

Fish Oils and Vitamin E

Summaries of the latest research concerning fish oils and vitamin E

Fish oils in cancer prevention

STOCKHOLM, SWEDEN. Several test tube (*in vitro*) and animal experiments have clearly shown that the long-chain omega-3 polyunsaturated fatty acids (PUFAs) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the main components of fish oil, help inhibit the promotion and progression of cancer. Their beneficial effect is particularly pronounced in hormone-dependent cancers such as breast and prostate cancer. Some, but not all, epidemiologic studies have also found a beneficial effect. Researchers at Sweden's famous Karolinska Institutet have just published a comprehensive review of the current knowledge regarding the role of PUFAs in carcinogenesis. They conclude that omega-3 PUFAs are protective against cancer progression, while omega-6 PUFAs, notably arachidonic acid and its derivatives, help promote the growth of cancer. They believe the n-3 PUFAs exert their beneficial effects in several different ways: * They suppress the synthesis of pro-inflammatory eicosanoids from arachidonic acid and thus produce an overall anti-inflammatory effect. * They positively affect gene expression or the activities of signal transduction molecules involved in the control of cell growth, differentiation apoptosis, angiogenesis and metastasis. * They suppress excessive production of nitrogen oxide (NO) during chronic inflammation and thereby help prevent DNA damage and impaired DNA repair. * They decrease estrogen production and thus reduce the estrogen-stimulated growth of hormone-dependent cancer cells. * Fish oils improve insulin sensitivity and cell membrane fluidity and may help prevent metastasis through these effects. Free radicals and reactive oxygen species produced in cells may attack PUFAs resulting in the formation of more free radicals, specifically hydroperoxides. The hydroperoxides, in turn, may damage DNA ultimately leading to cancer. These effects have indeed been observed in some *in vitro* experiments, but not in actual human beings. Many studies have shown that fish oils actually retard aging and suppress so-called free radical diseases such as atherosclerosis and cancer. Other studies have shown that a daily EPA + DHA intake in excess of 2.3 grams decreases the production of superoxide, a potent cancer promoter. At least one *in vitro* and one animal experiment have observed that EPA + DHA kill human breast cancer cells via the formation of hydroperoxides, but that this effect is strongly inhibited by vitamin E. Thus, at this point, it is not entirely clear whether EPA + DHA exert part of their beneficial effect through an increase or a decrease in the production of free radicals and reactive oxygen species. The researchers recommend more work in this area, but emphasize that the major benefits of fish oils probably are associated with their ability to inhibit the synthesis of arachidonic acid-derived, pro-inflammatory eicosanoids. The Swedish researchers also confirm that fatty, cold-water fish are the best sources of EPA and DHA and that the conversion rate of alpha-linolenic acid (flaxseed oil) to EPA is very low, even in healthy humans - probably in the order of 2-5%. / Larsson, SC, et al. Dietary long-chain n-3 fatty acids for the prevention of cancer: a review of potential mechanisms. *American Journal of Clinical Nutrition*, Vol. 79, June 2004, pp. 935-45/ *Editor's comment:* There would appear to be a growing body of evidence to the effect that long-chain omega-3 fatty acids, in particular EPA and DHA, help prevent the promotion and progression of certain cancers, notably hormone-dependent ones. Some of the mechanisms involved in this protective effect are well understood. While others, notably the role of free-radical formation, clearly need more work. Of some concern is the uncertainty surrounding vitamin E. Both vitamin E and fish oils have been found to help prevent hormone-dependent cancers, so taking both for cancer prevention is probably desirable. The situation is much less clear when it comes to slowing down an existing cancer and preventing it from spreading. Should one just rely on vitamin E (particularly the succinate form) or place one's faith in fish oils, or is the combination of the two the best way to go? Clearly more research in this area is urgently required.

Fish oils do not promote harmful peroxidation

CORVALLIS, OREGON. There is ample evidence that fish consumption and fish oil supplementation help protect against heart disease. However, the main components of fish oils, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are highly unsaturated and would therefore be prone to oxidation. This has prompted some researchers to express concern that fish oils might contribute to the lipid peroxidation involved in the development of atherosclerosis. Researchers at the Oregon State University have just released two major studies designed to further explore this concern. The first study involved 15 postmenopausal women who were randomized to supplement with 15 grams/day of sunflower oil, 15 grams/day of safflower oil or 15 grams/day of fish oil (providing 2.0 grams of EPA and 1.4 grams of DHA per day) in a 3-treatment crossover trial. The researchers conclude that there is no evidence that fish oil supplementation increases lipid peroxidation when assessed by measuring the levels of blood plasma malondialdehyde (MDA) and F2-isoprostanes. However, a slight increase in thiobarbituric acid reactive substances (TBARS) was noted in the fish oil supplemented group. The researchers believe this to be insignificant and point out that the TBARS test is somewhat unreliable. The second study involved 46 postmenopausal women who were randomly assigned to receive a daily fish oil supplement (providing 2.5 grams of EPA and 1.8 grams of DHA) combined with 0, 100, 200 or 400 mg of synthetic vitamin E (RRR-alpha-tocopherol acetate). Each of the 5-week treatment periods was followed by a 4-week washout interval in a 4-treatment, 4-period crossover design. The researchers noted substantial increases in blood plasma levels of EPA (from 0.110 to 0.734 mmol/L) and DHA (from 0.283 to 0.515 mmol/L). They also observed an average drop in triglyceride concentrations of almost 30%. Vitamin E (alpha-tocopherol) levels rose by about 50% after supplementation with 100 mg/day (50 IU) of alpha-tocopherol-acetate and by about 69% after supplementation with 400 mg/day (200 IU). The increase in alpha-tocopherol level was accompanied by a significant decrease in gamma-tocopherol level. The researchers evaluated the effect of supplementation on lipid oxidation (TBARS) and protein oxidation (carbonyl groups). They did not observe any increased protein oxidation, but did find a small but statistically significant increase in TBARS concentration after fish oil supplementation; they dismiss this finding as being likely to be clinically irrelevant. The size of the increase did not change with increased vitamin E intake. The researchers conclude, "If fish oil consumption does not cause an increase in oxidation as measured by protein carbonyls, then an increased intake of vitamin E [during fish oil supplementation] is not necessary." / Higdon, Jane V., et al. Supplementation of postmenopausal women with fish oil rich in eicosapentaenoic acid and docosahexaenoic acid is not associated with greater in vivo lipid peroxidation compared with oils rich in oleate and linoleate as assessed by plasma malondialdehyde and F2-isoprostanes. *American Journal of Clinical Nutrition*, Vol. 72, September 2000, pp. 714-22 Wander, Rosemary C. and Du, Shi-Hua. Oxidation of plasma proteins is not increased after supplementation with eicosapentaenoic and docosahexaenoic acids. *American Journal of Clinical Nutrition*, Vol. 72, September 2000, pp. 731-37/

Polyunsaturated fatty acids are safe

OSLO, NORWAY. Polyunsaturated fatty acids (PUFAs) of the n-6 and n-3 configurations cannot be synthesized by humans and must be obtained from the diet. The most common PUFAs are linoleic acid, linolenic acid, and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) found in fish oils. Linoleic acid is an n-6 configuration while linolenic acid, EPA and DHA are of the n-3 configuration. Because of the unsaturated nature (multiple double bonds) of PUFAs they are prone to oxidation which makes them rancid and potential initiators of chain reactions which can lead to oxidation of fat and cholesterol molecules in the body. This so-called lipid peroxidation reaction is believed to be implicated in atherosclerosis, cancer and inflammation. Dr. Jan Eritsland, a cardiologist at the Ullevål University Hospital, has just released a major study dealing with the safety of n-3 and n-6 PUFAs. Based on numerous reports published in the medical literature Dr. Eritsland concludes that a high intake of n-3 PUFAs reduces the risk for

cardiovascular disease and heart attack and is entirely safe at least up to a level corresponding to 10% of the daily calorie intake. He does caution though that the intake of dietary antioxidants (especially vitamin E) needs to be increased if the PUFA intake is increased. Supplementation with 4 grams/day of highly concentrated fish oil (containing 3.4 g of EPA and DHA) was found to lower triglyceride levels, but had no effect on cholesterol levels or glycemic control (plasma glucose and insulin levels). Although fish oils are known to reduce the tendency of blood to aggregate (clot) a recent major trial showed no difference in bleeding episodes among heart disease patients supplementing with 2 to 5 grams/day of fish oils and the controls. This held true even if the patients were also taking warfarin or aspirin. PUFAs of the n-3 family may help prevent cancer and there is no evidence at all that they promote it. There is, however, some limited evidence that n-6 PUFAs (linoleic acid) may indeed be involved in the initiation or promotion of cancer. Most experts recommend that the intake of linoleic acid not exceed 10% of daily calorie intake. [73 references] *Eritsland, Jan. Safety considerations of polyunsaturated fatty acids. American Journal of Clinical Nutrition, Vol. 71 (suppl), January 2000, pp. 197S-201S/*

Fish oils protect against death from heart disease

SANTA MARIA IMBARO, ITALY. There is clear evidence that a diet rich in oily fish confers considerable protection against heart disease. What is less clear is whether concentrated fish tissue oils in capsule form confer similar benefits. A very large group of Italian researchers (Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico) has just completed a major study which shows the benefits of fish oil supplementation in patients who have survived a first heart attack. Their study involved over 11,000 heart attack survivors who were randomly assigned to one of four groups. Group one received a one-gram gelatin capsule containing about 580 mg of eicosapentaenoic acid (EPA) and 290 mg of docosahexaenoic acid (DHA) as ethyl esters every day. Group two received 300 mg of synthetic vitamin E daily; group three both fish oil and vitamin E; and group four served as the control group. All participants ate a largely Mediterranean diet and continued to take their prescribed medications (beta-blockers, aspirin, and ACE-inhibitors). After 3.5 years of follow-up it was clear that the participants who had received fish oil or fish oil plus vitamin E had lowered their risk of dying or having another heart attack or a stroke by 10 to 15 per cent. The group who had taken vitamin E alone derived no statistically significant benefit from doing so. (Editor's note: The 300 mg of synthetic vitamin E used in the study corresponds to about 150 IU of natural vitamin E. This would be much less effective than the 200-400 IU/day of *natural* vitamin E used in studies which have shown a benefit of vitamin E in regard to heart disease and stroke). The researchers conclude that daily supplementation with fish oils (equivalent of consuming 100 grams of fish per day) is beneficial for patients who have survived a first heart attack. They suggest that the role of vitamin E needs further exploration. (Editor's note: Other studies have shown that vitamin E protects fish oils from going rancid so it is a good idea to take a combination of the two). NOTE: This study was funded in part by Bristol-Myers Squibb, Pharmacia-Upjohn, Societa Prodotti Antibiotici, and Pfizer. *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 Brown, Morris. Do vitamin E and fish oil protect against ischaemic heart disease? The Lancet, Vol. 354, August 7, 1999, pp. 441-42 (commentary)/*

Fish oil and vitamin E go together

BELTSVILLE, MARYLAND. Fish oils are beneficial in the prevention of cancer and cardiovascular disease. They do, however, oxidize very easily and therefore add to the oxidant stress on the body. An experiment was recently carried out by the U.S. Department of Agriculture to see if an increased intake of vitamin E could counteract this detrimental effect of fish oils. Forty men aged 32 to 44 were involved. The men consumed a controlled diet for a total of 28 weeks. For the first 10 weeks they received placebo oil capsules (15 g/day), for the next 10 weeks they received fish oil capsules (15 g/day), and for the last 8 weeks they received the fish oil plus 200 mg of vitamin

E (all-/rac-alpha/-tocopherol). The urinary excretion of peroxidation products (malondialdehyde) more than doubled when the fish oil capsules were introduced but then dropped by a factor of four when vitamin E was added. The vitamin E concentration in the red blood cells dropped very significantly when fish oil was ingested but more than recovered with the vitamin E supplement. It is concluded that the negative effects of fish oil consumption can be overcome by taking them together with vitamin E. *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/*

Fish oil supplements increase requirements for Vitamin E

LONDON, ENGLAND. A recent experiment carried out at King's College in London showed that daily intake of fish oil supplement reduces the plasma concentration of vitamin E to below normal range. Nine healthy male subjects were given a daily fish oil supplement containing 2.1 g docosahexaenoic acid (DHA) and 0.8 g eicosapentaenoic acid (EPA) for a six week period. The proportion of DHA and EPA in the blood increased during the trial while the concentration of very-low-density-lipoprotein-cholesterol and triacylglycerol decreased. Blood pressure fell slightly during treatment, but rose again once the fish oil supplementation was discontinued. Of particular interest was the finding that alpha-tocopherol (vitamin E) concentration in the blood fell from 20 micromol/l to about 10 micromol/l during the experiment. This raises the question whether fish oil supplementation increases the need for antioxidant supplementation. / 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/* Coromega *OILOFPISCES.COM* *INTERNATIONAL HEALTH NEWS* Copyright © 2006 by Hans R. Larsen Oilofpisces.com does not provide medical advice. Do not attempt self- diagnosis or self-medication based on our reports.

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