

The NUTRITION REPORTER™

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Studies Support Use of Glucosamine and Chondroitin in Treating Osteoarthritis

A few years ago, clinical research on glucosamine sulfate (and hydrochloride) and chondroitin sulfate was limited. Today, supported by a growing and impressive body of human trials, these two supplements are increasingly being used to prevent and reverse osteoarthritis.

Both glucosamine and chondroitin provide some of the biological building blocks needed for the body's production of cartilage, which forms a cushion against physical stresses in joints. Vitamin C is also needed for cartilage formation.

In one recent study, Alan F. Philippi, M.D., of the U.S. Navy, administered supplements containing 1,500 mg of glucosamine hydrochloride, 1,200 mg of chondroitin sulfate, and 228 mg of manganese ascorbate (a form of vitamin C) to 32 men suffering from osteoarthritis, specifically chronic knee or low-back pain. The men, all Navy SEALs in their 40s, took either the supplements or placebos daily for eight weeks, then were crossed over to the opposite regimen for another eight weeks.

"The study demonstrated the effectiveness of an over-the-counter combination of glucosamine HCl, chondroitin sulfate, and manganese ascorbate in relieving symptoms of knee osteoarthritis," Philippi wrote. About one-half of the knee patients improved while taking the supplements. However, the supplements showed no benefits in low-back pain.

The findings, based on clinical assessments and the patients' subjective impressions, showed reductions in symptoms ranging from 26 to 43 percent, depending on how the symptoms were measured.

In a separate study, Wesley E. Shankland II, DDS, PhD, of Cleveland, Ohio, reported that a similar supplement improved symptoms of osteoarthritis and temporomandibular joint (TMJ) disease in patients. All of the patients suffered from osteoarthritis and "popping" and other sounds resulting from movement of the TMJ, such as while chewing food. TMJ is a form of osteoarthritis affecting the jaw.

Shankland asked 50 patients with osteoarthritis and TMJ disease to take 1,600 mg of glucosamine HCl, 1,200 mg of chondroitin sulfate, and 1,000 mg of calcium ascorbate twice daily. The patients' conditions were assessed every two to three weeks.

Eighty percent of Shankland's patients improved—that is, had a perceived decrease in TMJ noises—though the paper did not identify the average length of treatment. Eight percent of the patients had no change, 2 percent reported a worsening of symptoms, and 10 percent did not comply with the study's protocol.

Finally, a letter in *Lancet* last summer raised questions about whether glucosamine supplements could cause insulin resistance and increase the risk of diabetes. The comment, paraphrased in the *UC Berkeley Wellness Letter* and the *Tufts University Health & Nutrition Letter*, caused some alarm. Several researchers responded to the letter and noted in *Lancet* that human studies have found glucosamine supplements did not increase insulin resistance and, in fact, appeared to improve it.

References: Leffler CT, Philippi AF, Leffler SG, et al. Glucosamine, chondroitin, and manganese ascorbate for degenerative joint disease of the knee or low back: a randomized, double-blind, placebo-controlled pilot study. *Military Medicine*, 1999;164:85-91. Shankland WE II. The effects of glucosamine and chondroitin sulfate on osteoarthritis of the TMJ: a preliminary report of 50 patients. *Orofacial Pain*, 1999;16:230-235. Adams ME. Hype about glucosamine. *Lancet*, 1999;354:353-354. Rovati LC, Anfeld M, Giacobelli G. Glucosamine in osteoarthritis. *Lancet*, 1999;354:1640. □

Antioxidant Cocktail Reduces Symptoms in Hepatitis C Patients

A "conservative" natural treatment of hepatitis C infections appears effective and inexpensive, according to a report describing three cases histories in the German journal *Medizinische Klinik*. Hepatitis C, a chronic liver infection, affects an estimated 4 million Americans and accounts for 10,000 deaths annually.

Burton M. Berkson, MD, PhD, of Las Cruces, N.M., described three of 50 hepatitis C patients he has treated with a regimen including daily supplements of 600 mg of alpha-lipoic acid, 900 mg of silymarin, and 400 mcg of selenium.

"There is no reliable and effective therapy for

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chronic hepatitis C since interferon and antivirals work no more than 30% of the time, and liver transplant surgery is uncertain and tentative over the long run," Berkson wrote.

According to Berkson, both alpha-lipoic acid and silymarin (an extract of the herb milk thistle) have been shown to improve liver function. Selenium may be helpful by countering a deficiency induced by selenium-coding RNA viruses, including hepatitis C.

One of the cases described was a 35-year-old woman who contracted hepatitis C from a blood transfusion 15 years ago. In 1996, she was diagnosed with cirrhosis of the liver. She was weak, had hypertension, suffered constant pain around her liver and spleen, and had a fasting glucose of 300 mg/dl.

Seeking an alternative to liver transplantation, the woman consulted Berkson, who put her on the supplement program and encouraged her to follow a 2,000-calorie diet for diabetics. "Within two weeks she began to feel much better and recovered quickly. Her blood sugar fell into the normal range and the pain in her liver and spleen ended," Berkson wrote. "She became energized and was able to do her normal work as a housewife. She returned to college the next semester..."

Berkson added, "One year of the triple antioxidant therapy...costs less than \$2,000, as compared to more than \$300,000 a year for liver transplant surgery. It appears reasonable that, prior to liver transplant surgery evaluation, or during the transplant evaluation process, this conservative triple antioxidant treatment approach should be considered. If there is a significant betterment in the patient's condition, liver transplant surgery may be avoided."

Reference: Berkson BM. A conservative triple antioxidant approach to the treatment of hepatitis C. *Medizinische Klinik*, 1999;94 (Suppl 3):84-89. □

Researchers Report St. John's Wort Works As Well As Drug Therapy

German researchers have confirmed, in a double-blind placebo-controlled study, that an extract of St. John's wort works as well as – if not better than – imipramine, an antidepressant drug. Even better, St. John's wort causes fewer side effects among patients.

Michael Philipp, MD, a professor of psychiatry at the Imerem Institute for Medical Research Management and Biometrics, Nuremberg, tested 1,050 mg of St. John's wort extract, 100 mg of imipramine, or placebo on a group of 263 men and women with moderate depression. Subjects took the herb, drug, or placebo daily for eight weeks.

Philipp and his colleagues measured the degree of depression among patients through a variety of

standard clinical tests, such as the Hamilton depression scale. In general, St. John's wort and imipramine outperformed the placebo about equally, but the herb resulted in a greater improvement in some of the tests.

Benefits from St. John's wort became noticeable after four weeks of supplementation. The most common side effect to St. John's wort supplementation was nausea. However, the number of patients experiencing side effects was about the same in the groups taking St. John's wort and the placebo, whereas they were about double in the group taking imipramine.

Philipp wrote that the herbal extract may "be considered as an alternative first choice treatment in most cases of mild to moderate depression without psychotic symptoms."

Reference: Philipp M, Kohnen R, Hiller K-O. Hypericum extract versus imipramine or placebo in patients with moderate depression: randomized multicentre study of treatment for eight weeks. *British Medical Journal*, 1999;319:1534-1539. □

Researchers Link Consumption of Refined Grains to Cancer Risk

Diets high in refined grains – primarily bread, pasta, and rice – may increase the risk of several different types of cancer.

Liliane Chatenoud, PhD, of the Ricerche Farmacologiche Mario Negri, Milan, analyzed data on 2,711 Italians with various types of cancer and 3,526 subjects hospitalized for other reasons.

She and her colleagues found that people who consumed the most refined grains were twice as likely to develop thyroid cancer, compared with people eating relatively few refined grains. In addition, those who ate a lot of grains had a 60 percent higher risk of cancer of the mouth, pharynx, esophagus, or larynx; a 50 percent higher risk of cancer of the stomach or colon; and a 30 percent higher risk of cancer of the rectum.

Fifty percent of the refined grains came from bread, 35 percent from pasta, and the rest from rice.

"These findings agree with those of several other studies....Similar associations were observed with sugar, which, from a nutritional viewpoint, confirms the metabolic similarities between sugars and refined cereals," wrote Chatenoud and her colleagues. Diets high in sugars and other refined carbohydrates increase glucose and insulin levels, as well as insulin-like growth factor I, which can stimulate tumor growth.

Reference: Chatenoud L, La Vecchia C, Franceschi S, et al. Refined-cereal intake and risk of selected cancers in Italy. *American Journal of Clinical Nutrition*, 1999;70:1107-1110. □

Study Finds Vitamin C Supplements Have Major Effect on Blood Pressure

Daily supplements of 500 mg of vitamin C can significantly reduce blood pressure, according to a study of 39 subjects with mild to moderate hypertension.

The double-blind study by researchers from the Boston University School of Medicine and the Linus Pauling Institute, Oregon State University, gave vitamin C supplements or placebos to the subjects. After one month, people taking vitamin C had a 9.1 percent decline in blood pressure. Subjects taking placebos had only a 2.7 decrease.

The effect of vitamin C was comparable to prescription drugs used to lower blood pressure.

"This study shows that long-term ascorbic acid treatment reduces blood pressure in patients with hypertension," wrote Joseph A. Vita, MD. "This reduction was of similar magnitude to that predicted by previous population-based and preliminary intervention studies."

Vita and his colleagues noted that free radicals may play a role in hypertension and that vitamin C may help by quenching some of those radicals.

Reference: Duffy SJ, Gokce N, Holbrook M, et al. Treatment of hypertension with ascorbic acid. *Lancet*, 1999;354:2048-2049. □

Blueberries, Strawberries, Spinach May Help Keep the Mind Sharp

Blueberries, rich in antioxidants called flavonoids, may help keep the mind young, according to a study using laboratory rats.

In experiments, James A. Joseph, PhD, and his colleagues at the USDA Human Nutrition Research Center on Aging, Tufts University, used aged rats that were biologically similar to people in their mid- to late 60s. Some were given standard laboratory rat chow, and others received extracts of blueberry, strawberry, or spinach. The extracts were comparable to about one-half cup of the fruit or vegetable daily.

Normally, the rats' neural and cognitive skills decline in old age. However, the rats receiving blueberries, strawberries, or spinach did a better job of navigating mazes, a sign of good short-term memory.

In addition, rats eating the blueberry extract were able to walk on a narrow rod for 11 seconds, close to the norm of 13 seconds. Unsupplemented rats were able to walk on the rod for only five seconds.

The researchers suggested that an increase of free radicals appears to increase neurodegenerative diseases with age, and that the antioxidants in blueberries and other foods are protective.

"In addition, the phytochemicals contained in

spinach, strawberries, and blueberries may produce effects other than antioxidant protection," Joseph and his colleagues wrote. "It is known, for example, that flavonoids can increase membrane fluidity... and...reduce inflammatory responses."

Blueberries are the American version of bilberries, a European fruit that has had a long folk history of use in disease prevention.

Reference: Joseph JA, Shukitt-Hale B, Denisova NA, et al. Reversals of age-related declines in neuronal signal transduction, cognitive, and motor behavioral deficits with blueberry, spinach, or strawberry dietary supplementation. *Journal of Neuroscience*, 1999;19:8114-8121. □

Beta-Carotene May Reduce Prostate Cancer Risk for Some Men

Beta-carotene supplements – battered by contradictory studies on their health benefits – may help some men reduce their risk of prostate cancer.

In the ongoing Physicians Health Study, thousands of male doctors took either a 50 mg beta-carotene supplement or a placebo every other day. Earlier analyses of data found that beta-carotene supplements had no bearing on the risk of either cancer or heart disease.

In this latest report, Nancy R. Cook, ScD, of the Harvard Medical School, found that men entering the study with low blood levels of beta-carotene – indicating that they ate few vegetables – were 45 percent more likely to develop prostate cancer than were men who had high baseline levels of beta-carotene.

However, if men with low initial beta-carotene levels took beta-carotene supplements, they had a 32 percent lower risk of prostate cancer.

Ultimately, there may be an optimal intake of beta-carotene. "It also was apparent that those with the highest levels [of beta-carotene] at baseline had a possible but nonsignificant increase in risk with supplementation," wrote Cook and her colleagues.

Reference: Cook NR, Stampfer MJ, Ma J, "β-carotene supplementation for patients with low baseline levels and decreased risks of total and prostate cancer," *Cancer*, 1999;86:1783-1792. □

Lutein and Zeaxanthin Protect Cells

Lutein and zeaxanthin, antioxidant carotenoids found in broccoli and spinach, have been associated with a reduced risk of macular degeneration, cataracts, and some types of cancer. A recent study revealed how these nutrients protect against disease.

Researchers believe that lutein and zeaxanthin shield

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Quick Reviews of Recent Research

• Magnesium linked to reduced death risk

Analyzing data from the National Health and Nutrition Examination Survey Epidemiologic Followup Study, researchers noted that high blood levels of magnesium, an essential mineral, were associated with a reduced risk of death from ischemic heart disease and reduced mortality from all causes.

Ford ES. *International Journal of Epidemiology*, 1999;28:645-651.

• Alpha-lipoic acid supplements act as antioxidant

Although alpha-lipoic acid is recognized as an antioxidant, relatively few studies have investigated this activity in people. Researchers asked 31 subjects to take either 600 mg of alpha-lipoic acid or 400 IU of natural vitamin E daily for two months. They then took both supplements for another two months. Using vitamin E's effects as the baseline, the researchers found that alpha-lipoic acid slowed free radical damage to cholesterol. Alpha-lipoic acid also reduced several markers of free radicals, including isoprostane, carbonyl, and conjugated dienes.

Marangon K, et al. *Free Radical Biology & Medicine*, 1999;27:1114-1121.

• Low vitamin E levels common

A large body of research indicates that vitamin E can reduce the risk of heart disease and cancer. In a study of 16,000 Americans representative of the overall population, researchers found that 27 percent of the population had low levels of vitamin E. Low vitamin E levels were found in

41 percent of African-Americans.

Ford ES and Sowell A. *American Journal of Epidemiology*, 1999;150:290-300.

• Vitamin E protects skin from age-related changes

Aging and exposure to air pollution increase the body's production of collagenase, an enzyme that breaks down collagen, one of the principal structural proteins of the skin. In a cell-culture study, researchers found that natural vitamin E blocked the activity of protein kinase C, an enzyme that promotes collagenase activity.

Ricciarelli R, et al. *Free Radical Biology & Medicine*, 1999;27:729-737.

• Resveratrol may protect against disease

Resveratrol, an antioxidant found in red wine and grapes, may account for some of the health benefits of these foods. In a cell-culture study, researchers noted that resveratrol inhibited the growth of endothelial cells. Uncontrolled growth of such cells could contribute to a higher risk of coronary artery disease and cancer.

Hsieh T-C, et al. *Cancer Research*, 1999;59:2596-2601.

• Shaken martinis have antioxidant properties

The fictional British secret agent James Bond may have been on the right track with his preference for shaken, not stirred, martinis. In an unusual study, Canadian researchers found that shaken martinis were superior to stirred martinis in quenching hydrogen peroxide, a potent generator of free radicals. The antioxidant properties of martinis were attributed to flavonoids. According to the researchers, though, Bond might have done better with either Sauvignon white wine or Scotch whiskey, both of which are substantially higher in flavonoids. (Bear in mind that vegetables and fruits are far healthier sources of flavonoids. -Editor)

Trevithick CC, et al. *BMJ*, 1999;319:1600-1602.

Lutein and Zeaxanthin...

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lipid-rich membranes from free radicals and also screen out damaging ultraviolet radiation in the eyes. So in a study focusing on egg yolk membranes, Agnieszka Sujak, PhD, of the Maria Curie-Skłodowska University, Lublin, Poland, investigated how lutein and zeaxanthin might retard free radical damage.

Both nutrients were incorporated into the structure of the egg yolk membrane, though in different ways. Lutein and zeaxanthin protected against chemically initiated free radicals, as well as those generated by ultraviolet radiation. Although both were equally effective in protecting against ultraviolet radiation in the short term, zeaxanthin turned out to be better in the long term.

Reference: Sujak A, Gabrielska J, Grudzinski W, et al. Lutein and zeaxanthin as protectors of lipid membranes against oxidative damage: the structural aspects. *Archives of Biochemistry and Biophysics*, 1999;371:301-307. □

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