Omega-3 Fatty Acid

Types of fats in food

- Unsaturated fat
- Monounsaturated fat
- Polyunsaturated fat
- Trans fat
- Omega fatty acids:
- 3
- 6
- 9
- Saturated fat
- Interesterified fat

n3 Fatty acids (popularly referred to as 3 fatty acids or omega-3 fatty acids) are a family of unsaturated fatty acids that have in common a final carbon–carbon double bond in the n3 position; that is, the third bond from the methyl end of the fatty acid.

Important nutritionally-essential n3 fatty acids are: -linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), all of which are polyunsaturated. The human body cannot synthesize n3 fatty acids de novo, but it can form 20-carbon unsaturated n3 fatty acids (like EPA) and 22-carbon unsaturated n3 fatty acids (like DHA) from the eighteen-carbon n3 fatty acid -linolenic acid. These conversions occur competitively with n6 fatty acids, which are essential closely related chemical analogues that are derived from linoleic acid. Both the n3 -linolenic acid and n6 linoleic acid are essential nutrients which must be obtained from food. Synthesis of the longer n3 fatty acids from linolenic acid within the body is competitively slowed by the n6 analogues. Thus accumulation of long-chain n3 fatty acids in tissues is more effective when they are obtained directly from food or when competing amounts of n6 analogs do not greatly exceed the amounts of n3.

Although omega-3 fatty acids have been known as essential to normal growth and health since the 1930s, awareness of their health benefits has dramatically increased in the past few years. The heart-health benefits of the long-chain omega-3 fatty acids — DHA and EPA omega-3 — are the best known. These benefits were discovered in the 1970s by researchers studying the Greenland Eskimos. The Greenland Eskimos consumed large amounts of fat from seafood, but displayed virtually no cardiovascular disease. The high level of omega-3 fatty acids consumed by the Eskimos reduced triglycerides, heart rate, blood pressure, and atherosclerosis.

On September 8, 2004, the U.S. Food and Drug Administration gave “qualified health claim” status to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) n3 fatty acids, stating that “supportive but not conclusive research shows that consumption of EPA and DHA [n3] fatty acids may reduce the risk of coronary heart disease.” This updated and modified their health risk advice letter of 2001 (see below). Currently regulatory agencies do not accept that there is sufficient evidence for any of the other suggested benefits of DHA and EPA other than for cardiovascular health, and further claims should be treated with caution.

The Canadian Government has recognized the importance of DHA omega-3 and permits the following biological role claim for DHA: “DHA, an omega-3 fatty acid, supports the normal development of the brain, eyes and nerves.”

As the importance of omega-3 fatty acids to health has received increasing awareness, the number of food products enriched in omega-3 fatty acids has increased. Many companies add fish oil or flax oil into their final product to enrich it in omega-3 fatty acids. Some animal products, such as milk and eggs, can be naturally enriched for omega-3 fatty acids by feeding the animals a diet that is rich in omega-3 fatty acids.

Chemistry

Chemical structure of alpha-linolenic acid (ALA), an essential n3 fatty acid, (18:39c,12c,15c, which means a chain of 18 carbons with 3 double bonds on carbons numbered 9, 12 and 15). Although chemists count from the carbonyl carbon (Blue Numbering), physiologists count from the n () carbon (red numbering). Note that from the n end (diagram right), the first double bond appears as the third carbon-carbon bond (line segment), hence the name "n3". This is explained by the fact that the n end is almost never changed during physiologic transformations in the human body, as it is more stable energetically, and other carbohydrates compounds can be synthesized from the other carbonyl end, for example in glycerides, or from double bonds in the middle of the chain.
Chemical structure of docosahexaenoic acid (DHA).
The term n3 (also called 3 or omega-3) signifies that the first double bond exists as the third carbon-carbon bond from the terminal methyl end (n) of the carbon chain.

n3 fatty acids which are important in human nutrition are: -linolenic acid (18:3, n3; ALA), eicosapentaenoic acid (20:5, n3; EPA), and docosahexaenoic acid (22:6, n3; DHA). These three polyunsaturates have either 3, 5 or 6 double bonds in a carbon chain of 18, 20 or 22 carbon atoms, respectively. All double bonds are in the cis-configuration, i.e. the two hydrogen atoms are on the same side of the double bond.

Most naturally-produced fatty acids (created or transformed in animalia or plant cells with an even number of carbon in chains) are in cis-configuration where they are more easily transformable. The trans-configuration results in much more stable chains that are very difficult to further break or transform, forming longer chains that aggregate in tissues and lacking the necessary hydrophilic properties. This trans-configuration can be the result of the transformation in alkaline solutions, or of the action of some bacterias that are shortening the carbonic chains. Natural transforms in vegetal or animal cells more rarely affect the last n3 group itself. However, n3 compounds are still more fragile than n6 because the last double bond is geometrically and electrically more exposed, notably in the natural cis configuration.

Biological Significances

The biological effects of the n3 are largely mediated by their interactions with the n6 fatty acids; see Essential fatty acid interactions for detail.
A 1992 article by biochemist William E.M. Lands provides an overview of the research into n3 fatty acids, and is the basis of this section.

The 'essential' fatty acids were given their name when researchers found that they were essential to normal growth in young children and animals. (Note that the modern definition of 'essential' is more strict.) A small amount of n3 in the diet (~1% of total calories) enabled normal growth, and increasing the amount had little to no additional effect on growth.

Likewise, researchers found that n6 fatty acids (such as -linolenic acid and arachidonic acid) play a similar role in normal growth. However, they also found that n6 was "better" at supporting dermal integrity, renal function, and parturition. These preliminary findings led researchers to concentrate their studies on n6, and it was only in recent decades that n3 has become of interest.

In 1963 it was discovered that the n6 arachidonic acid was converted by the body into pro-inflammatory agents called prostaglandins. By 1979 more of what are now known as eicosanoids were discovered: thromboxanes, prostacyclins and the leukotrienes. The eicosanoids, which have important biological functions, typically have a short active lifetime in the body, starting with synthesis from fatty acids and ending with metabolism by enzymes. However, if the rate of synthesis exceeds the rate of metabolism, the excess eicosanoids may have deleterious effects. Researchers found that n3 is also converted into eicosanoids, but at a much slower rate. Eicosanoids made from n3 fats are often referred to as anti-inflammatory, but in fact they are just less pro-inflammatory than those made from n6 fats. If both n3 and n6 are present, they will "compete" to be transformed, so the ratio of n3:n6 directly affects the type of eicosanoids that are produced.

This competition was recognized as important when it was found that thromboxane is a factor in the clumping of platelets, which leads to thrombosis. The leukotrienes were similarly found to be important in immune/inflammatory-system response, and therefore relevant to arthritis, lupus, and asthma. These discoveries led to greater interest in finding ways to control the synthesis of n6 eicosanoids. The simplest way would be by consuming more n3 and fewer n6 fatty acids.

Health Benefits

The 18 carbon -linolenic acid has not been shown to have the same cardiovascular benefits as DHA or EPA. Currently there are many products on the market which claim to contain health promoting 'omega 3', but contain only -linolenic acid (ALA), not EPA or DHA. These products contain mainly higher plant oils and must be converted by the body to create DHA and therefore considered less efficient. DHA and EPA are made by microalgae that live in seawater. These are then consumed by fish and accumulate to high levels in their internal organs. If a person is concerned about mercury and oceanborne contaminants in fish, DHA can be produced directly from microalgae as a vegetarian source. People with certain circulatory problems, such as varicose veins, benefit from fish oil because it contains the EPA and DHA derived from microalgae. Fish oil stimulates blood circulation, increases the breakdown of fibrin, a compound involved in clot and scar formation, and additionally has been shown to reduce blood pressure. There is strong scientific evidence that n3 fatty acids reduce blood triglyceride levels and regular intake reduces the risk of secondary and primary heart attack.

Some benefits have been reported in conditions such as rheumatoid arthritis and cardiac arrhythmias.

There is preliminary evidence that n-3 fatty acids supplementation might be helpful in cases of depression and anxiety. Studies report highly significant improvement from n-3 fatty acids supplementation alone and in conjunction with medication.

Some research suggests that fish oil intake may reduce the risk of ischemic and thrombotic stroke. However, very large amounts may actually increase the risk of hemorrhagic stroke (see below). Lower amounts are not related to this risk, 3 grams of total EPA/DHA daily are considered safe with no increased risk of bleeding involved and many studies used substantially higher doses without major side effects (for example: 4.4 grams EPA/2.2 grams DHA in 2003 study).

Cancer

Several studies report possible anti-cancer effects of n3 fatty acids (particularly breast, colon and prostate cancer). Omega-3 fatty acids reduced prostate tumor growth, slowed histopathological progression, and increased survival. Among n-3 fatty acids [omega-3], neither long-chain nor short-chain forms were consistently associated with breast cancer risk. High levels of docosahexaenoic acid, however, the most abundant n-3 PUFA [omega-3] in erythrocyte membranes, were associated with a reduced risk of breast cancer. A 2009 trial found that a supplement of eicosapentaenoic acid helped cancer patients retain muscle mass.

A 2006 report in the Journal of the American Medical Association concluded that their review of literature covering cohorts from many countries with a wide variety of demographic concluded that there was no link between n3 fatty acids and cancer. This is similar to the findings of a review by the British Medical Journal of studies up to February 2002 that failed to find clear effects of long and shorter chain n3 fats on total mortality, combined cardiovascular events and cancer.

Cardiovascular disease

In 1999, the GISSI-Prevenzione Investigators reported in the Lancet, the results of major clinical study in 11,324 patients with a recent myocardial infarction. Treatment 1 gram per day of n3 fatty acids reduced the occurrence of death, cardiovascular death and sudden cardiac death by 20%, 30% and 45% respectively. These beneficial effects were seen already from three months onwards.

In April 2006, a team led by Lee Hooper at the University of East Anglia in Norwich, UK, published a review of almost 100 separate studies into n3 fatty acids, found in abundance in oily fish. It concluded that they do not have a significant protective effect against cardiovascular disease. This meta-analysis was controversial and stands in stark contrast with two different reviews also performed in 2006 by the American Journal of Clinical Nutrition and a second JAMA review that both indicated decreases in total mortality and cardiovascular incidents (i.e. myocardial infarctions) associated with the regular consumption of fish and fish oil supplements. In addition n3 has been shown to reduce symptoms of other mental disorders such as aggression and ADHD.

Several studies published in 2007 have been more positive. In the March 2007 edition of the journal Atherosclerosis, 81 Japanese men with unhealthy blood sugar levels were randomly assigned to receive 1800 mg daily of eicosapentaenoic acid (EPA — an n3 essential fatty acid from fish oil) with the other half being a control group. The thickness of the carotid arteries and certain measures of blood flow were measured before and after supplementation. This went on for approximately two years. A total of 60 patients (30 in the EPA group and 30 in the control group) completed the study. Those given the EPA had a statistically significant decrease in the thickness of the carotid arteries along with improvement in blood flow. The authors indicated that this was the first demonstration that administration of purified EPA improves the thickness of carotid arteries along with improving blood flow in patients with unhealthy blood sugar levels.

In another study published in the American Journal of Health System Pharmacy March 2007, patients with high triglycerides and poor coronary artery health were given 4 grams a day of a combination of EPA and DHA along with some monounsaturated fatty acids. Those patients with very unhealthy triglyceride levels (above 500 mg/dl) reduced their triglycerides on average 45% and their VLDL cholesterol by more than 50%. VLDL is a bad type of cholesterol and elevated triglycerides can also be deleterious for cardiovascular health.

Another study on the benefits of EPA was published in The Lancet in March 2007. This study involved over 18,000 patients with unhealthy cholesterol levels. The patients were randomly assigned to receive either 1,800 mg a day of EPA with a statin drug or a statin drug alone. The trial went on for a total of five years. It was found at the end of the study those patients in the EPA group had superior cardiovascular function. Non-fatal coronary events were also significantly reduced in the EPA group. The authors concluded that EPA is a promising treatment for prevention of major coronary events, especially non-fatal coronary events.

Similar to those who follow a Mediterranean diet, Arctic-dwelling Inuit - who consume high amounts of n3 fatty acids from fatty fish - also tend to have higher proportions of n3, increased HDL cholesterol and decreased triglycerides (fatty material that circulates in the blood) and less heart disease. Eating walnuts (the ratio of n3 to n6 is circa 1:4 respectively) was reported to lower total cholesterol by 4% relative to controls when people also ate 27% less cholesterol.

A study carried out involving 465 women showed serum levels of eicosapentaenoic acid is inversely related to the levels of anti-oxidized-LDL antibodies. Oxidative modification of LDL is thought to play an important role in the development of atherosclerosis.

Immune Function

Another study regarding fish oil was published in the Journal of Nutrition in April 2007. Sixty four healthy Danish infants from nine to twelve months of age received either cow's milk or infant formula alone or with fish oil. It was found that those infants supplemented with fish oil had improvement in immune function maturation with no apparent reduction in immune activation.

Brain Health

There was yet another study on n3 fatty acids published in the April 2007 Journal of Neuroscience. A group of mice were genetically modified to develop accumulation of amyloid and tau proteins in the brain similar to that seen in people with poor memory. The mice were divided into four groups with one group receiving a typical American diet (with high ratio of n6 to n3 fatty acids being 10 to 1). The other three groups were given food with a balanced 1 to 1 n6 to n3 ratio and two additional groups supplemented with DHA plus long chain n6 fatty acids. After three months of feeding, all the DHA supplemented groups were noted to have a lower accumulation of beta amyloid and tau protein. Some research suggests that these abnormal proteins may contribute to the development of memory loss in later years.

There is also a study published regarding n3 supplementation in children with learning and behavioral problems. This study was published in the April 2007 edition of the Journal of the Developmental and Behavioral Pediatrics, where 132 children, between the ages of seven to twelve years old, with poor learning, participated in a randomized, placebo-controlled, double-blinded interventional trial. A total of 104 children completed the trial. For the first fifteen weeks of this study, the children were given polyunsaturated fatty acids (n3 and n6, 3000 mg a day), polyunsaturated fatty acids plus multi-vitamins and minerals or placebo. After fifteen weeks, all groups crossed over to the polyunsaturated fatty acids (PUFA) plus vitamins and mineral supplement. Parents were asked to rate their children's condition after fifteen and thirty weeks. After thirty weeks, parental ratings of behavior improved significantly in nine out of fourteen scales. The lead author of the study, Dr. Sinn, indicated the present study is the largest PUFA trial to date with children falling in the poor learning and focus range. The results support those of other studies that have found improvement in poor developmental health with essential fatty acid supplementation.

A study examining whether omega-3 exerts neuroprotective action in Parkinson's disease found that it did, using an experimental model, exhibit a protective effect (much like it did for Alzheimer's disease as well). The scientists exposed mice to either a control or a high omega-3 diet from two to twelve months of age and then treated them with a neurotoxin commonly used as an experimental model for Parkinson's. The scientists found that high doses of omega-3 given to the experimental group completely prevented the neurotoxin-induced decrease of dopamine that ordinarily occurs. Since Parkinson's is a disease caused by disruption of the dopamine system, this protective effect exhibited could show promise for future research in the prevention of Parkinson's disease.

Rheumatoid arthritis

Research in 2005 and 2006 has suggested that the in-vitro anti-inflammatory activity of n3 acids translates into clinical benefits. Cohorts of neck pain patients and of rheumatoid arthritis sufferers have demonstrated benefits comparable to those receiving standard NSAIDs. Those who follow a Mediterranean-style diet tend to have less heart disease, higher HDL ("good") cholesterol levels and higher proportions of n3 in tissue highly unsaturated fatty acids.

Health risks

In a letter published October 31, 2000, the United States Food and Drug Administration Center for Food Safety and Applied Nutrition, Office of Nutritional Products, Labeling, and Dietary Supplements noted that known or suspected risks of EPA and DHA n3 fatty acids may include the possibility of:

- Increased bleeding if overused (normally over 3 grams per day) by a patient who is also taking aspirin or warfarin. However, this is disputed.
- Hemorrhagic stroke (only in case of very large doses).
- Reduced glycemic control among diabetics.
- An increase in concentration of LDL cholesterol in some individuals.

Subsequent advises from the FDA and national counterparts have permitted health claims associated with heart health.

Cardiac Risk

Persons with congestive heart failure, chronic recurrent angina or evidence that their heart is receiving insufficient blood flow are advised to talk to their doctor before taking n3 fatty acids. There have been concerns if such persons take n3 fatty acids or eating foods that contain them in substantial amounts. In a recent large study, n3 fatty acids on top of standard heart failure therapy produced a small but statistically significant benefit in terms of mortality and hospitalization.

In congestive heart failure, cells that are only barely receiving enough blood flow become electrically hyperexcitable. This, in turn, can lead to increased risk of irregular heartbeats, which, in turn, can cause sudden cardiac death. n3 fatty acids seem to stabilize the rhythm of the heart by effectively preventing these hyperexcitable cells from functioning, thereby reducing the likelihood of irregular heartbeats and sudden cardiac death. For most people, this is obviously beneficial and would account for most of the large reduction in the likelihood of sudden cardiac death. Nevertheless, for people with congestive heart failure, the heart is barely pumping blood well enough to keep them alive. In these patients, n3 fatty acids may eliminate enough of these few pumping cells that the heart would no longer be able to pump sufficient blood to live, causing an increased risk of cardiac death.

Research Frontiers

Developmental Differences

Although not supported by current scientific evidence as a primary treatment for ADHD, autism, and other developmental differences, omega-3 fatty acids have gained popularity for children with these conditions. A 2004 Internet survey found that 29% of surveyed parents used essential fatty acid supplements to treat children with autism spectrum disorders.

Omega-3 fatty acids offer a promising complementary approach to standard treatments for ADHD and developmental coordination disorder. Fish oils appear to reduce ADHD-related symptoms in some children. Double blind studies have showed "medium to strong treatment effects of omega 3 fatty acids on symptoms of ADHD" after administering amounts around 1 gram for three to six months.

There is very little scientific evidence supporting the effectiveness of omega-3 fatty acids for autism spectrum disorders. One randomized controlled trial found that omega-3 fatty acids did not significantly affect aberrant behavior in autistic children, and although the investigators noted reduced hyperactivity, their later reanalysis reported that the reduction was not statistically significant.

Low Birth Weight

In a study of nearly 9,000 pregnant women, researchers found women who ate fish once a week during their first trimester had 3.6 times less risk of low birth weight and premature birth than those who ate no fish. Low consumption of fish was a strong risk factor for preterm delivery and low birth weight. However, attempts by other groups to reverse this increased risk by encouraging increased pre-natal consumption of fish were unsuccessful.

Psychiatric Disorders

n3 fatty acids are known to have membrane-enhancing capabilities in brain cells. One medical explanation is that n3 fatty acids play a role in the fortification of the myelin sheaths. Not coincidentally, n3 fatty acids comprise approximately eight percent of the average human brain according to Dr. David Horrobin, a pioneer in fatty acid research. Ralph Holman of the University of Minnesota, another major researcher in studying essential fatty acids, who gave Omega-3 its name, surmised how n3 components are analogous to the human brain by stating that "DHA is structure, EPA is function."

A benefit of n3 fatty acids is helping the brain to repair damage by promoting neuronal growth. In a six-month study involving people with schizophrenia and Huntington's disease who were treated with EPA or a placebo, the placebo group had clearly lost cerebral tissue, while the patients given the supplements had a significant increase of grey and white matter.

In the prefrontal cortex (PFC) of the brain, low brain n3 fatty acids are thought to lower the dopaminergic neurotransmission in this brain area, possibly contributing to the negative and neurocognitive symptoms in schizophrenia. This reduction in dopamine system function in the PFC may lead to an overactivity in dopaminergic function in the limbic system of the brain which is suppressively controlled by the PFC dopamine system, causing the positive symptoms of schizophrenia. This is called the n3 polyunsaturated fatty acid/dopamine hypothesis of schizophrenia (Ohara, 2007). This mechanism may explain why n3 supplementation shows effects against both positive, negative and neurocognitive symptoms in schizophrenia.

Consequently, the past decade of n3 fatty acid research has procured some Western interest in n3 fatty acids as being a legitimate 'brain food'. Still, recent claims that one's intelligence quotient, psychological tests measuring certain cognitive skills, including numerical and verbal reasoning skills, are increased on account of n3 fatty acids consumed by pregnant mothers remain unreliable and controversial. An even more significant focus of research, however, lies in the role of n3 fatty acids as a non-prescription treatment for certain psychiatric and mental diagnoses and has become a topic of much research and speculation.

In 1998, Andrew L. Stoll, MD and his colleagues at Harvard University conducted a small double-blind placebo-controlled study in thirty patients diagnosed with bipolar disorder. Most subjects in this study were already undergoing psychopharmacological treatment (e.g. 12 out of the 30 were taking lithium). Over the course of four months, he gave 15 subjects capsules containing olive oil, and another 15 subjects capsules containing nine grams of pharmaceutical-quality EPA and DHA. The study showed that subjects in the n3 group were less likely to experience a relapse of symptoms in the four months of the study. Moreover, the n3 group experienced significantly more recovery than the placebo group. However, a commentary on the Stoll study notes that the improvement in the n3 group was too small to be clinically significant. Though Stoll believes that the 1999 experiment was not as optimal as it could have been and has accordingly pursued further research, the foundation has been laid for more researchers to explore the theoretical association between absorbed n3 fatty acids and signal transduction inhibition in the brain.

“Several epidemiological studies suggest covariation between seafood consumption and rates of mood disorders. Biological marker studies indicate deficits in omega3 fatty acids in people with depressive disorders, while several treatment studies indicate therapeutic benefits from omega-3 supplementation. A similar contribution of omega-3 fatty acids to coronary artery disease may explain the well-described links between coronary artery disease and depression. Deficits in omega-3 fatty acids have been identified as a contributing factor to mood disorders and offer a potential rational treatment approach.” In 2004, a study found that 100 suicide attempt patients on average had significantly lower levels of EPA in their blood as compared to controls.

In 2006, a review of published trials in the American Journal of Clinical Nutrition found that “the evidence available provides little support” for the use of fish or the n–3 long-chain polyunsaturated fatty acids contained in them to improve depressed mood. The study used results of twelve randomized controlled trials in its meta-analysis. The review recommended that “larger trials with adequate power to detect clinically important benefits” be performed. A further 2007 study published in the British Journal of Nutrition, which was placebo-controlled and used 218 participants, found that increasing EPA and DHA in the diet “was found not to have beneficial or harmful effects on mood in mild to moderate depression,” confirming previous meta-analysis “that there is an overall negligible benefit of n-3 UFA supplementation for depressed mood”.

Dietary Sources

Daily Values

As macronutrients, fats are not assigned recommended daily allowances. Macronutrients have AI (Acceptable Intake) and AMDR (Acceptable Macronutrient Distribution Range) instead of RDAs. The AI for n3 is 1.6 grams/day for men and 1.1 grams/day for women while the AMDR is 0.6% to 1.2% of total energy.

“A growing body of literature suggests that higher intakes of linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) may afford some degree of protection against coronary heart disease. Because the physiological potency of EPA and DHA is much greater than that for linolenic acid, it is not possible to estimate one AMDR for all n3 fatty acids. Approximately 10 percent of the AMDR can be consumed as EPA and/or DHA.” There was insufficient evidence as of 2005 to set a UL (upper tolerable limit) for n3 fatty acids.

A perceived risk of fish oil n3 supplementation has been heavy metal poisoning by the body’s accumulation of traces of heavy metals, in particular mercury, lead, nickel, arsenic and cadmium as well as other contaminants (PCBs, furans, dioxins), which potentially might be found especially in less-refined fish oil supplements. However, in reality, heavy metal toxicity from consuming fish oil supplements is highly unlikely. This is because heavy metals selectively bind with protein in the fish flesh rather than accumulate in the oil. An independent test in 2006 of 44 fish oils on the US market found that all of the products passed safety standards for potential contaminants. The FDA recommends that total dietary intake of n3 fatty acids from fish not exceed 3 grams per day, of which no more than 2 grams per day are from nutritional supplements.

Historically, the Council for Responsible Nutrition (CRN) and the World Health Organization (WHO) have published acceptable standards regarding contaminants in fish oil. The most stringent current standard is the International Fish Oils Standard (IFOS). Fish oils that typically make this highest grade are those that are molecularly distilled under vacuum, and have virtually no measurable level of contaminants (measured parts per billion and parts per trillion).

n3 supplementation in food has been a significant recent trend in food fortification, with global food companies launching n3 fortified bread, mayonnaise, pizza, yogurt, orange juice, children's pasta, milk, eggs, confections and infant formula.

Fish

The most widely available source of EPA and DHA is cold water oily fish such as salmon, herring, mackerel, anchovies and sardines. Oils from these fish have a profile of around seven times as much n3 as n6. Other oily fish such as tuna also contain n3 in somewhat lesser amounts. Consumers of oily fish should be aware of the potential presence of heavy metals and fat-soluble pollutants like PCBs and dioxins which may accumulate up the food chain.

Even some forms of fish oil may not be optimally digestible. Of four studies that compare bioavailability of the triglyceride form of fish oil vs. the ester form, two have concluded that the natural triglyceride form is better, and the other two studies did not find a significant difference. No studies have shown the ester form to be superior although it is cheaper to manufacture.

Although fish is a dietary source of n3 fatty acids, fish do not synthesize them; they obtain them from the algae or plankton in their diet.

This article may contain wording that promotes the subject in a subjective manner without imparting real information. Please remove or replace such wording or find sources which back the claims.

Flax

Flax seeds produce linseed oil, which has a very high n3 content
Six times richer than most fish oils in n3, Flax (aka linseed) (Linum usitatissimum) and its oil are perhaps the most widely available botanical source of n3. Flaxseed oil consists of approximately 55% ALA (alpha-linolenic acid). Flax, like chia, contains approximately three times as much n3 as n6.

15 grams of flaxseed oil provides ca. 8 grams of ALA, which is converted in the body to EPA and then DHA at an efficiency of 2–15% and 2–5%, respectively.

Botanical Sources of n3 Fatty Acids

Table 1. n3 content as the percentage of ALA in the seed oil.

Common name	Alternative name	Linnaean name	% n3
Chia	Chia Sage	Salvia hispanica	64
Kiwifruit	Chinese gooseberry	Actinidia chinensis	62
Perilla	Shiso	Perilla frutescens	58
Flax	Linseed	Linum usitatissimum	55
Lingonberry	Cowberry	Vaccinium vitis-idaea	49
Camelina	Gold-of-pleasure	Camelina sativa	36
Purslane	Portulaca	Portulaca oleracea	35
Black Raspberry		Rubus occidentalis	33

Table 2. n3 content as the percentage of ALA in the whole food.

Common name	Linnaean name	% n3
Flaxseed	Linum usitatissimum	18.1
Butternuts	Juglans cinerea	8.7
Hempseed	Cannabis sativa	8.7
Walnuts	Juglans regia	6.3
Pecan nuts	Carya illinoinensis	0.6
Hazel nuts	Corylus avellana	0.1

Eggs

Eggs produced by chickens fed a diet of greens and insects produce higher levels of n3 fatty acids (mostly ALA) than chickens fed corn or soybeans. In addition to feeding chickens insects and greens, fish oils may be added to their diet to increase the amount of fatty acid concentrations in eggs. The addition of flax and canola seeds to the diet of chickens, both good sources of alpha-linolenic acid, increases the omega-3 content of the eggs.

Meat

The n6 to n3 ratio of grass-fed beef is about 2:1, making it a more useful source of n3 than grain-fed beef, which usually has a ratio of 4:1.

In most countries, commercially available lamb is typically grass-fed, and thus higher in n3 than other grain-fed or grain-finished meat sources. In the United States, lamb is often finished (i.e. fattened before slaughter) with grain, resulting in lower n3.

The omega-3 content of chicken meat may be enhanced by increasing the animals' dietary intake of grains that are high in n3, such as flax, chia, and canola.

Other Sources

Milk and cheese from grass-fed cows may also be good sources of n3. One UK study showed that half a pint of milk provides 10% of the recommended daily intake (RDI) of ALA, while a piece of organic cheese the size of a matchbox may provide up to 88%".

The microalgae Crypthecodinium cohnii and Schizochytrium are rich sources of DHA (22:6 n3) and can be produced commercially in bioreactors. This is the only source of DHA acceptable to vegans. Oil from brown algae (kelp) is a source of EPA. Walnuts are one of few nuts that contain appreciable n3 fat, with approximately a 1:4 ratio of n3 to n6. Acai palm fruit also contains n3 fatty acids.

Omega-3 is also found in softgels in pharmacies and nowadays it is also found in combination with omega-6, omega-9 and shark liver oil

Some vegetables, too, contain a noteworthy amount of n-3, including strawberries and broccoli.

The n6 to n3 Ratio

Main article: Essential fatty acid interactions Clinical studies indicate that the ingested ratio of n6 to n3 (especially Linoleic vs Alpha Linolenic) fatty acids is important to maintaining cardiovascular health. However, two studies published in 2005 and 2007, found no such correlations in humans.

Both n3 and n6 fatty acids are essential, i.e. humans must consume them in the diet. n3 and n6 compete for the same metabolic enzymes, thus the n6:n3 ratio will significantly influence the ratio of the ensuing eicosanoids (hormones), (e.g. prostaglandins, leukotrienes, thromboxanes etc.), and will alter the body's metabolic function. Generally, grass-fed animals accumulate more n3 than do grain-fed animals which accumulate relatively more n6. Metabolites of n6 are significantly more inflammatory (esp. arachidonic acid) than those of n3. This necessitates that n3 and n6 be consumed in a balanced proportion; healthy ratios of n6:n3 range from 1:1 to 4:1.Studies suggest that the evolutionary human diet, rich in game animals, seafood and other sources of n3, may have provided such a ratio.

Typical Western diets provide ratios of between 10:1 and 30:1 — i.e., dramatically skewed toward n6.Here are the ratios of n6 to n3 fatty acids in some common oils: canola 2:1, soybean 7:1, olive 3–13:1, sunflower (no n3), flax 1:3, cottonseed (almost no n3), peanut (no n3), grapeseed oil (almost no n3) and corn oil 46 to 1 ratio of n6 to n3.

Conversion Efficiency of ALA, EPA and DHA

It has been reported that conversion of ALA to EPA and further to DHA in humans is limited, but varies with individuals.Women have higher ALA conversion efficiency than men, probably due to the lower rate of utilization of dietary ALA for beta-oxidation. This suggests that biological engineering of ALA conversion efficiency is possible. Goyens et al. argue that it is the absolute amount of ALA, rather than the ratio of n3 and n6 fatty acids, which affects the conversion.