

# Biosynthesis of Omega 3' fatty Acids and the Activation of Anticancerous Effect in Human

Dr. Y. Thangam<sup>1</sup>, B. Ranchitha<sup>2</sup>

Assistant Professor of Zoology, J. K. K. Nataraja College of Arts and Science, Komarapalayam, Namakkal Dt, Tamilnadu, India

**Abstract:** *Omega-3 fatty acids play a crucial role in brain function, as well as normal growth and development. They have also become popular because they may reduce the risk of heart disease. Fish contain unsaturated fatty acids, which, when substituted for saturated fatty acids such as those in meat, may lower cholesterol. The main beneficial nutrient appears to be omega-3 fatty acids in fatty fish. Omega-3 fatty acids are a type of unsaturated fatty acid that may reduce inflammation throughout the body. Inflammation in the body can damage the blood vessels and lead to heart disease. Patients taking more than 3 grams of omega-3 fatty acids from capsules should do so only under a physician's care. High intakes could cause excessive bleeding in some people. However, more recent research suggests that other nutrients in fish or a combination of omega-3 fatty acids and other nutrients in fish may actually be responsible for the health benefits and the prevention of diseases like Coronary heart disease, Atherosclerosis, Rheumatic arthritis, Cancer diagnosis, Breast cancer, and Cardio vascular diseases.*

**Keywords:** Alpha linolenic acid, Eicosapentaenoic acid, Docosahexaenoic acid, Diagnosis of Coronary heart disease, Atherosclerosis, Rheumatic arthritis, Cancer diagnosis, Breast cancer, and Cardio vascular diseases

## 1. Introduction

Omega-3 fatty acids are considered essential fatty acids. They are necessary for human health, but the body can't make them. Omega-3 fatty acids are found in fish. Fish is a good source of protein and, unlike fatty meat products; it's not high in saturated fat. Fish is a good source of omega-3 fatty acids. Omega-3 fatty acids benefit the heart of healthy people, and those at high risk of cardiovascular disease. Research has shown that omega-3 fatty acids decrease risk of arrhythmias (abnormal heartbeats), which can lead to sudden death. Omega-3 fatty acids also decrease triglyceride levels, slow growth. Fish processing generates valuable byproducts that are high in protein and lipids, such as viscera, skin, tails, heads and frames. The disposal of these nutrient-rich byproducts can often increase costs. By using enzymes to valorize byproducts, processors can potentially obtain additional revenue from nutritional supplements, ingredients for pet food, biodiesels, fertilizers, agricultural products, animal and fish feeds. Many processors do not capture the full value of these byproducts. This may be due to inefficient secondary processing and over-reliance on mechanical, heat or chemical methods. (Cho, 1999).

Omega-3 fatty acids include docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA) and alpha-linolenic acid (ALA). A number of clinical studies have shown omega-3 fatty acids are essential for normal infant vision development. DHA and other omega-3 fatty acids are found in maternal breast milk and also are added to some supplemented infant formulas. Omega-3 supplemental formulas appear to stimulate vision development in infants. According to an analysis of several studies conducted by researchers at Harvard School of Public Health, the authors found that healthy pre-term infants who were fed DHA-supplemented formula showed significantly better visual acuity at 2 and 4 months of age, compared with similar pre-term infants who were fed formula that did not contain the omega-3 supplement. Adequate amounts of DHA and other omega-3 fatty acids in the diet of pregnant women also

appear to be important in normal infant vision development. There are three major types of omega-3 fatty acids that are ingested and used by the body (Davidson, 2013).

- Alpha-linolenic acid (ALA)
- Eicosapentaenoic acid (EPA)
- Docosahexaenoic acid (DHA)

The body converts ALA to EPA and DHA. ALA is short for alpha-linolenic acid. This is the most common omega-3 fatty acid in the diet. It is 18 carbons long, with three double bonds. ALA is mostly found in plant foods, and needs to be converted into the EPA or DHA before it can be utilized by the human body. However, this conversion process is inefficient in humans. Only a small percentage of ALA is converted into EPA, and even less into DHA. When ALA is not converted to EPA or DHA, it remains inactive and is simply stored or used as energy, like other fats. Some observational studies have found an association between a diet rich in ALA and a reduced risk of heart disease deaths, while others have found an increased risk of prostate cancer. This increase in prostate cancer risk was not associated with the other main omega-3 types, EPA and DHA, which actually had a protective effect. ALA is found in many plant foods, including kale, spinach, purslane, soybeans, walnuts and many seeds such as chia, flax and hemp seeds. ALA is also found in some animal fats. Some seed oils, such as flaxseed oil and rapeseed (canola) oil are also high in ALA (Conquer, *et al.*, 1997; Burdge, 2004).

EPA is short for eicosapentaenoic acid. It is 20 carbons long, with 5 double bonds. Its main function is to form signaling molecules called eicosanoids, which play numerous physiological roles. Eicosanoids made from omega-3s reduce inflammation, while those made from omega-6s tend to increase inflammation. For this reason, a diet high in EPA may reduce inflammation in the body. Chronic, low-level inflammation is known to drive several common diseases. Several studies have shown that fish oil, which is high in EPA and DHA, may reduce symptoms of depression. Both EPA and DHA are mostly found in seafood, including fatty

fish and algae. For this reason, they are often called marine omega-3s. EPA concentrations are highest in herring, salmon, eel, shrimp and sturgeon. Grass-fed animal products, such as dairy and meats, also contain some EPA (Flock *et al.*, 2013).

DHA is short for docosahexaenoic acid. It is 22 carbons long, with 6 double bonds. DHA is an important structural component of skin and the retina in the eye ( SanGiovanni and Chew, 2005). Fortifying baby formula with DHA leads to improved vision in infants. DHA is absolutely vital for brain development and function in childhood, as well as brain function in adults. Early-life DHA deficiency is associated with problems later on, such as learning disabilities, ADHD, aggressive hostility and several other disorders. A decrease in DHA during aging is also associated with impaired brain function and the onset of Alzheimer's disease. DHA is also reported to have positive effects on diseases such as arthritis, high blood pressure, type 2 diabetes and some cancers. The role of DHA in heart disease is also well established. It can reduce blood triglycerides, and may lead to fewer harmful LDL particles. DHA also causes the breakup of so called *lipid rafts* in membranes, making it more difficult for cancer cells to survive and for inflammation to occur. Several studies suggest omega-3 fatty acids may help protect adult eyes from macular degeneration and dry\_eye syndrome. Essential fatty acids also may help proper drainage of intraocular fluid from the eye, decreasing the risk of high eye pressure and glaucoma. Also, a 2009 National Eye Institute (NEI) study that used data obtained from the Age-Related Eye Disease Study (AREDS) found participants who reported the highest level of omega-3 fatty acids in their diet were 30 percent less likely than their peers to develop macular degeneration during a 12-year period (Calder, 2013).

(DHA) and eicosapentaenoic acid (EPA) play a host of vital roles in neuronal structure and function, protecting them from oxidative damage, inflammation, and the cumulative destruction inflicted. The long-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are important in generating bioactive lipid mediators important in inflammation resolution. As key components of phospholipid membranes and lipid rafts that serve to organize or separate molecules, these fatty acids also affect cell signaling thought to impact breast carcinogenesis. The ability of long-chain omega-6 fatty acids to modulate inflammation and other Women with evidence of high intake ratios of the marine omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) relative to the omega-6 arachidonic acid have been found to have a reduced risk of breast cancer compared with those with low ratios in some but not all case-control and cohort studies. If increasing EPA and DHA relative to arachidonic acid is effective in reducing breast cancer risk, likely mechanisms include reduction in pro inflammatory lipid derivatives, inhibition of nuclear factor- $\kappa$ B-induced cytokine production, and decreased growth factor receptor signaling as a result of alteration in membrane lipid rafts. Primary prevention trials with either risk biomarkers or cancer incidence as endpoints are underway but final results of these trials are currently unavailable. EPA and DHA supplementation is also being explored in an effort to help prevent or alleviate common

problems after a breast cancer diagnosis, including cardiac and cognitive dysfunction and chemotherapy-induced peripheral neuropathy (Harris, 2009; Hooper, *et al.*, 2006).

Evidence for Coronary heart disease suggests that people who have low levels of EPA and DHA may have a higher risk of coronary heart disease and heart failure. Clinical trials suggest that omega-3 fatty acids may have benefits in terms of reducing total and heart disease mortality (death). It is believed that omega-3 fatty acids may help lower triglycerides and inflammation. Daily intake has been linked to a reduced risk of sudden heart failure. Coronary heart disease and heart failure. High blood pressure: Many studies report that omega-3 fatty acids may help reduce blood pressure. However, effects have generally been small, and other trials reported no benefit. Effects may be greater in people who have higher blood pressure and may depend on the dose. DHA may have greater benefits than EPA. Hyperlipidemia (triglyceride lowering): Maternal nutrition guidelines have always stressed a diet including sufficient caloric and protein requirements, but recently fatty acids have also been deemed important. This is partially due to the fact that EPA and DHA supplementation during pregnancy has been associated with multiple benefits for the infant. During pregnancy, the placenta transfers nutrients, including DHA, from the mother to the fetus. The amount of omega-3 fatty acid in the fetus is correlated with the amount ingested by the mother, so it is essential that the mother has adequate nutrition (Horvath, 2007).

Fish oil when consumed, activities like weight loss, exercise performance and muscle strength, muscle soreness after exercise, pneumonia, cancer, lung disease, seasonal allergies, chronic fatigue syndrome, and for preventing blood vessels from re-narrowing after surgery to widen them. Fish oil is also used for diabetes, prediabetes, asthma, a movement and coordination disorder called dyspraxia, dyslexia, eczema, autism, obesity, weak bones (osteoporosis), rheumatoid arthritis (RA), osteoarthritis, psoriasis, an autoimmune disease called systemic lupus erythematosus (SLE), multiple sclerosis, HIV/AIDS, cystic fibrosis, gum disease, Lyme disease, sickle cell disease, and preventing weight loss caused by some cancer drugs. Fish oil is used intravenously (by IV) for scaly and itchy skin (psoriasis), blood\_infection, cystic fibrosis, pressure ulcers. Fish oil is applied to the skin for psoriasis. A lot of the benefit of fish oil seems to come from the omega-3 fatty acids that it contains. Interestingly, the body does not produce its own omega-3 fatty acids. Nor can the body make omega-3 fatty acids from omega-6 fatty acids, which are common in the Western diet. A lot of research has been done on EPA and DHA, two types of omega-3 acids that are often included in fish oil supplements. Omega-3 fatty acids reduce pain and swelling. This may explain fish oil is likely effective for psoriasis and dry eyes. These fatty acids also prevent the blood from clotting easily. This might explain the fish oil is helpful for some heart conditions. (Kris-Etherton, *et al.*, 2002).

CHD is caused by atherosclerosis. This is a long-term process in which fatty acid deposits of plaque buildup on the inside of the coronary arteries. These are the blood vessels that supply the heart muscle with oxygen and nutrients. In

the long run, the coronary arteries become so narrow that the flow of blood to the heart muscle is decreased or easily blocked by plaque or a blood clot. CHD can produce chest pain, called angina, heart attack, or both. Atherosclerosis begins when the inside wall of an artery is damaged by inflammation or high levels of cholesterol and triglycerides. Triglycerides is another form of fat in the blood. A diet high in fat, especially saturated fat, increases cholesterol and triglycerides. Artery damage can also be caused by high blood pressure, tobacco smoke, or diabetes. Cholesterol and triglycerides should be below recommended levels. This could help prevent heart disease. According to the National Heart, Lung, and Blood Institute, that means a total cholesterol level of less than 200 mg/dl and a triglyceride level of less than 150 mg/dl. To lower the levels of cholesterol and triglycerides, one should maintain a healthy weight, do moderately demanding physical activity most days of the week, eat a diet rich in vitamins, minerals, and fiber. Also include fish containing omega-3 fatty acids at least twice a week (Zheng, *et al.*, 2012; Bemelmans, *et al.*, 2004).

In clinical trials eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in the form of fish oils along with anti rheumatic drugs improve joint pain in patients with rheumatoid arthritis; have a beneficial effect in patients with ulcerative colitis; and in combination with drugs, improve the skin lesions, lower the hyperlipidemia from exterminates, and decrease the toxicity of cyclosporin in patients with psoriasis. In various animal models omega 3 fatty acids decrease the number and size of tumors and increase the time elapsed before appearance of tumors. Studies with nonhuman primates and human newborns indicate that DHA is essential for the normal functional development of the retina and brain, particularly in premature infants. Because omega 3 fatty acids are essential in growth and development throughout the life cycle, they should be included in the diets of all humans. Omega-3 and omega 6 fatty acids are not inter convertible in the human body and are important components of practically for all cell membranes. Whereas cellular proteins are genetically determined, the polyunsaturated fatty acid (PUFA) composition of cell membranes to a great extent dependent on the dietary intake (Peet, *et al.*, 1998).

The cardio protective power of omega-3 fatty acids has been thoroughly documented in clinical literature. Less well known is their paramount role in optimizing many facets of brain function, from depression, cognition, and memory to mental health. Recent research has opened up a new horizon in our understanding of omega-3s' profound ability to half age-related decline and pathology, shattering the long-held medical belief that brain shrinkage and nerve cell death is progressive and irreversible. Omega-3s have been shown to possess antidepressant and neuro protective properties. One recent landmark study found that aging humans who consumed more omega-3s had increased gray matter brain volume and that most new tissue development was observed in the part of the brain associated with *happiness*.<sup>1</sup> Similar findings appeared in the prestigious journal *Lancet*.<sup>2</sup> In one of the largest studies of its kind, scientists analyzing the diets of 12,000 pregnant women found that children of those who consumed the least omega-3 were 48% more likely to

score in the lowest quartile on IQ tests. In this article, the latest research on these essential fatty acids' importance to the growth, development, and function of the human brain is detailed and the intrinsic power to preserve cognition and memory and *reverse* age-related loss of brain function and also discover exciting findings on their unique capacity to combat multiple forms of mental illness, neuropsychiatric disorders, and aberrant behavior, from Alzheimer's disease and aggression to bipolar disorder and depression. Key Nutrient from the Cradle to the Grave Approximately 8% of the brain's weight is comprised of omega-3 fatty acids the building block for an estimated 100 billion neurons (Hibbeln, 1998; Hooijmans 2008).

## 2. Materials and Methods

Omega3' fattyacid isolated by Hazura K and Monatshin 1887. The exact structure was clarified by Erdmann 1909 and was synthesized by Nigama and Weedonin1956. It is produced *de novo* from **linoleic acid**, in a desaturation reaction catalyzed by  $\Delta 15$ -desaturase. In turn **linoleic acid** is formed from **oleic acid converted into EPA and DHA** in a desaturation reaction. It is a **polyunsaturated fatty acid** (PUFA) with three *cis* (Z) double bounds (the first one from the methyl end is in omega-3 ( $\omega$ -3) or n-3, 18:3n-3) member of the sub-group called long chain fatty acids (LCFA), from 14 to 18 carbon atoms.

### 1. Coronary heart disease(CHD)

Coronary heart disease diagnosed by Electrocardiogram (ECG), Echocardiogram, Stress test, Cardiac catheterization or angiogram, Heart scan.

### 2. Atherosclerosis (ATS)

Blood tests, Doppler ultrasound, Ankle-brachial index.

### 3. Rheumatoid Arthritis (RA)

Can Nerve Stimulation Therapy, Blood Tests, Inflammation, Antibodies, Imaging Tests.

### 4. Cancer Diagnosis

LabTests, Imaging Procedures, CTScan, Nuclearscan, MRI-scan, PETscan, X-rays and Biopsy.

**With a needle:** The doctor uses a needle to withdraw tissue or fluid.

**With an endoscope:** The doctor looks at areas inside the body using a thin, lighted tube called an endoscope.

**With surgery:** Surgery may be excisional or incisional. In an excisional biopsy, the surgeon removes the entire tumor. Often some of the normal tissue around the tumor also is removed. In an incisional biopsy, the surgeon removes just part of the tumor.

### 5. Breast cancer

Mammogram, Ultrasound, MRI-scan, Biopsy, Lab Tests.

### 6. Cardio vascular disease

Cardio vascular disease is diagnosed by Electrocardiogram (ECG), Holter monitoring, Echocardiogram, Cardiac catheterization, Cardiac computerized tomography (CT) scan, Cardiac magnetic resonance imaging (MRI).

### 3. Results

Table 1 Represents the synthesis and changes of omega 3' fatty acids , in Alpha linolenic acid (ALA), Docosahexaenoic acid (DHA), Eicosapentaenoic Acid (EPA). These acids are utilized as drugs for patients with combination of other drugs to recover the diseases like Prostate cancer (PC), Abnormal heart rhythms (AHR), Menopausal in women and Depression (MDP), Macular degeneration (MD), and Alzheimizers (ALZM) in different number of patients were observed. ALA were injected along with other drugs the prostate cancer were improved to 23% and 16% of the patient were died. In 62 patient the disease affected by AHR, the DHA were induced and about 92% were improved and death percent decreased to 5%. The patient affected by MPD, the improved percent were increased when compared with death percent due to the injection of EPA. The improved percent is 86% and death percent is 9%.

**Table 1:** Synthesis of omega 3' fatty acids in different disease in number of patients with improved and death percent

S. No	Number of patient	Omega 3 fatty acid	Diseases	Improved %	Death%
1	68	ALA	Prostate cancer	23%	16%
2	62	DHA	Abnormal heart rhythms	92%	5%
3	56	EPA	Menopausal in women, Depression	86%	9%
4	40	ALA	Macular degeneration	16%	4%
5	59	DHA	Alzheimer's disease	42%	1.5%

**Table II.** Evaluate the changes and synthesis of omega 3' fatty acids and the combination of fatty acids , DHA+EPA, EPA+DHA, ALA+DHA in patient and the diseases are the Coronary heart disease (CHD), Atherosclerosis (ATS), Breast cancer (BC), Rheumatoid arthritis (RA), and Cardiovascular disorder (CVD).The coronary heart disease improved due to the exposure of DHA+EPA and the improved percent were 20% and the death percent is 8%. When EPA+DHA acids with combination of drugs 10% were improved in patients undergone with ATS. The deaths were 2%. The BC improved 32%, while the deaths were 14% due to the injestion of EPA+DHA. The patient with RA disease were improved 48% when omega 3' fatty acids DHA+EPA were exposed. The combination of the drugs along with ALA+DHA the CVD patients improved 76% and the death rate about 33% were observed.

**Table 2:** Synthesis of omega 3' fatty acids in different disease in number of patients with improved and death percent

S. No	Number of patient	Omega 3 fatty acid	Diseases	Improved %	Death %
1	44	DHA+EPA	Coronary heart disease	20%	8%
2	14	EPA+DHA	Atherosclerosis	10%	2%
3	72	EPA+DHA	Breast cancer	32%	14%
4	58	DHA+EPA	Rheumatoid arthritis	48%	12%
5	66	ALA+DHA	Cardiovascular disorder	76%	33%

### 4. Discussion

Fatty acids are the "building blocks" of fat. These important nutrients are critical for the normal production and functioning of cells, muscles, nerves and organs. Fatty acids also are required for the production of hormone-like compounds that help to regulate the blood pressure, heart rate and blood clotting. Some fatty acids called essential fatty acids (EFAs) are necessary to our diet, because our body can't produce them. To stay healthy, we must obtain these fatty acids from our food. Two types of EFAs are omega-3 fatty acids and omega-6 fatty acids. Studies have found that omega-3 fatty acids, in particular, may benefit eye health. Several sources of information suggest that man evolved on a diet with a ratio of omega 6 to omega 3 fatty acids of approximately 1 whereas today this ratio is approximately 10:1 to 20-25:1, indicating that Western diets are deficient in omega 3 fatty acids compared with the diet on which humans evolved and their genetic patterns were established. Omega-3 fatty acids increase bleeding time; decrease platelet aggregation, blood viscosity, and fibrinogen; and increase erythrocyte deformability, thus decreasing the tendency to thrombus formation. In no clinical trial, including coronary artery graft surgery, has there been evidence of increased blood loss due to ingestion of omega 3 fatty acids. The American Heart Association (AHA) recommends eating fish (particularly fatty fish such as mackerel, lake trout, herring, sardines, albacore tuna, and salmon) at least 2 times a week. Research shows that omega-3 fatty acids reduce inflammation and may help lower risk of chronic diseases such as heart disease, cancer, and arthritis (Mozaffarian and Wu, 2011; Rangel-Huerta, *et al.*, 2012; Miles and Calder, 2012).

Omega-3 fatty acids are highly concentrated in the brain and appear to be important for cognitive (brain memory and performance) and behavioral function. In fact, infants who do not get enough omega-3 fatty acids from their mothers during pregnancy are at risk for developing vision and nerve problems. Symptoms of omega-3 fatty acid deficiency include fatigue, poor memory, dry skin, heart problems, mood swings or depression, and poor circulation. It is important to have the proper ratio of omega-3 and omega-6 (another essential fatty acid) in the diet. Omega-3 fatty acids help reduce inflammation, and most omega-6 fatty acids tend to promote inflammation. The typical American diet contains 14 to 25 times more omega-6 fatty acids than omega-3 fatty acids, which may nutritionally oriented physicians, consider to be too high on the omega-6 side.

Indeed, studies suggest that higher dietary omega-6 to omega-3 ratios appear to be associated with worsening inflammation over time and a higher risk of death among hemodialysis patients. The Mediterranean diet, on the other hand, has a healthier balance between omega-3 and omega-6 fatty acids. Many studies have shown that people who follow this diet are less likely to develop heart disease. The Mediterranean diet emphasizes foods that are rich in omega-3 fatty acids, including whole grains, fresh fruits and vegetables, fish, olive oil, garlic, and moderate wine consumption (Innis, 2008; Ameer *et al.*, 2012; Larque, *et al.*, 2002; AHA, 2015; US Department of Agriculture, Agricultural Research Service, 2014).

Omega-3 fatty acids used cautiously by people who bruise easily, have a bleeding disorder, or take blood-thinning medications, including warfarin (Coumadin), clopidogrel (Plavix), or aspirin. High doses of omega-3 fatty acids may increase the risk of bleeding, in people without a history of bleeding disorders, and even in those who are not taking other medications. Because of the potential for side effects and interactions with medications, should only take dietary supplements only under the supervision of a knowledgeable health care provider. Fish oil can cause gas, bloating, belching, and diarrhea. Time release preparations may reduce these side effects. People with either diabetes or schizophrenia may lack the ability to convert alpha-linolenic acid (ALA) to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the forms more readily absorbed by the body. People with these conditions should be sure to get enough EPA and DHA from their diets. Also, people with type 2 diabetes may experience increases in fasting blood sugar levels while taking fish oil supplements. For type 2 diabetes, use fish oil supplements only under the supervision of a health care provider. Although studies suggest that eating fish (which includes the omega-3 fatty acids EPA and DHA) may reduce the risk of macular degeneration, a more recent study including 2 large groups of men and women found that diets rich in ALA may increase the risk of this disease. Until more information becomes available, people with macular degeneration should get omega-3 fatty acids from sources of EPA and DHA, rather than ALA. Fish and fish oil may protect against prostate cancer, but some suggest that ALA may be associated with increased risk of prostate cancer in men. More research in this area is needed (Holman *et al.*, 1982; Jeppesen *et al.*, 2013; Friedberg *et al.*, 1998; Montori *et al.*, 2000).

The inflammation-resolving properties and favorable effects of EPA and DHA on oncogenic proteins, as well as on the cardiovascular, bone, and central nervous system, make them excellent candidates for primary and secondary breast cancer prevention trials for individuals at increased risk as well as breast cancer survivors. Interventional trials in these cohorts are ongoing. As shown by huge amount of assays in human as well as in animal models, w-3 Omega acids play important role in the development and maintenance of different organs, primarily the brain, and could be useful in the prevention of different pathologies, mainly the cardiovascular diseases, and, as proposed recently, some psychiatric, dermatological or rheumatologic disorders. The impact (qualitative and quantitative) of alterations in the

lipid composition of animal foods on the nutritional value of derived products (in terms of EPA and DHA content) eaten by humans are more important in single-stomach animals than multi-stomach animals (due to their hydrogenating intestinal bacteria). The potential for the prevention and treatment of cardiovascular disease through increased dietary intake of omega-3 (w-3) fish oils is not a recent scientific discovery. A historically important study in 1980 reported that high levels of omega-3 fatty acids in the diet of the Inuit people of Greenland were linked to a lower rate of death from acute myocardial infarction compared to the Danish population. An abundance of ensuing clinical trials supported the benefit of the omega-3 polyunsaturated fatty acids *cis*-5,8,11,14,17-eicosapentaenoic acid (EPA) and *cis*-4,7,10,13,16,19-docosahexaenoic acid (DHA). EPA and DHA have demonstrated many cardio protective effects including anti arrhythmic, blood triglyceride-lowering, and antithrombotic effects, as well as improving endothelial relaxation and inhibiting both atherosclerosis and inflammation.

**Rheumatoid arthritis:** Most clinical studies examining omega-3 fatty acid supplements for arthritis have focused on rheumatoid arthritis (RA), an autoimmune disease that causes inflammation in the joints. Several small studies have found that fish oil helps reduce symptoms of RA, including joint pain and morning stiffness. One study suggests that people with RA who take fish oil may be able to lower their dose of non-steroidal anti-inflammatory drugs (NSAIDs). However, unlike prescription medications, fish oil does not appear to slow progression of RA, only to treat the symptoms. Joint damage still occurs. Laboratory studies suggest that diets rich in omega-3 fatty acids may help people with osteoarthritis (Lee, 2012). More study is needed.

**Depression:** Research is not clear on whether taking omega-3 fatty acids can help relieve depression symptoms. Several studies show that people who took omega-3 fatty acids in addition to prescription antidepressants had a greater improvement in symptoms than those who took antidepressants alone. Other studies suggest that omega-3 fatty acid intake helps protect against postpartum depression, among other benefits. However, some studies found no benefit. Studies are also mixed on whether omega-3 fatty acids alone have any effect on depression. Depression is a serious illness. Omega-3 fatty acids have been found to play a role in atherosclerosis and peripheral arterial disease (PAD). It is thought that both EPA and DHA improve plaque stability, decrease endothelial activation, and improve vascular permeability, thereby decreasing the chance of experiencing a cardiovascular event. It was found that EPA supplementation is associated with significantly higher amounts of EPA in the carotid plaque. EPA+DHA supplementation has been shown to improve endothelial function in patients with PAD by decreasing plasma levels of soluble thrombomodulin. The results of this prospective study showed that baseline red blood cell membrane phospholipids *cis* omega-3 fatty acids is inversely associated, and *cis* omega-6 fatty acids are positively associated, with longitudinal weight gain in initially normal weight healthy human being (Zurier, *et al.*, 1996).

## 5. Conclusion

Among the fatty acids, it is the omega-3 polyunsaturated fatty acids (PUFA) which possess the most potent immune modulatory activities, and among the omega-3 PUFA, those from fish oil—eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)—are more biologically potent than  $\alpha$ -linolenic acid (ALA). Some of the effects of omega-3 PUFA are brought about by modulation of the amount and types of eicosanoids made, and other effects are elicited by eicosanoid-independent mechanisms, including actions upon intracellular signaling pathways, transcription factor activity and gene expression. Experimental and clinical intervention studies indicate that omega-3 fatty acids have anti-inflammatory properties and, therefore, might be useful in the management of inflammatory and autoimmune diseases. Coronary heart disease, major depression, aging and cancer are characterized by an increased level of interleukin 1 (IL-1), a proinflammatory cytokine. Similarly, arthritis, Crohn's disease, ulcerative colitis and lupus erythematosus are autoimmune diseases characterized by a high level of IL-1 and the proinflammatory leukotriene LTB<sub>4</sub> produced by omega-6 fatty acids. There have been a number of clinical trials assessing the benefits of dietary supplementation with fish oils in several inflammatory and autoimmune diseases in humans, including rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriasis, lupus erythematosus, multiple sclerosis and migraine headaches. The first evidence of the important role of dietary intake of omega-3 polyunsaturated fatty acids (PUFAs) in inflammation was derived from epidemiological observations of the low incidence of autoimmune and inflammatory disorders, such as psoriasis, asthma and type-1 diabetes, as well as the complete absence of multiple sclerosis (Swan and Allen, 2013; Schachter, *et al.*, 2004).

Population studies suggest that omega-3 fatty acids may have a preventive effect in rheumatoid arthritis. (Lee, *et al.*, 2012). Therefore, persons at a higher risk because of genetic susceptibility are good subjects to carry out preventive measures through dietary change by decreasing the omega-6 fatty acid and increasing the omega-3 fatty acid intake. Asthma is a mediator driven inflammatory process in the lungs and the most common chronic condition in childhood. The leukotrienes and prostaglandins are implicated in the inflammatory cascade that occurs in asthmatic airways. With low omega-3 ingestion, metacholine-induced respiratory distress increased. With high omega-3 fatty acid ingestion, alterations in urinary 5-series leukotriene excretion predicted treatment efficacy and a dose change in 40% of the test subjects (responders) whereas the non-responders had a further loss in respiratory capacity.

## Reference

[1] Cho, H. P., Nakamura, M., Clarke, S.D., 1999. Cloning, expression, and fatty acid regulation of the human delta-5 desaturase. *J Biol Chem.* 274(52):37335-37339. (PubMed)

[2] Davidson, M. H., 2013. Omega-3 fatty acids: new insights into the pharmacology and biology of docosahexaenoic acid, docosapentaenoic acid, and

eicosapentaenoic acid. *Curr Opin Lipidol.* 24(6):467-474. (PubMed)

[3] Conquer, J. A., Holub, B.J., 1997. Dietary docosahexaenoic acid as a source of eicosapentaenoic acid in vegetarians and omnivores. *Lipids.* 32(3):341-345. (PubMed)

[4] Burdge, G., 2004.  $\alpha$ -linolenic acid metabolism in men and women: nutritional and biological implications. *Curr Opin Clin Nutr Metab Care.* 7(2):137-144. (PubMed)

[5] Flock, M. R., Skulas-Ray, A. C., Harris, W. S., Etherton, T. D., Fleming, J. A., Kris-Etherton, P. M., 2013. Determinants of erythrocyte omega-3 fatty acid content in response to fish oil supplementation: a dose-response randomized controlled trial. *J Am Heart Assoc.* 2(6):e000513. (PubMed)

[6] SanGiovanni, J. P., Chew, E. Y., 2005. The role of omega-3 long-chain polyunsaturated fatty acids in health and disease of the retina. *Prog Retin Eye Res.* 24(1):87-138. (PubMed)

[7] Calder, P. C., 2013. n-3 fatty acids, inflammation and immunity: new mechanisms to explain old actions. *Proc Nutr Soc.* 72(3):326-336. (PubMed)

[8] Harris, W. S., Mozaffarian, D., Rimm, E., 2009. Omega-6 Fatty Acids and Risk for Cardiovascular Disease: A Science Advisory From the American Heart Association Nutrition Subcommittee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Cardiovascular Nursing; and Council on Epidemiology and Prevention. *Circulation.* 119(6):902-7. (PubMed)

[9] Hooper, L., Thompson, R. L., Harrison, R. A., 2006. Risks and benefits of omega 3 fats for mortality, cardiovascular disease, and cancer: systematic review. *BMJ.* 332(7544):752-760. (PubMed)

[10] Horvath, A., Koletzko, B., Szajewska, H., 2007. Effect of supplementation of women in high-risk pregnancies with long-chain polyunsaturated fatty acids on pregnancy outcomes and growth measures at birth: a meta-analysis of randomized controlled trials. *Br J Nutr.* 98(2):253-259. (PubMed)

[11] Kris-Etherton, P. M., Harris, W. S., Appel, L. J., 2002. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation.* 106(21):2747-2757. (PubMed)

[12] Zheng, J., Huang, T., Yu, Y., Hu, X., Yang, B., Li, D., 2012. Fish consumption and CHD mortality: an updated meta-analysis of seventeen cohort studies. *Public Health Nutr.* 15(4):725-737. (PubMed)

[13] Bemelmans, W. J., Lefrandt, J. D., Feskens, E. J., 2004. Increased  $\alpha$ -linolenic acid intake lowers C-reactive protein, but has no effect on markers of atherosclerosis. *Eur J Clin Nutr.* 58(7):1083-1089. (PubMed)

[14] Peet, M., Murphy, B., Shay, J., Horrobin, D., 1998. Depletion of omega-3 fatty acid levels in red blood cell membranes of depressive patients. *Biol Psychiatry.* 43(5):315-319. (PubMed)

[15] Hibbeln, J. R., 1998. Fish consumption and major depression. *Lancet.* 351(9110):1213. (PubMed)

[16] Hooijmans, C. R., Kiliaan, A. J., 2008. Fatty acids, lipid metabolism and Alzheimer pathology. *Eur J Pharmacol.* 585(1):176-196. (PubMed)

- [17] Mozaffarian, D., Wu, J. H., 2011. Omega-3 fatty acids and cardiovascular disease: effects on risk factors, molecular pathways, and clinical events. *J Am Coll Cardiol.* 58(20):2047-2067. (PubMed)
- [18] Rangel-Huerta, O. D., Aguilera, C. M., Mesa, M. D., Gil, A., 2012. Omega-3 long-chain polyunsaturated fatty acids supplementation on inflammatory biomarkers: a systematic review of randomised clinical trials. *Br J Nutr.* 107 Suppl 2:S159-170. (PubMed)
- [19] Miles, E. A., Calder, P. C., 2012. Influence of marine n-3 polyunsaturated fatty acids on immune function and a systematic review of their effects on clinical outcomes in rheumatoid arthritis. *Br J Nutr.* 107 Suppl 2:S171-184. (PubMed)
- [20] Innis, S. M., 2008. Dietary omega 3 fatty acids and the developing brain. *Brain Res.* 1237:35-43. (PubMed)
- [21] Aneur, A., Enroth, S., Johansson, A., 2012. Genetic adaptation of fatty-acid metabolism: a human-specific haplotype increasing the biosynthesis of long-chain omega-3 and omega-6 fatty acids. *Am J Hum Genet.* 90(5):809-820. (PubMed)
- [22] Larque, E., Demmelmair, H., Koletzko, B., 2002. Perinatal supply and metabolism of long-chain polyunsaturated fatty acids: importance for the early development of the nervous system. *Ann N Y Acad Sci.* 967:299-310. (PubMed)
- [23] American Heart Association. About Stroke. 2015. Available at: [http://www.strokeassociation.org/STROKEORG/AboutStroke/About-Stroke\\_UCM\\_308529\\_SubHomePage.jsp](http://www.strokeassociation.org/STROKEORG/AboutStroke/About-Stroke_UCM_308529_SubHomePage.jsp).
- [24] US Department of Agriculture, Agricultural Research Service. 2014. Nutrient Intakes from Food: Mean Amounts Consumed per Individual, by Gender and Age. Available at: <http://www.ars.usda.gov/ba/bhnrc/fsrg>.
- [25] Holman, R. T., Johnson, S. B., Hatch, T. F., 1982. A case of human linolenic acid deficiency involving neurological abnormalities. *Am J Clin Nutr.* 35(3):617-623. (PubMed)
- [26] Jeppesen, C., Schiller, K., Schulze, M. B., 2013. Omega-3 and omega-6 fatty acids and type 2 diabetes. *Curr Diab Rep.* 13(2):279-288. (PubMed)
- [27] Friedberg, C. E., Janssen, M. J., Heine, R. J., Grobbee, D. E., 1998. Fish oil and glyceemic control in diabetes. A meta-analysis. *Diabetes Care.* 21(4):494-500. (PubMed)
- [28] Montori, V. M., Farmer, A., Wollan, P. C., Dinneen, S. F., 2000. Fish oil supplementation in type 2 diabetes: a quantitative systematic review. *Diabetes Care.* 23(9):1407-1415. (PubMed)
- [29] Lee, Y. H., Bae, S. C., Song, G. G., 2012. Omega-3 polyunsaturated fatty acids and the treatment of rheumatoid arthritis: a meta-analysis. *Arch Med Res.* 43(5):356-362. (PubMed)
- [30] Harbige, L. S., 2003. Fatty acids, the immune response, and autoimmunity: a question of n-6 essentiality and the balance between n-6 and n-3. *Lipids.* 38(4):323-341. (PubMed)
- [31] Zurier, R. B., Rossetti, R. G., Jacobson, E. W., 1996.  $\gamma$ -linolenic acid treatment of rheumatoid arthritis. A randomized, placebo-controlled trial. *Arthritis Rheum.* 39(11):1808-1817. (PubMed)
- [32] Swan, K., Allen, P. J., 2013. Omega-3 fatty acid for the treatment and remission of Crohn's disease. *J Complement Integr Med.* 10. (PubMed)
- [33] Schachter, H. M., Reisman, J., Tran, K., 2004. Health effects of omega-3 fatty acids on asthma. *Evid Rep Technol Assess (Summ).* (91):1-7. (PubMed)