AMERICAN BOTANICAL COUNCIL

P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

HerbClip™

FILE: ▪Essential Fatty Acids
▪Cardiovascular Disease
▪Omega 3 Fatty Acids

HC 110253-302

Date: April 14, 2006

RE: Dietary Influences of Omega 3 Fatty Acids in Cardiovascular Disease and Cancer

Shahidi F and Miraliakbari H. Omega-3 (*n*-3) fatty acids in health and disease: Part 1—cardiovascular disease and cancer. *J Med Food*. 2004;7(4):387-401.

Lipids are essential for human life. In this category of compounds are fatty acids, which have diverse physiological effects depending on the number of carbon atoms in the molecule (length of the fatty acid) and degree of unsaturation (number of double bonds). Short-chain fatty acids contain 2 to 6 carbon atoms, medium-chain 8 to 10, and long-chain 12 to 24. Omega-3 and omega-6 fatty acids are long-chain fatty acids. Omega-3 fatty acids include alpha-linolenic acid (ALA; 18 carbons long), eicosapentaenoic acid (EPA; 20 carbons long), and docosahexaenoic acid (DHA; 22 carbons long), which are found in high quantities in cold water fish. Although fish oil content of omega-3 fatty acids varies with the species, season, and harvest site, fish oil generally contains approximately 1 gram of omega-3 fatty acids per 100 grams of fish (3.5 ounces). Omega-3 fatty acids have been extensively studied for the prevention of cardiovascular disease and cancer. This article reviews data from experimental, epidemiological, and intervention studies on the use of omega-3 fatty acids for cardiovascular disease and cancer.

Long-chain fatty acids help maintain cell membrane fluidity, and "are key components in the membranes of highly specialized cells such as neurons [nerves], erythrocytes [red blood cells], cardiomyocytes [heart muscle cells], retinocytes [cells that detect light in the eye], germ cells [cells from which all other cells derive], and immune cells." ALA is found in abundance in flaxseed (*Linum usitatissimum*), canola (*Brassica napus*), soybean (*Glycine max*), and walnut (*Juglans regia*) oils. Alpha-linolenic acid is converted in humans to the longer omega-3 fatty acid EPA, which is then transformed to DHA; however, this process is not very efficient. Estimates of the rate of conversion of ALA to EPA range from 0.1–21%, while ALA-to-DHA conversion rates range from undetectable to 9%.[1]

Cardiovascular Disease

Fish oils were first postulated to protect against cardiovascular disease in the 1950s. Epidemiological studies in Greenland Inuits and Danish settlers of Greenland revealed what has been called the "Eskimo paradox." That is, in this study "Greenland Inuits had a significantly lower incidence of heart disease compared with the Danish settlers, despite comparable fat intakes (40% of caloric intake) and a higher intake of dietary cholesterol." Additional studies concluded that this paradox resulted from a high consumption of fish and marine mammals, both rich sources of long-chain omega-3 fatty acids, and was confirmed in Japanese and Alaskan populations. Eating two fish meals per week (30 grams of any type of fish) decreased by 50% the risk of death from cardiovascular disease compared to those people who ate less than two fish meals per week. Additional studies in the U.S. have also concluded that eating fish significantly decreases the risk of death from cardiovascular disease.

Basic research discovered the potential underlying mechanisms for the cardioprotective effects of long-chain omega-3 fatty acids. Metabolites of EPA have anti-inflammatory actions. Additionally, there is a finite number of fatty acids that can reside in cell membranes, and EPA and DHA compete with arachadonic acid (AA; an omega-6 fatty acid), which is pro-inflammatory. An increase in the EPA-to-AA ratio decreases the production away from the pro-aggregatory (increasing cell clumping, a risk factor for cardiovascular disease) molecules prostaglandin I_2 (PGI_2) and thromboxane A_2 (TXA_2), and increases production of the anti-aggregatory molecules TXA_3 and PGI_3. Omega-3 fatty acids have also shown antiarrhythmic (irregular rhythm) potential in animal and in vitro studies; however, findings from clinical trials are inconsistent. One study of omega-3 fatty acids in people with ventricular arrhythmias found no benefit, and even potential harm in some subjects,[2] while a second clinical trial detected a significant protective effect against atrial fibrillation from omega-3 fatty acid supplementation after coronary artery bypass graft (CABG; commonly called angioplasty) surgery.[3] And a human observational study found an inverse correlation between serum omega-3 fatty acid concentration and ventricular arrhythmias.[4] Clearly more research is needed to determine which cardiovascular patients and pathologies might benefit from omega-3 fatty acids. Similarly, intake of ALA from plant sources was inversely correlated with cardiovascular disease risk in several studies.

Multiple prospective, randomized clinical trials have shown an overall protective effect of long-chain omega-3 fatty acids against myocardial infarction and death from cardiovascular disease; however, the authors point out that these studies "are limited by the numerous dietary changes in these trials and the possibility that the cardioprotective effects observed in these trials are due to other components in the diets of these subjects."

Cancer

In vitro, in vivo animal, and epidemiological studies point to a possible protective role of omega-3 fatty acids in the prevention of prostate and colorectal cancers. A 30-year prospective study on Swedish men found "an inverse association between fatty fish consumption and prostate cancer;" however, fish consumption was also related to "healthy diet and lifestyle habits," making it impossible to conclude that consuming fish alone decreases prostate cancer risk. Frequently in observational dietary analyses, the variable being studied is merely an indicator for changes in the intake of many other nutrients as well; therefore, the controlled clinical trial remains the gold standard for dietary analyses.[5]

Compelling data have accumulated since that study, however, which points to a possible protective role of omega-3 fatty acids in cancer prevention. One study compared serum and prostate tissue concentrations of fatty acids in patients with prostate cancer to those with benign prostatic hyperplasia (BPH; a non-cancerous condition). They concluded, "cancer patients had elevated adipose tissue levels of saturated fatty acids and reduced adipose tissue levels of monounsaturated fatty acids," while "compared with hyperplasia patients, cancer patients had reduced prostate tissue stearic acid to oleic acid ratios and total stearic acid levels." Cancer patients also had lower prostate tissue concentrations of AA, EPA, DHA, and total omega-3 fatty acids compared to non-cancerous tissue. In vitro studies showed beneficial effects on experimental prostate cancer cell lines when given omega-3 fatty acids. However, clinical trials are lacking, so definitive conclusions about the beneficial effects of omega-3 fatty acids on prostate cancer development cannot be made.

Omega-3 fatty acids have also been studied for their effects on the genesis of colorectal cancer. While extensive human clinical trials are also lacking, one study "examined the effects of *n*-3 fatty acids on colonic cell proliferation in subjects at high risk for colon cancer." The conclusion was that "*n*-3 fatty acids may reduce the progression of colorectal polyps to colorectal carcinoma and may protect high-risk individuals from colon cancer," according to the authors of this review article. However, the majority of data on this topic come from animal experiments. The authors review these studies in detail. Specifically, animal studies showed that mustard oil, which is rich in alpha-linolenic acid, decreased the incidence of colon cancer in rats by 50%, compared to a 25% reduction with fish oil and a 10% reduction with corn oil. Additional studies have confirmed these general findings.

Even less is known about the role of omega-3 fatty acids in breast cancer initiation and progression. The authors review two epidemiological studies that show a potential protective role of omega-3 fatty acids for breast cancer, and in vitro studies of experimental breast cancer cell lines also point to a protective role. However, no clinical trials have been conducted, and are needed to understand which omega-3 fatty acids, if any, are helpful in preventing and treating breast cancer.

Conclusion

The authors conclude this review article by summarizing the biological roles of omega-3 fatty acids, dosages used in human studies (3–10 g/day of fatty acids), and mentioning adverse events reported experienced by subjects supplementing with greater than 3 g/day of fish oil (nausea, belching, diarrhea, and bad oral taste). They did not report the frequency of these adverse events. Future research will undoubtedly reveal additional molecular mechanisms of omega-3 fatty acids and their role in clinical medicine.

—John Neustadt, ND

References

[1]Geppert J, Kraft V, Demmelmair H, Koletzko B. Docosahexaenoic acid supplementation in vegetarians effectively increases omega-3 index: a randomized trial. *Lipids.* Aug 2005;40(8):807-814.
[2]Raitt MH, Connor WE, Morris C, et al. Fish oil supplementation and risk of ventricular tachycardia and ventricular fibrillation in patients with implantable defibrillators: a randomized controlled trial. *Jama.* Jun 15 2005;293(23):2884-2891.
[3]Calo L, Bianconi L, Colivicchi F, et al. N-3 Fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a randomized, controlled trial. *J Am Coll Cardiol.* May 17 2005;45(10):1723-1728.
[4]Christensen JH, Riahi S, Schmidt EB, et al. n-3 Fatty acids and ventricular arrhythmias in patients with ischaemic heart disease and implantable cardioverter defibrillators. *Europace.* Jul 2005;7(4):338-344.
[5]Campbell TC. *The China Study*. Dallas, TX: Benbella Books; 2005.