

# Fish Oils: The Essential Nutrients

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**Fish oils help prevent heart disease, depression and cancer.  
A comprehensive review of the many health benefits of fish oils.**

There are good fats and there are bad fats. Artificially produced *trans*-fatty acids are bad in any amount and saturated fats from animal products should be kept to a minimum. The best fats or oils rather, since they are liquid at room temperature, are those that contain the **essential fatty acids** so named because without them we die. Essential fatty acids are polyunsaturated and grouped into two families, the omega-6 EFAs and the omega-3 EFAs.

Seemingly minor differences in their molecular structure make the two EFA families act very differently in the body. While the metabolic products of omega-6 acids promote inflammation, blood clotting, and tumor growth, the omega-3 acids act entirely opposite. Although we do need both omega-3s and omega-6s it is becoming increasingly clear that an excess of omega-6 fatty acids can have dire consequences. Many scientists believe that a major reason for the high incidence of heart disease, hypertension, diabetes, obesity, premature aging, and some forms of cancer is the profound imbalance between our intake of omega-6 and omega-3 fatty acids. Our ancestors evolved on a diet with a ratio of omega-6 to omega-3 of about 1:1. A massive change in dietary habits over the last few centuries has changed this ratio to something closer to 20:1 and this spells trouble. [1-3]

## Sources and requirements

The main sources of omega-6 fatty acids are vegetable oils such as corn oil and soy oil that contain a high proportion of linoleic acid. Omega-3 acids are found in flaxseed oil, walnut oil, and marine plankton and fatty fish. The main component of flaxseed and walnut oils is alpha-linolenic acid while the predominant fatty acids found in fatty fish and fish oils are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The most beneficial and active of these fatty acids are EPA and DHA. Alpha-linolenic acid can be converted to EPA and DHA in the body, but the conversion is quite inefficient especially in older people. [1, 2]

Scientists were first alerted to the many benefits of EPA and DHA in the early 1970s when Danish physicians observed that Greenland Eskimos had an exceptionally low incidence of heart disease and arthritis despite the fact that they consumed a high-fat diet. Intensive research soon discovered that two of the fats (oils) they consumed in large quantities, EPA and DHA, were actually highly beneficial. More recent research has established that fish oils (EPA and DHA) play a crucial role in the prevention of atherosclerosis, heart attack, depression, and cancer. Clinical trials have shown that fish oil supplementation is effective in the treatment of many disorders including rheumatoid arthritis, diabetes, ulcerative colitis, and Raynaud's disease. [1-5]

Recognizing the unique benefits of EPA and DHA and the serious consequences of a

deficiency the US National Institutes of Health recently published Recommended Daily Intakes of fatty acids. They recommend a total daily intake of 650 mg of EPA and DHA, 2.22 g/day of alpha-linolenic acid and 4.44 g/day of linoleic acid. Saturated fat intake should not exceed 8 per cent of total calorie intake or about 18 g/day.

### **Good for the brain and children too**

The human brain is one of the largest "consumers" of DHA. A normal adult human brain contains more than 20 grams of DHA. Low DHA levels have been linked to low brain serotonin levels which again are connected to an increased tendency to depression, suicide, and violence. A high intake of fish has been linked to a significant decrease in age-related memory loss and cognitive function impairment and a lower risk of developing Alzheimer's disease. A recent study found that Alzheimer's patients given an omega-3-rich supplement experienced a significant improvement in their quality of life.[6-9]

Several studies have established a clear association between low levels of omega-3 fatty acids and depression. Other studies have shown that countries with a high level of fish consumption have fewer cases of depression. Researchers at Harvard Medical School have successfully used fish oil supplementation to treat bipolar disorder (manic-depressive illness) and British researchers report encouraging results in the treatment of schizophrenia. [10-15]

An adequate intake of DHA and EPA is particularly important during pregnancy and lactation. During this time the mother must supply all the baby's needs for DHA and EPA because it is unable to synthesize these essential fatty acids itself. DHA makes up 15 to 20% of the cerebral cortex and 30 to 60% of the retina so it is absolutely necessary for normal development of the fetus and baby. There is some evidence that an insufficient intake of omega-3 fatty acids may increase the risk of premature birth and an abnormally low birth weight. There is also emerging evidence that low levels of omega-3 acids are associated with hyperactivity in children. [1, 3, 16- 22]

The constant drain on a mother's DHA reserves can easily lead to a deficiency and some researchers believe that preeclampsia (pregnancy-related high blood pressure) and postpartum depression could be linked to a DHA deficiency. Experts recommend that women get at least 500-600 mg of DHA every day during pregnancy and lactation. The easiest way to ensure this intake is to take a good fish oil supplement daily. [17-19]

Researchers at the University of Sydney have found that children who regularly eat fresh, oily fish have a four times lower risk of developing asthma than do children who rarely eat such fish. They speculate that EPA present in the fish may prevent the development of asthma or reduce its severity by reducing airway inflammation and responsiveness. Researchers at the University of Wyoming have found that supplementation with 3.3 grams/day of fish oil markedly reduces breathing difficulties and other symptoms in asthma patients. Other research has found fish oil to be beneficial in the treatment of other lung diseases such as cystic fibrosis and emphysema. [23- 29]

### **The heart's best friend**

An enormous amount of medical literature testifies to the fact that fish oils prevent and may help to ameliorate or reverse atherosclerosis, angina, heart attack, congestive heart failure, arrhythmias, stroke, and peripheral vascular disease. Fish oils help maintain the elasticity of artery walls, prevent blood clotting, reduce blood pressure and

stabilize heart rhythm. [1-4, 30-33]

Danish researchers have concluded that fish oil supplementation may help prevent arrhythmias and sudden cardiac death in healthy men. An Italian study of 11,000 heart attack survivors found that patients supplementing with fish oils markedly reduced their risk of another heart attack, a stroke or death. A group of German researchers found that fish oil supplementation for 2 years caused regression of atherosclerotic deposits and American medical researchers report that men who consume fish once or more every week have a 50% lower risk of dying from a sudden cardiac event than do men who eat fish less than once a month. [34-40]

Greek researchers report that fish oil supplementation (10 grams/day) reduces the number of attacks by 41% in men suffering from angina. Norwegian medical doctors have found that fish oil supplementation reduces the severity of a heart attack and Indian researchers report that supplementation started immediately after a heart attack reduces future complications. Bypass surgery and angioplasty patients reportedly also benefit from fish oils and clinical trials have shown that fish oils are safe for heart disease patients. The evidence is indeed overwhelming. An adequate daily intake (about 1 gram) of EPA and DHA is essential to maintain a healthy heart. Fish oils are especially important for diabetics who have an increased risk of heart disease. [41- 49]

Researchers at the University of Cincinnati have found that supplementing with as little as 2 grams/day of fish oil (410 mg of EPA plus 285 mg of DHA) can lower diastolic pressure by 4.4 mm Hg and systolic pressure by 6.5 mm Hg in people with elevated blood pressure. Enough to avoid taking drugs in cases of borderline hypertension. Several other clinical trials have confirmed that fish oils are indeed effective in lowering high blood pressure and that they may work even better if combined with a program of salt restriction. [50-55]

#### **Reduces pain and helps prevent cancer**

Fish oils are particularly effective in reducing inflammation and can be of great benefit to people suffering from rheumatoid arthritis or ulcerative colitis. Daily supplementation with as little as 2.7 grams of EPA and 1.8 grams of DHA can markedly reduce the number of tender joints and increase the time before fatigue sets in. Some studies have also noted a decrease in morning stiffness and at least two clinical trials concluded that arthritis patients who took fish oils could eliminate or sharply reduce their use of NSAIDs and other arthritis drugs. [56-61]

Patients with ulcerative colitis have abnormally low blood levels of EPA. Clinical trials have shown that supplementation with fish oil (2.7 grams of EPA and 1.8 grams of DHA daily) can reduce the severity of the condition by more than 50% and enable many patients to discontinue anti-inflammatory medication and steroids. [62-64]

There is now also considerable evidence that fish oil consumption can delay or reduce tumor development in breast cancer. Studies have also shown that a high blood level of omega-3 fatty acids combined with a low level of omega-6 acids reduces the risk of developing breast cancer. Daily supplementation with as little as 2.5 grams of fish oils has been found effective in preventing the progression from benign polyps to colon cancer and Korean researchers recently reported that prostate cancer patients have low blood levels of omega-3 fatty acids. Greek researchers report that fish oil supplementation improves survival and quality of life in terminally ill cancer patients. [65-73]

### **Safe and easily available**

It is estimated that 85% or more of people in the Western world are deficient in omega-3 fatty acids and most get far too much of the omega-6 fatty acids. Vegetarian diets, for example, tend to be very high in omega-6.

The recommended daily intake of EPA plus DHA is about 650 mg rising to 1000 mg/day during pregnancy and lactation. Clinical trials have used anywhere from 1 g/day to 10 g/day, but little additional benefit has been observed at levels above 5 g/day of EPA and DHA combined. The benefits of therapeutic supplementation may become evident in a few weeks when blood parameters (triglycerides, fibrinogen) are involved, but may take 3 months or longer to materialize in degenerative diseases like atherosclerosis and rheumatoid arthritis. [74, 75]

The processing and packaging of the fish oil are crucial in determining its quality. Low quality oils may be quite unstable and contain significant amounts of mercury, pesticides, and undesirable oxidation products. High quality oils are stabilized with adequate amounts of vitamin E and are packaged in individual foil pouches or other packaging impervious to light and oxygen. Some very recent research carried out at the University of Minnesota found that emulsified fish oils are much better absorbed than the straight oils in gelatin capsules. [76]

Cod liver oils and fish oils are not the same. Cod liver oil is extracted from cod **liver** and is an excellent source of vitamins A and D. Fish oils are extracted from the **tissues** (flesh) of fatty fish like salmon and herring and are good sources of EPA and DHA. Fish oils contain very little vitamin A and D, but cod liver oil does contain EPA and DHA. However, you would probably exceed the recommended daily intake of vitamins A and D if you were to try to obtain therapeutic amounts of EPA and DHA from cod liver oil.

Supplementing with fish oils has been found to be entirely safe even for periods as long as 7 years and no significant adverse effects have been reported in hundreds of clinical trials using as much as 18 grams/day of fish oils. Fish oil supplementation does, however, lower blood concentrations of vitamin E so it is a good idea to take extra vitamin E when adding fish oils to your diet. A clinical trial carried out by the US Department of Agriculture found that taking 200 mg/day of synthetic vitamin E (equivalent to about 100 IU of natural alpha-tocopherol) is sufficient to completely counteract this effect of fish oil supplementation. [74, 75, 77, 78]

## **REFERENCES**

1. Simopoulos, Artemis. Omega-3 fatty acids in health and disease and in growth and development. *American Journal of Clinical Nutrition*, Vol. 54, 1991, pp. 438-63
2. Pepping, Joseph. Omega-3 essential fatty acids. *American Journal of Health-System Pharmacy*, Vol. 56, April 15, 1999, pp. 719-24
3. Uauy-Dagach, Ricardo and Valenzuela, Alfonso. Marine oils: the health benefits of n-3 fatty acids. *Nutrition Reviews*, Vol. 54, November 1996, pp. S102-S108
4. Connor, William E. Importance of n-3 fatty acids in health and disease. *American Journal of Clinical Nutrition*, Vol. 71 (suppl), January 2000, pp. 171S-75S
5. DiGiacomo, Ralph A. , et al. Fish-oil Dietary Supplementation in Patients with Raynaud's Phenomenon: A Double-Blind, Controlled, Prospective Study. *The American Journal of Medicine*, Vol. 86, February 1989, pp. 158-164
6. Levine, Barbara S. Most frequently asked questions about DHA. *Nutrition Today*, Vol. 32, November/December 1997, pp. 248-49
7. Kalmijn, S., et al. Polyunsaturated fatty acids, antioxidants, and cognitive function in very old men. *American Journal of Epidemiology*, Vol. 145, January 1, 1997, pp. 33-41
8. Kalmijn, S., et al. Dietary fat intake and the risk of incident dementia in the Rotterdam Study. *Annals of Neurology*, Vol. 42(5), November 1997, pp. 776-82
9. Yehuda, S., et al. Essential fatty acids preparation (SR-3) improves Alzheimer's patients quality of life.

- International Journal of Neuroscience, Vol. 87(3-4), November 1996, pp. 141-9
10. Edwards, R., et al. Omega-3 polyunsaturated fatty acid levels in the diet and in red blood cell membranes of depressed patients. *Journal of Affective Disorders*, Vol. 48, March 1998, pp. 149-55
  11. Hibbeln, Joseph R. Fish consumption and major depression. *The Lancet*, Vol. 351, April 18, 1998, p. 1213 (correspondence)
  12. Hibbeln, Joseph R. and Salem, Norman. Dietary polyunsaturated fatty acids and depression: when cholesterol does not satisfy. *American Journal of Clinical Nutrition*, Vol. 62, July 1995, pp. 1-9
  13. Stoll, Andrew L., et al. Omega 3 fatty acids in bipolar disorder. *Archives of General Psychiatry*, Vol. 56, May 1999, pp. 407-12 and pp. 415-16 (commentary)
  14. Calabrese, Joseph R., et al. Fish oils and bipolar disorder. *Archives of General Psychiatry*, Vol. 56, May 1999, pp. 413-14 (commentary)
  15. Laugharne, J.D.E., et al. Fatty acids and schizophrenia. *Lipids*, Vol. 31 (suppl), 1996, pp. S163-S65
  16. Jensen, Craig L., et al. Effect of docosahexaenoic acid supplementation of lactating women on the fatty acid composition of breast milk lipids and maternal and infant plasma phospholipids. *American Journal of Clinical Nutrition*, Vol. 71 (suppl), January 2000, pp. 292S-99S
  17. Makrides, Maria and Gibson, Robert A. Long-chain polyunsaturated fatty acid requirements during pregnancy and lactation. *American Journal of Clinical Nutrition*, Vol. 71 (suppl), 2000, pp. 307S-11S
  18. Connor, William E., et al. Increased docosahexaenoic acid levels in human newborn infants by administration of sardines and fish oil during pregnancy. *Lipids*, Vol. 31 (suppl), 1996, pp. S183-S87
  19. Cunnane, S.C., et al. Breast-fed infants achieve a higher rate of brain and whole body docosahexaenoate accumulation than formula-fed infants not consuming dietary docosahexaenoate. *Lipids*, Vol. 35, January 2000, pp. 105-11
  20. Carlson, S.E., et al. Long-chain polyunsaturated fatty acids and development of human infants. *Acta Paediatr Suppl*, Vol. 88 (430), August 1999, pp. 72-7
  21. Mitchell, E.A., et al. Clinical characteristics and serum essential fatty acid levels in hyperactive children. *Clin Pediatr (Phila)*, Vol. 26, August 1987, pp. 406-11
  22. Stevens, Laura J., et al. Essential fatty acid metabolism in boys with attention-deficit hyperactivity disorder. *American Journal of Clinical Nutrition*, Vol. 62, No. 4, October 1995, pp. 761-68
  23. Hodge, Linda, et al. Consumption of oily fish and childhood asthma risk. *Medical Journal of Australia*, Vol. 164, February 5, 1996, pp. 137-40
  24. Broughton, K. Shane, et al. Reduced asthma symptoms with n-3 fatty acid ingestion are related to 5-series leukotriene production. *American Journal of Clinical Nutrition*, Vol. 65, April 1997, pp. 1011-17
  25. Dry, J. and Vincent, D. Effect of a fish oil diet on asthma: results of a 1-year double-blind study. *International Archives of Allergy and Applied Immunology*, Vol. 95, No. 2/3, 1991, pp. 156-7
  26. Shahar, Eyal, et al. Dietary n-3 polyunsaturated fatty acids and smoking-related chronic obstructive pulmonary disease. *The New England Journal of Medicine*, Vol. 331, No. 4, July 28, 1994, pp. 228-33
  27. Lawrence, R. and Sorrell, T. Eicosapentaenoic acid in cystic fibrosis: evidence of a pathogenetic role for leukotriene B4. *The Lancet*, Vol. 342, August 21, 1993, pp. 465-69
  28. Katz, D.P., et al. The use of an intravenous fish oil emulsion enriched with omega-3 fatty acids in patients with cystic fibrosis. *Nutrition*, Vol. 12, May 1996, pp. 334-39
  29. Schwartz, Joel. Role of polyunsaturated fatty acids in lung disease. *American Journal of Clinical Nutrition*, Vol. 71 (suppl), January 2000, pp. 393S-96S
  30. Daviglius, Martha L., et al. Fish consumption and the 30-year risk of fatal myocardial infarction. *New England Journal of Medicine*, Vol. 336, April 10, 1997, pp. 1046-53
  31. Christensen, Jeppe Hagstrup, et al. Effect of fish oil on heart rate variability in survivors of myocardial infarction. *British Medical Journal*, Vol. 312, March 16, 1996, pp. 677-78
  32. Simon, Joel A., et al. Serum fatty acids and the risk of coronary heart disease. *American Journal of Epidemiology*, Vol. 142, No. 5, September 1, 1995, pp. 469-76
  33. Flaten, Hugo, et al. Fish-oil concentrate: effects of variables related to cardiovascular disease. *American Journal of Clinical Nutrition*, Vol. 52, 1990, pp. 300-06
  34. Christensen, Jeppe Hagstrup, et al. Heart rate variability and fatty acid content of blood cell membranes: a dose-response study with n-3 fatty acids. *American Journal of Clinical Nutrition*, Vol. 70, September 1999, pp. 331-37
  35. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. *The Lancet*, Vol. 354, August 7, 1999, pp. 447-55
  36. Brown, Morris. Do vitamin E and fish oil protect against ischaemic heart disease? *The Lancet*, Vol. 354, August 7, 1999, pp. 441-42 (commentary)
  37. von Schacky, Clemens, et al. The effect of dietary omega-3 fatty acids on coronary atherosclerosis. *Annals of Internal Medicine*, Vol. 130, April 6, 1999, pp. 554-62
  38. Albert, Christine M., et al. Fish consumption and risk of sudden cardiac death. *Journal of the American Medical Association*, Vol. 279, January 7, 1998, pp. 23-28
  39. Kromhout, Daan. Fish consumption and sudden cardiac death. *Journal of the American Medical Association*, Vol. 279, January 7, 1998, pp. 65-66 (editorial)
  40. Siscovick, David S., et al. Dietary intake and cell membrane levels of long-chain n-3 polyunsaturated fatty acids and the risk of primary cardiac arrest. *Journal of the American Medical Association*, Vol. 274, No. 17, November 1, 1995, pp. 1363-67
  41. Salachas, A., et al. Effects of low-dose fish oil concentrate on angina, exercise tolerance time, serum triglycerides, and platelet function. *Angiology*, Vol. 45, December 1994, pp. 1023-31
  42. Landmark, K., et al. Use of fish oils appears to reduce infarct size as estimated from peak creatine kinase and lactate dehydrogenase activities. *Cardiology*, Vol. 89 (2), 1998, pp. 94- 102
  43. Singh, R.B., et al. Randomized, double-blind, placebo-controlled trial of fish oil and mustard oil in patients with suspected acute myocardial infarction. *Cardiovasc Drugs Ther*, Vol. 11, July 1997, pp. 485-91
  44. Eritsland, J., et al. Long-term effects of n-3 polyunsaturated fatty acids on haemostatic variables and

- bleeding episodes in patients with coronary artery disease. *Blood Coagul Fibrinolysis*, Vol. 6, February 1995, pp. 17-22
45. von Schacky, Clemens. n-3 fatty acids and the prevention of coronary atherosclerosis. *American Journal of Clinical Nutrition*, Vol. 71 (suppl), January 2000, pp. S224-27S
  46. Connor, William E. Diabetes, fish oil, and vascular disease. *Annals of Internal Medicine*, Vol. 123, No. 12, December 15, 1995, pp. 950-52
  47. McManus, Ruth M., et al. A comparison of the effects of n-3 fatty acids from linseed oil and fish oil in well-controlled type II diabetes. *Diabetes Care*, Vol. 19, May 1996, pp. 463-67
  48. Luo, Jing, et al. Moderate intake of n-3 fatty acids for 2 months has no detrimental effect on glucose metabolism and could ameliorate the lipid profile in type 2 diabetic men. *Diabetes Care*, Vol. 21, May 1998, pp. 717-24
  49. Rivellese, Angela A., et al. Long-term effects of fish oil on insulin resistance and plasma lipoproteins in NIDDM patients with hypertriglyceridemia. *Diabetes Care*, Vol. 19, November 1996, pp. 1207-13
  50. Appel, Lawrence J., et al. Does supplementation of diet with "fish oil" reduce blood pressure? *Archives of Internal Medicine*, Vol. 153, June 28, 1993, pp. 1429-38
  51. Radack, Kenneth, et al. The effects of low doses of n-3 fatty acid supplementation on blood pressure in hypertensive subjects. *Archives of Internal Medicine*, Vol. 151, June 1991, pp. 1173-80
  52. Morris, Martha Clare, et al. Does fish oil lower blood pressure? A meta-analysis of controlled trials. *Circulation*, Vol. 88, No. 2, August 1993, pp. 523-33
  53. Andreassen, A.K., et al. Hypertension prophylaxis with omega-3 fatty acids in heart transplant recipients. *J Am Coll Cardiol*, Vol. 29, May 1997, pp. 1324-31
  54. Cobiac, L., et al. Effects of dietary sodium restriction and fish oil supplements on blood pressure in the elderly. *Clin Exp Pharmacol Physiol*, Vol. 18, May 1991, pp. 265-68
  55. Toft, Ingrid, et al. Effects of n-3 polyunsaturated fatty acids on glucose homeostasis and blood pressure in essential hypertension. *Annals of Internal Medicine*, Vol. 123, No. 12, December 15, 1995, pp. 911-18
  56. Kremer, Joel M., et al. Fish-oil fatty acid supplementation in active rheumatoid arthritis: A double-blinded, controlled, crossover study. *Annals of Internal Medicine*, Vol. 106, April 1987, pp. 497-503
  57. Kremer, Joel M. n-3 fatty acid supplements in rheumatoid arthritis. *American Journal of Clinical Nutrition*, Vol. 71 (suppl), January 2000, pp. 349S-51S
  58. Fortin, Paul R., et al. Validation of a meta-analysis: the effects of fish oil in rheumatoid arthritis. *Journal of Clinical Epidemiology*, Vol. 48, 1995, pp. 1379-90
  59. Kremer, J.M., et al. Effects of high-dose fish oil on rheumatoid arthritis after stopping nonsteroidal anti-inflammatory drugs - clinical and immune correlates. *Arthritis and Rheumatology*, Vol. 38, August 1995, pp. 1107-14
  60. Geusens, P., et al. Long-term effect of omega-3 fatty acid supplementation in active rheumatoid arthritis: a 12-month, double-blind, controlled study. *Arthritis and Rheumatology*, Vol. 37, June 1994, pp. 824-29
  61. Navarro, Elisabet, et al. Abnormal fatty acid pattern in rheumatoid arthritis - A rationale for treatment with marine and botanical lipids. *Journal of Rheumatology*, Vol. 27, February 2000, pp. 298-303
  62. Aslan, Alex and Triadafilopoulos, George. Fish oil fatty acid supplementation in active ulcerative colitis: A double-blind, placebo-controlled, crossover study. *American Journal of Gastroenterology*, Vol. 87, April 1992, pp. 432-37
  63. Salomon, P., et al. Treatment of ulcerative colitis with fish oil n-3 omega fatty acid: an open trial. *Journal of Clinical Gastroenterology*, Vol. 12, April 1990, pp. 157-61
  64. Siguel, E.N. and Lerman, R.H. Prevalence of essential fatty acid deficiency in patients with chronic gastrointestinal disorders. *Metabolism*, Vol. 45, January 1996, pp. 12-23
  65. Simonsen, Neal, et al. Adipose tissue omega-3 and omega-6 fatty acid content and breast cancer in the EURAMIC Study. *American Journal of Epidemiology*, Vol. 147, No. 4, 1998, pp. 342-52
  66. Cave, W.T. Jr. Dietary omega-3 polyunsaturated fats and breast cancer. *Nutrition*, Vol. 12 (suppl), January 1996, pp. S39-42
  67. Fernandez-Banares, F., et al. Changes of the mucosal n3 and n6 fatty acid status occur early in the colorectal adenoma-carcinoma sequence. *Gut*, Vol. 38, 1996, pp. 254-59
  68. Anti, M., et al. Effects of different doses of fish oil on rectal cell proliferation in patients with sporadic colonic adenomas. *Gastroenterology*, Vol. 107, December 1994, pp. 1709-18
  69. Yang, Y.J., et al. Comparison of fatty acid profiles in the serum of patients with prostate cancer and benign prostatic hyperplasia. *Clinical Biochemistry*, Vol. 32, August 1999, pp. 405-09
  70. Norrish, A.E., et al. Prostate cancer risk and consumption of fish oils: a dietary biomarker- based case-control study. *British Journal of Cancer*, Vol. 81, No. 7, December 1999, pp. 1238-42
  71. Gogos, Charalambos A., et al. Dietary omega-3 polyunsaturated fatty acids plus vitamin E restore immunodeficiency and prolong survival for severely ill patients with generalized malignancy. *Cancer*, Vol. 82, January 15, 1998, pp. 395-402
  72. Wigmore, S.J., et al. The effect of polyunsaturated fatty acids on the progress of cachexia in patients with pancreatic cancer. *Nutrition*, Vol. 12 (suppl), January 1996, pp. S27-30
  73. Barber, M.D., et al. The effect of an oral nutritional supplement enriched with fish oil on weight-loss in patients with pancreatic cancer. *British Journal of Cancer*, Vol. 81, No. 1, September 1999, pp. 80-86
  74. Saynor, R. and Gillott, T. Changes in blood lipids and fibrinogen with a note on safety in a long term study on the effects of n-3 fatty acids in subjects receiving fish oil supplements and followed for seven years. *Lipids*, Vol. 27, July 1992, pp. 533-38
  75. Eritsland, Jan. Safety considerations of polyunsaturated fatty acids. *American Journal of Clinical Nutrition*, Vol. 71 (suppl), January 2000, pp. 197S-201S
  76. Bibus, Douglas M., et al. Bioavailability Studies of Emulsified Flavored Fish Oil. The University of Minnesota, Austin, MN. January 21, 2000
  77. Nair, Padmanabhan P., et al. Dietary fish oil-induced changes in the distribution of alpha-tocopherol, retinol, and beta-carotene in plasma, red blood cells, and platelets: modulation by vitamin E. *American*

- Journal of Clinical Nutrition, Vol. 58, July 1993, pp. 98-102
78. Sanders, T.A.B. and Hinds, Allison. The influence of a fish oil high in docosahexaenoic acid on plasma lipoprotein and vitamin E concentrations and haemostatic function in healthy male volunteers. British Journal of Nutrition, Vol 68, July 1992, pp. 163-73