor Jack Challem has just published a 48-page health guide describing the dangers of homocysteine and how B vitamins can help. To order your copy of *Homocysteine*, send a $6 check to The Nutrition Reporter, PO Box 5505, Aloha OR 97007. □

Rating the Flavonoids

You've no doubt heard a lot about the antioxidant properties of flavonoids, a large group of water-soluble pigments found in fruits and vegetables. But have you wondered how the different flavonoids stack up against each other?

Catherine Rice-Evans, PhD, of Guy's Hospital, London, recently compared the antioxidant properties of many flavonoids.

The most potent antioxidant flavonoids were epigallocatechin gallate and epicatechin gallate, found in green and black teas. Close behind was quercetin, found in onion, apple skin, berries, black grape, tea, and broccoli. And right behind quercetin was cyanidin, a type of anthocyanidin found in grapes, raspberries, and strawberries, according to Rice-Evans' article in *Biochemical Society Transactions* (1996;24:790-4).

A note of caution, though. Although some antioxidants do a better job than others when it comes to quenching free radicals, a diversity of antioxidants is better than any single one. The flavonoids function in the watery regions of cells, whereas vitamin E, coenzyme Q10, and carotenoids work in the fatty regions, such as cell membranes. □

Low Tryptophan Hurts Autistics

The essential amino acid tryptophan has long been thought to be involved in modulating autistic behavior, including aggression and repetitive behavior. According to a new study, low tryptophan diets can make the symptoms of autism much worse.

Christopher J. McDoughle, MD, and his colleagues from the Connecticut Mental Health Center, New Haven, studied the behavior of 20 non-medicated autistic adults on tryptophan-deficient diets.

Eleven (65 percent) of the 17 autistic patients who completed the study got worse after eating a tryptophan-deficient diet.

"Tryptophan depletion led to a significant increase in behaviors such as whirling, flapping, pacing, banging and hitting self, rocking, and toe walking. In addition, patients were significantly less calm and happy and more anxious," McDoughle wrote in the *Archives of General Psychiatry* (Nov 1996;53:989-96).

Would supplemental tryptophan help such patients? It's possible, but not clear from McDoughle's study. Supplemental tryptophan was banned by the FDA several years ago after consumers became sick from a contaminated batch of the nutrient. However, a number of vitamin companies recently began selling a tryptophan precursor, L-5-hydroxy-tryptophan. □

Vitamins Protect Against Toxins

Vitamins E and C can protect the heart from bacterial toxins associated with life-threatening infections, such as sepsis, researchers have reported.

In an animal experiment, G. Barja, PhD, of Complutense University, Spain, exposed guinea pigs to a bacterial endotoxin. Like people, guinea pigs do not produce their own vitamin C.

The endotoxin increased oxidative stress in the heart muscle. However, supplemental vitamins E and C were protective, according to an article by Barja in *Life Sciences* (1996;59:649-57). □

The Little Antioxidants Around Us

When you regularly follow nutrition research, it often seems as though half the world is made of free radicals and the other half consists of protective antioxidants. Yet most people think of only the major antioxidants—vitamins C and E, the carotenoids, and alpha-lipoic acid. Many other nutrients serve as beneficial antioxidants, and many common foods and herbs contain potent amounts of them. Here's a brief rundown of some of them—and some surprises—from recent studies.

• Curcumin, a common spice, functions as an antioxidant and can attack and induce death in cancerous cells.

Jiang M-C, et al., *Nutrition and Cancer*, 1996:26:111-20.

• Provençal herbs and rosemary are rich in the antioxidants carnosol and carnosic acid. Both substances prevent the oxidation of fats. Purified carnosol also showed anti-HIV activity.

Aruoma OI, et al., *Food and Chemical Toxicology*, 1996:34:449-56.

• Both green and black tea, rich in antioxidant flavonoids, prevented precancerous changes in liver cells and reduced excretion of toxic compounds, suggesting they were effectively broken down.

Xu M, et al., *Carcinogenesis*, 1996;17:1429034.

• In an epidemiological study, consumption of non-herbal teas (i.e., green or black teas) by post-menopausal women was associated with a lower risk of digestive and urinary tract cancers. Women who consumed two or more cups of tea daily had a 32 percent lower risk of digestive tract cancer and a 60 percent lower risk of urinary tract cancer, compared with women who rarely, if ever, drank tea.

Zheng W, et al., *American Journal of Epidemiology*, 1996;144:175-82.

• Caffeine, the stimulant found in coffee, prevented oxidative damage to liver cell membranes. It was most effective against hydroxyl free radicals, moderately effective against singlet oxygen radicals, and only modestly effective against peroxyl radicals. Interestingly, the researchers concluded that "the antioxidant ability of caffeine was similar to that of the established biological antioxidant glutathione and significantly higher than ascorbic acid."

Devasagayam TPA, et al., *Biochimica et Biophysica Acta*, 1996;1282:63-70.

• The flavonoid quercetin, found in apples, onions, and grapes, inhibited the growth of cheek tumors and papillomas (epithelial tumors) in hamsters.

Balasubramanian S and Govindasamy S, *Carcinogenesis*, 1996;17:877-9.

• Hesperidin, a flavonoid found in orange peel, lowered blood pressure and water retention in hypertensive rats.

Galati EM, et al., *Il Farmaco*, 1996;51:219-21.

• Blood levels of two little known carotenoids, lycopene and canthaxanthin (as well as beta-carotene and vitamin E) appeared to protect against cervical cancer and cervical intraepithelial neoplasia.

Palan PR, et al., *Clinical Cancer Research*, 1996;2:181-5.

• Phenolic flavonoids extracted from cocoa powder and chocolate were potent antioxidants, capable of preventing oxidation of low-density lipoprotein (LDL). The researchers noted that "a cup of hot chocolate contains 7.3 grams (two tablespoons of cocoa would have 146 mg total phenol), whereas a 41 gram (1.5 oz) piece of milk chocolate would have 205 mg total phenol. For comparison, a standard 140 mL (5 oz) serving of red wine contains about 210 mg total phenols."

Waterhouse AL, et al., *Lancet*, 1996;348:834.

• Various fractions of the vitamin E complex were found in four different varieties of the spice oregano. Gamma tocopherol was the most abundant fraction.

Lagouri V and Boskou D, *International Journal of Food Sciences and Nutrition*, 1996;47:493-7.

• Antioxidants in *Ginkgo biloba* prevented oxidative stress and the loss of viability in macrophages (a type of white blood cell) and endothelial cells (which line arteries).

Rong Y, et al., *Free Radical Biology & Medicine*, 1996;20:121-7.

• Capsaicin, the pungent component of hot peppers, and diallyl sulfide, one of the many sulfur-containing compounds found in garlic, can prevent mutational and carcinogenic changes triggered by toxic chemicals.

Surh Y-J, et al., *Carcinogenesis*, 1995;16:2467-71.

• In comparing the antioxidant properties of 12 fruits and 5 commercial fruit juices, researchers found that fresh and dried strawberry had the greatest ability to quench free radicals. Among juices, grape juice had the greatest antioxidant activity.

Wang H, et al., *Journal of Food Chemistry*, 1996;44: 701-5. □

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