

Long-chain fatty acids (LC-PUFAs: ARA, DHA and EPA)

AT A GLANCE

Introduction

LC-PUFAs or long chain polyunsaturated fatty acids are mainly found in the form of two families of conditionally essential fatty acids: omega-3 (n-3) and omega-6 (n-6) fatty acids. Essential fatty acids are fatty acids that cannot be synthesized within the human body, and therefore must be obtained from the diet.

Conditionally essential fatty acids are fatty acids where limited endogenous production occurs but it is insufficient to meet the nutritional requirements. Fatty acids that are not saturated with hydrogen (H) atoms (and contain more than one double bond between the atoms) are called 'polyunsaturated fatty acids' (PUFAs). Long chain polyunsaturated fatty acids LC-PUFAs possess a chain of 20 or more carbon molecules. Most LC-PUFAs are of plant and fatty fish origin.

There are three major types of omega-3 fatty acids that are ingested in foods and used by the body:

- The alpha-linolenic acid (ALA)
- The LC-PUFAs eicosapentaenoic acid (EPA)
- And the docosahexaenoic acid (DHA).

Once eaten, the body converts very limited amounts of ALA to EPA and DHA, the two types of omega-3 fatty acids most readily utilised by the body. However, for the vast majority of individuals the level of conversion is so low that ALA does not make a useful contribution to their metabolic requirement of EPA and DHA.

Most omega-6 fatty acids are consumed in the diet from vegetable oils as linoleic acid (LA). Linoleic acid is converted in the body to the long-chain polyunsaturated fatty acids gamma-linolenic acid (GLA) and arachidonic acid (ARA). Limited quantities of ARA can be obtained from the diet by the consumption of some meat and egg products. GLA can be ingested from several plant-based oils (e.g. borage oil and evening primrose oil).

Health Functions

A sufficient intake of LC-PUFAs in the form of omega-3 and omega-6 fatty acids is important as they play a critical role in:

- the development and maintenance of proper brain function
- the visual process
- immune and inflammatory responses
- and the production of hormone-like molecules.

The European Food Safety Authority (EFSA), which provides scientific advice to assist policy makers, has confirmed that clear cardiovascular health benefits have been established for the dietary intake of the LC-PUFAs omega-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) in contributing to:

- the maintenance of normal blood pressure;

- the maintenance of normal concentrations of triglycerides
- the normal function of the heart

Disease Risk Reduction

Preterm infants

The long-chain omega-3 fatty acid docosahexaenoic acid (DHA) is a major and essential building block of membranes of the brain and other nervous tissues, including the retina. Moreover, DHA appears to be important for visual and neurological processes.

Term infant formula containing at least 0.3% of the total fatty acids as DHA has been shown to aid visual maturation. Overall the studies suggest that feeding infants formula enriched with DHA and long-chain omega-6 fatty acids (arachidonic acid, AA) contribute to the visual and neurological development of preterm or term infants.

Pregnancy and breast-feeding

As the mother is the sole source of omega-3 fatty acids (e.g., docosahexaenoic acid, DHA) for the foetus and exclusively breast-fed infant, a sufficient intake during pregnancy and breast-feeding is thought to be essential to meet the infant's requirements.

Results of studies assessing effects of long-chain polyunsaturated fatty acids (PUFA) on pregnancy duration as well as the physical and mental development of children born to supplemented mothers have been mixed. However, expert panels recommended that during pregnancy and lactation women should consume at least 200 mg DHA per day and EFSA recommended that during pregnancy and lactation women should consume an additional 100 to 200 mg of DHA in addition to the 250 mg/day of EPA plus DHA recommended for healthy adults.

Heart disease

Studies have shown that higher intake levels of long-chain omega-3 fatty acids (eicosapentaenoic acid, EPA, and docosahexaenoic acid, DHA) will aid in lowering the risk factors for heart disease, most importantly high blood pressure ('hypertension') and high blood triglyceride levels.

Studies of heart attack victims have found that supplementing the diet with omega-3 fatty acids daily can reduce the risk of stroke, follow-on heart attacks, and death.

Cancer

The balance between omega-3 and omega-6 fatty acids appears to play an important role in the development and growth of some cancer forms, such as breast, colon, and prostate cancer. While further research is still needed to understand the effect that omega-3 fatty acids may have on cancer prevention or treatment, researchers speculate that omega-3 fatty acids in combination with other nutrients (e.g. vitamin C, vitamin E, beta-carotene, and coenzyme Q10) may be of particular value in the prevention and treatment of breast cancer and other hormone-induced cancers.

Some studies have shown slowing or reversing in the progression of colon cancer with daily consumption of long-chain omega-3 fatty acids (eicosapentaenoic acid, EPA, and docosahexaenoic acid, DHA).

One animal study has shown that in rats with spreading colon cancer, omega-3 fatty acids (specifically the omega-3 fatty acid alpha-linolenic acid, ALA) in fact promoted the growth of cancer cells in the liver. The reason for this is not clear and needs further investigation.

Both population studies as well as clinical studies suggest that omega-3 fatty acids may inhibit the growth of prostate cancer.

While in one study, the omega-3 fatty acid alpha-linolenic acid (ALA) has been seen in higher levels in individuals with prostate cancer, suggesting ALA may have a cancer-promoting role, more recent studies that were specifically designed to look for prostate cancer risk factors in humans and a systematic review found no such link.

Age-related eye disease

A clinical study comparing people with age-related macular degeneration, a serious eye condition that can progress to blindness, to individuals without the eye disease found that those with a healthy dietary balance of omega-3 and omega-6 fatty acids and higher intake of fish in their diets were less likely to have this particular eye disorder.

Another larger clinical study confirms that consuming long-chain omega-3 fatty acids (eicosapentaenoic acid, EPA, and docosahexaenoic acid, DHA) from fish four or more times per week may reduce the risk of developing macular degeneration. Notably, however, this same study suggests that omega-3 fatty acid alpha-linolenic acid (ALA) may actually increase the risk of this eye condition; the reason for this is not clear.

Alzheimer's disease

An insufficient intake of long-chain omega-3 fatty acids (docosahexaenoic acid, DHA) may be a risk factor for cognitive decline, Alzheimer's disease and other types of dementia, but it is not yet known whether DHA supplementation can help prevent or treat such cognitive disorders.

Other Applications

Please note:

Any dietary or drug treatment with high-dosed micronutrients needs medical supervision.

Heart disease

There is some evidence that omega-3 fatty acids may treat and even prevent atherosclerosis by inhibiting the development of plaque and blood clots which can clog arteries.

Diabetes

Individuals with diabetes tend to have high blood fat (triglyceride) levels. Studies have shown that omega-3 fatty acids from fish oil can help to lower triglycerides, so people with diabetes may benefit from eating foods or taking supplements that contain long-chain omega-3 fatty acids (eicosapentaenoic acid, EPA, and docosahexaenoic acid, DHA).

The omega-3 fatty acid alpha-linolenic acid (ALA) may not have the same benefit as DHA and EPA because some people with diabetes lack the ability to efficiently convert ALA to a form of omega-3 fatty acids that the body can use readily.

There have been slight increases reported in fasting blood sugar levels in patients with type 2 diabetes while taking very high doses of fish oil supplements.

Inflammatory diseases

Several studies investigating the use of omega-3 fatty acid supplements for inflammatory joint conditions (e.g., rheumatoid arthritis) concluded that the supplements reduce tenderness in joints, decrease morning stiffness, and allow for a reduction in the amount of medication needed for people with rheumatoid arthritis.

In addition, some studies suggest that diets rich in omega-3 fatty acids (and low in the inflammatory omega-6 fatty acids) may benefit people with other inflammatory disorders, such as Crohn's disease and asthma. However, study results have been mixed and more evidence is needed to draw any definitive conclusions.

Mental disorders

Omega-3 fatty acids are important components of nerve cell membranes; they help nerve cells communicate with each other, which is an essential step in maintaining good mental health. In particular, the long-chain omega-3 fatty acid docosahexaenoic acid (DHA) is involved in a variety of nerve cell processes.

Levels of omega-3 fatty acids were found to be measurably low and the ratio of omega-6 to omega-3 fatty acids were particularly high in a clinical study of patients hospitalized for depression. In a clinical study of individuals with depression, those who ate a healthy diet consisting of fatty fish 2–3 times per week for 5 years experienced a significant reduction in feelings of depression. A recent meta-analysis concluded that beneficial effects on depression only occur when the ratio of EPA to DHA in the marine oil favours EPA.

In a clinical study in people with bipolar disorder, those who were treated with the long-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in combination with their usual mood stabilizing medications experienced fewer mood swings and recurrence of either depression or mania than those who received a placebo. However, another study treating individuals with bipolar depression did not find evidence of efficacy for the use of EPA in these patients.

Preliminary clinical evidence suggests that people with schizophrenia experience an improvement in symptoms when given omega-3 fatty acids. However, a recent well-designed study concluded that EPA supplements are no better than placebo in improving symptoms of this condition. The conflicting results suggest that more research is needed before conclusions can be drawn.

Children with attention deficit/hyperactivity disorder (ADHD) may have low levels of certain essential fatty acids (including EPA and DHA) in their bodies. Several clinical studies using omega-3 and omega-6 fatty acid supplementation in children and adolescents with ADHD found improvements in reading and level of attention and hyperactivity. The results of the studies have been mixed but overall, they indicate an improvement in the ADHD symptoms. More studies, including comparisons with drug therapies, are needed to evaluate these results.

Clinical studies suggest that men and women with the eating disorder anorexia nervosa have lower than optimal levels of polyunsaturated fatty acids (including omega-3 fatty acid alpha-linolenic acid, ALA, and long-chain omega-6 fatty acid gamma-linolenic acid, GLA.) To prevent the complications associated with essential fatty acid deficiencies, some experts recommend that treatment programs for anorexia nervosa include polyunsaturated fatty acid-rich foods such as fish and organ meats.

Osteoporosis

Studies suggest that long-chain omega-3 fatty acid eicosapentaenoic acid (EPA) may help increase calcium levels in the body, deposit calcium in the bones, and improve bone strength.

In a study of women over 65 with osteoporosis, those given EPA and long-chain omega-6 fatty acid gamma-linolenic acid (GLA) supplements experienced significantly less bone loss over a three-year period than those who were given a placebo. . However, more studies are needed to confirm those results.

Weight loss

Clinical studies suggest that overweight people who follow a weight loss program that includes exercise tend to achieve better control over their blood sugar and cholesterol levels when fish rich in omega-3 fatty acids (such as salmon, mackerel, and herring) is a staple in their low-fat diet.

Other disorders

While further research is needed, some evidence suggests that omega-3 fatty acids may also prove helpful in protecting against some infections and treating a variety of additional conditions including emphysema, glaucoma, menstrual pain, migraine headaches, concussion, multiple sclerosis, lupus, Lyme disease, panic attacks, preeclampsia, preterm delivery, psoriasis, stress, and ulcers.

Intake Recommendations

European health authorities have established intake recommendations for LC-PUFAs for adults:

- an omega-3 fatty acid intake of 2 g/day alpha-linolenic acid (ALA) and 250 mg/day long-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)
- an omega-6 fatty acid intake of 10 g/day linoleic acid (LA).

Scientists have suggested a minimum daily intake of 500 mg EPA and DHA combined for healthy individuals.

In the U.S., adequate intakes for adults have been set at 1.6 g omega-3 fatty acids (ALA) per day for men, 1.1 g/day for women respectively, and 17 g omega-6 fatty acids (LA) per day for men (19–50 years of age), 12 g/day for women (19–50 years of age) respectively.

The American Heart Association recommends eating fish (particularly fatty fish such as mackerel, lake trout, herring, sardines, albacore tuna, and salmon) at least twice a week.

It is advised that pregnant women and mothers, nursing mothers, young children, and women who might become pregnant not eat several types of fish, including swordfish, shark, and king mackerel, which have higher levels of contaminants (e.g., mercury). They are advised to consume polyunsaturated fatty acid supplements.

It is important to maintain an appropriate balance of omega-3 and omega-6 in the diet, as these two substances work together to promote health. Omega-3 fatty acids, for example, help reduce inflammation, and most omega-6 fatty acids tend to promote inflammation. An inappropriate balance of these essential fatty acids contributes to the development of disease whereas a proper balance helps maintain and even improve health.

A healthy diet should consist of roughly 2–4 times more omega-6 fatty acids than omega-3 fatty acids. The typical diet in developed countries ('Western diet') tends to contain 14–25 times more omega-6 fatty acids than omega-3 fatty acids, and many researchers believe this imbalance is a significant factor in the rising rate of inflammatory disorders. In contrast, the 'Mediterranean diet' consists of a healthier balance between omega-3 and omega-6 fatty acids, and many studies have shown that people who follow this diet are less likely to develop heart disease.

Supply Situation

In general, dietary intakes of omega-6 fatty acids are well above the recommendations defined in most European countries, while the intakes of long-chain omega-3 fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are mostly lower than recommended by national authorities.

A similar situation exists in the U.S.: while a healthy diet should consist of roughly 2–4 times more omega-6 fatty acids than omega-3 fatty acids, the typical American (Western) diet tends to contain 14–25 times more omega-6 fatty acids than omega-3 fatty acids.

Deficiency

Essential fatty acid deficiency is rare and has been found to occur in patients with a chronic poor absorption of fat from food, some patients nourished intravenously, and in patients with cystic fibrosis.

Because the last three months of pregnancy are a critical period for the accumulation of the omega-3 fatty acid docosahexaenoic acid (DHA) in the brain and retina, new born term and preterm infants are thought to be particularly vulnerable to adverse effects of insufficient DHA. Therefore, it has been proposed that term and preterm infant formulas be supplemented with enough DHA to bring blood and cellular DHA levels of formula-fed infants up to those of breast-fed infants.

Symptoms of omega-3 fatty acid deficiency include extreme tiredness (fatigue), poor memory, dry skin, heart problems, mood swings or depression, and poor circulation.

Infants who do not get enough omega-3 fatty acids from their mothers during pregnancy are at risk of developing vision and nerve problems.

Sources

The LC-PUFA Omega-3 fatty acids EPA and DHA can be found in fatty fish, such as salmon, tuna, anchovies and sardines, and other marine life such as algae and krill. The terrestrial omega 3 fatty acid ALA is found in some vegetable (e.g. rape seed/canola, chia) and nut (e.g. walnut) oils.

Food sources of omega-6 fatty acids include vegetable oils, such as soybean, safflower, and corn oil, nuts, seeds, and - in small amounts - in meat, poultry, and eggs.

In addition, supplements containing omega-3 fatty acids (based on fish oils or algae) and omega-6 fatty acids (based on borage or black current seed oil, as well as evening primrose oil) are available.

Safety

Omega-3 fatty acids

High doses of omega-3 fatty acids should be used cautiously by people who bruise easily, have a bleeding disorder, or take blood-thinning medications, because excessive amounts of omega-3 fatty acids may lead to bleeding. EFSA has determined that a daily intake of 5g per day of EPA and DHA is safe for healthy adults.

Fish oil can cause flatulence, bloating, belching, and diarrhoea in a few individuals.

Individuals with type 2 diabetes may experience increases in fasting blood sugar levels while taking high doses of fish oil supplements; supervision by a health care provider is recommended.

Studies have shown that some omega-3 fatty acids may reduce the risk of developing macular degeneration.

In contrast, some studies suggest that high doses of ALA may increase the risk of developing this disorder.

As these studies are inconclusive, more research is needed to evaluate any potential risk.

Some studies have shown that omega-3 fatty acids may reduce the risk of developing some cancers. In contrast, an analysis has suggested that consumption of high doses of ALA may increase the risk of prostate cancer. However, more recent studies and a systematic review found no such link. Fish (and fish oil supplements) may contain potentially harmful contaminants, such as heavy metals

(including mercury), dioxins, and polychlorinated biphenyls (PCBs). Excessive exposure to those toxic substances can cause brain and kidney damage. The developing fetus, infants, and young children are especially vulnerable to the toxic effects of mercury on the brain. In order to limit the exposure of these groups to mercury, health authorities recommend women who may become pregnant, pregnant women, and breast-feeding women not to eat fish that contain high mercury levels (e.g., shark, swordfish, king mackerel, or golden snapper) but to consume a variety of fish that are lower in mercury (e.g., tuna, shrimp, salmon, catfish, and pollock.)

Omega-6 fatty acids

Omega-6 fatty acids should not be used in individuals with seizure disorder because there have been reports of these supplements (e.g., evening primrose oil) inducing seizures.

Borage seed oil, and possibly other sources of gamma-linolenic acid (GLA), should not be used during pregnancy because they may be harmful to the fetus and induce early labor.

Doses of GLA greater than 3,000 mg per day should be avoided because, at that point, production of arachidonic acid (ARA) increases, which may cause and increase inflammation in adults.

Side effects of evening primrose oil can include occasional headache, abdominal pain, nausea, and loose stools.

Animal studies have shown that omega-6 fatty acids (linoleic acid and arachidonic acid), such as the fat found in corn oil, promote the growth of prostate tumor cells. More research is needed to evaluate potential cancer-promoting effects in humans.

Drug interactions

Please note:

Because of the potential for interactions, dietary supplements should not be taken with medication without first talking to an experienced healthcare provider.

Nutrient interactions

It has been suggested that the amount of vitamin E required increases with the amount of polyunsaturated fatty acids consumed.

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