

# The NUTRITION REPORTER™

THE INDEPENDENT NEWSLETTER THAT REPORTS VITAMIN AND MINERAL THERAPIES © JULY 1997 VOL 8 NO 7 BY JACK CHALLEM

## Soy Isoflavones: Can These Nutrients Help Protect Against Women's Health Problems?

The terms are hardly household words—at least for now—but a group of nutrients found in soy foods may help forestall some of the most common women's health problems, including breast cancer, heart disease, osteoporosis, and the discomfort of menopause.

The nutrients are called isoflavones, a group of flavonoids that include genistein, daidzein, and glycitein. Although found in a variety of legumes, isoflavones are particularly abundant in soy foods. A serving of tofu or a glass of soy milk contains "therapeutic" levels of these substances.

The isoflavones play at least three distinct roles in health, each with a cascade of beneficial effects. According to a surge of research in the past several years—more than 1,000 published studies since 1993—the isoflavones are:

- powerful antioxidants that minimize cell damage from free radicals,
- very weak estrogens that block the hazardous effects of too much hormonal estrogen and synthetic estrogens
- inhibitors of tumor cell growth by blocking activity of the enzyme tyrosine kinase.

Interest in the isoflavones comes out of epidemiological studies showing that Asian women and men have a low risk of breast and prostate cancer, respectively, compared with Americans. This low risk has been attributed largely to diet and lifestyle, rather than to genetics, because the risk of cancer among Asians increases when they move to the United States and adopt American diets.

Traditional Asian diets are high in soy foods and isoflavones, whereas American diets are very low in them. (Soybean oil does not contain these flavonoids.) Furthermore, levels of genistein, the predominant isoflavone, are higher in fermented soy foods, such as Japanese miso and natto. That's because bacteria help break down the isoflavone genistin into the much more biologically active genistein. (Fukutake M, et al., *Food and Chemical Toxicology*, 1996;34:457-61.)

The weakestrogenic effects of isoflavones help maintain bone density, according to a study by John W. Erdman, PhD, of the University of Illinois. Erdman presented his findings at the Second International Symposium on the Role of Soy in Preventing and Treating Chronic Disease, held last year in Brussels, Belgium.

The isoflavones attach to cell receptors for estrogen and prevent attachment by more powerful hormonal estrogen.

Because the estrogenic properties of isoflavones are so mild, they function as anti-estrogens and prevent the true hormone from stimulating cell growth. This is one reason why researchers believe isoflavones protect against breast cancer, according to experiments by various researchers. (See Zava DT, et al., *Nutrition and Cancer*, 1997;27:31-40.) Isoflavones might also protect against the estrogen-like effects of pesticides, according to an article by Devra Lee Davis, PhD, in *Science & Medicine* (May/June 1997:56-63).

In fact, genistein may have even broader anticancer properties, according to findings by a team of doctors at the University of Vermont College of Medicine. Paul L. Penar, MD, and his colleagues reported in *Neurosurgery* (1997;40:141-151) that, in a cell-culture study, genistein inhibited the activity of tyrosine kinase and the invasiveness of glioblastoma, an aggressive type of brain cancer. □

## Vitamin E Supplements Boost Immune System in Elderly Men

Vitamin E supplements can boost immunity in healthy older people and may help protect them from cancer and infections, according to a study by researchers at Tufts University.

The researchers, led by Simin Nikbin Meydani, DVM, PhD, gave vitamin E supplements to 88 volunteer subjects for four months. Seventy-eight of them completed the study, and they averaged a 65 percent improvement in their delayed-type hypersensitivity skin response (DTH). The DTH skin test measures how quickly and forcefully the immune system responds to challenges.

The subjects also averaged a six-fold increase in antibodies in response to a challenge with hepatitis B and a lesser but significant response to the tetanus vaccine.

The subjects took 60 IU, 200 IU, or 800 IU of vitamin E daily, and the immune response was greatest among subjects taking 200 IU. The vitamin E worked in part by lowering levels of prostaglandin E<sub>2</sub>, which interferes with immune function. Patients taking dummy pills had no change in their immune response.

Immune system activity typically decreases with age, and the researchers noted that it is difficult to enhance the immunity of older patients.

"Few interventions have been successful in changing

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the age-associated decline of the immune response," Meydani and her colleagues wrote in the *Journal of the American Medical Association* (May 7, 1997;277:1380-86). "In the present study, we demonstrate that supplementation of healthy elderly with vitamin E, an antioxidant vitamin that inhibits prostaglandin E2 production, significantly improves certain clinically relevant in vivo indexes of cell-mediated immune response, without an adverse effect in this population."

Although the study was not designed to measure whether vitamin E reduced the number of infections, Meydani did report an intriguing finding. "When the three vitamin E-treated groups were combined, their incidence of self-reported infections...was 30 percent lower than that of the placebo group," she wrote.

In a related editorial, Ranjit Kumar Chandra, MD, of Memorial University, St. John's, Newfoundland, wrote, "The era of nutrient supplements to promote health and reduce illness is here to stay....It is expensive and impractical to estimate dietary intake or blood levels of various nutrients in individuals. Since there is no evidence to suggest that physiological amounts of vitamins and trace elements given for prolonged periods have any toxic or adverse consequences...it would be prudent to opt for a suitable micronutrient supplement in modest amounts for all elderly individuals..." □

## Folic Acid Deficiency Common, Leads to DNA Damage and Diseases

A deficiency of the B-vitamin folic acid can lead to the break up of deoxyribonucleic acid (DNA), the complex protein that constitutes your genes. However, taking folic acid supplements can reduce this DNA damage, according to a study by researchers at the University of California, Berkeley.

And in a separate study, conducted in Ireland, researchers have found that large numbers of people have a genetic defect that interferes with their ability to utilize folic acid. High supplemental levels of the nutrient may compensate for the defect.

In the first study, Bruce N. Ames, PhD, identified the precise way that folic acid deficiency causes DNA damage. Normally, thymine is one of the four proteins that make up DNA. When a person is deficient in folic acid, another compound, called uracil, accumulates in place of thymine in DNA. When the body tries to remove the excess uracil, it leaves breaks in DNA and chromosomes, according to an article in the *Proceedings of the National Academy of Sciences* (April 1997;94:3290-95).

Although single-strand DNA breaks can often be repaired by the body, the large quantity of uracil in DNA increases the risk of double-strand breaks, which are harder to repair and more hazardous, according to Ames.

When Ames and his colleagues gave their human

subjects folic acid supplements, the amount of uracil being incorporated into DNA decreased significantly, "suggesting that, in folate-deficient people, increased folate intake may decrease the risk of many types of cancer."

Folic acid deficiency affects about 10 percent of the U.S. population as a whole and one-half of adolescents, the elderly, and low-income African-Americans. Its deficiency is also associated with an increased risk of coronary heart disease, decreased mental function, and colon, esophageal, and cervical cancer, Ames explained.

"The optimum intake of folate and other micronutrients for long-term health is likely to be greater than that necessary to prevent overt symptoms of deficiency," he wrote.

In fact, because of genetics, 5-15 percent of people might have very high folic acid requirements. John Scott, PhD, of Trinity College, Dublin, studied mutations in a gene that creates 5,10-methylenetetrahydrofolate reductase, an enzyme essential for folic acid activity in the body.

Normally, people carry two copies of this gene, one inherited from the mother and one from the father. Scott found that one in every seven Irish women had mutated versions of this gene.

Women with two mutated (damaged) versions of the gene had abnormally low blood levels of folic acid, as did pregnant women with one mutated gene. Nonpregnant women with one damaged gene were able to maintain normal folic acid levels through the diet.

"These results suggest that a substantial minority of people in general populations may have increased folate needs," Scott wrote in *Lancet* (May 31, 1997;349:1591-3).

He added that "if genetic variations that cause altered nutrient status are common, as this study suggests, there may be no such thing as a 'normal' population with respect to nutrient requirements, as was assumed when dietary reference values were established." □

## Depressives Have Low Folic Acid

Most adults require folic acid in infinitesimal amounts—400 mcg, or about 1/70,000 of an ounce daily. People who fail to obtain even this small amount of folic acid, found in leafy green vegetables, are more likely to be depressed—and not respond well to antidepressant therapy.

In a study of 213 outpatients with serious depressive disorders, Maurizio Fava, MD, of Massachusetts General Hospital, found that patients with low folic acid levels were far more likely to suffer specifically from melancholic depression. They were also less likely to respond to the antidepressant drug fluoxetine.

"Overall, the results are consistent with findings linking low folate levels to poorer response to antidepressant treatment," Fava wrote in the *American Journal of Psychiatry* (March 1997;1154:426-8). "Folate levels might be considered in the evaluation of depression patients who do not respond to antidepressant treatment." □

## High Beta-Carotene Linked to Better Lung Function, Breathing

Taking beta-carotene and vitamin A supplements increases lung function among smokers and asbestos workers, according to a new analysis of data from the Carotene and Retinol Efficacy Trial (CARET).

John R. Balmes, MD, of the University of California, San Francisco, analyzed the relationship between blood levels of beta-carotene and vitamin A in a group of 816 men in the CARET study. He found that lung capacity was strongly associated with high blood levels of beta-carotene and vitamin A, even when he accounted for the effects of smoking and asbestos exposure, according to his article in the *American Journal of Respiratory and Critical Care Medicine* (March 1997;155:1066-1071).

Increasing blood levels of beta-carotene and vitamin A, through supplementation, further increased lung capacity. "These results provide support for the hypothesis that beta-carotene and retinol [vitamin A] have a protective effect on loss of ventilatory function," Balmes wrote.

"Retinol is an important regulator of epithelial cell proliferation, differentiation, and morphogenesis," he added. "Beta-carotene, in addition to being metabolized to retinol, has antioxidant properties...It is reasonable to postulate that antioxidant defenses play a critical role in the respiratory tracts where both a high natural exposure to oxygen and the inhalation of oxidant pollutants occur." □

## Lutein May Protect Against Cancer, Macular Degeneration

High dietary intake of lutein, a carotenoid found in kale, broccoli, and spinach, is associated with a low risk of macular degeneration, the leading cause of blindness among the elderly. It might also provide some protection against cancer, according to a recent animal study.

Researchers at Washington State University injected laboratory mice with breast cancer cells, which led to solid cancers in 60-70 percent of the mice. Some of the mice were also fed diets that included various percentages of lutein. Very small quantities of lutein—about two-thousandths of a percent (0.002) of the diet—decreased the incidence, appearance, and growth of tumors, according to an abstract by J. S. Park, PhD, in the *FASEB Journal* (Feb 28, 1997;11:A447, #2586).

In a separate study, scientists at Florida International University gave 30 mg of lutein daily for 150 days to five human subjects. The density of the macular pigment increased in both eyes of three subjects. The fourth subject showed an increase in one eye, and the fifth subject showed no improvement at all. In macular degeneration, the macular pigment becomes thin or nonexistent, and this study showed that supplements can increase its density. The abstract was also published in the *FASEB Journal* (1997;11:A447, #2586). □

## Vitamin C Supplements Ease Exercise-Triggered Asthma

Exercise-induced asthma, which includes coughing, wheezing, and shortness of breath, affects 70 percent of all children with asthma. It typically begins several minutes after starting exercise. However, vitamin C supplements can reduce the severity of exercise-induced asthma attacks.

Herman A. Cohen, MD, of the Rabin Medical Center, Israel, gave 2 grams of vitamin C or placebo to 20 men and women, ages 7 to 28, in double-blind crossover study. Cohen compared the subjects' lung function before taking the vitamin C and exercising afterward.

Patients taking the placebo suffered a significant decline in lung function after exercising. In contrast, nine of the patients taking vitamin C had considerably milder asthma attacks, and two had "borderline" benefits. These 11 subjects "experienced a concomitant clinical well-being without coughing attacks or any pulmonary discomfort," Cohen wrote in *Archives of Pediatric and Adolescent Medicine* (Apr 1997;151:467-70).

Five of the vitamin C-responsive subjects were asked to continue 500 mg of vitamin C daily for two additional weeks, and they benefited from the same protective effect.

"Vitamin C is the major antioxidant substance present in the airway surface liquid of the lung, where it could be important in protecting against endogenous and exogenous oxidants," Cohen wrote. □

## High Potassium Intake Lowers Blood Pressure

High blood pressure, with its stress on blood vessels, increases the risk of heart attack and cardiovascular diseases in general. Many physicians recommend that their hypertensive patients decrease their intake of sodium, believing that high blood pressure is caused in part by an imbalance in the body's sodium-potassium ratio.

The use of potassium supplements in the treatment of high blood pressure dates back to a clinical trial published in 1928. However, many studies have showed minor or mixed benefits. In a recent meta, or collective, analysis of 2,600 patients in 33 studies, Paul K. Whelton, MD, currently with the Tulane University School of Public Health, New Orleans, La., confirmed that potassium supplements or high-potassium diets do in fact decrease blood pressure.

On average, people who ate high-potassium diets or took potassium supplements (in various dosages) had decreases of about 3 mm Hg in their systolic blood pressure and almost 2 mm Hg in their diastolic blood pressure, according to Whelton's article in the *Journal of the American Medical Association* (May 28, 1997;277:1624-32).

The most dramatic finding was among patients who consumed large amounts of sodium. When they increased

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## Quick Reviews of Recent Research

### • Anthocyanidins ranked as antioxidants

Anthocyanidins, a class of flavonoids, are found in many fruits (particularly berries), red wine, herbs, and Pycnogenol® (French maritime pine bark extract). They function as antioxidants, and may help plants resist insect attacks. Researchers recently ranked the antioxidant activity of 14 anthocyanidins. The most potent antioxidant anthocyanidins were types of cyanidin compounds. At the top of the ranking was cyanidin-3-glucoside (also known as kuromanin), followed by cyanidin-3-rhamnoglucoside (keracyanin) and cyanidin. The richest dietary sources of anthocyanidins were red wine, blueberries, sweet cherries, black raspberries, and blackberries.

Wong H, et al., *Journal of Agriculture and Food Chemistry*, 1997;45:304-9.

### • Vitamin B12 associated with slow AIDS progression

In a study of vitamins and HIV progression, researchers found that low blood levels of vitamin B12 were strongly associated with a faster progression to full-blown AIDS. HIV-positive men with high B12 levels lived an average of 8 years before developing AIDS. In contrast, men with low B12 levels developed AIDS after an average of four years.

Tang AM, et al., *Journal of Nutrition*, 1997;127:345-51.

### • High fish intake helps brain

In an epidemiological study of elderly Dutch men, researchers found that high fish consumption was inversely associated with cognitive impairment. In contrast, high linoleic acid, from vegetable oils, may be associated with mental deterioration.

Kalmijn S, et al., *American Journal of Epidemiology*, 1997;145:33-41.

### • Grape juice, wine, and beer protect heart

Drinking three glasses of purple grape juice daily reduces the stickiness of blood platelet cells and is as effective as taking aspirin, according to research conducted by John D. Folts, PhD, at the University of Wisconsin and presented at the annual meeting of the American College of Cardiology, in Anaheim, Calif. In a separate study, researchers at Kaiser Permanente in Oakland, Calif., found that drinking one glass of wine or beer daily reduced the risk of heart disease by 20 percent.

Mann J, Medical Tribune News Service, March 18, 1997.

### • Baker's yeast linked to vaginal infections

Baker's yeast, used in baking bread, may sometimes

cause vaginal yeast infections in women. Researchers investigated yeast infections among 16 Italian women and identified baker's yeast as the causative microorganism. The yeast was inadvertently transferred from fingers to the vagina.

Susman E, Medical Tribune News Service, May 8, 1997.

### • Wine may protect against macular degeneration

Modest wine consumption may reduce the risk of macular degeneration, the leading cause of blindness among the elderly. In a study conducted at the Howard University School of Medicine, Washington, D.C., researchers found that people who drank two to 12 glasses of either red or white wine a year had half the risk of developing macular degeneration, compared with people who consumed no alcohol.

Watson V, Medical Tribune News Service, May 12, 1997.

### • Green tea protects against cancer

Green tea contains several catechins, types of flavonoids, which appear to have anti-cancer activity. One of these catechins, called epigallocatechin-3 gallate (EGCG), inhibits the activity of urokinase, an enzyme cancer cells need to invade normal tissues and metastasize. The brewing of black tea destroys EGCG. A single cup of green tea contains more EGCG and is safer than synthetic urokinase inhibitors.

Jankin J, et al., *Nature*, June 5, 1997;387:561.

### • Vitamins associated with mental performance

In a study of 137 elderly people, researchers found that dietary intake and blood levels of vitamins B1, B2, B3, and folic acid were associated with better thinking and abstraction abilities. Protein intake correlated to better memory.

La Rue A, et al., *American Journal of Clinical Nutrition*, 1997;65:20-9.

### • Folic acid reduces risk of colon cancer

In a study of 98 patients with ulcerative colitis, researchers found that folic acid supplementation for at least six months reduced the risk of colon cancer.

Kashner BA, et al., *Gastroenterology*, 1997;112:29-32.

## Potassium and blood pressure...

Continued from previous page  
their potassium intake (without decreasing sodium intake), systolic blood pressure dropped by 4.4 mm Hg and diastolic blood pressure went down by 2.5 mm Hg.

Bananas, kiwi, apricots, dried beans, and sweet potatoes are high in potassium. □

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