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Bioscience Research

Print ISSN: 1811-9506 Online ISSN: 2218-3973

*Journal by Innovative Scientific Information & Services Network*

REVIEW ARTICLE BIOSCIENCE RESEARCH, 2023 20(2): 474-481. OPEN ACCESS

# An Overview of Omega-3 Fatty Acids (OM3FAs) and their benefits to human health

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Omega-3 fatty acids (OM3FAs) are essential nutrients for the human body's numerous physiological and neurological functions. This review article aims to overview of benefits of OM3FAs, highlighting their importance in improving human health. Mechanisms through which OM3FA promotes neurological and metabolic health include activating G protein-coupled receptors (GPR40 and GPR120) and peroxisome proliferator-activated receptors (PPAR). It activates receptors that promote neurological health, reduces inflammation, improves glucose absorption, increases the density of synaptic vesicles in hippocampus, and improves metabolic health. Adequate intake of OM3FA is critical for optimal mood regulation, preventing neurological disorders, and enhancing brain learning, cognition, and blood circulation. OM3FAs deficiency or insufficiency increases risk of dementia, depression, and behavioral problems. Benefits of OM3FA supplements in preventing or managing Alzheimer's disease, depression, ADHD, and age-related cognitive decline. Long-chain OM3FAs have neuroprotective effects due to their anti-inflammatory and antioxidant properties. In addition, it has cardiovascular and neurodevelopmental benefits throughout life. An adequate intake of OM3FA supplements can help prevent or reduce the likelihood of or manage heart disease, arrhythmias, atherosclerosis, and dyslipidemia, as well as promote healthy aging that supports optimal development in children. OM3FAs are promising nutraceuticals to maintain health of brain, cardiovascular, pregnant women, and babies.

**Keywords: Omega-3, OM3FAs, DHA, EPA, Health**

## INTRODUCTION

Long-chain omega-3 fatty acids (OM3FAs), including eicosatetraenoic acid (EPA) and docosahexaenoic acid (DHA), are required for brain growth, cell signaling, and memory formation (Seo, Blaner and Deckelbaum, 2005; Brew et al. 2015). OM3FAs are critical components of neuronal membranes. They play role in developing intellect, the neurological system, vision, neurotransmitter metabolism, endothelial function, brain barrier integrity, neuronal survival, and neurodegenerative prevention (Wang et al. 2018). Approximately 50 to 60% of dry weight is a lipid, of which 35% is OM3FAs, and DHA accounts for more than 40% of the total OM3FAs in neuronal tissue, mainly grey matter (Heras-Sandoval, Pedraza-Chaverri and Pérez-Rojas, 2016; Fang et al. 2020). DHA is generally advised throughout pregnancy and is regularly added to newborn formula due to its apparent favorable effect on visual and cognitive development (Brew *et al.* 2015; Fang et al. 2020). In particular, endogenous DHA synthesis in mammals is restricted, and breast milk provides newborns with a highly accessible amount of DHA (Wang et al. 2018). DHA is derived from the animal diet, mainly fish, after weaning (Heras-Sandoval, Pedraza-Chaverri and Pérez-Rojas, 2016). According to one study, OM3FAs ingestion may improve neuronal composition, neurotransmission, and cognitive performance. Two mechanisms influence neurotransmission: changing membrane fluidity and increasing neurotransmitter release (Bos et al. 2016). OM3FAs deficiencies have been reported in individuals with range of mental illnesses, including attention deficit hyperactivity disorder (ADHD), depression, schizophrenia, and autism spectrum disorder (Walker, Jebb and Calder, 2013). Based on this information, many intervention studies have been conducted to assess the effectiveness of supplementation with OM3FAs for treating children with ADHD and other conditions. OM3FAs helpful in treatment of Alzheimer's disease (Wang et al. 2018). Clinical research also showed that OM3FAs are effective in various mental states. Bipolar illness, borderline personality disorder, and better cognitive performance are all examples of dysregulated mood and impulse control (Simopoulos, 2002; Yuen *et al.* 2005). Several human studies have examined the preventive benefits of OM3FAs and their components in frequency (Yuen et al. 2005). Furthermore, OM3FAs are transformed into eicosanoids, which may govern various homeostatic and inflammation processes related to different disorders such as infectious diseases, cancer, and cardiovascular disorders (Dennis and Norris, 2015). As a result, this review aims to identify benefits of OM3FAs in human health.

### Mechanism of Action

OM3FAs decrease lipogenic gene expression, improve beta-oxidation of fatty acids, enhance the term lipoprotein-lipase, and regulate overall body lipid accretion (Park and Harris, 2003; Bays *et al.* 2008; Noreen *et al.* 2010). They suppress the expression of phosphatidic acid phosphatase and sterol regulatory element binding proteins (SREBP) (Horton *et al.* 1998; Noreen *et al.* 2010; Logan and Spriet, 2015). This reduces synthesis of SREBP and the cholesterol-producing enzymes it regulates, 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase (Noreen et al. 2010; Backes et al. 2016). Furthermore, they can increase metabolic rate and decrease total body fat by acting as ligands for peroxisome proliferator-activated receptors (PPAR). Alterations in body composition can also increase fat utilization and energy expenditure (KOTA, HUANG and ROUFOGALIS, 2005; He et al. 2018). Figure 1 summarizes mechanism of action of OM3FAs.

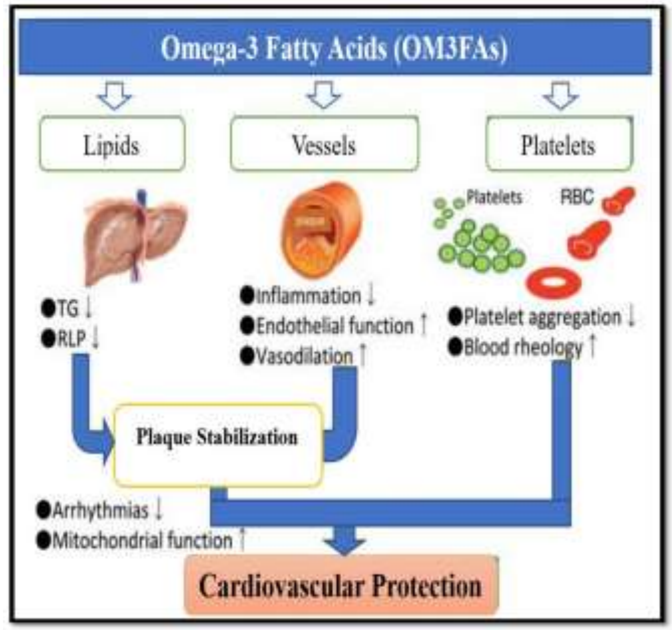


**Figure 1: Summarize the mechanism of action of OM3FAs.**

### Traditional Sources of OM3FAs

Most crop seeds and vegetable oils, such as canola, soybean, and sunflower oils, are high in OM3FAs in form of linoleic acid (LA), with low levels of Alpha-linolenic acid (ALA) (Moghadasian, 2008). ALA levels are notably high in chia, perilla, and flax seeds. Diet rich in fish, beef, and lamb may also provide EPA, DHA, and arachidonic acid (ARA), which can be used directly for normal physiological functioning (Saini, Shetty and Giridhar, 2014; Saini et al. 2016). Green leafy vegetables are also abundant in OM3FAs in ALA (Saini, Shetty and Giridhar, 2014; Kim et al. 2018) (Table 1).

**Table 1: summarize OM3FAs sources**

| Source | Type | Omega-3 Fatty Acids |
|---|---|---|
| Fatty fish | Animal-based | EPA and DHA |
| Fish oil | Animal-based | EPA and DHA |
| Krill oil | Animal-based | EPA and DHA |
| Algae oil | Plant-based | DHA and sometimes EPA |
| Flaxseeds | Plant-based | ALA |
| Flaxseed oil | Plant-based | ALA |
| Chia seeds | Plant-based | ALA |
| Walnuts | Plant-based | ALA |
| Canola oil | Plant-based | ALA |
| Abbreviations: EPA: Eicosapentaenoic acid. DHA: Docosahexaenoic acid. ALA: Alpha-linolenic acid | | |

In most regions, lacking OM3FAs increases risk of chronic diseases. To date, several ways have been presented to improve body's intake of OM3FAs, including the following: increased intake of fish and other meals rich in OM3FAs, fortification of food items with fish oil, krill oil, or ALA, enhancement of OM3FAs in animal products by feeding rich diets, and genetic engineering fortification of polyunsaturated fatty acids (PUFAs) in oilseed crops (Garg et al. 2006; Lane and Derbyshire, 2018). It has been established that providing an ALA-rich diet to animals may enhance the concentration of long-chain PUFA in animal-derived products. On other hand, extent of increase in long chain-PUFA content seems dependent on the kind of food supplementation (Moghadasian, 2008). For example, broiler breast and thigh meat fed high-ALA-rich flaxseed oil for six weeks had 2 to 5-fold higher EPA and DHA (Kanakri *et al.* 2017). Organic milk production improves nutritional quality by changing fatty acid content (Benbrook et al. 2013).

### Effects of OM3FAs on the Brain

OM3FAs account for about 20% of the weight of the brain. Highly critical in brain function and mental disorders (Logan, 2003). OM3FAs promote neurological and metabolic health by activating G protein-coupled receptors (GPR40 and GPR120) and PPAR. PPAR-alpha activity promotes fatty acid oxidation and decreases triglyceride production, while PPAR-gamma activation enhances insulin sensitivity and decreases inflammation. DHA and EPA increase GPR120-mediated gene activation, reducing inflammation and improving adipocyte glucose absorption. These effects lead to improved brain health (Calder, 2015; Bahadorpour et al. 2023). Long-chain OM3FAs can help reduce inflammatory cytokines in brain, which could enhance the way neurotransmitters work. OM3FAs deficiency in brain is associated with reduced dopamine and serotonin signaling. Furthermore, OM3FAs deficiency can cause a 30% decrease in synaptic vesicle density in hippocampus, a 30–35% reduction in phosphatidylserine levels, a 30% decrease in glucose uptake in neurons, and a 90% reduction in tyramine-stimulated dopamine release (Logan, 2003; Layé et al. 2018). Because OM3FAs consumption improves learning, cognition, mental well-being, and blood circulation in brain, people who are more socially isolated, seniors, and people who consume less healthy foods containing OM3FA may benefit from taking OM3FA (Dighriri *et al.* 2022). OM3FAs levels and intake correlate with better brain function and lower risk of age-related cognitive decline, according to several recent studies. A study in elderly discovered that greater amounts of DHA were related to larger volumes of hippocampus, a critical brain region for memory (Pottala et al. 2014). Clinical trials show that OM3FAs supplements may improve working memory, episodic memory, cognitive flexibility, and learning in older (Yurko-Mauro, Alexander and Van Elswyk, 2015). OM3FAs help prevent and slow age-related mental decline by reducing inflammation and oxidative stress, two factors linked to neurodegeneration. Studies show that OM3FAs levels tend to be lower in patients with dementia or Alzheimer's disease (Cederholm, Salem and Palmblad, 2013; Bazinet and Layé, 2014).

### Benefits of OM3FAs in mood disorders and depression

The prevalence of depression has increased since World War II, and up to 40% of patients (Logan, 2003; Friedrich, 2017). This mental health problem burdens individuals, society, and healthcare costs. OM3FAs have mood-regulating effects and may reduce risk of depression and anxiety. A trial in 33 young, healthy participants found that DHA/EPA (2400 mg per day) for 35 days improved mood and vigor, reducing anxiety and depression (Fontani et al. 2005). Meta-analysis of 19 clinical trials in 2019 found that OM3FAs supplements significantly reduced symptoms of depression, especially in adults over 60 years (Liao *et al.* 2021). Other analyses link increased seafood intake or OM3FAs blood levels to a lower likelihood of being associated with bipolar disorder, psychotic disorders, or depression (Grosso et al. 2014; Jacka et al. 2017)

### Benefits of OM3FAs on attention deficit hyperactivity disorder (ADHD)

ADHD affects 4-15% of children in United States and often persists into adulthood. Children and adults with ADHD have lower levels of OM3FAs,which are associated with academic and behavioral issues. Several trials have found that OM3FAs supplementation (ranging from 120-500 mg of DHA/EPA per day) in children with ADHD-type symptoms improves attention, behavior, and oppositional defiant disorder (Hirayama, Hamazaki and Terasawa, 2004). A study also found that supplementing underperforming children with 600 mg that did not perform well In studies, 600 mg DHA enhanced parent-reported ADHD-like behavior (Richardson et al. 2012).

In children with impaired sustained visual attention, esterified OM3FAs with phosphatidylserine showed a more significant improvement in symptoms compared to the fish oil or control groups (Carlson, Werkman and Tolley, 1996). This finding was supported by another study using a similar OM3FAs supplement (Carlson et al. 1993; Carlson, Werkman and Tolley, 1996). Supplementing children with ADHD with long-chain marine OM3FAs may significantly reduce symptoms.

### Benefits of OM3FAs on Alzheimer

Alzheimer's is a progressive neurodegenerative disease characterized by a gradual decline in cognitive function, memory loss, and changes in behavior. OM3FAs, particularly DHA and EPA, have a potential role in preventing and managing Alzheimer's disease (Cole and Frautschy, 2010). The interest in OM3FAs is derived from their anti-inflammatory and neuroprotective properties, which might assist in their positive effects on Alzheimer's disease (Cole and Frautschy, 2010). Inflammation is believed to play significant role in pathogenesis of Alzheimer's. OM3FAs, particularly EPA, have been found to reduce production of pro-inflammatory molecules in brain. By mitigating inflammation, OM3FAs can help slow progression of Alzheimer's (Calder, 2015). OM3FAs are essential fats that must be obtained from diet. They are integral components of brain cell membranes and play crucial role in brain plasticity, neuronal survival, and protection against inflammation and oxidative stress, all relevant to Alzheimer's. Several studies have found that OM3FAs supplementation can reduce amyloid beta plaques, inhibit tau hyperphosphorylation, decrease inflammation, and support cognitive functions in animal models of Alzheimer's disease (Lim *et al.* 2001; Calder, 2015). Epidemiological studies also suggest that higher fish consumption and OM3FAs intake are associated with a lower risk of Alzheimer's disease and a slower rate of cognitive decline (Mazereeuw *et al.* 2012). Supplementation of OM3FAs for patients with established Alzheimer's disease may help slow its progression and maintain cognitive functions. However, the effects depend on the dosage, treatment duration, and condition stage (Mazereeuw *et al.* 2012).

### Effects of OM3FAs on cardiovascular disorders

The research of the Greenland Eskimos was the first to demonstrate that diet rich in OM3FAs reduces coronary heart disease mortality (Bang, Dyerberg and Hjørne, 2009). Several additional studies have proven that OM3FAs maintain heart health by minimizing the likelihood of arrhythmias (Geelen *et al.* 2005; Leaf, 2006; Voronin et al. 2022). Evaluating data from controlled studies with 32,000 individuals provided the most significant evidence that OM3FAs benefit the heart. According to this study, cardiovascular events were reduced by 19–45% (Lee et al. 2008). According to fatty acid antiarrhythmic experiment, individuals with myocardial infarction who received OM3FA had a 38% reduction in risk of malignant ventricular arrhythmias (Leaf et al. 2005). In addition, OM3FAs reduced heart rate and helped reduce proportion of people who developed atrial fibrillation after coronary artery bypass surgery (Dallongeville et al. 2003; Geelen et al. 2005; Bang, Dyerberg and Hjørne, 2009). The antiarrhythmic action of OM3FAs is assumed to be generated by change in electrophysiology of heart, which causes the heart rate to slow and the QT interval to shorten (Bang, Dyerberg and Hjørne, 2009). Furthermore, according to a meta-analysis, eating fish was associated with relative risk of 0.83 for fatal coronary heart disease versus 86 compared to eating little or no fish (Leaf et al. 2005). Diet rich in OM3FA is a vital part of changing your lifestyle to prevent coronary heart disease from occurring in first place. A diet has been shown to delay coronary atherosclerosis, cure coronary artery stenosis, and avoid restenosis after coronary angioplasty (Mozaffarian, 2005).

### Effects of OM3FAs on atherosclerosis

Most of beneficial effects of OM3FA on atherosclerosis are due to how they impact plasma lipids. Reduced blood pressure, fewer inhibitors of plasminogen activity, the way endothelial cells work, and improved health for those suffering from metabolic syndrome (Esposito *et al.* 2004; Chan *et al.* 2006). Since atherosclerosis is an inflammatory disease, anti-inflammatory effects of OM3FA may help prevent it from occurring. Proinflammatory cytokine concentrations in serum and peripheral blood mononuclear cells, such as interleukin-1 beta (IL1b), tumor necrosis factor-a, and Interleukin-6 (IL6), were shown to be lower in people with high cholesterol who received OM3FA (Esposito *et al.* 2004; Morgan *et al.* 2006). Platelet monocyte aggregation, a sensitive sign of platelet activation leading to atherothrombosis, can be slowed by eating oily fish. Because they suppress inflammation, OM3FAs can prevent development and stabilize atherosclerotic plaques (Erkkilä *et al.* 2004).

### Effects of OM3FAs on dyslipidemia

Dyslipidemia is a significant risk factor for cardiovascular disease, leading cause of death worldwide. The main impact of OM3FAs on lipids is their ability to reduce blood triglyceride levels (Kabir *et al.* 2007). The atherogenic index, calculated as ratio of triglycerides to high-density lipoprotein (HDL) cholesterol, was lower in those who received OM3FA, and cholesterol from the lipoprotein decreased. This is a significant risk factor for development of atherosclerosis (Kabir et al. 2007; Hartweg et al. 2008). Multiple epidemiological studies and randomized controlled trials have shown that OM3FAs can reduce serum triglyceride levels by up to 50% in some individuals. In addition, OM3FAs are well tolerated and have a very safe side effect profile. Due to their triglyceride-lowering effects, OM3FAs supplements or OM3FAs-rich foods are often used as adjunct to conventional lipid-lowering medications (Eslick et al. 2009; Mori, 2014). Trials found that OM3FAs supplementation significantly reduced triglyceride levels (-26.7 mg/dL) and very low-density lipoprotein (LDL) cholesterol levels. EPA and DHA also produced small but significant increases in HDL cholesterol (+2.4 mg/dL). However, OM3FAs did not significantly reduce total cholesterol or LDL cholesterol levels. The effects were most potent in individuals with severe hypertriglyceridemia (triglycerides >500 mg/dL). The results confirm that OM3FAs can significantly lower triglyceride levels with minimal effects on other lipids (Chen, Yu and Shao, 2015; Bhatt et al. 2019)

### OM3FAs for hypertension

Hypertension is a significant risk factor for cardiovascular disease and stroke. Although conventional antihypertensive drugs effectively lower blood pressure, alternative strategies such as diet and lifestyle changes can also help control hypertension. OM3FAs reduce the upper and lower values of blood pressure are reduced by OM3FAs in patients with and without high blood pressure. People who use OM3FA daily have a lower risk of developing hypertension (Dallongeville et al. 2003; Hartweg et al. 2008). Previous research used higher doses to examine how fish oils reduce blood pressure. The median dose was 3.7 g / day, and a decrease of 2.1 mm Hg was found in systolic blood pressure and 1.6 mm Hg in diastolic pressure (Campbell et al. 2013; Miller, Van Elswyk and Alexander, 2014). A meta-analysis of observational studies found that a high OM3FAs dietary intake was associated with a statistically significant reduction in risk of hypertension (relative risk 0.89, 95% CI 0.83 to 0.96) (Miller, Van Elswyk and Alexander, 2014). OM3FAs are believed to reduce blood pressure through several mechanisms, including improved endothelial function, reduced inflammation, decreased arterial stiffness, and reduced renin-angiotensin-aldosterone system activity. In addition, EPA and DHA can act as natural calcium channel blockers and angiotensin-converting enzyme inhibitors (Mozaffarian and Wu, 2011; Cicero et al. 2017)

### OM3FAs for pregnant women

Inflammation during pregnancy can cause several problems, including preterm delivery and hypertension. Due to their anti-inflammatory properties, OM3FAs can help reduce overall inflammation levels (Layé et al. 2018). Pregnant women who consume enough OM3FAs have lower chance of developing cardiovascular disease, stroke, improved lipid profiles, decreased inflammation, and lower blood pressure (Shahidi and Ambigaipalan, 2018). OM3FAs are vital for brain growth in infants and children. They are essential for forming neural networks and maturation of central nervous system and retina. Studies show that pregnant women and children with higher intake or blood levels tend to have children with better cognitive outcomes, memory, problem-solving skills, and motor development (Innis, 2008).

## CONCLUSION

OM3FAs play vital role in brain function and have numerous benefits for mental health disorders. They activate receptors that promote neurological and metabolic health, reduce inflammation, improve glucose absorption, and increase the density of synaptic vesicles in hippocampus. Studies have shown that OM3FAs can improve learning, cognition, mental well-being, and blood circulation in brain, which makes it beneficial for socially isolated individuals, seniors, and people who consume less healthy foods. OM3FAs also have mood-regulating effects and can reduce risk of depression and anxiety. In addition, they can improve attention and behavior. Furthermore, OM3FAs, particularly DHA and EPA, can potentially prevent and manage Alzheimer's disease, as they can reduce inflammation, support cognitive functions, and slow disease progression. Benefits of OM3FAs on brain make it a valuable dietary supplement to maintain optimal brain health and prevent mental health disorders. OM3FAs have numerous benefits for cardiovascular health. They have been shown to reduce the likelihood of arrhythmias, cardiovascular events, and atrial fibrillation while also helping to slow progression of atherosclerosis. OM3FAs also effectively reduce blood triglyceride levels and improve lipid profiles, making them a valuable adjunct to conventional lipid-lowering medications. Additionally, OM3FAs can help control hypertension and reduce overall inflammation levels, which is especially beneficial for pregnant women.

## CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

## ACKNOWLEDGEMENT

We would like to express our sincere gratitude to all those who have supported and contributed to this research. Special thanks go to our colleagues and mentors for their valuable insights, constructive feedback, and unwavering encouragement throughout the development of this paper.

## AUTHOR CONTRIBUTIONS

All authors have contributed equally to the research, writing, and editing of this paper. All authors read and approved the final version.



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