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Means of Delivering Recommended Levels of Long Chain n-3 Polyunsaturated Fatty Acids in Human Diets

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ABSTRACT: n-3 Polyunsaturated fatty acids (n-3PUFA) of marine origin have been shown to be essential for brain development and cognitive function. In addition to their essentiality, the scientific literature is full of evidence to suggest that regular consumption and/or dietary supplementation with long chain n-3PUFA give several health benefits including: prevention of cardiovascular diseases, inflammatory diseases, dyslexia, and depression. Long chain n-3PUFA intake in the Western countries, including Australia, has been shown to be inadequate. This is largely due to the fact that the Western populations do not eat seafood on a regular basis because of its cost and availability, and many individuals do not like the flavor/taste/odor of seafood. Foods fortified with long chain n-3PUFA could play an important role in meeting the demands for optimal health. Marine n-3PUFA are not likely to compete with saturated, monounsaturated, and n-6PUFA as a major source of dietary fat; however, increasing the intake of foods containing marine n-3PUFA is an important strategy for the prevention of chronic illnesses. Recent developments in food technology allow fortification of foods, such as bread, dairy products, eggs, pasta, biscuits, margarines, and other spreads, without the undesirable fish odor/taste and with reasonable shelf life. There is a need to increase the amount of long chain n-3PUFA consumed per serve and optimize their bioavailability. This article reviews the foods fortified with marine n-3PUFA and their role in meeting daily requirements, and highlights the need for further research in this important area of functional foods.

Keywords: n-3 fatty acids, eicosapentaenoic acid, docosahexaenoic acid, fish oil, functional foods

Introduction

The human diet contains polyunsaturated fatty acids (PUFA) belonging to the n-6 and n-3 fatty acid families. Major dietary n-6PUFA include linoleic (18:2), γ-linolenic (18:3), and arachidonic (20:4) acids, whereas major dietary n-3PUFA include α-linolenic (18:3), eicosapentaenoic (20:5), docosapentaenoic (22:5), and docosahexaenoic (22:6) acids. Linoleic, γ-linolenic, and α-linolenic acids are present in large quantities in foods of plant origin, such as corn or maize oil, sunflower seed oil, cottonseed oil, soybean oil, linseed oil, evening primrose oil, and canola oil. Arachidonic acid originates from muscle and organ meats, or alternatively may be synthesized within the body via successive desaturation and chain elongation of linoleic acid. The longer chain n-3PUFA are found mainly in foods of marine origin or are synthesized via desaturation and chain elongation of α-linolenic acid within the human body. Recent evidence suggests that lean meat contributes significantly to the longer chain n-3PUFA content of the Western diet (Sinclair and others 1982; Meyer and others 2003; Li and others 2005). When present in equimolar concentration, linoleic acid and α-linolenic acid compete for conversion to their respective longer chain products, arachidonic acid and eicosapentaenoic acid (Contreras and Rapoport 2002). Recent studies have demonstrated that, for maximum conversion of α-linolenic acid to eicosapentaenoic acid and a maximum reduction in the formation of arachidonic acid, the α-linolenic acid should be supplemented with saturated fatty acids (SFA) rather than n-6PUFA (Garg and others 1989; MacDonald-Wicks and Garg 2004).

Saturated, monounsaturated, and n-6PUFA will continue to form a majority of the fatty acids present in the human diet. n-3PUFA, particularly the longer chain fatty acids of marine origin, constitute a small proportion of the total fat intake. For individuals or populations who consume no seafood or muscle or organ meats, such as vegetarians, α-linolenic acid is the only potential source of n-3PUFA. However, recent studies have demonstrated that the extent of conversion of α-linolenic acid to longer chain n-3PUFA is modest, and it is uncertain as to whether meaningful amounts of conversion occur to support normal growth and development. Emken and others (1994) found 15% conversion, whereas Pawlosky and others (2001) reported 0.2% conversion; both reported that the conversion to docosahexaenoic acid was much less than that to eicosapentaenoic acid and docosapentaenoic acid. However, the longer chain n-3PUFA that accumulates in tissue membranes is docosahexaenoic acid. Therefore, in some individuals, supplementation of the diet using fish oil capsules or foods fortified with fish oil fatty acids may be the only option to supply the recommended levels of longer chain n-3PUFA. As the dose of marine n-3PUFA required to achieve targeted health benefits is much higher than the recommended levels for maintenance of general health, it becomes even more challenging to meet the required amount of these fatty acids in order to minimize the risk of chronic disease.

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Dietary Intakes and Recommendations for Long Chain n-3PUFA

The dietary intake of total n-3PUFA has been estimated from a large dietary survey in the United Kingdom to be 2000 mg for men and 1410 mg for women (Gregory and others 1990), but these estimates do not distinguish between plant and marine n-3PUFA. In the United States, the dietary intake of total n-3PUFA has been reported to be 1600 mg/d, of which 100 to 200 mg/d is 20:5n-3 and 22:6n-3 (Kris-Etherton and others 2000). A recent study reported an average daily intake of 189 mg of marine n-3PUFA (20:5, 22:5, and 22:6 at 56, 26, and 106 mg/d, respectively) (Meyer and others 2003) in the diets of Australians. The major food sources contributing to n-3PUFA intakes include seafoods (71%), meats (20%), and eggs (6%). This study indicated that Australians are failing to meet the recommendations as outlined in the draft document of the new Australian Nutrient Reference Values (previously known as Recommended Dietary Intakes) in which adequate intake has been set at 190 mg/d. The paper also highlighted the need for strategies to increase the availability and consumption of foods enriched with long chain n-3PUFA. In contrast to these Western diets, Japanese eat about 80 g of fish and shellfish per day, providing approximately 1000 to 2000 mg/d of 20:5n-3 and 22:6n-3 (Sugano and Hirahara 2000). This high fish consumption is believed to contribute to the reduced incidence of coronary heart disease (CHD) in this population (Lands and others 1990).

A host of health agencies and professional organizations worldwide have issued recommendations on the intake of long chain n-3PUFA (Table 1). A number of recommendations to increase marine oil intake in people with or at risk of cardiovascular disease (CVD) have been made. These recommendations are based on evidence derived from sound clinical trials linking dietary deficiency of long chain n-3PUFA with cardiovascular events, and a recent meta-analysis of 13 cohort studies including more than 220,000 individuals followed for CHD mortality rates for an average of 12 y (He and others 2004). The British Nutrition Foundation Task Force recommends a daily intake of 500 to 1000 mg/d of long chain n-3PUFA, which is equivalent to 1 to 2 portions of oily fish per week (British Nutrition Foundation 1992). In contrast, the U.K. Department of Health recommends a daily intake of 200 mg of 20:5n-3 and 22:6n-3 (Department of Health 1994). Sweden recommends that the ratio of n-6PUFA to n-3PUFA be 5:1 (Nordic Working Group on Diet and Nutrition 1996). The World Health Organization recommends 1 to 2 servings of fish per week, each containing 200 to 500 mg of 20:5n-3 and 22:6n-3 (Kris-Etherton and others 2002). The American Heart Association (AHA) recommends that people with no CVD should eat oily fish twice/week and foods rich in α-linolenic acid (walnuts, canola, soy, and flaxseed). However, those with documented CVD should eat approximately 1 g of 20:5n-3 and 22:6n-3 per day, preferably from oily fish but also in supplement form. The AHA further recommends that, for triglyceride-lowering effects, 2 to 4 g of n-3PUFA should be consumed per day as a supplement under a physician's care (Kris-Etherton and others 2003). The International Society for the Study of Fatty Acids and Lipids (ISSFAL) recommends adequate 18:2n-6 intake as 2% energy, healthy 18:3n-3 intake as 0.7% energy, and, for cardiovascular health, a minimum of 500 mg of 20:5n-3 and 22:6n-3 per day (ISSFAL 2004). The expert panel supported by the National Institutes of Health recommends 300 mg of docosahexaenoic acid per day for pregnant or lactating females (Simopoulos and others 1999). The Joint FAO/WHO Expert Consultation on Fats and Oils in Human Nutrition made no specific recommendations for n-3PUFA, but recommended that individuals with linoleic-to-linolenic acid ratio in excess of 10:1 should be encouraged to consume foods rich in n-3PUFA, such as green leafy vegetables, legumes, fish, and other seafood (FAO/WHO Consultation on Fats and Oils 1994).

In summary, dietary recommendations for long chain n-3PUFA supplementation are still a matter of debate. Recommendations vary depending on desired disease prevention: daily ranges for 20:5n-3 and 22:6n-3 begin at 180 mg (for healthy adults) to 500 mg (decrease in heart disease) to 1000 mg (decrease in mental illness) (Ruxton and others 2004).

It is also recommended that the ratio of n-6PUFA to n-3PUFA should not exceed 4 to 1 in order to optimize the bioavailability, metabolism, and incorporation into membrane phospholipids (Garg and others 1988c, 1990; Volker and Garg 1996). There are three possible ways to achieve this: (1) simply increasing long chain n-3PUFA consumption in the diet; (2) keeping the SFA, monounsaturated fatty acids (MUFA), and long chain n-3PUFA content constant and decreasing n-6PUFA in the diet (however, taking a whole-diet approach and in the light of general dietary advice to decrease the proportion of SFA in the diet, to concomitantly decrease n-6PUFA will encourage a low-fat intake which has the potential to reduce the level of circulating high density lipoprotein (HDL) cholesterol (Katan 1998; Terpstra and others 2000)); (3) maintaining the level of long chain n-3PUFA, decreasing total n-6PUFA and making up the shortfall in dietary fat intake with MUFA and/or SFA (this will improve the n-6PUFA-to-n-3PUFA ratio without reducing the fat content in the diet and will therefore avoid the detrimental effects of a reduction in circulating HDL cholesterol level). Whether either of the last two options is suitable to optimize the n-6PUFA-to-n-3PUFA ratio without adverse effects on the plasma lipid profile remains to be established.

Health Benefits and Mechanisms of Action of n-3PUFA

Epidemiological and experimental evidence suggests that consumption of marine n-3PUFA is associated with a reduced risk of CVD, certain types of cancer, inflammatory disease (rheumatoid

Table 1—Recommended Daily Intake of Long Chain n-3 Polyunsaturated Fatty Acids

Organization	Recommended daily dose of 20:5n-3 plus 22:6n-3 (mg)	Population
National Health and Medical Research Council (Australian Nutrient Reference Values)	190	General population
British Nutrition Foundation Task Force	500–1000	People at risk of CVD
U.K. Department of Health	200	General population
European Academy of Nutritional Science	200	General population
ISSFAL	650	General population
AHA	1000	People at risk of CVD
	Oily fish (twice/week)	General population
	>3 g/d	To reduce triglyceride levels
NIH	300	Pregnant and lactating females

arthritis, asthma, lupus, and ulcerative colitis), diabetes mellitus, multiple sclerosis, and clinical depression (Ruxton 2004; Wang and others 2004). It is noteworthy that, if the population under study already has a high overall intake of fish, eating more fish is not associated with increased health benefits. These effects are mediated by alterations in circulating lipid levels, eicosanoids, cytokines, and physico-chemical properties of the cellular membranes. n-3PUFA are pleiotropic molecules with a broad variety of different biological actions, including hypotriglyceridemic, anti-aggregatory, anti-inflammatory, and anti-arrhythmic responses. Long chain n-3PUFA have been shown to reduce the size of the chylomicrons synthesized in the intestinal mucosa and released into the thoracic lymph following consumption of foods containing fats (Chan and others 2003). They have also been shown to reduce circulating levels of triglyceride and to reduce secretion of very low density lipoprotein (LDL) from the hepatic tissue (Parks and others 1990; Ikeda and others 2001). Dietary supplementation with long chain n-3PUFA has been shown to inhibit delta-6 desaturase activity, and reduce plasma and tissue levels of arachidonic acid (20:4n-6) (Garg and others 1988a, 1988b). Dietary 20:5n-3 and 22:6n-3 have also been shown to compete at the cyclo-oxygenase and lipo-oxygenase levels with 20:4n-6 to reduce the formation of series-2 eicosanoids (von Schacky and others 1985; Kurlandsky and others 1994; Nordoy and others 1994). Consumption of long chain n-3PUFA has also been associated with a reduction in plasma levels of pro-inflammatory cytokines (interleukins and tumor necrosis factor) (Endres and others 1994; Wallace and others 1995; Wachtler and others 1997; Seljeflot and others 1999). Dietary supplementation with fish oil high in long chain n-3PUFA is accompanied by a reduction in fibrinogen content and down regulation of the expression of adhesion molecules such as VCAM-I and ICAM-I (Gans and others 1988; Collie-Duguid and Wahle 1996; Hughes and others 1996; Vanschoonbeek and others 2004). Dietary long chain n-3PUFA are incorporated into the platelet phospholipids and concomitantly reduce platelet aggregation (Skeaff and Holub 1988; Chen and others 2000). Recent studies have demonstrated that dietary supplementation with long chain n-3PUFA improves vascular compliance and favorably modifies blood pressure (Cobiac and others 1992; Appel and others 1993; McVeigh and others 1994; Geleijnse and others 2002). Incorporation of long chain n-3PUFA into the membrane phospholipids can alter the physico-chemical properties of the membrane and influence membrane-associated functions, such as hormone binding, ion channels, enzyme activities, and so on. (Clandinin and others 1991).

The U.S. Food & Drug Administration has granted a qualified health claim for dietary n-3PUFA supplements: "Consumption of Omega-3 fatty acids may reduce the risk of CHD. FDA evaluated the data and determined that, although there is scientific evidence supporting the claim, the evidence is not conclusive" (US Food & Drug Administration 2004). The United Kingdom has become the first country outside the United States to grant an n-3 fish-oil health claim that manufacturers throughout Europe have begun applying to their products. The claim, issued by the Joint Health Claims Initiative, made up of consumer protection groups, food law enforcers, and members of the food industry, states: "Eating 3 g weekly, or 0.45 g daily, long chain n-3PUFA, as part of a healthy lifestyle, helps maintain heart health." (Joint Health Claims Initiative 2005).

Given that most Western populations fall well short of recommended oily fish servings per week, food formulators are working hard to develop other ways of increasing fish oil intake, and a wide range of products including eggs, breads, crackers, milks, cheeses, and juices are expected to carry the claim in the near future. Apart from well-informed health seekers, the majority of the consumers in Australia and New Zealand display poor understanding of omega-3 fatty acid types and sources (Patch and others 2005a, 2005b). Moreover, for a vast majority of consumers, improved heart health remains the health benefit most readily linked with n-3PUFA intake/supplementation.

Safety concerns relating almost exclusively to the administration of large doses of LCn-3PUFA have been expressed by some experts. Subjects reported a higher incidence of belching and unpleasant taste (Belluzzi and others 1994) when taking fish oil capsules as supplements, but not experienced by those who increased their n-3PUFA intake purely by dietary means. Since LCn-3PUFA are known to exert a dose-related increase in bleeding time, concerns have been raised about the possibility of increase in blood loss during labor or during surgical operations. However, there are no documented cases of abnormal bleeding even when high dosages of LCn-3PUFA were supplemented along with anticoagulant medications. High doses of LCn-3PUFA have the potential to increase LDL cholesterol levels and/or increase oxidizability of LDLs; however, clear evidence and clinical relevance of these findings remain unclear. People who bruise easily, have a bleeding disorder, or take blood thinning medications are advised to take LCn-3 supplements under the supervision of a healthcare provider.

Food Sources of n-3PUFA

Common plant sources of n-3PUFA (in the form of α-linolenic acid) include canola oil, soybean oil, walnuts, and flaxseed (linseed) oil. However, plant biologists are removing α-linolenic acid from these sources by genetic manipulation and/or by chemical hydrogenation to improve the shelf-life stability and cooking qualities (Robert and others 2005). Enriched eggs, produced by the addition of fish meal or canola/linseed oil to chicken feed, are also a good source of long chain n-3PUFA (Scheideler and others 1997; Smuts and others 2003; Bourre 2005a). However, concerns with cholesterol present in yolk prohibit frequent consumption of eggs. It is also possible to enrich poultry and pig meat with long chain n-3PUFA by supplementing the feed with fish meal or canola/linseed oil (Metcalf and others 2003; Bourre 2005b). Food sources of long chain n-3PUFA (20:5n-3 and 22:6n-3) include seafoods, fish oils such as cod liver oil, menhaden oil, and herring oil, lipid extracts from fungi, and algae of marine origin. With increased consumption of seafood and impure marine oils, concerns have been raised about the toxins, such as parachlorobenzoic acid, DDT, dioxin, and methyl mercury, that may be present in these foods (Mahaffey 2004; Melanson and others 2005).

Regardless of the source, all long chain n-3PUFA are highly susceptible to oxidation, which leads to unpleasant off-flavors and taste in the final product (Nawar 1996; Watkins and German 1998). The oxidative instability of long chain n-3PUFA is markedly higher than that of oleic acid (18:1n-7) and linoleic acid (18:2n-6). Exposure to high temperatures and air during processing and storage can cause rapid deterioration of these fatty acids. Another problem is the residual "fish" aroma and taste that often remain in the product even if n-3 oils are properly processed and stored. These problems can often be minimized by refining and deodorizing the oil, and packaging in an inert gas like nitrogen to prevent oxidation. Natural and synthetic antioxidants such as tocopherols and ascorbyl palmitate are commonly used to help prevent oil oxidation (Frankel and others 1994; Huang and others 1994; Chen and Ho 1997). However, the effectiveness of antioxidants depends on several factors, such as pH, temperature, polarity and concentration of antioxidants, and the physical properties of the food system. Consequently, great variations can be seen in different food systems.

Microencapsulation of oil can be used to delay or inhibit oxidation and allow the manufacturer to handle and incorporate oil in

Table 2—Examples of Some Commercially Available Microencapsulated n-3 Powder Products

Company/Product	Product description	Ingredients
BASF/Dry n-3 18:12	Microencapsulated fish oil rich in EPA and DHA, light yellow	Gelatin and sucrose matrix, coated in starch, sodium ascorbate (E310), ascorbic acid (E300), tocopherol (E306), tricalcium phosphate (E341)
BASF/Dry n-3 5:25C	Microencapsulated fish oil high in DHA, light yellow	Caseinate and sucrose matrix, coated in starch, ascorbyl palmitate (E304), sodium ascorbate
Nu-Mega/Driphorm Hi-DHA 50	Powder containing 48% Hi DHA tuna oil, bland taste	Tuna oil, sodium caseinate, dextrose monohydrate, dried glucose syrup, sodium ascorbate (E301), mixed natural tocopherols, lecithin, dl-alpha tocopherol (E307), ascorbyl palmitate (E304)
Salkat/Vana Sana EPA/DH, A Rich Powder, 50A 070	Powder, typical taste	Natural fish oil concentrate, carbohydrates, antioxidants, free flowing agent

food products (Kolanowski and others 1999; Klinkesorn and others 2005). The microencapsulation process can also help mask undesirable fishy odors and flavors in the final product. A number of companies, including BASF, Roche, Clover, and Ocean Nutrition, manufacture and sell microencapsulated fish oil powders for use in food products (Table 2). Moreover, several patents on microencapsulation technologies for the protection and encapsulation of fish oil exist. Most of these encapsulated n-3 oil products are based on the formation of fish oil emulsions using proteins, polysaccharides, lecithin, and other low molecular weight emulsifiers, individually and in various combinations. The emulsions are then spray-dried to form microcapsules. However, the amount of oil that can be delivered in these formats varies from 1% to 30%. During spray-drying, a significant proportion of the oil can migrate into the surface of the powder particle, which readily oxidizes and can cause off-flavors in food products. To improve the oxidative stability of the microencapsulated product, antioxidants can be added to either the oil or the powder, or both. Microemulsification has added advantages, such as long shelf life, masking of the taste and flavor of fish, and improved bioavailability of the n-3PUFA. However, particular attention needs to be paid to the material used for microencapsulation for maximum bioavailability. These technologies have allowed the fortification of frequently consumed foods, such as breads, biscuits, soups, fruit juices, and spreads with reasonable consumer acceptability. However, the levels of incorporation that can be achieved with existing technologies are very low and the amounts of long chain n-3PUFA required to meet recommended allowances are impractical in most cases. Further work in this area needs to concentrate on the development of convenience foods, suitable for fortifying with larger amounts of n-3PUFA per serve, in a palatable format.

Facts about Foods Fortified with Long Chain n-3PUFA

There is a constantly growing range of foods enriched in n-3PUFA available to the consumer (Table 3). One of the limitations of currently available foods fortified with long chain n-3PUFA is that they need to be consumed in large quantities to meet a dietary recommendation of 200 mg/d for healthy adults, or even in larger amounts to meet a dietary recommendation of 1000 mg/d of long chain n-3PUFA for people at high risk of CVD. Australian food examples include:

- Dairy Farmers (Farmers Best) milk provides at most 31.2 mg of 20:5n-3 and 22:6n-3 per 250 mL serving, which is no more than 15% of what is needed per day to benefit heart health, and less than 3% of the recommended dose for people at high risk of CVD.
- Brownes (Heart Plus) milk drink has been specially formulated to improve the performance of the heart and cardiovascular system as part of a balanced diet with regular physical activity. This product does better. One serve (250 mL) contains about 75% of our daily requirement of long chain n-3PUFA, but still needs to be consumed at a dose of over 1.5 L to meet a dietary recommendation of 1000 mg/d of long chain n-3PUFA for people at high risk of CVD.
- Coles (High Top) bread provides only 37 mg of 20:5n-3 and 22:6n-3 per serve (2 slices). Buttercup (Wonder White) DHA bread contains only 34 mg of 20:5n-3 and 22:6n-3 in 2 slices. Both breads contain per serve less than 15% of what is needed for good heart health and less than 3% of the recommended dose for people at high risk of CVD.
- AP Foods (Seachange) omega-3 spread contains 600 mg of long chain n-3PUFA per 100 g. Approximately 35 g/d of this spread must be consumed for a healthy heart and 175 g/d would need to be consumed to obtain sufficient long chain n-3PUFA to benefit those at high risk of CVD.
- Biomedical Laboratories (IQ3 Brainstorm) cereal bars in the United Kingdom are made using Nu-Mega's Driphorm powdered fish oils. The fruit-flavored bars, containing 150 mg of 20:5n-3/22:6n-3, are marketed as a way to improve children's performance at school. This appears to be a good way of supplying long chain n-3PUFA in the diets of children.

Conclusions

Clearly, there is a need to develop foods that can deliver the recommended level of long chain n-3PUFA in convenience foods consumed on a regular basis. n-3PUFA, particularly of marine origin, will continue to be a minority of all the fatty acid classes present in the human diet, even after making a recommendation of 2 to 3 servings of fish and seafood per week. It is not likely that we will

Table 3—Examples of Some Commercially Available Foods Fortified with n-3 Polyunsaturated Fatty Acids

Product	20:5n-3/22:6n-3	% of daily dose (general population)	% of daily dose (for those at high risk of CVD)	Country
Dairy Farmers (Farmers Best) milk	31.2 mg per 250 mL serve	15	3	Australia
Brownes (Heart Plus) milk	150 mg per 250 mL serve	75	15	Australia
Coles (High Top) bread	37 mg per serve of 2 slices	16	3.2	Australia
AP Foods (Seachange) omega-3 spread	200 mg per 35 g serve	100	20	Australia
Fish oil capsules (most brands)	300 mg per 1 g capsule	150	30	Australia
Cereal bars (Biomedical Laboratories)	150 mg per bar	75	15	United Kingdom

start eating fish on a daily basis just because the n-3PUFA are beneficial to health. If everyone in the world starts consuming even 2 to 3 servings of fish per week, the supply of fish will run out very quickly. Innovative methods of providing required amounts of long chain n-3PUFA are needed. Species of algae and fungi have been isolated and cultured for mass production of long chain n-3PUFA free of the toxins that are typically found in some fish. Efforts are being made to insert genes in plants and animals to enable endogenous synthesis of long chain n-3PUFA. Until such gene manipulations are successfully implemented and their safety established, it is imperative that the delivery and the bioavailability of n-3PUFA are optimized. There is some evidence to suggest that the bioavailability of long chain n-3PUFA can be improved by providing n-3PUFA in a food matrix that accelerates their entry into the mucosal cells. Some important points to optimizing the benefits from n-3PUFA supplements, such as fish oil capsules, include the following:

1. Keep n-6PUFA in the diet as low as possible.
2. Consume n-3PUFA supplements with a background diet rich in MUFA.
3. Consume supplements with the meal.
4. Ensure that sufficient preformed long chain n-3PUFA foods are consumed, rather than relying on foods containing the parent 18:3n-3.
5. Prefer microencapsulated fish oil capsules over normal capsules.

Research Needs

It is evident from the information presented in this article that there is a need to develop functional foods that can provide the recommended levels of long chain n-3PUFA, including for those who have already had a cardiovascular event and those at a high risk of developing CHD. It is noteworthy that although foods fortified with higher levels of long chain n-3PUFA need to be developed, the total fat content, particularly the level of SFA, must not exceed the dietary guidelines. The fortified food must be convenient, palatable, with no fishy odor/flavor and no fishy eructation following consumption. The food matrix should provide minimum or no resistance for release of long chain n-3PUFA in the gastrointestinal tract to ensure maximum bioavailability. Particular attention needs to be paid to the material used for microemulsification, as this may be an important criterion for the bioavailability of long chain n-3PUFA. Quantitative data on bioavailability of long chain n-3PUFA from the n-3PUFA enriched foods is lacking in the literature, although acute and chronic effects of consuming these foods on n-3PUFA incorporation have been extensively reported. Other factors, dietary or physiological, which might affect the bioavailability of long chain n-3PUFA also merit further investigation. Perhaps, long chain n-3PUFA can be combined with other nutrients in a single food to optimize their health benefits. One such ideal combination may be the synergistic effects of long chain n-3PUFA and plant sterols on plasma lipids. Plant sterols are known to reduce plasma and LDL cholesterol, while the triglyceride lowering properties of long chain n-3PUFA are well established. The combination of the two may be ideal to achieve overall lipid-lowering effects from a single food. Similarly, long chain n-3PUFA can be combined with other dietary ingredients, such as carotenoids, in order to maximize the anti-inflammatory effects for the prevention of rheumatoid arthritis, asthma, and inflammatory bowel disease. The development of functional foods enriched with larger amounts of long chain n-3PUFA and testing for bioavailability, biological and clinical effects require a concerted team effort, including food scientists/technologists, human/clinical nutritionists, and food producers. Some of these aspects of long chain n-3PUFA are under active investigation in our research laboratories.

References

Appel LJ, Miller ER III, Seidler AJ, Whelton PK. 1993. Does supplementation of diet with 'fish oil' reduce blood pressure? A meta-analysis of controlled clinical trials. Arch Intern Med 153:1429–38.

Belluzzi A, Brignola C, Campieri M, Camporesi EP, Gionchetti P, Rizzello F, Belloli C, De Simone G, Boschi S, Miglioli M, Barbara L. 1994. Effects of new fish oil derivative on fatty acid phospholipid-membrane pattern in a group of Crohn's disease patients. Dig Dis Sci 39:2589–94.

Bourre JM. 2005a. Where to find omega-3 fatty acids and how feeding animals with diet enriched in omega-3 fatty acids to increase nutritional value of derived products for human: what is actually useful? J Nutr Health Aging 9:232–42.

Bourre JM. 2005b. Effect of increasing the omega-3 fatty acid in the diets of animals on the animal products consumed by humans. Med Sci (Paris) 21:773–9.

British Nutrition Foundation. 1992. Task force on unsaturated fatty acids. London: Chapman and Hall.

Chan DC, Watts GF, Mori TA, Barrett PH, Redgrave TG, Beilin LJ. 2003. Randomized controlled trial of the effect of n-3 fatty acid supplementation on the metabolism of apolipoprotein B-100 and chylomicron remnants in men with visceral obesity. Am J Clin Nutr 77:300–307.

Chen JH, Ho CT. 1997. Antioxidant activities of caffeic acid and its related hydroxycinnamic acid compounds. J Agric Food Chem 45:2374–8.

Chen LY, Jokela R, Li DY, Bavry AA, Sandler H, Sjoquist M, Saldeen T, Mehta JL. 2000. Effect of stable fish oil on arterial thrombogenesis, platelet aggregation, and superoxide dismutase activity. J Cardiovasc Pharmacol 35:502–5.

Clandinin MT, Cheema S, Field CJ, Garg ML, Venketraman J, Clandinin TR. 1991. Dietary fat: the exogenous determination of membrane structure and cell function. FASEB J 5:2761–9.

Cobiac L, Nestel PJ, Wing LM, Howe PR. 1992. A low-sodium diet supplemented with fish oil lowers blood pressure in the elderly. J Hypertens 10:87–92.

Collie-Duguid ES, Wahle KW. 1996. Inhibitory effect of fish oil N-3 polyunsaturated fatty acids on the expression of endothelial cell adhesion molecules. Biochem Biophys Res Commun 220:969–74.

Contreras MA, Rapoport SI. 2002. Recent studies on interactions between n-3 and n-6 polyunsaturated fatty acids in brain and other tissues. Curr Opin Lipidol 13:267–72.

Department of Health. 1994. Report on health and social subjects, No. 46. Nutritional aspects of cardiovascular disease. Report of the Cardiovascular Review Group, COMA. London: Her Majesty's Stationery Office.

Emken EA, Adlof RO, Gulley RM. 1994. Dietary linoleic acid influences desaturation and elongation of deuterium labelled linoleic and linolenic acids in young adult males. Biochim Biophys Acta 1213:277–88.

Endres S, Sinha B, Eisenhut T. 1994. Omega-3 fatty acids in the regulation of cytokine synthesis. World Rev Nutr Diet 76:89–94.

FAO/WHO Consultation on Fats and Oils. 1994. Fats and oils in human nutrition: report of a joint consultation, FAO Food and Nutrition paper No. 57. Rome: Food and Agriculture.

Frankel EN, Huang SW, Kanner J, German JB. 1994. Interfacial phenomena in the evaluation of antioxidants: bulk oils vs emulsions. J Agric Food Chem 42:1054–9.

Gans RO, Bilo HJ, Schouten JA, Rauwerda JA. 1988. Fish oil and plasma fibrinogen. Br Med J 297:978–9.

Garg ML, Sebokova E, Thomson ABR, Clandinin MT. 1988a. Delta-6 desaturase activity in liver microsomes of rats fed diets enriched with cholesterol and/or (n-3) fatty acids. Biochem J 249:351–6.

Garg ML, Thomson ABR, Clandinin MT. 1988b. Effect of dietary cholesterol and/or (n-3) fatty acids on lipid composition and delta-5 desaturase activity of rat liver microsomes. J Nutr 118:661–8.

Garg ML, Wierzbicki A, Sebokova E, Thomson ABR, Clandinin MT. 1988c. Differential effects of dietary linoleic and alpha-linolenic acids on lipid metabolism in rat tissues. Lipids 23:847–52.

Garg ML, Wierzbicki A, Thomson ABR, Clandinin MT. 1989. Dietary saturated fat level alters the competition between alpha-linolenic and linoleic acid. Lipids 24:334–9.

Garg ML, Thomson ABR, Clandinin MT. 1990. Interactions of saturated, n-6 and n-3 fatty acids to modulate arachidonic acid metabolism. J Lipid Res 31:271–7.

Geleijnse JM, Grobbee DE, Donders AR, Kok FJ. 2002. Blood pressure response to fish oil supplementation: metaregression analysis of randomized trials. J Hypertens 20:1493–9.

Gregory J, Foster K, Tyler H, Wiseman M. 1990. The dietary and nutritional survey of British adults. Office of Population Censuses and Surveys, Social Survey Division. London: Her Majesty's Stationery Office.

He K, Song Y, Daviglus ML, Liu K, Van Horn L, Dyer AR, Greenland P. 2004. Accumulated evidence on fish consumption and coronary heart disease mortality: a meta-analysis of cohort studies. Circulation 109:2705–11.

Huang SW, Frankel EN, German JB. 1994. Antioxidant activity of alpha-tocopherols and gamma-tocopherols in bulk oils and in oil-in-water emulsions. J Agric Food Chem 42:2108–14.

Hughes DA, Pinder AC, Piper Z, Johnson IT, Lund EK. 1996. Fish oil supplementation inhibits the expression of major histocompatibility complex class II molecules and adhesion molecules on human monocytes. Am J Clin Nutr 63:267–72.

Ikeda I, Kumamaru J, Nakatani N, Sakono M, Murota I, Imaizumi K. 2001. Reduced hepatic triglyceride secretion in rats fed docosahexaenoic acid-rich fish oil suppresses postprandial hypertriglyceridemia. J Nutr 131:1159–64.

ISSFAL. 2004. Recommendations for intake of polyunsaturated fatty acids in healthy adults. ISSFAL Newsl 11:12–18.

Joint Health Claims Initiative. 2005. Generic health claim for LC n-3 PUFA and heart health. Available from: http://www.jhci.org.uk/approv/omega.htm. Accessed February 2, 2006.

Katan MB. 1998. Effect of low fat diets on plasma high density lipoprotein concentrations. Am J Clin Nutr 67:573S–6S.
Klinkesorn U, Sophanodora P, Chinachoti P, McClements DJ, Decker EA. 2005. Stability of spray-dried tuna oil emulsions encapsulated with two-layered interfacial membranes. J Agric Food Chem 53:8365–71.
Kolanowski W, Swiderski F, Berger S. 1999. Possibilities of fish oil application for food products enrichment with omega-3 PUFA. Int J Food Sci Nutr 50:39–49.
Kris-Etherton PM, Taylor DS, Yu-Poth S, Huth P, Moriarty K, Fishell V, Hargrove RL, Zhao G, Etherton TD. 2000. Polyunsaturated fatty acids in the food chain in the United States. Am J Clin Nutr 71:179S–88S.
Kris-Etherton P, Harris WS, Appel LJ. 2002. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Circulation 106:2747–57.
Kris-Etherton PM, Harris WS, Appel LJ. 2003. Omega-3 fatty acids and cardiovascular disease: new recommendations from the American Heart Association. Arterioscler Thromb Vasc Biol 23:151–2.
Kurlandsky LE, Bennink MR, Webb PM, Ulrich PJ, Baer LJ. 1994. The absorption and effect of dietary supplementation with omega-3 fatty acids on serum leukotriene B4 in patients with cystic fibrosis. Pediatr Pulmonol 18:211–17.
Lands WEM, Hamazaki T, Yamazaki K, Okuyama H, Sakai K, Goto Y, Hubbard V-S. 1990. Changing dietary patterns. Am J Clin Nutr 51:991–3.
Li D, Siriamornpun S, Wahlqvist ML, Mann NJ, Sinclair AJ. 2005. Lean meat and heart health. Asia Pac J Clin Nutr 14:113–19.
MacDonald-Wicks L, Garg ML. 2004. Incorporation of n-3 fatty acids into plasma and liver lipids of rats: importance of background dietary fat. Lipids 39:545–51.
Mahaffey KR. 2004. Fish and shellfish as dietary sources of methylmercury and the omega-3 fatty acids, eicosahexaenoic acid and docosahexaenoic acid: risks and benefits. Environ Res 95:414–28.
McVeigh GE, Brennan GM, Cohn JN, Finkelstein SM, Hayes RJ, Johnston GD. 1994. Fish oil improves arterial compliance in non-insulin-dependent diabetes mellitus. Arterioscler Thromb 14:1425–9.
Melanson SF, Lewandrowski EL, Flood JG, Lewandrowski KB. 2005. Measurement of organochlorines in commercial over-the-counter fish oil preparations: implications for dietary and therapeutic recommendations for omega-3 fatty acids and a review of the literature. Arch Pathol Lab Med 129:74–7.
Metcalf RG, James MJ, Mantzioris E, Cleland LG. 2003. A practical approach to increasing intakes of n-3 polyunsaturated fatty acids: use of novel foods enriched with n-3 fats. Eur J Clin Nutr 57:1605–12.
Meyer BJ, Mann NJ, Lewis JL, Milligan GC, Sinclair AJ, Howe PRC. 2003. Dietary intakes and food sources of omega-6 and omega-3 polyunsaturated fatty acids. Lipids 38:391–8.
Nawar WW. 1996. Lipids. In: Fennema OR, editor. Food chemistry. New York: Marcel Dekker.
Nordic Working Group on Diet and Nutrition. 1996. Nordic nutrition recommendations. Scand J Nutr 40:161–5.
Nordoy A, Hatcher L, Goodnight S, Fitzgerald GA, Conner WE. 1994. Effects of dietary fat content, saturated fatty acids, and fish oil on eicosanoid production and hemostatic parameters in normal men. J Lab Clin Med 123:914–20.
Parks JS, Johnson FL, Wilson MD, Rudel LL. 1990. Effect of fish oil diet on hepatic lipid metabolism in nonhuman primates: lowering of secretion of hepatic triglyceride but not apoB. J Lipid Res 31:455–66.
Patch CS, Tapsell LC, Williams PG. 2005a. Attitudes and intentions toward purchasing novel foods enriched with omega-3 fatty acids. J Nutr Educ Behav 37:235–41.
Patch CS, Tapsell LC, Williams PG. 2005b. Overweight consumers' salient beliefs on omega-3-enriched functional foods in Australia's Illawarra region. J Nutr Educ Behav 37:83–9.
Pawlosky RJ, Hibbelin JR, Novotny JA, Salem N. 2001. Physiological compartmental analysis of alpha-linolenic acid metabolism in adult humans. J Lipid Res 42:1257–65.
Robert SS, Singh SP, Zhou XR, Petrie JR, Blackburn SI, Mansour PM, Nichols PD, Liu Q, Green AG. 2005. Metabolic engineering of Arabidopsis to produce nutritionally important DHA in seed oil. Funct Plant Biol 32:1–7.
Ruxton C. 2004. Health benefits of omega-3 fatty acids. Nurs Stand 18:38–42.
Ruxton CH, Reed SC, Simpson MJ, Millington KJ. 2004. The health benefits of omega-3 polyunsaturated fatty acids: a review of the evidence. J Hum Nutr Diet 17:449–59.
Scheideler SE, Froning G, Cuppett S. 1997. Studies of consumer acceptance of high omega-3 fatty acid enriched eggs. J Appl Poultry Res 6:137–46.
Seljeflot I, Johansen O, Arnesen H, Eggesbo JB, Westvik AB, Kierulf P. 1999. Procoagulant activity and cytokine expression in whole blood cultures from patients with atherosclerosis supplemented with omega-3 fatty acids. Thromb Haemost 81:566–70.
Simopoulos AP, Leaf A, Salem N. 1999. Workshop on the essentiality of and recommended dietary intakes for omega-6 and omega-3 fatty acids. J Am Coll Nutr 18:487–9.
Sinclair AJ, Slattery W, O'Dea K. 1982. The analysis of polyunsaturated fatty acids in meat by capillary gas liquid chromatography. J Sci Food Agric 33:771–6.
Skeaff CM, Holub BJ. 1988. The effect of fish oil consumption on platelet aggregation responses in washed human platelet suspensions. Thromb Res 51:105–15.
Smuts CM, Borod E, Peeples JM, Carlson SE. 2003. High-DHA eggs: feasibility as a means to enhance circulating DHA in mother and infant. Lipids 38:407–14.
Sugano M, Hirahara F. 2000. Polyunsaturated fatty acids in the food chain in Japan. Am J Clin Nutr 71:189S–96S.
Terpstra AHM, van den Berg P, Jansen H, Beynen AC, van Tol A. 2000. Decreasing dietary fat saturation lowers HDL-cholesterol and increases hepatic HDL binding in hamsters. Br J Nutr 83:151–9.
U.S. Food & Drug Administration. 2004. FDA allows qualified health claim to decrease risk of coronary heart disease. Available from: http://www.fda.gov/bbs/topics/news/2004/NEW01129.html. Accessed February 2, 2006.
Vanschoonbeek K, Feijge MA, Paquay M, Rosing J, Saris W, Kluft C, Giesen PL, de Maat MP, Heemskerk JW. 2004. Variable hypocoagulant effect of fish oil intake in humans: modulation of fibrinogen level and thrombin generation. Arterioscler Thromb Vasc Biol 24:1734–40.
Volker D, Garg ML. 1996. Dietary n-3 fatty acid supplementation in rheumatoid arthritis—mechanisms, clinical outcomes, controversies and future directions. J Clin Biochem Nutr 20:83–97.
von Schacky C, Fischer S, Weber PC. 1985. Long-term effects of dietary marine omega-3 fatty acids upon plasma and cellular lipids, platelet function, and eicosanoid formation in humans. J Clin Invest 76:1626–31.
Wachtler P, Konig W, Senkal M, Kemen M, Koller M. 1997. Influence of a total parenteral nutrition enriched with omega-3 fatty acids on leukotriene synthesis of peripheral leukocytes and systemic cytokine levels in patients with major surgery. J Trauma-Injury Infect Crit Care 42:191–8.
Wallace JM, Turley E, Gilmore WS, Strain JJ. 1995. Dietary fish oil supplementation alters leukocyte function and cytokine production in healthy women. Arterioscler Thromb Vasc Biol 15:185–9.
Wang C, Chung M, Lichtenstein A, Balk E, Kupelnick B, DeVine D, Lawrence A, Lau J. 2004. Effects of Omega-3 Fatty Acids on Cardiovascular Disease. Evidence Report/Technology Assessment No. 94, Agency for Healthcare Research and Quality Publication No. 04-E009-2. Rockville, MD.
Watkins SM, German JB. 1998. Omega fatty acids. In: Akoh CC, Min DB, editors. Lipid chemistry. New York: Marcel Dekker.