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Antioxidant Flavonoids Provide Multiple Benefits to Cardiovascular System

Three new studies have found that flavonoids – a family of antioxidant pigments in fruits and vegetables – can improve cardiovascular health.

In the first study, Frank Enseleit, MD, of University Hospital, Zurich, Switzerland, and his colleagues asked 23 patients to take 200 mg of Pycnogenol®, an antioxidant complex obtained from French maritime pine bark, daily for eight weeks. After a two-week "washout" period the subjects were then given placebos for eight weeks.

At the start of the study and after each treatment period, the subjects' blood vessel tone – technically known as endothelial function – was measured using ultrasound.

The Pycnogenol supplements led to an improvement in blood vessel tone compared with placebos. In addition, a marker of free radical activity decreased more during the Pycnogenol phase of the study, compared with the placebo phase.

In another study, Amy Jennings, PhD, of the Norwich Medical School, United Kingdom, and her colleagues studied 1,898 women ages 18 to 75 years. Jennings analyzed the subjects dietary consumption of total flavonoids and their subclasses.

She found that higher intake of anthocyanins (closedly related to anthocyanidins), found in blueberries and other dark-colored fruits, were associated with significantly lower systolic blood pressure. Meanwhile, high intake of flavones, found in celery and parsley, were associated with better blood vessel tone.

"The intakes of anthocyanins associated with these findings could be incorporated into the diet by the consumption of one to two portions of berries daily..." wrote Jennings.

Finally, Yan Yang, MD, PhD, of Sun Yat-Sen University, China, and her colleagues treated 150 men and women with elevated cholesterol levels.

The subjects were asked to take either 320 mg of a mix of supplemental anthocyanins or placebos daily for 24 weeks. By the end of the study, people averaged a 10.4 percent decrease in the "bad" low-density lipoprotein (LDL) cholesterol and a 14 percent increase in the "good" high-density lipoprotein (HDL) cholesterol.

In addition, people taking anthocyanin supplements had a 21.6 percent decrease in C-reactive protein (CRP) levels, a marker of inflammation, compared with only a 2.5 percent decrease in the placebo group. Two other markers of inflammation – vascular adhesion molecules and interleuken-1 beta – decreased substantially among people taking anthocyanidins, but not among those taking placebos.

References: Enseleit F, Sudano I, Periat D, et al. Effects of Pycnogenol on endothelial function in patients with stable coronary artery disease: a double-blind, randomized, placebo-controlled cross-over trial. *European Heart Journal*, 2012:33:1589-1597. Jennings A, Welch AA, Faireather-Tait SJ, et al. Higher anthocyanin intake is associated with lower arterial stiffness and central blood pressure in women. *American Journal of Clinical Nutrition*, 2012;96:781-788. Zhu Y, Ling W, Guo H, et al. Anti-inflammatory effect of purified dietary anthocyanin in adults with hypercholesterolemia: a randomized controlled trial. *Nutrition, Metabolism, and Cardiovascular Diseases*, 2012: epub ahead of print. ❑

Perspectives

Now, a Fish Oil Controversy?

Here we go again.

By now, most of you have heard about the *Journal of the AMA* study that supposedly found omega-3 fish oil supplements don't reduce the risk of heart disease. Well, as you might imagine, there's more to the story.

First, in our headline-driven world, there was no context for the study – or any other study that gets media attention. The context is that thousands of studies have shown that fish oils *do* protect the heart in numerous ways. So why should one "study"

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cancel the findings of thousands of others?

Second, you probably noticed that I just put "study" in quotes. That's because it was a statistical analysis of other studies, which I prefer to call a statistical machination.

Third, about half of the subjects had advanced heart disease, so they were taking a lot of prescription drugs. When people take a lot of drugs, it's hard to tease out the benefits of one more therapy, e.g. fish oils. At the very least, drugs mask the benefits of fish oils or other nutrients. (See the next story for more on this topic.)

Fourth, I would argue that fish oil supplements are more effective and safer than any drug therapy. They're also less expensive than drugs. *–JC*

Statin Drugs Negate Benefits of Omega-3 Fish Oil Supplements

Life often boils down to a choice: stay healthy with the help of omega-3 fish oil supplements, or take cholesterol-lowering triglyceride drugs and risk dealing with their side effects.

A new study by Dutch researchers suggests that it's not wise to take both.

Simone R.B.M. Eussen, PhD, of Utrecht University, The Netherlands, and her colleagues studied 3,740 people who had previously suffered at least one heart attack. The subjects were asked to take either placebos or an omega-3 supplement containing 400 mg of eicosapentaenoic acid (EPA), plus docosahexaenoic acid (DHA), and alpha-linolenic acid (the "parent" molecule of EPA and DHA).

Among people taking statins, omega-3 fish oils provided no additional benefits during the 41-month study. The reason, it turned out, was that statins negated the benefits of fish oils.

Meanwhile, people who took supplements containing EPA, DHA, and alpha-linolenic acid – but no statins – were 54 percent less likely to suffer another heart attack.

Eussen noted that among people who did not use statins, only 9 percent of people taking fish oils had a heart attack, compared with 18 percent of those taking placebos.

"In patients with a history of myocardial infarction who are not treated with statins, low-dose supplements with omega-3 fatty acids may reduce major cardiovascular events," wrote Eussen.

Reference: Eussen SRBM, Geleijnse JM, Giltay EJ, et al. Effects of n-3 fatty acids on major cardiovascular events in statin users and non-users with a history of myocardial infarction. *European Heart Journal*, 2012;33:1582-1588. ❑

Excess Carbs Affect Liver, While Weight Loss Corrects Problem

Eating large amounts of refined sugars and starches, such as white bread and pasta, can certainly increase weight. But the more serious problem might actually be an increase in liver fat, also known as steatohepatitis, which can reduce normal functioning of this organ and boost the risk of type 2 diabetes.

Ksenia Sevastianova, MD, of the Minerva Foundation for Medical Research in Helsinki, Finland, and her colleagues placed 16 obese men and women on a diet containing an extra 1,000 calories daily of simple sugars, mostly from candy and sugary beverages. After three weeks, the subjects then followed a low-calorie diet for six months.

Overfeeding the subjects simple carbohydrates increased weight by 2 percent, but liver fat by an average of 27 percent. In other words, liver fat increased 10-fold more than body fat.

After six months of dieting, the study participants lost an average of 4 percent of their weight, an average of about seven pounds. They also lost 25 percent of their liver fat.

The researchers pointed out that the extra sugar calories increased lipogenesis – that is, production of liver fat.

"Weight loss restores liver fat to normal," wrote Sevastianova.

Reference: Sevastianova K, Santos A, Kotronen A, et al. Effect of short-term carbohydrate overfeeding and long-term weight loss on liver fat in overweight humans. *American Journal of Clinical Nutrition*, 2012;96:727-734. ❑

Chinese Mushroom Extract Helps in Treating Rare Type of Cancer

Exotic types of mushrooms – including supplements containing mushroom extracts – have long been used for their medicinal properties. In a new study, researchers have found that extracts of a Chinese mushroom slowed the progression of a specific type of cancer in dogs and extended their life expectancy.

Dorothy Cimino Brown, DVM, of the University of Pennsylvania, Philadelphia, treated 15 dogs that had been diagnosed with hemangiosarcoma, an aggressive type of cancer that originates in blood vessels. Although this type of cancer occurs in people, it is rare.

Cimino Brown used a polysaccharopeptide extract of the *Coriolus versicolor* mushroom, also known as *yunzhi* in Chinese. This extract is also sold as a dietary supplement.

The dogs were treated with one of three doses of

the mushroom extract – 25, 50, or 100 mg per kilogram of body weight daily. (A 20-pound dog would have received 900 mg daily.)

The extract delayed the progression of metastases and significantly increased survival time.

According to Cimino Brown, the longest average survival on record of a dog with hemangiosarcoma was 86 days. Some dogs given the mushroom extract in the study lived more than a year without any other type of treatment.

Although there was no statistical difference between the different dosages, the longest survivals were in the dogs receiving 100 mg of the extract daily. Those dogs lived an average of 199 days.

Reference: Cimino Brown D, Reetz J. Single agent polysaccharopeptide delays metastases and improves survival in naturally occurring hemangiosarcoma. *Evidence-Based Complementary and Alternative Medicine*, 2012: doi 10.1155/2012/384301. ❑

Omega-3 Supplements Help Improve Childrens' Behavior

Docosahexaenoic acid (DHA), one of the two most important forms of omega-3 fats, is essential for normal brain development in children. In a recent study, British researchers found that supplemental DHA reduced behavior problems in children.

Alexandra J. Richardson, PhD, and her colleagues at Oxford University tested 600 mg of DHA and placebos 362 children, ages seven to nine years, with poor reading skills. The study ran for 16 weeks.

Children in the 20th percentile – that is, with a reading ability two years behind their peers – had an eight-month gain in reading ability while taking DHA supplements. Similarly, children in the 10th percentile had a 1.9-month gain in their reading ability while taking the supplements.

However, children with higher reading scores at the start of the study improved just a little, as much as those taking placebos.

In addition, parents but not teachers reported that children taking DHA had fewer behavior problems.

Reference: Docosahexaenoic acid for reading, cognition and behavior in children aged 7-9 years: a randomized controlled trial (the DOLAB study). *PLoS One*, 2012;7:e43909. ❑

Vitamin C Reduces Post-Exercise Fatigue, Improves Heart Rate

Taking a modest amount of supplemental vitamin C eases feelings of fatigue after exercise and reduces heart rate.

Carol S. Johnston, PhD, of Arizona State University, Phoenix, and her colleagues asked 20 obese men and women to take either 500 mg of vitamin C or placebos daily for four weeks. At the beginning and end of the study, the researchers assessed the subjects' feelings of fatigue after walking for 60 minutes on a treadmill.

After four weeks, feelings of post-exercise fatigue decreased substantially among people taking vitamin C, but increased among those taking placebos. In addition, people taking vitamin C had an 11-beat-per-minute decrease in their heart rate – a sign that their hearts were working more efficiently. Meanwhile, heart rates decreased by only three beats per minute in the placebo group.

People in both groups lost about the same amount of weight, almost nine pounds.

Vitamin C is a cofactor in the body's production of carnitine, which is needed to help burn fats for energy.

Reference: Huck CJ, Johnston CS, Beezhold BL, et al. Vitamin C status and perception of effort during exercise in obese individuals adhering to a calorie reduced diet. *Nutrition*, 2012: epub ahead of print. ❑

Researchers Find Link Between Refined Carbs and Breast Cancer

A large study by researchers from a variety of European nations has found a strong link between intake of processed sugars and other carbohydrates and the risk of some types of breast cancer.

Isabelle Romieu, MD, of the International Agency for Research on Cancer, Lyon, France, and her colleagues studied data collected from 334,849 women, ages 34 to 66 years when the study began. Over an average follow up of 11.5 years, 11,576 women were diagnosed with breast cancer.

Overall, there was no relationship between "glycemic load" and breast cancer. Glycemic load is a way of calculating a diet rich in refined sugars and carbs that sharply increase blood sugar levels.

However, the researchers found a strong association between high glycemic load diets and the risk of estrogen-negative (ER-) breast cancer in postmenopausal women. In this group, women eating a lot of high glycemic load foods were 36 percent more likely to develop ER- breast cancer.

Furthermore, the researchers found a slightly stronger association between ER- and progesterone-negative (PR-) breast cancer if postmenopausal women had a history of eating high glycemic load diets.

Reference: Romieu I, Ferrari P, Rinaldi S, et al. Dietary glycemic index and glycemic load and breast cancer risk in the European prospective investigation into cancer and nutrition (EPIC). *American Journal of Clinical Nutrition*, 2012;

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Quick Reviews of Recent Research

• Mixed benefits in calorie-restriction study

Animal studies since the 1930s have found that reducing calorie intake by about 30 percent increased life expectancy by about the same amount. Because it is not feasible to conduct a life-long study of this sort in people, researchers compared calorie-restricted rhesus monkeys to those allowed to eat as much food as they wanted in a laboratory setting. The study began in 1987, and a recent report found that severe calorie restriction has not so far extended life expectancy. Calorie restriction did reduce the risk of cancer and possibly diabetes in the monkeys, although it might have slightly increased the risk of cardiovascular disease.

Mattison JA. *Nature*, 2012: doi 10.1038/nature11432.

• Mercury versus omega-3s from fish

Swedish and Finnish researchers investigated the relationship between omega-3 fat and methylmercury intake from fish in a total of 572 men from their countries. High mercury levels, based on analyzing the subjects' hair was associated with an increased risk of heart attack, whereas higher blood levels of omega-3s was related to a lower risk. The researchers noted that even a small (1 percent) increase in omega-3 intake would reduce the risk of heart attack by 7 percent and thereby offset the risk posed by mercury. Still, they concluded that the ideal approach might be to consume fish high in omega-3s but low in mercury.

Wennberg M. *American Journal of Clinical Nutrition*, 2012;96:706-713.

• Royal jelly leads to health benefits

Royal jelly supplements, made from the nutrient-rich food that produces queen bees, has long been used by people as a dietary supplement. Japanese researchers gave 61 men either 300 mg of royal jelly or placebos daily for six months. By the end of the study, men taking the royal jelly supplements had increases in red blood cells, improvements in glucose tolerance, and better moods.

Morita H. *Nutrition Journal*, 2012;11: doi 10.1186/1475-2891-11-77.

• Nutrients protect sperm from damage

Researchers from the Lawrence Berkeley National Laboratory in California studied 80 men with no signs of fertility problems. Older men with the highest intake of vitamin C had 20 percent less sperm damage, with similar findings for vitamin E and zinc. Older men with high intake of various micronutrients had levels of sperm damage similar to that of young men.

Schmid TE. *Fertility and Sterility*, 2012: epub ahead of print.

• Green tea extracts enhance mental focus

A combination of green tea extract and L-theanine has been shown to improve mental focus and increase a sense of relaxation. Korean researchers provided either a combination of 360 mg of green tea extract and 60 mg of L-theanine or placebos for 16 weeks to 91 men and women with mild cognitive impairment. Tests showed that the subjects benefited from improved memory and an increase in brain theta waves, an indicator of cognitive alertness. High-quality green tea is rich in L-theanine.

Park SK. *Journal of Medicinal Food*, 2011;14:334-343.

• Magnesium may lower colon cancer risk

A team of British and Dutch researchers has found that higher intakes of dietary magnesium are associated with a lower risk of colorectal adenomas, a type of precancerous polyp. The researchers compared magnesium intake in 768 cases and 709 polyp-free men and women. The inverse relationship between magnesium and adenomas was found in people who were overweight and 55 years of age or older. For every 100 mg of daily magnesium intake, subjects had a 13 percent lower risk of adenomas.

Wark PA. *American Journal of Clinical Nutrition*, 2012: doi 10.3945/ajcn.111.030924.

• Some veggies reduce breast cancer risk

Cruciferous vegetables, such as broccoli, cauliflower, and brussel sprouts, are rich in antioxidants and sulfur, which help the body break down carcinogens and other toxins. Chinese researchers analyzed data from 13 population-based studies to determine whether consumption of cruciferous vegetables lower the risk of breast cancer. They concluded that women eating relatively large quantities of cruciferous vegetables had a 15 percent lower risk of developing breast cancer.

Liu X. *The Breast*, 2012:epub ahead of print.

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