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INNOVATIVE DIETARY SOURCES OF N-3 FATTY ACIDS

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■ **Abstract** It is now established that dietary n-3 polyunsaturated fatty acids (PUFAs) are involved in health promotion and disease prevention, particularly those traditionally derived from marine sources (e.g., eicosapentaenoic acid and docosahexaenoic acid). A number of organizations have made specific recommendations for the general population to increase their intakes of these nutrients. In response to and along with these recommendations, n-3 PUFAs are being incorporated into nontraditional food sources because of advances in the technology to safely enrich/fortify our food supply. Fatty acid compositions of traditional oils (e.g., canola and soybean) are being genetically modified to deliver more highly concentrated sources of n-3 PUFA. The advent of algal sources of docosahexaenoic acid provides one of the few terrestrial sources of this fatty acid in a concentrated form. All of this is possible because of newer technologies (microencapsulation) and improved processing techniques that ensure stability and preserve the integrity of these unstable fatty acids.

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ABBREVIATIONS

ALA, α-linolenic acid; CVD, cardiovascular disease; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; FDA, Food and Drug Administration; HUFA, highly unsaturated fatty acid; LDL, low density lipoprotein; MMP, matrix metalloproteinase; n-3, omega-3; PUFA, polyunsaturated fatty acid; SDA, stearidonic acid; USDA, United States Department of Agriculture; VLDL, very-low-density lipoprotein.

INTRODUCTION

Over the past 30 years, the beneficial effects of omega-3 (n-3) polyunsaturated fatty acids (PUFAs) have been extensively explored. Beginning with the original set of articles explaining the reduced incidence of ischemic heart disease in Greenland Eskimos (3, 12, 78), to the extensive, systematic review of epidemiological data (7), these bioactive compounds have marched to the forefront of dietary constituents promoting health and preventing disease. In an effort to capitalize on the health and commercial benefits of n-3 PUFA, there is a growing industry designed to enrich or fortify foods with this family of lipids. Newer technologies and processing techniques minimize oxidation, and in some instances mask flavor and smell for improved palatability. This chapter reviews how the landscape of n-3 PUFA-containing foods is rapidly changing via the incorporation of n-3 PUFA into foods typically devoid or deficient of these nutrients. Eggs, breads, pasta, dairy products, baby food, milk, baby formula, juices, cereals, meats, and salad dressings are some of the foods affected. The availability of these novel products is limited in the United States as compared with Europe, South America, and Australia, where public acceptance appears to be higher. Nevertheless, newer and innovative technologies are making it easier to more cost-effectively produce and design foods containing higher levels of these nutrients, thus satisfying a growing marketplace of a health-conscience public.

N-3 PUFA METABOLISM

N-3 fatty acids are a family of 18–24-carbon fatty acids with three or more methylene-interrupted double bonds where the last double bond (from the carboxyl group) is three carbons from the methyl end of the molecule. Mammalian cells do not contain enzymes capable of adding double bonds (desaturate) to fatty acids after the ninth carbon from the carboxyl end of the molecule. As such, n-3 fatty acids cannot be synthesized and must be provided in the diet.

The parent compound of the n-3 PUFA is α-linolenic acid (ALA, 18:3 n-3) from which all n-3 PUFAs are derived (Figure 1). This PUFA contains three methylene-interrupted double bonds and is initially desaturated to stearidonic acid (SDA, 18:4 n-3) via the Δ-6 desaturase, the rate-limiting enzyme in the metabolic pathway. Eicosapentaenoic acid (EPA, 20:5 n-3) is formed following the elongation of SDA to eicosatetraenoic acid (20:4 n-3) with the addition of two carbons and the subsequent addition of a double bond via the Δ-5 desaturase. Both the Δ-5 and Δ-6 desaturases are membrane-bound enzymes associated with the endoplasmic reticulum (ER) of mammalian cells (80). EPA is further metabolized to docosahexaenoic acid (DHA, 22:6 n-3) via a unique set of reactions previously attributed to a putative mammalian Δ-4 desaturase (102, 114). EPA undergoes two elongation steps, generating docosapentaenoic acid (DPA, 22:5 n-3) and 24:5 n-3 at the ER (61). This product is then desaturated to 24:6 n-3 via Δ-6 desaturase, presumably by the same protein that catalyzes the first step in the pathway (80). DHA is formed from 24:6 n-3 following the removal of two carbons via peroxisomal β-oxidation.

DIETARY SOURCES

α-Linolenic Acid

ALA is the major n-3 PUFA in the diet, with daily mean intakes estimated to be 1.6 g and 1.1 g per day for men and women, respectively (23). The major dietary sources are found in vegetable oils such as soybean and canola oils. Although there are other vegetable oils with ALA contents >50% (Table 1), they are consumed by only a small percentage of the population in any appreciable amounts. However, ALA is also found in a wide range of plant products, such as nuts, seeds, vegetables, legumes, grains, and fruits, contributing to the total ALA intake. Although some of these products have a relatively high ALA content (e.g., English walnuts, 10%), most foods have relatively low levels (0.1%–0.7%) (42).

It is known that dietary ALA can be converted to EPA and DHA following consumption; however, the extent of this conversion appears to be minimal at current intakes. Utilizing stable isotopes, conversion of ALA to DHA in omnivorous adults was estimated to be <1% (11, 82, 83). Similarly, when evaluating changes in plasma phospholipid DHA levels, supplementation of ALA, up to 5 g per day, does

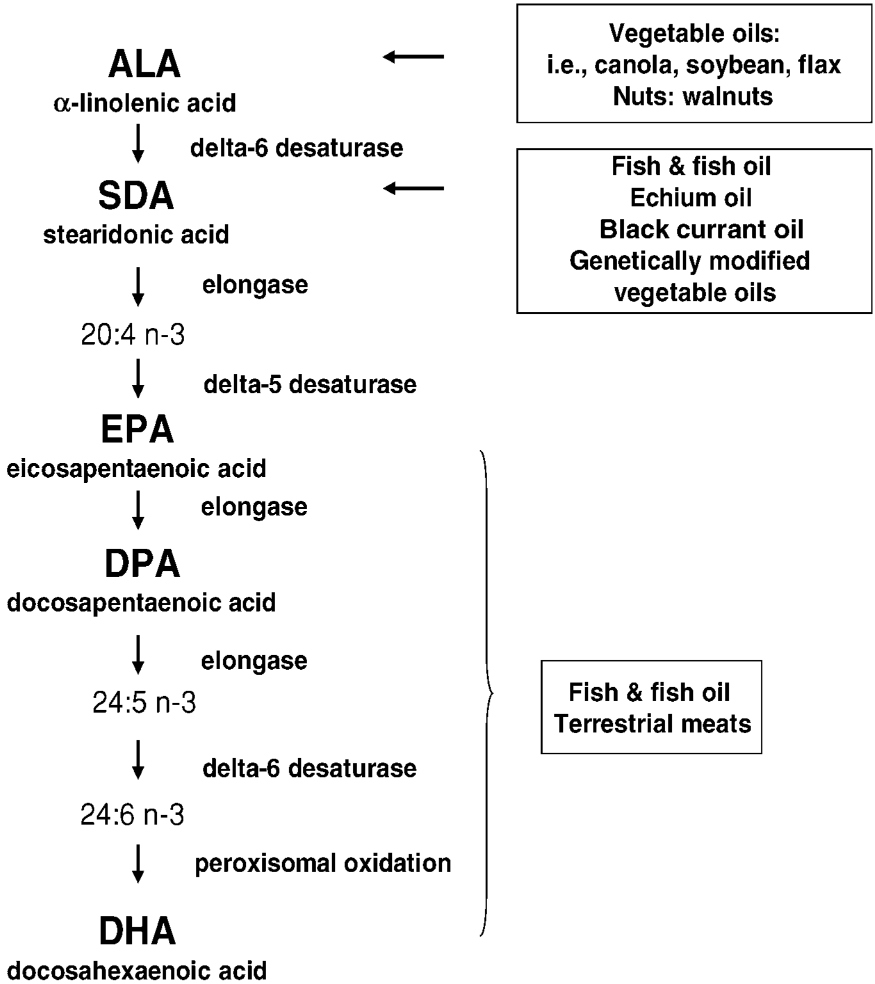

Figure 1 Metabolic pathway of n-3 polyunsaturated fatty acids (PUFAs) and traditional food sources of these fatty acids in the U.S. diet. Abbreviations: ALA, α-linolenic acid; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; LA, linoleic acid; SDA, stearidonic acid.

not increase plasma (or erythrocyte) DHA phospholipid levels (Table 2). As part of a typical western diet, the major metabolic fate of supplemented ALA appears to be oxidation and not long-chain n-3 fatty acid synthesis (11, 45, 58, 62, 83, 99, 107, 111, 115). It appears the only effective way to enrich tissue phospholipids with DHA is to consume DHA (Table 3).

TABLE 1 α-Linolenic acid content of selected vegetable oils

Oil	α-Linolenic acid content (g/100 g of oil)	Reference
Perilla	54–65	(55)
Linseed	50–54	(9, 54, 89)
Flaxseed	53	(110)
Modified canola	22–44	(34)
Cohni	5.9–14.5	(2)
Canola	9–11	(54, 110)
Wheat germ	6.9	(54)
Soybean	6.8	(110)

SDA

As previously mentioned, SDA is the immediate metabolic derivative of ALA. Since supplemental ALA is poorly converted to EPA and DHA, SDA could be an alternative for increasing EPA levels because it enters the metabolic pathway after the Δ-6 desaturase step. Following consumption of SDA, it is readily metabolized to EPA (45, 72, 73, 103) and can be considered a "pro-EPA" fatty acid. Consumption of SDA is low, with few dietary sources. At ∼9% by weight, echium oil appears

TABLE 2 The effects of dietary supplementation of α-linolenic acid on changes of EPA and DHA levels in plasma phospholipids in humans

Dietary ALA[a] (g/d)	EPA (% change from baseline)	DHA (% change from baseline)	Reference
0.37	33[b]	12	(99)
0.75	15	−3	(45)
0.82	−57[b]	−21[b]	(111)
1.5	23	−7	(45)
1.8	39[b]	92[b]	(96)
2.0	14	−2	(107)
2.8	13	0	(62)
3.5	60[b]	3	(115)
5.9	−13	−15[b]	(111)

[a]Values represent the amount of ALA supplemented to the baseline diet.

[b]Values are significantly different from baseline at $p < 0.05$.

ALA, α-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid.

TABLE 3 The effects of dietary supplementation of DHA on changes of DHA levels in plasma phospholipids

Dietary DHA[a] (g/d)	DHA (% change from baseline)	Reference
0.17	23[b]	(46)
0.18	24[b]	(21)
0.28	25	(107)
0.39	91	(37)
0.7	38	(107)
1.68	86[b]	(113)
2.25	190[b]	(15)
3.6	69[b]	(27)
4.0	173[b]	(75)

[a]Values represent the amount of DHA supplemented to the baseline diet.
[b]Values are significantly different from baseline at $p < 0.05$.
DHA, docosahexaenoic acid.

to be the richest commercially available plant source of SDA (103), followed by black currant oil at 2%–4% (Table 4) (93). Surprisingly, fish and fish oils are not particularly rich in SDA, which emphasizes the importance of a terrestrial source. The availability of SDA as a metabolic source for EPA could be enhanced by the development of SDA-enriched vegetable oils through biotechnology (70, 109). Commonly consumed vegetable oils contain no SDA, but a modified canola oil has been generated to contain up to 23% SDA (109), potentially providing a terrestrial source for highly unsaturated n-3 PUFA with similar biological properties of EPA (50, 86, 103).

EPA, DPA, and DHA

SDA is converted to EPA via the metabolic intermediate 20:4 n-3, a fatty acid not found in the food supply because of its rapid conversion to EPA. Foods that contain EPA also contain its metabolic derivatives DPA and DHA in various amounts. Fish and fish oils are the richest sources of these fatty acids, with contents ranging from 30% to 50% for both fresh and saltwater fish (49). DHA is the major n-3 PUFA in

TABLE 4 Stearidonic acid content of selected vegetable oils

Oil	Stearidonic acid content (g/100 g oil)	Reference
Modified canola	16–23	(109)
Echium	3.5–8.8	(28)
Black currant	3.4	(93)

fish whose levels are typically 2 to 5 times greater than EPA. However, per capita food disappearance data show that fish intake in the United States is small compared with other meats (54). Although they are not thought of in this context, terrestrial meats (such as beef, pork, chicken, etc.) may contribute significant amounts of n-3 highly unsaturated fatty acids (HUFAs, those fatty acids with >3 double bonds). Howe et al. (41) have estimated that terrestrial meats, such as beef, pork, mutton, poultry, and game, contribute 43% of the n-3 HUFA in the Australian diet, and the largest portion was in the form of DPA (41, 71). They revised these levels up 20% from their original values due to their improved fatty acid analysis of meats (41).

Similarly, reanalysis of the U.S. food supply and commonly used food consumption databases may be necessary to assess accurately n-3 HUFA intakes and their relative contributions to the U.S. diet (105). At present, accurately determining total n-3 HUFA intakes is difficult. For example, the n-3 HUFA content of meats is in the range of 20–50 mg per 100g, but fats are traditionally reported in gram quantities and values less than 0.1 g are many times not reported in the U.S. Department of Agriculture (USDA) database (105, 110). As an illustration, no values for n-3 HUFA are reported for rib eye (NDB NO: 13,098), although rib eye clearly contains these fatty acids (105). Many times these values, when present in the database, are not derived from direct analyses of the food, but are imputed, e.g., determined from preset mathematical formulas (105). Nevertheless, EPA and DHA intakes (not including contributions from DPA) are estimated to be between 100–200 mg/d in the United States (53). This is in comparison with n-3 HUFA intakes of 246 mg/d by Australians (41), 400–500 mg/d by the French (6), and 215–315 mg/d by Germans (63).

HEALTH EFFECTS

Cardiovascular Disease

A number of review articles have outlined the relationship of n-3 PUFA and risk for cardiovascular disease (1, 14, 31, 53, 116). A more comprehensive review of epidemiological literature can be found in a technical report from the Agency for Healthcare Research and Quality (U.S. Public Health Service) (7). This report screened more than 7464 abstracts and evaluated 39 studies that examined n-3 PUFA intake and outcomes related to cardiovascular disease. A number of studies demonstrated beneficial effects from n-3 HUFA and ALA supplementation/consumption. However, the evidence for a beneficial effect, primarily from cohort and secondary prevention trials, was clearer for n-3 HUFA than it was for ALA, although it was pointed out that dose and duration is an important factor in establishing overall efficacy. It is unclear whether any beneficial effects of ALA can be attributed to its conversion to EPA and DHA, given the doses in the studies and the poor rates of conversion as determined by changes in tissue phospholipid levels when compared with supplementation by n-3 HUFA.

Sudden Death

A major benefit of n-3 HUFA is reducing the risk of sudden death (17, 47, 53, 59, 60, 63, 79). Proposed mechanisms have included their effects on fibrinolysis and reductions in circulating triacylglycerol levels, platelet activation, and the expression of vascular adhesion molecules (53, 112). There is growing evidence that a reduction in sudden cardiac death may be the greatest impact of dietary n-3 HUFA. Sudden death accounts for as much as 50% of cardiovascular disease (CVD) deaths, and up to 80% of these are due to ventricular fibrillation. As such, attention has shifted from antithrombotic effects to their antiarrhythmic and plaque stabilization effects (17, 43, 47, 59, 60, 79, 90). It is suggested that these HUFAs reduce arrhythmic events by modifying lipid microdomains of plasma membranes, thereby affecting the conductance of ion channels (60). Furthermore, the generation of an atherogenic plaque involves remodeling of the extracellular matrix. Important in this process are matrix metalloproteinases (MMPs), a family of collagenases involved in the degradation of extracellular matrix. The stability of the cap of the fibrous plaque is dependent upon interstitial collagen fibers. Overexpression of MMPs weakens this protective cover, increasing plaque instability and potential atheroma formation (25). N-3 PUFAs from fish oils reduce MMP expression increasing plaque stability, potentially reducing sudden coronary events (4, 16, 25, 30, 39).

Neurological Disorders

Of late, there is an increasing interest in the relationship of n-3 HUFA and the brain. The brain is 65% lipid and DHA is a significant portion of that. N-3 HUFAs have been associated with neurological function (67). Consumption has been inversely linked to impulsivity/aggression/hostility (13, 44) and homicides (34), as well as a number of neurologically based disorders such as bipolar disorder (81), depression (35, 106), suicide (106), and various forms of dementia, including Alzheimer's disease (77).

Potential Adverse Effects

Interest in the potential adverse effects of n-3 PUFA intake has focused on the HUFAs, especially EPA and DHA. These concerns particularly apply to elevated intakes, e.g., >3 g/day. Because consumption of dietary n-3 HUFAs is inversely associated with CVD risk and individuals with type 2 diabetes are at increased risk, dietary intervention with n-3 fats seems logical. However, among the concerns were early reports that n-3 HUFA above 3 g/d could adversely influence glycemic control, particularly with diabetics (24, 26, 48, 117). Since then, a number of follow-up studies with more moderate doses have found little effect on indices of glycemia and insulin response/sensitivity (5, 65, 68, 84, 91, 100), results confirmed with a recent meta-analysis evaluating 18 trials with fish oil doses ranging from 3–18 g/d (74). In regard to lipid profiles, n-3 HUFAs are consistently hypotriglyceridemic

(66), but there is some concern that they also may raise LDL cholesterol levels (66, 74, 88, 104). Both phenomena appear to be related to increased turnover of VLDL and its subsequent conversion to LDL (64, 74), but these particles tend to be larger. This is important because smaller LDL particles are more atherogenic (104, 108). Further concern is the oxidizability of LDL, where oxidized LDL is the underlying etiology of the atherosclerotic process. Some studies, but not all (36), report the susceptibility of LDL oxidation is enhanced following fish oil consumption as measured by in vitro assays (69, 104), but it is difficult to determine applicability because these effects are not observed with measures of in vivo oxidation (76, 108). Nevertheless, susceptibility to oxidation could counter some of the overall beneficial effects of n-3 HUFA. Probably the greatest concern of the public relates to potential contamination of fish (for example, methyl mercury) because fish is an important dietary source of n-3 HUFA. The FDA has specific recommendations for the type and amount of fish to be consumed (http://www.cfsan.fda.gov/~dms/admehg3.html). These recommendations target pregnant or nursing women, those who are about to become pregnant, and small children. There are no specific recommendations for individuals outside of these targeted groups. Furthermore, these concerns do not appear to be applicable with regard to this chapter.

RECOMMENDED INTAKES

Recommended intakes for n-3 PUFA are not uniform (Table 5). In 2000, Simopoulos (97) recommended daily intakes for EPA + DHA at 650 mg, with at least 222 mg for both EPA and DHA, and 2.22 g/d for ALA. The American Heart Association recommends adults eat fish (in particular fatty fish) at least two times per week (52, 53). Wijendran & Hayes (116) recommend intakes of ALA and EPA + DHA to be 0.75% and 0.25%–0.5% of energy, respectively. In 2004, at their annual meeting, the International Society for the Study of Fatty Acids and Lipids recommended a "healthy intake" of ALA at 0.7% of energy and EPA + DHA intakes at ≥500 mg/d (19). The guidelines proposed by the Food and Nutrition Board (Institute of Medicine) established adequate intakes for ALA at 1.6 g/d and 1.1 g/d for adult men and women, respectively, and that EPA + DHA could account for up to 10% of the total n-3 fatty acid intake as a contribution toward the adequate intake for ALA (23).

FORTIFYING FOODS WITH N-3 PUFA

FDA Guidelines

In September 2004, the Food and Drug Administration (FDA) announced a qualified health claim for n-3 PUFA. This claim for labeling conventional food products stated, "Supportive but not conclusive research shows that consumption of EPA

TABLE 5 Recommended intakes of n-3 PUFA[a]

Date	Organization	Recommendations
		n-3 PUFA intakes
2004	International Society for the Study of Fatty Acids and Lipids (19)	ALA: 0.7% energy EPA + DHA: ≥500 mg/d
2004	Wijendran & Hayes (116)	ALA: 0.75% energy EPA + DHA: 0.25% energy
2003	World Health Organization	Total n-3 PUFA: 1%–2% energy
2002	Food and Nutrition Board (U.S.) (23)	ALA, women: 1.1 g/d of which 10% can be EPA + DHA ALA, men: 1.6 g/d of which 10% can be EPA + DHA
2002	American Heart Association	Eat fish (fatty fish) at least 2 times per week
2002	Scientific Advisory Committee on Nutrition (U.K.)	Total n-3 PUFA: >0.2 g/d Eat 2 portions of fish weekly (one being oily)
2001	Health Councils of the Netherlands	Total n-3 PUFA: 1% energy DHA: 150–200 mg/d
2000	Simopoulos et al. (98)	ALA: 2.22 g/d EPA: ≥220 mg/d DHA: ≥220 mg/d EPA + DHA: 650 mg/d
1999	British Nutrition Foundation (U.K.)	ALA: 0.2% energy Total n-3 PUFA: 1.25 g/d

[a]In part, modified from PUFA Newsletter, September 2003 (87).

ALA, α-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; PUFA, polyunsaturated fatty acid.

and DHA omega-3 fatty acids may reduce the risk of coronary heart disease. One serving of [name of food] provides [grams] of EPA and DHA omega-3 fatty acids" (for information about this quality health claim, visit the following FDA Web site: http://www.cfsan.fda.gov/~dms/lab-qhc.html). This claim was not extended to ALA, where the cardioprotective effects are more equivocal. The FDA also recommends that the combined daily intakes of EPA and DHA not exceed 3 g per day (with no more than 2 g per day from dietary supplements) because of the possible adverse effects on glycemic control, increased bleeding times, and elevation in LDL cholesterol.

Delivery of n-3 PUFA to Foods

The FDA has approved as "generally recognized as safe" a number of fish oils (e.g., menhaden, salmon, tuna, and anchovy) and algal oils rich in DHA (*Crypthero-dinium cohnii, Schizochytrium* sp.), allowing for food fortification with these products (see the FDA Web site: http://www.cfsan.fda.gov/~rdb/opa-gras.html).

The primary sources for algal oils rich in DHA (~40%) are Martek Biosciences (Columbia, Maryland) with DHASCO®, and the German ingredients firm Nutrinova (Frankfurt/Main, Germany) with Nutrinova® DHA. These algal products offer an advantage over vegetable oils because they are far superior in modifying tissue DHA levels in comparison with ALA (Tables 2 and 3). Furthermore, algal oils also offer an advantage over fish products because they are considered plant sources of n-3 PUFA and thus vegetarians can consume them; in addition, they eliminate concerns about potential contaminants associated with fish products.

These oils can be directly added to foods, and a number of processing techniques have been developed to enhance stabilization (due to their high unsaturation indexes). One of these is microencapsulation, a process by which minute droplets of oil are coated with a stable film (38, 51). Encapsulation of oils increases shelf life, minimizes the fishy taste and odor, and stabilizes the product by reducing oxidation potential. For example, one such product, Meg-3® (Ocean Nutrition Canada, Dartmouth, Nova Scotia, Canada), is a blend of microencapsulated refined fish oils (anchovy, sardine, mackerel), generating a very fine, free-flowing, nongranulated powder with negligible odor. Another method of enriching foods with n-3 PUFA is via bio-delivery. This is accomplished by feeding animals food products that contain n-3 PUFA with the desired effect of enriching their tissues with n-3 PUFA. For example, enriching DHA content of egg phospholipids is accomplished by providing hens with rations containing ALA or fish meal. ALA and DHA content in egg yolks increase in a dose-dependent manner when the diets of hens are modified with increasing levels of ALA (8, 22, 94). Feeding hens diets containing 0%, 10%, or 20% flaxseed progressively increased content of ALA (28, 261, and 527 mg/egg, respectively) and DHA (51, 81, and 87 mg/egg, respectively) (22). When hens are fed diets containing EPA and/or DHA, the eggs are further enriched with DHA (29, 32, 33, 40). Similar results can be achieved with foods such as pork, chicken, sheep, and beef, despite the significant biohydrogenation of dietary PUFA that occurs in ruminants (18, 20, 40, 95). Feeding pigs and chickens rations containing fishmeal or feeding ruminants n-3 PUFA-containing feed results in meat products significantly enriched in n-3 HUFA, in particular EPA and DHA (18, 20, 40, 95). However, when swine are only provided n-3 PUFA in the form of ALA, EPA is the major n-3 HUFA enriched in tissues (92, 101), a finding that suggests dietary DHA is needed to significantly enrich tissues with DHA.

FOOD PRODUCTS FORTIFIED WITH N-3 FATTY ACIDS

When the FDA affirmed that certain fish oils were generally recognized as safe, it established guidelines for their use. The food categories listed in Table 6 illustrate the wide range of foods that can be fortified (for more information, see the FDA Web site: http://www.cfsan.fda.gov/~rdb/opa-gras.html). Similar categories of foods have been identified for use with algal oils. Indeed, many of these targeted applications have already found the marketplace, particularly in Europe, Australia,

TABLE 6 Novel foods as sources for dietary N-3 PUFAs

Food	Serving (g)	ALA (mg)	EPA (mg)	DHA (mg)	Source of information
Bread/pasta					
Tip Top Up	100	113	8	36	http://www.tiptopup.comau/driver.asp? page=main/brands/l Sold in Australia in all major supermarkets, corner stores, petrol stations Source of n-3: HiDHA®, tuna oil (0.16%)
Barilla PLUS	100	360	–	–	http://www.barillaus.com/PLUS_Omega_3.aspx Sold at: local groceries, Kroger's Source of n-3: flaxseed
Warburton Good Health Loaf for Women	100	–	–	30	http://www.nutraingredients.com Sold at: ASDA and Sainsbury's supermarkets in the United Kingdom Source of n-3: source not revealed No longer available
Vans Gourmet Flax Waffles	90	1600	–	–	http://vanswaffles.com/images/gourmet_pop_ftr.gif Sold at: Kroger's Source of n-3: flax meal
Valfleuri Spaghetti	N/A	N/A	N/A	N/A	Sold in France Source of n-3: eggs derived from hens fed linseed oil Provides 20% of French recommendations
Men's Bread	34	48	–	–	http://www.frenchmeadow.com/nut_men.htm Sold at: natural food markets, health food stores, food cooperatives, retail stores with natural markets. Whole Foods, Wild Oats, Kroger's, and SuperTarget in the "specialty bread" refrigerated and frozen section of stores across the United States Source of n-3: organic flaxseed

Wegmans Breads with Omega-3s	114	0	80		http://www.wegmans.com/eatwelllivewell/hearthealth/03,3103_differentfats.asp Sold at: stores in New York, Pennsylvania, New Jersey, and Virginia Source of n-3: microencapsulated powder (Ocean's Nutritional)
Dimpflmeier Flaxseed Rye Bread	102	1200	–	–	http://www.dimpfbreadex.com/dbx2k-html/Order%20Splash%20(nav)/dimpf-order-splsh.htm Sold at: Dimpflmeier Bakery in Toronto, Canada, and online Source of n-3: flaxseed and flaxseed oil
Arnold Smart and Health Omega 3 Bread	36	–	33		http://arnold.gwbakeries.com/healthLifeFact.cfm/factType/omega Sold at: Wal-Mart and other grocers in Pennsylvania, Maryland, Connecticut, Florida, Georgia, Indiana, and Michigan Source of n-3: Meg-3 (Ocean's Nutritional)
Cereal					
Uncle Sam Cereal	55	2000	–	–	Sold at: Bi-Lo, Kroger, Wal-Mart, Wild Oats, Harris Teeter Source of n-3: whole flaxseed
Zoe's Flax and Soy Granola Cereal*	50	2200	–	–	Sold at: http://www.zoefoods.com/zoe_info/products/ Source of n-3: one tablespoon of ground flaxseed *Flavors: cranberry currants/honey almond/apple cinnamon
Organic Golden Flax Cereal	50	1000	–	–	http://www.shopnatural.com/html/16,465.htm Sold at: various Web sites Source of n-3: organic golden flaxseeds
Hearty Apple Cinnamon Hot Cereal	35	3400	–	–	Sold at: www.romanmeal.comSource of n-3: defatted flaxseed meal

(*Continued*)

TABLE 6 (*Continued*)

Food	Serving (g)	ALA (mg)	EPA (mg)	DHA (mg)	Source of information
Milk					
Leche Omega Extra of Nestle	200 ml	–	–	N/A	http://translate.google.com/translate?hl=en&sl=es&u=http://www.nestle.com.ar/pages/ProductosPack.asp%3FIDProducto%3D285%26IDMarca%3D39&prev=/search%3Fq%3DLeche%2BOmega%2Bof%2BNestle%26hl%3Den%26lr%3D Sold in Argentina Source of n-3: source not revealed
Vitalat Omega 3 Milk	200 ml	–	60	60	http://www.parmalat.com.br/portal/page?_pageid=398,62,135&_dad=portal&_schema=PORTAL Sold in Brazil, Uruguay, Argentina Source of n-3: source not revealed
Natrel Omega 3	250 ml	300	–	–	www.natrel.ca/english/whatsnew/omega_press.htm Sold at: retail grocery trade throughout Ontario, Quebec, and British Columbia Source of n-3: flaxseed oil
Neilson Dairy Oh! 1% Milk	250 ml	–	–	10	http://www.dairy-oh.com/nutrition.htm Sold at: Loblaws, Zehrs, Fortinos, No Frills, Valu-mart, independent grocers, Sobeys, Price Chopper, selected IGA and Foodlands in Ontario Source of n-3: dairy cows are fed a unique diet containing DHA
Neilson Dairy Oh! 2% Milk	250 ml	–	–	10	
Neilson Dairy Oh! Whole Milk	250 ml	–	–	20	

St Ivel Advance with Omega 3—semi-skimmed	250 ml	–	63		http://www.omega3.co.uk/omega3/pages/omega3_product>formula.php Sold at: Waitrose stores and selected Tesco, Sainsbury's, and Morrisons stores in the United Kingdom Source of n-3: omega 3 in an emulsion format (containing sardine oils)
St Ivel Advance with Omega 3—whole	250 ml	–	113		
Mark & Spencer's Super Whole Milk	250 ml	–	48		Sold in United Kingdom Source of n-3: fish oils incorporated into cow feed
Dawn Omega Milk Lowfat	250 ml	–	25		Sold in Ireland Source of n-3: DSM's ROPUFA '30'
Whole Milk	250 ml	–	50		
Candia	250 ml	–	190		Sold in France Source of n-3: source not revealed
Primevere Sterilized Drink	250 ml	210	–	47.5	Sold in France Source of n-3: colza and fish oils
So Good Fortified Soy Omega Vanilla	250 ml	1000	–	–	Sold in Vancouver, B.C. Source of n-3: flaxseed oil
Eggs					
Gold Circle Farms	50	–	–	150	http://www.goldcirclefarms.com/productso3_eggs.html Sold at: primarily sold at health food stores Source of n-3: hens fed a special DHA-rich diet, a patented feed protocol
Stonegate	58	–	–	100	Sold at: Waitrose groceries, Sainsbury, Ocado, and ASDA in the United Kingdom Source of n-3: Nu-Mega's DHA-rich tuna oil

(*Continued*)

TABLE 6 (*Continued*)

Food	Serving (g)	ALA (mg)	EPA (mg)	DHA (mg)	Source of information
Christopher Eggs, Columbus (U.K.)	50	600	–	–	Sold at: 500 Wal-Mart Supercenters in 13 South-Central and Midwestern states Source of n-3: "patented, natural, all-vegetarian feed for hens"
Eggs Plus by Pilgrim's Pride	50	100	–	100	Sold at: grocery stores in Texas, Oklahoma, and Arkansas Source of n-3: add flaxseed and fish oil to the feed with an additional supplement of vitamin E
Born 3 Eggs	50	400	–	–	http://www.born3.com/b3_eggs.htm#anchor1323509 Sold in British Columbia, Canada Source of n-3: flaxseed
Omega Pro Liquid Eggs	100	–	149	144*	Sold at: Food Lion, Albertson's, Wal-Mart Supercenters, Whole Foods, Canada Source of n-3: menhaden oil*30mg DPA included
Country Hen Eggs	50	310	–		http://www.countryhen.com/order.php Sold at: Web site listed above Source of n-3: feed contains long-chain polyunsaturated fatty acids (specific content unknown)
Egg* Land's Best	50	–	2	100	http://www.eggland.com/egglandsbest/egnb.html Sold at: Food City, Food Lion, HG Hill Co., Ingles Markets, Kroger, Piggly Wiggly, Sack N Save/Mega Mart, Schnuck's Markets, Seessel's Inc., Wal-Mart Supercenter, Winn Dixie Source of n-3: "patented, all-natural vegetarian diet" containing canola oil

Wegmans Omega 3 Eggs	50	320	130		http://www.wegmans.com/eatwelllivewell/hearthealth/03,3103_differentfats.asp Sold at: stores in New York, Pennsylvania, New Jersey, and Virginia Source of n-3: flaxseed and microencapsulated powder are incorporated into hen's feed
Meats					
Birds Eye Ocean Hake Fillets	100	490	40	100	http://www.simplot.com.au/Hosting/corp/SimSite.nsf/pages/Brands.Birds%20Eye.Birds%20Eye%20Smart%20Choice Sold in Australia Source of n-3: enriched with unknown source of EPA/DHA. ALA source: par-fried in canola oil
Hans Sliced Chicken	100	–	45	135	http://www.hans.com.au/omega3/default.asp?p=32 Sold in Australia: Coles, Bi Lo, Action stores in Queensland only. Nationally: Woolworths Source of n-3: microencapsulated tuna oil
Hans Strassburg	100	–	23	65	http://www.hans.com.au/omega3/default.asp?p=33 Sold in Australia: Coles, Bi Lo, and Action stores in Queensland only. Nationally: Woolworths Source of n-3: microencapsulated tuna oil
Juice					
Supajus	250 ml	–	–	100	Sold at: vending machines in U.K. schools Source of n-3: pure tuna oil
Nutrition bars					
Zoneperfect Lemon Yogurt	50	–	3		http://www.zoneperfect.com Sold at: CVS Pharmacy, GNC, Ingles, Sam's Club, SuperTarget, Target, Vitamin Depot Plus, Vitamin World, Wal-Mart Supercenter, Walgreens Source of n-3: molecular distilled fish oil

(*Continued*)

TABLE 6 (*Continued*)

Food	Serving (g)	ALA (mg)	EPA (mg)	DHA (mg)	Source of information
Zoe's Flax and Soy Bars—Apple Crisp and Lemon Bars	52	2200	–	–	http://www.zoefoods.com/zoe_info/products/barapple.htm Sold at: Earthfare, Knoxville Food Co-op, Nature's Pantry Source of n-3: ground flaxseed
Peanut Butter and Chocolate Bars	52	1500	–	–	
Health By Chocolate	25	35	–	–	http://www.ecobella.com/_health_by_chocolate.html Sold at: www.Eccobella.com Source of n-3: cranberry seed oil
Oh Mama! Nutritional Bar	50	–	–	115	http://www.ohmamabar.com/page/nutrition.html Sold at: Motherhood Maternity, Buy Buy Baby, or at www.ohmamabar.com Source of n-3: DHA algal oil (Martek)
IQ3 Brainstorm Bar	N/A	N/A	N/A	N/A	http://www.iq3-brainstorm.co.uk/brainstorm.php Sold at: at most quality health food shops in the United Kingdom Source of n-3: vegetable margarine, microencapsulated tuna oil (3.1%)
Salad dressing					
Au Bon Pain Salad Dressing	71	–	–	N/A	http://www.aubonpain.com/nutrition.php?ID=322&HEADER=dressings&GROUP_ID=17&DOUBLELIST= Sold at: N/A Source of n-3: refined menhaden oil
Omega-3 Mayonnaise	14	2000	–	–	Sold at: local health food stores Source of n-3: flaxseed oil

Omega-3 Balsamic Vinaigrette, Organic or Raspberry Vinaigrette	31	2000	–	–	http://www.spectrumorganics.com/index.php?id=7 Sold at: local health food stores Source of n-3: flaxseed oil
Spectrums Spread, Essentials Omega-3	14	1000	–	–	Sold at: local health food stores Source of n-3: flaxseed oil
Primevere Margarine	100	300	–	–	Sold in France Source of n-3: colza oil
Meadow Lea Hi Omega Spread	10	440	60		http://www.goodmanfielder.com.au/dir065/gfsite/gflimited.nsf/Content/About+us+−+Media+Release+97 Sold in Australia Source of n-3: source not revealed
Smart Balance Omega Plus Buttery Spread	100	–	150		http://www.smartbalance.com/product.html Sold at: Reisbecks, Buehlers, Roundy's Supermarkets; Wal-Mart Supercenter Source of n-3: menhaden oil
Cindy's Kitchen Salad Dressing	N/A	–	700		Sold at: Food Lion, Albertson's, Wal-Mart Supercenter, Whole Foods Source of n-3: menhaden oil
Infant formula					
Similac by Ross	5 fl. oz.	–	–	8	Sold at: local grocery stores, Wal-Mart Supercenter, drug stores Source of n-3: *Crypthecondinium cohnii* oil

(*Continued*)

TABLE 6 (*Continued*)

Food	Serving (g)	ALA (mg)	EPA (mg)	DHA (mg)	Source of information
Enfamil Lipil w/ iron by Mead Johnson	–	–	17		Sold at: local grocery stores, Wal-Mart Supercenter, drug stores Source of n-3: *Crypthecondinium cohnii* oil
Nestle Gold Start w/ DHA and ARA			N/A		Sold at: local grocery stores, Wal-Mart Supercenter, drug stores Source of n-3: *Crypthecondinium cohnii* oil
Mother's Horlicks	75	–	–	60	Sold in India Source of n-3: powder—microalgae
Junior's Horlicks	100	–	–	40	Sold in India Source of n-3: powder—microalgae
Impact Novaritis Nutritional Support	1 liter	–	1700		Sold at: provided at medical facilities Source of n-3: menhaden oil (omega protein)
Beech-Nut First Advantage baby foods	4 oz.	–	–	~60	http://www.beechnut.com Sold in Food Lion Source of n-3: "omega-3 enhanced egg yolks"
Other					
Omega-3 Enriched Pizza	N/A			32	http://www.nardonebros.com/ Sold at: www.nardonebros.com Source of n-3: microencapsulated tuna fish oil (Nu-Mega ingredients)

Canada, and South America. The United States is lagging behind these countries in availability of foods fortified with n-3 PUFA. Three major forms of n-3 PUFA are used for fortification: ALA-rich vegetable oils, fish oils (and n-3 enriched fish oils), and algal oils rich in DHA. Table 6 lists a representative sample of novel commercial products currently available, their n-3 PUFA contents, and where they are sold. This list is not exhaustive, but rather is a snapshot of the current marketplace; an expansion of the number of products to be developed is anticipated in response to the recent FDA announcement regarding health claims of n-3 PUFA.

Eggs

A standard egg (50 g) contains 34 mg of DHA, with very little EPA (<5 mg) (105). This ratio of DHA to EPA is typical of eggs, even when hens consume EPA, because EPA acts primarily as an intermediate for the synthesis in DHA (this latter aspect is unique for eggs). DHA-enriched eggs can be found all over the world, and their DHA content ranges from 50–150 mg/egg. Those eggs that are derived from ALA-fed hens have higher ALA contents, while hens fed EPA and/or DHA produce eggs with higher DHA levels. In either case, arachidonic acid levels are significantly reduced. This is important because eggs are particularly rich in arachidonic acid, and attenuating arachidonic acid and its subsequent metabolism to eicosanoids is believed to be a targeted effect underlying some of the benefits of n-3 PUFA (56, 57, 85).

Milk Products

The Italian dairy group Parmalat (http://www.parmalat.com) has been a leader in marketing n-3-fortified milk products across the globe, in particular in Europe and South America. Both whole milk and low-fat milk can be fortified. Dawn® Omega Milk is fortified with ROPUFA® (Roche, Basel, Switzerland), which contains a combination of EPA, DPA, and DHA (25%). This marine oil is dispersed in gelatin, sucrose, and starch, stabilized with a mixture of tocopherols, ascobyl palmitate, and rosemary extract (personal communication). In general, the levels of EPA and DHA for 200 ml of fortified milk ranges from 10 mg to 190 mg, while the levels of ALA in the ALA-fortified milk can be as high as 800 mg ALA/200 ml milk. Other dairy products such as yogurts are being fortified with distilled fish oils.

Margarines/Spreads/Salad Dressings

Similar to milk products, this category is divided into those fortified with ALA or EPA/DHA. The ALA in margarines are typically derived from flaxseed or colza oils and ranges from 30–36 mg per 10 g serving; salad dressings are fortified with as much as 2000 mg ALA per serving. Spreads containing EPA/DHA are typically derived from fish oils at levels of ~15 mg per 10 g serving; salad dressings are fortified at much higher levels. Some products include a combination of ALA and EPA/DHA. For example, Smart Balance® spread is fortified with n-3 PUFAs from soybean, canola, and menhaden oils, providing 150 mg EPA/DHA and 400 mg ALA per 14 g serving.

Pasta and Breads

A number of bread products are fortified with ALA from flaxseed (up to 300 mg per 25 g slice) and some with a combination of fish oil and a product identified as HiDHA® (a product containing DHA and EPA in a ratio of 3.5:1). Some n-3-fortified pasta products are being made with eggs from hens fed linseed oil (>50% ALA), a novel approach for the use of these eggs.

Cereals and Cereal (Granola) Bars

Cereals and cereal bars high in n-3 PUFA are typically fortified with ALA from flaxseed, with levels ranging from 2000–5343 mg per 55 g serving (one cup) for cereals, and 1500–2200 mg ALA per bar. No cereals that contained EPA/DHA could be identified.

Infant Formulas and Baby Foods

The major infant formula companies have infant formulas fortified with algae-derived DHA (10) at levels designed to mimic human breast milk. And for those infants eating solid foods, new baby food products using n-3-enriched egg yolks (60 mg DHA per 4 oz) have also made their way to the marketplace.

Other Food Products

Juices fortified with n-3 HUFA have appeared and disappeared from the market-place. Supajuice®, an orange-flavored beverage containing 100 mg EPA/DHA (from tuna oil), is sold in the United Kingdom and is available in school vending machines. GlaxoSmithKline, using DHA-rich algal oil, has developed a DHA-fortified powder that is added to liquids. A 75 g serving contains 30–60 mg DHA and is being marketed to pregnant and breast-feeding women and young children in India under the names of Mother's Horlicks and Junior's Horlicks, respectively. In addition, processed meat products containing microencapsulated fish oil were identified in French supermarkets.

SUMMARY

As more products are being developed that are enriched or fortified with n-3 PUFA, a challenge for the scientific community is to differentiate the biological effects of ALA from its downstream metabolites, SDA, EPA, DPA, and DHA. It is increasingly clear that form and amount are important with regard to n-3 PUFA. The challenge for the public will be to understand that not all n-3 PUFAs are the same: ALA is not the same thing as EPA and DHA. With the ever-changing composition of the food supply, social scientists face even greater challenges with regard to their ability to ascertain health risks associated with diet. Similar difficulties extend to government agencies whose job it is to maintain accurate, up-to-date food composition databases. Currently, it is very difficult to quantitate accurately n-3 HUFA consumption in a typical western diet, and with the development of new technologies (e.g., microencapsulation) that improve the palatability and stability of n-3 PUFA, this becomes even more challenging. Our current databases provide nutrient levels that link food with the raw products from which they were derived, e.g., bread derived from wheat, yogurt derived from milk, etc., providing consistency and stability within food categories. However, as commercial development of new and innovative sources of n-3 PUFAs (algal oils, genetically modified plants) provide a cheaper and safer supply of these fatty acids (say, compared with fish), this will result in the rapid development of nontraditional foods that are enriched or fortified, thus challenging our ability to accurately keep track of these changes. This is further complicated because some of these foods influence the composition of products from which they are derived (e.g., pasta made from DHA-enriched eggs). In summary, the landscape of foods containing n-3 PUFA is changing and it will be interesting to evaluate the impact of these changes.

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