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IN THE NEWS

Resveratrol Protects Against Atherosclerosis

Resveratrol, a phytopolyphenol compound found abundantly in red wine, protects against atherosclerosis by multiple mechanisms.* Atherosclerosis develops from an excess of low-density lipoprotein (LDL) in the arteries, oxidative stress, inflammation, and endothelial cell injury and dysfunction; the process leads to the formation of fibrous plaques that may rupture.

Several activities of resveratrol help inhibit the progression of atherosclerosis. Studies show that the compound regulates the production of both vasoconstricting and vasodilating substances, inhibits oxidative stress and the generation of reactive oxygen species, inhibits inflammation, prevents the oxidation and uptake of LDL, suppresses platelet aggregation at plaque sites, and decreases the accumulation of smooth muscle cells in the blood vessels.

These findings support previous data on the wide-ranging benefits of resveratrol, including protection against cancer and neurodegenerative diseases, and suggest its future role in the prevention of cardiovascular disease.

—Laura J. Ninger, ELS



Reference

* Fan E, Zhang L, Jiang S, Bai Y. Beneficial effects of resveratrol on atherosclerosis. *J Med Food*. 2008 Dec;11(4):610-4.

Home Blood Pressure Monitoring More Accurate Than Office Measurement

Continuous blood pressure monitoring at home appears to be more accurate than measurements taken at office visits in predicting heart disease outcomes, according to a recent study.*

A total of 556 patients with treatment-resistant hypertension underwent both office measurements of blood pressure and 24-hour ambulatory blood pressure measurements at home (every 15-30 minutes) while wearing a small device. After blood pressure was recorded, patients were monitored for cardiovascular events including heart attack, heart failure, stroke, and death. An average of five years later, 20% of patients had experienced a cardiovascular event or had died. Blood pressure measured in the doctor's office showed no statistical association with outcomes, whereas high blood pressure measurements at home—especially values recorded at night—were associated with heart disease events.

Home blood pressure monitoring eliminates “white coat hypertension,” the phenomenon of elevated blood pressure from the stress of being in a doctor's office, and provides important information about night-time levels.

—Laura J. Ninger, ELS

Reference

* Salles GF, Cardoso CR, Muxfeldt ES. Prognostic influence of office and ambulatory blood pressures in resistant hypertension. *Arch Intern Med*. 2008 Nov 24;168(21):2340-6.

Fish Oil Keeps Arteries Supple

Fish oil supplementation improves arterial elasticity compared with placebo in overweight patients with high blood pressure.* Arterial stiffness in hypertensive or elderly patients may predispose to cardiovascular disease.

The 52 Chinese patients were randomly assigned to take fish oil capsules (3,000 mg/day) or placebo. After eight weeks, large-artery elasticity was significantly improved in the fish oil group compared with baseline, but no effect was found in the placebo group. No changes occurred in small-artery elasticity or blood pressure in either group. The increase in arterial elasticity correlated with the degree of increase in the ratio of polyunsaturated fatty acids to saturated fatty acids in the blood.

The results suggest that omega-3 fatty acids from fish oil exert a direct and rapid effect on improving arterial elasticity in overweight, hypertensive patients, but further study is needed to prove a similar benefit for aging-related arterial stiffness

—Laura J. Ninger, ELS

Reference

* Wang S, Ma AQ, Song SW, Quan QH, Zhao XF, Zheng XH. Fish oil supplementation improves large arterial elasticity in overweight hypertensive patients. *Eur J Clin Nutr.* 2008 Dec;62(12):1426-31.

B Vitamin Prevents Memory Loss

A recent article in the *Journal of Neuroscience* reveals a protective effect of nicotinamide, otherwise known as niacinamide, against memory loss in mice bred to develop a condition that mimics Alzheimer's disease in humans.*

The team from the University of California, Irvine, added nicotinamide (the amide of nicotinic acid [vitamin B3]) daily to the drinking water of Alzheimer's mice and normal mice, while other groups of mice received untreated water for four months. They found lower levels of phosphorylated tau in the brains of the Alzheimer's mice that received nicotinamide, as well as an increase in proteins that strengthen the brain's microtubules. While untreated Alzheimer's mice demonstrated memory loss, those that received nicotinamide performed at the same level as the normal mice.

"The results presented here suggest that nicotinamide has a potential as a novel, safe and inexpensive Alzheimer's disease therapy, either alone or in combination with amyloid beta-lowering therapies," the scientists concluded.

—Dayna Dye



Reference

* Green KN, Steffan JS, Martinez-Coria H, et al. Nicotinamide restores cognition in Alzheimer's disease transgenic mice via a mechanism involving sirtuin inhibition and selective reduction of Thr231-phosphotau. *J Neurosci.* 2008 Nov 5;28(45):11500-10.

Endothelial Progenitor Cells May Reduce Cardiovascular Disease

Endothelial progenitor cells (EPCs), which circulate in the bloodstream, play a role in normal blood vessel function and may find application as both a marker of cardiovascular disease and a potential treatment, according to a recent review.¹

Endothelial progenitor cells help create and repair blood vessels by giving rise to endothelial cells (cells that line the blood vessels). Current research suggests that EPCs are biomarkers for cardiovascular disease risk. Oxidative stress, especially associated with aging, impairs endothelial cell function, and the response of EPCs to oxidative stress is therefore critical to prevent disease. Because a higher number of EPCs is related to a lower risk of disease, EPCs are also a potential therapeutic strategy to repair blood vessels.¹



Further understanding of the relationship between oxidative damage and EPC function will lead to future antioxidant treatments,

and EPCs may become “a method to evaluate the effectiveness of interventions to reduce vascular morbidities and mortalities.”¹

One of resveratrol’s multiple benefits is its ability to upregulate endothelial progenitor cells.²

—Laura J. Ninger, ELS

Reference

1. Case J, Ingram DA, Haneline LS. Oxidative stress impairs endothelial progenitor cell function. *Antioxid Redox Signal*. 2008 Nov;10(11):1895-907.
2. Balestrieri ML, Schiano C, Felice F, et al. Effect of low doses of red wine and pure resveratrol on circulating endothelial progenitor cells. *J Biochem*. 2008 Feb;143(2):179-86.

Vitamin E Reduces Inflammation

A recent issue of the journal *Experimental Physiology* published the discovery of researchers at the University of Illinois of an anti-inflammatory effect for vitamin E in an animal model of inflammation.*

Kinesiology and community health professor Kimberly Huey, PhD, and colleagues administered vitamin E or a placebo to mice for three days before injecting the animals with a low dose of *E. coli* lipopolysaccharide to induce inflammation. A control group of animals received saline instead of the lipopolysaccharide.

The team found increased levels of the cytokines interleukin-6 and interleukin-1-beta in the skeletal and cardiac muscle of mice that received lipopolysaccharide, yet among those that received vitamin E, levels of these cytokines were significantly lower than those of the placebo group. The cytokines function as intercellular communicators that assist in immune response, yet can lead to excessive inflammation.

Dr. Huey concluded that vitamin E “may be beneficial in individuals with chronic inflammation, such as the elderly.”

—Dayna Dye

Reference

- * Huey KA, Fiscus G, Richwine AF, Johnson RW, Meador BM. In vivo vitamin E administration attenuates interleukin-6 and interleukin-1beta responses to an acute inflammatory insult in mouse skeletal and cardiac muscle. *Exp Physiol*. 2008 Dec;93(12):1263-72.

Pharmaceutical Advertising Biases Journals Against Non-Drug Therapies

According to a study conducted at the Wake Forest University School of Medicine, advertising by pharmaceutical companies in medical journals is clearly associated with bias against “non-drug” therapies in those journals.*

Researchers examined a year’s worth of issues from 11 “major medical journals,” including influential publications, such as *The New England Journal of Medicine*, the *Journal of the American Medical Association*, and the *British Medical Journal*. Investigators tallied the amount and content of advertising per journal, and noted any coverage of dietary supplements, including the conclusions reached regarding those nutritional supplements.

Journals with the greatest amount of pharmaceutical company-sponsored advertising were least likely to feature articles about dietary supplements. More to the point, when such journals did feature articles regarding supplements, the conclusions were more likely to be negative rather than positive, or merely neutral.

“The results are consistent with the hypothesis that pharmaceutical advertising biases journals against non-drug therapies,” wrote investigators. “In major medical journals, more pharmaceutical advertising is associated with publishing fewer articles about [dietary supplements] and having more negative conclusions about [dietary supplements]’ safety.”

—Dale Kiefer

Reference

* Kemper KJ, Hood KL. Does pharmaceutical advertising affect journal publication about dietary supplements? *BMC Complement Altern Med.* 2008 Apr 9;8:11.

Dietary Inorganic Phosphate Linked to Elevated Risk of Lung Cancer

Escalating amounts of inorganic phosphate in the diet may damage lung health and set the stage for lung cancer, according to a new report.*

Phosphate is an essential nutrient that occurs naturally in the diet. Escalating amounts of inorganic phosphate have entered the modern food supply, as manufacturers frequently add them to processed foods such as meats, cheeses, beverages, and baked goods to improve product texture and water retention.

Since excess phosphate has been shown to stimulate a metabolic pathway associated with lung cancer promotion, Korean researchers investigated the effects of excess dietary phosphate on lab mice bred to model human lung cancer. Mice received either a normal (0.5%) or high (1.0%) phosphate level in the diet for four weeks. Analysis revealed that mice receiving the higher amount of dietary phosphate experienced “increased lung tumor progression and growth compared with normal diet.”

The findings suggest that “careful regulation of dietary phosphate may be critical for lung cancer prevention as well as treatment.”

—Dale Kiefer

Reference

* Jin H, Xu CX, Lim HT, et al. High dietary inorganic phosphate increases lung tumorigenesis and alters Akt signaling. *Am J Respir Crit Care Med.* 2009 Jan 1;179(1):59-68.

Selenium May Slash Women’s Bladder Cancer Risk by One-Third

A new study by researchers at Dartmouth Medical School suggests that increased levels of the essential micronutrient selenium may play an important role in preventing bladder cancer, at least among women and moderate smokers. Increased selenium intake was also associated with a reduced incidence of a particular class of cancers, related to mutations in the tumor suppressor gene p53.¹

Researchers measured levels of selenium in the toenails of more than 1,800 people, including subjects with newly diagnosed bladder cancer and healthy control subjects. Higher selenium levels were associated with a 34% reduced risk of bladder cancer among females, a 39% risk reduction among moderate smokers, and a 43% reduction in the risk of p53-positive bladder cancer.¹

While previous studies have identified a link between selenium intake and bladder cancer risk,^{2,3} this is believed to be the first study to link selenium with a reduced risk of p53-positive bladder cancer.¹

—Dale Kiefer



Reference

1. Wallace K, Kelsey KT, Schned A, Morris JS, Andrew AS, Karagas MR. Selenium and risk of bladder cancer: a population-based case-control study. *Cancer Prev Res (Phila Pa).* 2009 Jan;2(1):70-3.
2. Navarro Silvera SA, Rohan TE. Trace elements and cancer risk: a review of the epidemiologic evidence. *Cancer Causes Control.* 2007 Feb;18(1):7-27.
3. Kellen E, Zeegers M, Buntinx F. Selenium is inversely associated with bladder cancer risk: a report from the Belgian case-control study on bladder cancer. *Int J Urol.* 2006 Sep;13(9):1180-4.

L-Carnitine Decreases Oxidized LDL in Diabetic Patients

Supplementation with L-carnitine significantly reduces levels of oxidized low-density lipoprotein (LDL) in patients with diabetes.* Oxidized LDL plays a role in atherosclerosis and coronary artery disease, especially when blood sugar is elevated. L-carnitine is a micronutrient with antioxidant and lipid-lowering effects.

In this study, 81 men and women with type 2 diabetes were randomly assigned to take L-carnitine (2,000 mg/day) or placebo for three months along with a low-calorie diet. The L-carnitine group showed significant decreases in lipids including total cholesterol, LDL, triglycerides, and apolipoproteins, as well as a significant increase in beneficial high-density lipoprotein (HDL), compared with placebo. Supplementation also decreased oxidized LDL and other measures of oxidative stress.

Glycosylated hemoglobin, a long-term measure of blood sugar, also decreased in the L-carnitine group.

The reduction in oxidized LDL after only three months of L-carnitine supplementation may indicate a preventive effect on cardiovascular disease.

—Laura J. Ninger, ELS

Reference

* Malaguarnera M, Vacante M, Avitabile T, Malaguarnera M, Cammalleri L, Motta M. L-Carnitine supplementation reduces oxidized LDL cholesterol in patients with diabetes. *Am J Clin Nutr.* 2009 Jan;89(1):71-6.

New Drug Approved for Advanced Prostate Cancer

The US Food and Drug Administration has approved a new injectable hormone treatment for advanced prostate cancer.¹ The medication, currently known as degarelix, was developed by Ferring Pharmaceuticals.

Testosterone suppression (“medical castration”) is a major treatment strategy in advanced prostate cancer. Degarelix works by binding with and blocking the receptor for gonadotropin-releasing hormone in the pituitary gland, an action that suppresses the release of gonadotropins and testosterone. This mechanism of action differs from that of current drugs such as leuprolide.

In a pivotal clinical study, men with prostate cancer were randomly assigned to standard doses of degarelix (207 men) or leuprolide (201 men).² The study objective was to reduce testosterone levels below 50 ng/dL over 12 months. Degarelix was just as effective as leuprolide but had a faster onset of action. After three days of treatment, 96% of men taking degarelix had reduced levels of testosterone, compared with 0% with leuprolide; respective rates were 99% and 18% at day 14 and 100% for both agents by day 28. Testosterone remained suppressed at one year in both groups. Levels of prostate-specific antigen (PSA), an indicator of tumor activity and progression, were 64% lower after two weeks of degarelix and 95% lower after three months, and remained low throughout one year of treatment.

Degarelix was generally safe and most adverse reactions were mild-to-moderate in severity.

—Laura J. Ninger, ELS

Reference

1. Available at: <http://www.medicalnewstoday.com/articles/134153.php>. Accessed January 15, 2009.

2. Available at: <http://www.fda.gov/cder/foi/label/2008/022201lbl.pdf>. Accessed January 15, 2009.

Berry Compounds Have Brain Anti-Aging Effects

Supplementation with polyphenolic compounds from fruits and vegetables helps prevent age-related declines in cognitive and motor function in adult rats.*

The authors fed rats for nine months with a regular diet or a diet supplemented with vitamin E, strawberry extract, or spinach extract. The antioxidant diets prevented several chemical processes involved in oxidative stress and improved spatial memory and learning ability.

In other experiments, aged rats showed significant reversal of age-related cognitive declines and increase in motor performance after eight weeks of supplementation with spinach, strawberry, and especially blueberry extracts. Strawberry and blueberry supplementation even protected against radiation damage.

The authors conclude that “nutritional interventions containing polyphenolics, such as berry fruits, may prove to be a valuable asset in strengthening the brain against the ravages of time as they could retard or prevent the development of age-related neurodegenerative diseases... such as Alzheimer’s disease, because they can reduce oxidative stress and inflammation.”

—Laura J. Ninger, ELS

Reference

* Shukitt-Hale B, Lau FC, Joseph JA. Berry fruit supplementation and the aging brain. *J Agric Food Chem*. 2008 Feb 13;56(3):636-41.

Egg Consumption Associated With Increased Mortality, Diabetes Risk

Men who ate one or more eggs daily were nearly 25% more likely to die of cardiovascular disease than men who ate one or fewer eggs weekly, according to newly released results from a study of more than 21,000 American physicians.¹ The results were gleaned from a 20-year study of male doctors’ health and dietary habits. Eggs are a rich source of cholesterol; a large egg contains about 212 mg of cholesterol.

The study also concluded that diabetic subjects who consumed the greatest number of eggs per week were twice as likely to die of cardiovascular disease as diabetic subjects who consumed the fewest eggs.¹ A related report concluded that daily egg consumption significantly increases a person’s risk of becoming diabetic.²

Interestingly, the last definitive study to address the subject of eggs and heart disease, published nearly a decade ago, failed to find a significant link between egg consumption and cardiovascular disease. But even that study identified an increased risk of coronary heart disease among egg-eating diabetics.³

—Dale Kiefer

Reference

1. Djousse L, Gaziano JM. Egg consumption in relation to cardiovascular disease and mortality: the Physicians’ Health Study. *Am J Clin Nutr*. 2008 Apr;87(4):964-9.
2. Djousse L, Gaziano JM, Buring JE, Lee. Egg consumption and risk of type 2 diabetes in men and women. *Diabetes Care*. 2008 Nov 18.
3. Hu FB, Stampfer MJ, Rimm EB, et al. A prospective study of egg consumption and risk of cardiovascular disease in men and women. *JAMA*. 1999 Apr 21;281(15):1387-94

New Book Provides Definitive Guide to Supplement-Drug Interactions

The recent release of the landmark textbook *Herb, Nutrient, and Drug Interactions: Clinical Implications and Therapeutic Strategies* provides the most detailed, complete source of information available on how commonly used herbs and nutrients interact with medications. Using these therapies together can support or interfere with a drug’s action, or lead to adverse effects.

The book is co-authored by a team of practicing health care professionals with special expertise in integrative medicine: Dr. Mitchell Stargrove, a naturopathic physician, Jonathan Treasure, an authority on medical herbalism, and Dr. Dwight L. McKee, a diplomat of the boards of Internal Medicine, Medical Oncology, and Hematology. Over 60 of the most commonly used herbs and nutrients are covered in depth.

This collaborative effort goes beyond previous books on herb-drug-nutrient interactions in that it analyzes the source, strength, and relevance of the scientific studies, and clearly presents the information in a clinically relevant format. Special consideration is also given to how nutrients are depleted from the body by specific medications.

For instance, the book discusses 26 different classes of drugs that may interact with the essential B vitamin, folic acid. The

common antidiabetic drug metformin (Glucophage®), for example, reportedly depletes folic acid by affecting its absorption. This may partially explain why higher homocysteine levels are seen with long-term metformin use. Folic acid and other B vitamins help keep homocysteine levels down. Since both diabetes and high homocysteine levels are associated with increased cardiovascular risk, folic acid supplementation appears to be especially crucial for metformin users.

Folic acid may also benefit individuals who use the cardiovascular drug nitroglycerin by preventing drug tolerance (decreased efficacy with use). Nitroglycerin becomes less effective at over time by interfering with the enzymes that make nitric oxide (NO), which is needed for healthy arterial function and blood flow. Co-administering folic acid with nitroglycerin may help enhance the drug's therapeutic effects.

Folic acid may also play an important role for those taking lithium or selective serotonin-reuptake inhibitor (SSRI) medications such as fluoxetine (Prozac®) for depression. Clinical studies have shown that folic acid supplementation enhances the antidepressant action of these pharmaceuticals, likely due to its role as a cofactor in the production of neurotransmitters, which control mood.

Drug therapy may be detrimental to vitamin K levels, which can be depleted by several classes of medications. Oral corticosteroids such as prednisone, for example, can cause increased urinary loss of vitamin K. Vitamin K deficiency contributes to vascular calcification as well as bone loss.

Coenzyme Q10 (CoQ10) is another important nutrient depleted by numerous common medicines, including sulfonylureas and related oral hypoglycemic agents for diabetes, tricyclic antidepressants, cholesterol-lowering statins, and the chemotherapy agent doxorubicin (Adriamycin®). Individuals using these drugs may thus benefit from CoQ10 supplementation.

The authors examine the possible interaction of CoQ10 with the anti-coagulant warfarin and find that it lacks clear scientific support. While four case reports have documented that CoQ10 interfered with the action of warfarin, existing studies are merely suggestive and fragmentary. Still, individuals who use warfarin should have their international normalized ratio (INR) levels closely monitored if they choose to supplement with CoQ10.

Access to accurate, clinically relevant information on herb-drug and nutrient-drug interactions is vital to anyone combining these therapies. *Herb, Nutrient, and Drug Interactions: Clinical Implications and Therapeutic Strategies* provides consumers with the ability to work with their doctors to confidently design safe and effective integrative treatment plans.

—Michael J. Hall, ND

Reference

* Stargrove MB, Treasure J, McKee DL. *Herb, Nutrient, and Drug Interactions: Clinical Implications and Therapeutic Strategies*. St. Louis, MO: Mosby Elsevier; 2008.

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