The use of long-chain omega-3 fatty acid supplements to alleviate symptoms of schizophrenia or to mitigate adverse effects of antipsychotic medications has been investigated in a number of clinical trials (194, 199). In a recent randomized, placebo-controlled trial in 50 subjects with recent onset of schizophrenia who were medicated, daily supplementation with EPA (740 mg) and DHA (400 mg) reduced psychotic symptoms (assessed with the Brief Psychiatric Rating Scale) only in those who were not taking the anxiolytic, lorazepam (Ativan) (200). Overall, however, there was no effect of long-chain PUFA supplements on schizophrenia symptoms. Yet, given the high safety profile of fish oil supplements and some evidence of a positive effect of EPA supplementation in a subset of trials, some clinicians may consider EPA a useful adjunct to antipsychotic therapy in patients with schizophrenia.

Alzheimer's disease and dementia

Several mechanisms suggest that omega-3 PUFA supplementation may improve the cognitive performance of individuals with Alzheimer's disease and other types of dementia. In particular, the antioxidative and antiinflammatory properties of these PUFA may help protect neurons, promote synaptic plasticity, and limit cellular death. The PUFA composition of the diet appears to influence blood cholesterol, which may play a role in the pathology of Alzheimer's disease. However, the current evidence from clinical trials is not supportive of omega-3 supplementation in the treatment of Alzheimer's disease in humans. A 2016 Cochrane review identified three randomized, placebo-controlled trials in patients with Alzheimer's disease of mild-to-moderate severity (201). These trials compared daily supplementation with DHA (between 675 mg and 1,700 mg) and EPA (between 600 mg and 975 mg) to a placebo for 12 months (202, 203) or 18 months (204). Of note, the study by Quinn et al. (204) also included 4 mg/day of vitamin E (used as preservative — see also Nutrient interactions) in the intervention arm, and the study by Freund-Levi et al. (202) included DHA (900-1,100 mg/day) but no EPA. The pooled analysis of these trials showed no beneficial effect of omega-3 supplementation on measures of global and specific cognitive functions, measures of functional outcomes, and measures of dementia severity (201). There was no difference between intervention and placebo arms regarding the occurrence of adverse effects (201).

Sources

Food sources

Humans can synthesize arachidonic acid (AA) from linoleic acid (LA) and eicosapentaenoic acid (EPA) and docosapentaenoic acid (DHA) from α-linolenic acid (ALA) through a series of desaturation and elongation reactions.

EPA and docosapentaenoic acid (DPA) are also obtained from the retroconversion of DHA (see Metabolism and Bioavailability). Due to low conversion efficiency, it is advised to obtain EPA and DHA from additional sources.

Omega-6 fatty acids

Linoleic acid (LA): Food sources of LA include vegetable oils, such as soybean, safflower, and corn oil; nuts; seeds; and some vegetables. Dietary surveys in the US indicate that the average adult intake of LA ranges from 17 to 20 g/day for men and 12 to 13 g/day for women (78). Some foods that are rich in LA are listed in **Table 2**.

Food	Serving	Linoleic Acid (g)
Safflower oil	1 tablespoon	10.1
Sunflower seeds, oil roasted	1 ounce	9.7
Pine nuts	1 ounce	9.4
Sunflower oil	1 tablespoon	8.9
Corn oil	1 tablespoon	7.3
Soybean oil	1 tablespoon	6.9
Pecans, oil roasted	1 ounce	6.4
Brazil nuts	1 ounce	5.8
Sesame oil	1 tablespoon	5.6

Table 2. Food Sources of Linoleic Acid (18:2n-6) (205)

Arachidonic acid: Animals, but not plants, can convert LA to AA. Therefore, AA is absent in vegetable oils and fats and present in small amounts in meat, poultry, and eggs.

Omega-3 fatty acids

α-Linolenic acid (ALA): Flaxseeds, walnuts, and their oils are among the richest dietary sources of ALA. Canola oil is also an excellent source of ALA. Dietary surveys in the US indicate that average adult intakes for ALA range from 1.8 to 2.0 g/day for men and from 1.4 to 1.5 g/day for women (78). Some foods that are rich in ALA are listed in **Table 3**.

Food	Serving	α-Linolenic acid (g)
Flaxseed oil	1 tablespoon	7.3
Chia seeds, dried	1 ounce	5.1
Walnuts, English	1 ounce	2.6
Flaxseeds, ground	1 tablespoon	1.6
Walnut oil	1 tablespoon	1.4
Canola oil	1 tablespoon	1.3
Soybean oil	1 tablespoon	0.9
Mustard oil	1 tablespoon	0.8
Walnuts, black	1 ounce	0.6
Tofu, firm	½ cup	0.2

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA): Dietary surveys in the US indicate that average adult intakes of EPA range from 0.03 to 0.06 g/day, and average adult intakes of DHA range from 0.05 to 0.10 g/day (78). Oily fish are the major dietary source of EPA and DHA; omega-3 fatty acid-enriched eggs are also available in the US. Some foods that are rich in EPA and DHA are listed in **Table 4**.

Table 4. Food Sources of EPA (20:5n-3) and DHA (22:6n-3) (107)

Food	Serving	EPA (g)	DHA (g)	Amount Providing 1 g of EPA + DHA
Herring, Pacific	3 ounces*	1.06	0.75	1.5 ounces
Salmon, chinook	3 ounces	0.86	0.62	2 ounces
Sardines, Pacific	3 ounces	0.45	0.74	2.5 ounces
Salmon, Atlantic	3 ounces	0.28	0.95	2.5 ounces
Oysters, Pacific	3 ounces	0.75	0.43	2.5 ounces
Salmon, sockeye	3 ounces	0.45	0.60	3 ounces
Trout, rainbow	3 ounces	0.40	0.44	3.5 ounces

*A three-ounce serving of fish is about the size of a deck of cards.

Tuna, canned, white	3 ounces	0.20	0.54	4 ounces	
Crab, Dungeness	3 ounces	0.24	0.10	9 ounces	
Tuna, canned, light	3 ounces	0.04	0.19	12 ounces	
*A three-ounce serving of fish is about the size of a deck of cards.					

Supplements *Omega-6 fatty acids*

Borage seed oil, evening primrose oil, and black currant seed oil are rich in ylinolenic acid (GLA; 18:3n-6) and are often marketed as GLA or essential fatty acid (EFA) supplements (206).

Omega-3 fatty acids

Flaxseed oil (also known as flax oil or linseed oil) is available as an ALA supplement. A number of fish oils are marketed as omega-3 fatty acid supplements. The omega-3 fatty acids from natural fish oil are in the triglyceride form, often with only one of three attached fatty acids an omega-3; thus, up to 70% of fatty acids provided may be other types (3). Ethyl esters of EPA and DHA (ethyl-EPA and ethyl-DHA) are concentrated sources of longchain omega-3 fatty acids that provide more EPA and DHA per gram of oil. Krill oil contains both EPA and DHA and is considered comparable to fish oil as a source of these long-chain PUFA (207). Cod liver oil is also a rich source of EPA and DHA, but some cod liver oil preparations may contain excessive amounts of preformed vitamin A (retinol) and vitamin D (206). DHA supplements derived from algal and fungal sources are also available. Because dietary DHA can be retroconverted to EPA and DPA in humans, DHA supplementation represents yet another alternative to fish oil supplements (see Metabolism and Bioavailability).

The content of EPA and DHA varies in each of these preparations, making it necessary to read product labels in order to determine the EPA and DHA levels provided by a particular supplement. All omega-3 fatty acid supplements are absorbed more efficiently with meals. Dividing one's daily dose into two or three smaller doses throughout the day will decrease the risk of gastrointestinal side effects (see Safety).

Infant formula

In 2001, the FDA began permitting the addition of DHA and AA to infant formula in the United States (208). Presently, manufacturers are not required to list the amounts of DHA and AA added to infant formula on the label.