Chapter - 5
Omega-3 Fatty Acids as Nutraceuticals: Health Benefits and Therapeutic Applications

Authors

Punam Roy
Department of Nutrition, Nistarini College, Purulia, West Bengal, India

Ankita Panda
M.Sc. in Nutrition and Dietetics, Vidyasagar Institute of Health, West Bengal, India

Souvik Tewari
Assistant Professor, Department of Food and Nutrition, Swami Vivekananda University, Barrackpore, West Bengal, India

Chapter - 5

Omega-3 Fatty Acids as Nutraceuticals: Health Benefits and Therapeutic Applications

Punam Roy, Ankita Panda and Souvik Tewari

Abstract

Omega-3 fatty acids are among the most extensively studied bioactive lipids because of their diverse physiological functions and established health benefits. Classified as essential polyunsaturated fatty acids (PUFAs), omega-3 fatty acids cannot be synthesized in sufficient quantities by the human body and must therefore be obtained through dietary sources or supplementation. The principal omega-3 fatty acids include α-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), each possessing unique biological functions and therapeutic significance. Increasing evidence demonstrates that omega-3 fatty acids act as effective nutraceuticals in the prevention and management of cardiovascular diseases, metabolic disorders, inflammatory conditions, neurodegenerative diseases, mental health disorders, and certain cancers. This chapter reviews the chemistry, dietary sources, metabolism, mechanisms of action, health benefits, therapeutic applications, safety considerations, and future prospects of omega-3 fatty acids as nutraceuticals.

Keywords: Omega-3 fatty acids, Nutraceuticals, EPA, DHA, ALA, Functional foods, Cardiovascular disease, Inflammation, Brain health, Dietary supplements.

1. Introduction

Nutraceuticals have emerged as an important component of preventive healthcare by bridging the gap between nutrition and medicine. Defined as bioactive compounds or products derived from foods that provide physiological benefits beyond basic nutrition, nutraceuticals have gained considerable attention for their potential role in reducing the risk of chronic diseases and promoting overall health. Increasing scientific evidence supports the use of nutraceuticals as complementary strategies for disease prevention

and health promotion, particularly in the management of cardiovascular diseases, metabolic disorders, neurodegenerative conditions, and chronic inflammatory diseases (Calder, 2023; Baker, 2024).

Among the diverse classes of nutraceuticals, **omega-3 fatty acids** are one of the most extensively investigated because of their well-established physiological functions and therapeutic potential. Omega-3 polyunsaturated fatty acids (n-3 PUFAs), particularly **α-linolenic acid (ALA), eicosapentaenoic acid (EPA)**, and **docosahexaenoic acid (DHA)**, play critical roles in maintaining membrane integrity, regulating inflammatory responses, supporting cardiovascular function, and promoting neurological development and cognitive health. Numerous clinical trials and systematic reviews have demonstrated beneficial effects of omega-3 fatty acids in lowering serum triglycerides, reducing systemic inflammation, and improving cardiovascular outcomes in selected patient populations (Djuricic & Calder, 2023; Tutor *et al.*, 2024).

Omega-3 fatty acids belong to the family of long-chain polyunsaturated fatty acids characterized by the first double bond occurring at the third carbon atom from the methyl (ω) end of the fatty acid chain. Humans lack the Δ12 and Δ15 desaturase enzymes required for de novo synthesis of omega-3 fatty acids; consequently, **ALA is considered an essential fatty acid** that must be obtained from the diet. Although ALA can be converted to EPA and DHA through sequential desaturation and elongation reactions, the conversion efficiency is generally low, making direct dietary intake of EPA and DHA from marine or algal sources important for achieving adequate physiological levels (National Institutes of Health, 2025; Baker, 2024).

Modern dietary patterns, particularly in many industrialized countries, are characterized by relatively low consumption of marine-derived omega-3 fatty acids and higher intake of omega-6 polyunsaturated fatty acids. While an elevated omega-6/omega-3 ratio has historically been proposed as a contributor to chronic low-grade inflammation and non-communicable diseases, recent evidence suggests that **absolute intake and tissue levels of EPA and DHA are more clinically relevant than the dietary ratio alone.** Current recommendations therefore emphasize increasing consumption of omega-3-rich foods or supplements rather than focusing solely on reducing omega-6 intake (National Institutes of Health, 2025; Harvard T.H. Chan School of Public Health, 2025). Consequently, dietary enrichment with omega-3 fatty acids through functional foods and nutraceutical supplements has become an important public health strategy for improving cardiometabolic

health and reducing the burden of chronic diseases (Tutor *et al.*, 2024; Djuricic & Calder, 2023).

2. Classification and Chemistry of omega-3 fatty acids

Omega-3 fatty acids comprise three major nutritionally important members:

2.1 Alpha-Linolenic Acid (ALA)

Alpha-linolenic acid (ALA; **18:3 n−3**) is an essential **omega-3 polyunsaturated fatty acid (PUFA)** comprising 18 carbon atoms and three cis double bonds, with the first double bond located at the third carbon from the methyl (ω) end of the fatty acid chain. Since humans lack the Δ12 and Δ15 desaturase enzymes required for its endogenous synthesis, ALA must be obtained through dietary intake, making it an indispensable component of human nutrition. Rich dietary sources of ALA include flaxseed and flaxseed oil, chia seeds, walnuts, hemp seeds, perilla seed oil, canola oil, and soybean oil. Following absorption, ALA serves as the metabolic precursor for the long-chain omega-3 fatty acids **eicosapentaenoic acid (EPA)** and **docosahexaenoic acid (DHA)** through a series of desaturation and elongation reactions occurring primarily in the liver. However, the conversion efficiency of ALA to EPA is relatively low (approximately 5-10%), while conversion to DHA is generally less than 1-5%, owing to competition with omega-6 fatty acids for shared desaturase enzymes and individual factors such as age, sex, genetics, and nutritional status. Despite its limited conversion, ALA exerts independent biological effects, including antioxidant, anti-inflammatory, cardioprotective, and neuroprotective activities, and has been associated with a reduced risk of cardiovascular disease and all-cause mortality. Consequently, adequate dietary intake of ALA is recommended as part of a balanced diet, particularly for individuals with limited consumption of marine-derived omega-3 fatty acids, while direct sources of EPA and DHA remain important for achieving optimal physiological benefits (Baker, 2024; National Institutes of Health, 2025; Djuricic & Calder, 2023).

2.2 Eicosapentaenoic Acid (EPA)

Eicosapentaenoic acid (EPA; **20:5 n−3**) is a long-chain omega-3 polyunsaturated fatty acid consisting of 20 carbon atoms and five cis double bonds, with the first double bond located at the third carbon from the methyl (ω) end of the fatty acid chain. EPA is predominantly obtained from marine sources, including fatty fish such as salmon, mackerel, sardines, herring, anchovies, and tuna, as well as fish oil, krill oil, and marine microalgae, which

serve as the primary producers of long-chain omega-3 fatty acids in aquatic ecosystems. Although EPA can be synthesized endogenously from alpha-linolenic acid (ALA), the conversion rate in humans is limited and insufficient to meet physiological requirements, making dietary intake an important source. EPA is widely recognized for its potent anti-inflammatory properties, primarily through its ability to compete with arachidonic acid for cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, thereby reducing the production of pro-inflammatory eicosanoids while promoting the synthesis of specialized pro-resolving mediators (SPMs), including E-series resolvins, which facilitate the resolution of inflammation. In addition, EPA modulates immune cell function, suppresses inflammatory cytokine production, and influences gene expression through activation of peroxisome proliferator-activated receptors (PPARs). Clinically, EPA has demonstrated significant cardiovascular benefits by lowering serum triglyceride concentrations, improving endothelial function, reducing platelet aggregation, stabilizing atherosclerotic plaques, and decreasing the risk of major adverse cardiovascular events, particularly in high-risk individuals with hypertriglyceridemia. Beyond cardiovascular protection, EPA has also shown therapeutic potential in inflammatory disorders, depression, metabolic syndrome, and other chronic diseases, making it one of the most extensively studied nutraceutical omega-3 fatty acids (Djuricic & Calder, 2023; National Institutes of Health, 2025; Siscovick *et al.*, 2023).

2.3 Docosahexaenoic Acid (DHA)

Docosahexaenoic acid (DHA; **22:6 n−3**) is a long-chain omega-3 polyunsaturated fatty acid comprising 22 carbon atoms and six cis double bonds, making it the most unsaturated and structurally complex of the major dietary omega-3 fatty acids. DHA is primarily obtained from marine sources such as fatty fish (e.g., salmon, sardines, mackerel, herring, and tuna), fish oil, krill oil, and marine microalgae, the latter serving as an important vegetarian and sustainable source. Although DHA can be synthesized from α-linolenic acid (ALA) through sequential desaturation and elongation reactions, the conversion efficiency in humans is extremely limited, necessitating adequate dietary intake. DHA is highly concentrated in the phospholipid membranes of the brain, retina, and central nervous system, where it contributes to membrane fluidity, synaptic plasticity, neurotransmission, and signal transduction. Approximately 30-40% of the polyunsaturated fatty acids present in the cerebral cortex and up to 50% of those in retinal photoreceptor membranes consist of DHA, underscoring its indispensable role in maintaining normal

neuronal and visual function. Adequate DHA intake is particularly critical during pregnancy, lactation, and early infancy, when rapid fetal and neonatal brain growth and retinal development occur. Maternal DHA is actively transported across the placenta and subsequently supplied through breast milk, supporting optimal cognitive development, visual acuity, and neurobehavioral outcomes in infants. In adults, DHA has been associated with preservation of cognitive function, healthy aging, reduced risk of neurodegenerative disorders, and modulation of neuroinflammatory processes. Emerging evidence also suggests beneficial effects of DHA in cardiovascular health through improvements in endothelial function, heart rate regulation, and lipid metabolism, although its strongest evidence remains in neurological and developmental health. Owing to these diverse physiological functions, DHA is widely incorporated into infant formulas, prenatal supplements, functional foods, and nutraceutical formulations aimed at promoting lifelong brain and eye health (Baker, 2024; National Institutes of Health, 2025; Calder, 2023; Koletzko *et al.*, 2022).

3. Dietary sources of omega-3 fatty acids

Dietary intake is the primary means of obtaining omega-3 fatty acids, as humans have a limited capacity to synthesize these essential lipids endogenously. The nutritional value and biological activity of dietary omega-3 fatty acids vary according to their source and chemical form. Marine foods are the richest natural sources of the long-chain omega-3 fatty acids **eicosapentaenoic acid (EPA)** and **docosahexaenoic acid (DHA)**, whereas plant-derived foods predominantly provide **α-linolenic acid (ALA)**, the metabolic precursor of EPA and DHA. In recent years, microalgae have emerged as a sustainable and vegetarian alternative for the production of long-chain omega-3 fatty acids, particularly DHA and EPA, supporting the growing demand for plant-based nutraceuticals and functional foods (National Institutes of Health, 2025; Baker, 2024).

3.1 Marine sources

Marine organisms constitute the most abundant and bioavailable dietary sources of EPA and DHA. Fatty fish, including **salmon (*Salmo salar*)**, **sardines (*Sardina pilchardus*)**, **mackerel (*Scomber* spp.)**, **tuna (*Thunnus* spp.)**, **anchovies (*Engraulis* spp.)**, and **herring (*Clupea harengus*)**, accumulate these long-chain omega-3 fatty acids through the marine food chain, primarily by consuming phytoplankton and microalgae. Regular consumption of these fish has been consistently associated with reduced

cardiovascular risk, improved cognitive function, and lower incidence of chronic inflammatory diseases. Fish oil remains one of the most widely used omega-3 nutraceuticals because of its high concentrations of EPA and DHA, whereas **krill oil**, extracted from Antarctic krill (*Euphausia superba*), contains omega-3 fatty acids primarily in phospholipid form, which may enhance bioavailability and tissue incorporation. Marine-derived omega-3 supplements have become an important strategy for individuals who consume insufficient amounts of fatty fish or require therapeutic doses of EPA and DHA (Calder, 2023; Djuricic & Calder, 2023).

3.2 Plant sources

Plant-derived omega-3 fatty acids are primarily present as **α-linolenic acid (ALA)**. Rich dietary sources include **flaxseed (*Linum usitatissimum*)**, **chia seeds (*Salvia hispanica*)**, **hemp seeds (*Cannabis sativa*)**, **walnuts (*Juglans regia*)**, **perilla seed (*Perilla frutescens*)**, **canola oil**, and **soybean oil**. Among these, flaxseed and chia seeds are recognized as particularly concentrated sources of ALA and are widely incorporated into functional foods, bakery products, cereals, and dietary supplements. Although ALA contributes to cardiovascular and metabolic health, its conversion to EPA and DHA in humans is relatively inefficient because of limited enzymatic activity and competition with omega-6 fatty acids for shared desaturase enzymes. Consequently, while plant-based sources are valuable for increasing total omega-3 intake, they may not fully replace direct dietary sources of EPA and DHA, particularly in populations with increased physiological requirements such as pregnant women, older adults, and individuals with chronic inflammatory conditions (Baker, 2024; National Institutes of Health, 2025).

3.3 Algal sources

Microalgae are the primary biological producers of long-chain omega-3 fatty acids in marine ecosystems and represent a sustainable, environmentally friendly, and vegetarian source of EPA and DHA. Unlike fish, which accumulate omega-3 fatty acids through the food chain, microalgae synthesize these lipids directly, making algal oil an attractive alternative to fish-derived supplements. Commercially cultivated microalgal species such as ***Schizochytrium* spp.**, ***Crypthecodinium cohnii*** and ***Nannochloropsis* spp.** are widely used for the industrial production of DHA-and EPA-rich oils. Algal omega-3 oils are free from many marine contaminants, including methylmercury and persistent organic pollutants, and are therefore particularly suitable for vegetarians, vegans, pregnant women, and individuals with

seafood allergies. Owing to advances in biotechnology and fermentation technologies, algal-derived omega-3 fatty acids are increasingly incorporated into infant formulas, functional beverages, dairy products, dietary supplements, and pharmaceutical-grade nutraceutical formulations, offering a sustainable solution to the growing global demand for omega-3 fatty acids while reducing pressure on marine fish stocks (Baker, 2024; Calder, 2023; National Institutes of Health, 2025).

Fortified functional foods

The increasing consumer demand for health-promoting foods has accelerated the development of **omega-3-fortified functional foods,** which are designed to enhance dietary intake of essential fatty acids without requiring major changes in eating habits. These products are enriched with omega-3 fatty acids derived from fish oil, krill oil, algal oil, or plant-based sources such as flaxseed and chia seed oils. Commonly available fortified foods include **omega-3-enriched eggs**, **fortified milk**, **yogurt**, **bread**, **infant formulas**, **cheese**, **margarine**, and **functional beverages**. Omega-3-enriched eggs are typically produced by supplementing the diets of laying hens with flaxseed, fish oil, or microalgae, resulting in significantly higher concentrations of DHA and, to a lesser extent, EPA in the egg yolk. Similarly, dairy products such as milk and yogurt are fortified with microencapsulated fish or algal oils to improve their nutritional value while minimizing undesirable fishy flavors and oxidative deterioration. Bakery products, including bread and cereals, are increasingly formulated with omega-3-rich ingredients such as flaxseed flour or encapsulated omega-3 oils, providing consumers with convenient dietary sources of essential fatty acids. Functional beverages, including fruit juices, dairy-based drinks, and plant-based beverages, have also emerged as effective delivery vehicles for omega-3 fatty acids, often utilizing advanced encapsulation technologies to improve stability, bioavailability, and sensory acceptance. The incorporation of omega-3 fatty acids into functional foods not only enhances nutritional quality but also offers a practical public health strategy to address inadequate omega-3 intake in populations with low fish consumption. Continued advancements in food processing technologies, particularly microencapsulation, nanoemulsion, and lipid stabilization techniques, have substantially improved the oxidative stability, shelf life, and consumer acceptability of omega-3-fortified products, thereby expanding their application in the functional food and nutraceutical industries (Baker, 2024; Calder, 2023; Jacobsen *et al.*, 2021; National Institutes of Health, 2025).

4. Metabolism and Bioavailability

ALA undergoes enzymatic conversion into EPA and DHA through elongation and desaturation pathways. However, the conversion efficiency is generally low, with less than 10% converted to EPA and typically less than 5% converted to DHA in adults. Consequently, direct dietary intake of EPA and DHA is often recommended.

5. Mechanisms of action of omega-3 fatty acids

The biological activities of omega-3 fatty acids extend beyond their role as essential nutrients, encompassing a wide range of molecular and cellular mechanisms that contribute to their nutraceutical and therapeutic efficacy. The long-chain omega-3 polyunsaturated fatty acids, particularly **eicosapentaenoic acid (EPA)** and **docosahexaenoic acid (DHA)**, exert pleiotropic effects through modulation of inflammatory pathways, membrane architecture, gene expression, oxidative stress, and cellular signaling. These mechanisms collectively underlie their beneficial effects in cardiovascular diseases, metabolic disorders, neurodegenerative diseases, autoimmune conditions, and cancer. Rather than acting through a single biochemical pathway, omega-3 fatty acids influence multiple interconnected signaling networks, enabling them to regulate both physiological homeostasis and pathological processes. The principal mechanisms of action are discussed below.

5.1 Anti-inflammatory Effects

One of the most extensively studied mechanisms of omega-3 fatty acids is their potent anti-inflammatory activity. EPA and DHA are incorporated into cell membrane phospholipids, where they compete with arachidonic acid (AA), an omega-6 fatty acid, for cyclooxygenase (COX) and lipoxygenase (LOX) enzymes. This competition results in reduced synthesis of pro-inflammatory eicosanoids, including prostaglandin E_2 (PGE_2), thromboxane A_2 (TXA_2), and leukotriene B_4 (LTB_4), while simultaneously increasing the production of less inflammatory or anti-inflammatory lipid mediators. More importantly, EPA and DHA serve as precursors for a unique class of **specialized pro-resolving mediators (SPMs)**, including **E-series and D-series resolvins, protectins and maresins**, which actively promote the resolution of inflammation rather than merely suppressing inflammatory responses. These mediators inhibit neutrophil infiltration, enhance macrophage-mediated clearance of apoptotic cells, reduce the production of pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α),

interleukin-1β (IL-1β), and interleukin-6 (IL-6), and facilitate tissue repair. Additionally, omega-3 fatty acids suppress activation of the nuclear factor-kappa B (NF-κB) signaling pathway and NLRP3 inflammasome, thereby limiting chronic low-grade inflammation implicated in cardiovascular diseases, obesity, diabetes mellitus, rheumatoid arthritis, and neurodegenerative disorders (Calder, 2023; Djuricic & Calder, 2023; Serhan & Levy, 2023).

5.2 Membrane fluidity

Omega-3 fatty acids play a fundamental structural role by incorporating into the phospholipid bilayer of cellular membranes, thereby modifying membrane composition and increasing membrane fluidity. DHA, owing to its highly unsaturated structure containing six double bonds, has a particularly pronounced effect on membrane flexibility and permeability. Enhanced membrane fluidity influences the organization of lipid rafts, membrane-bound receptors, ion channels, transport proteins, and intracellular signaling complexes. These changes improve receptor-ligand interactions, facilitate neurotransmitter release, optimize signal transduction, and regulate cellular communication. In neuronal tissues, DHA-rich membranes support synaptic plasticity, neurotransmission, and neurogenesis, thereby contributing to learning, memory, and cognitive performance. Similarly, in cardiovascular tissues, increased membrane fluidity improves endothelial function, calcium handling, and cardiac electrical stability, reducing susceptibility to arrhythmias. The ability of omega-3 fatty acids to modify membrane architecture also influences immune cell activation and inflammatory signaling, highlighting their broad physiological significance (Calder, 2023; National Institutes of Health, 2025).

5.3 Gene regulation

Beyond their structural functions, omega-3 fatty acids regulate gene expression through interactions with several nuclear transcription factors and intracellular signaling pathways. EPA and DHA function as endogenous ligands for **peroxisome proliferator-activated receptors (PPAR-α, PPAR-γ, and PPAR-δ)**, which regulate genes involved in fatty acid oxidation, lipid transport, glucose metabolism, insulin sensitivity, and inflammatory responses. Activation of PPARs enhances β-oxidation of fatty acids, reduces hepatic triglyceride synthesis, improves lipid homeostasis, and suppresses the expression of inflammatory genes. Omega-3 fatty acids also inhibit the activation of **nuclear factor-kappa B (NF-κB)**, a key transcription factor

benefits. These long-chain polyunsaturated fatty acids exert multiple complementary actions that improve cardiovascular function and reduce the risk of atherosclerotic cardiovascular disease. One of their most well-established effects is the reduction of **serum triglyceride concentrations** through decreased hepatic very-low-density lipoprotein (VLDL) synthesis, enhanced fatty acid β-oxidation, and increased clearance of triglyceride-rich lipoproteins. Clinical studies have consistently shown that prescription omega-3 formulations containing EPA or EPA/DHA can reduce triglyceride levels by approximately 20-45%, depending on dosage and baseline triglyceride concentrations (Virani *et al.*, 2023; NIH, 2025).

Omega-3 fatty acids also improve **vascular endothelial function**, which is essential for maintaining vascular homeostasis and regulating blood flow. EPA and DHA enhance nitric oxide (NO) bioavailability, reduce oxidative stress within endothelial cells, and improve endothelial-dependent vasodilation, thereby contributing to better vascular function and reduced arterial stiffness. Furthermore, these fatty acids possess **antithrombotic properties** by decreasing platelet aggregation and thromboxane A_2 synthesis while promoting the formation of less thrombogenic eicosanoids. Although omega-3 supplementation may modestly prolong bleeding time, clinically significant bleeding complications are uncommon at recommended therapeutic doses (Djuricic & Calder, 2023; Siscovick *et al.*, 2023).

Another important mechanism underlying cardiovascular protection is the **anti-arrhythmic effect** of omega-3 fatty acids. By incorporating into cardiomyocyte membrane phospholipids, EPA and DHA influence membrane excitability, stabilize cardiac ion channels, and improve electrical conduction, thereby reducing susceptibility to ventricular arrhythmias and sudden cardiac death. Additionally, omega-3 fatty acids exert modest **blood pressure-lowering effects**, particularly in individuals with hypertension, through improved endothelial function, enhanced arterial compliance, reduced sympathetic nervous system activity, and modulation of the renin-angiotensin-aldosterone system. Meta-analyses indicate that regular omega-3 intake can produce small but clinically meaningful reductions in both systolic and diastolic blood pressure, contributing to overall cardiovascular risk reduction (Zhang *et al.*, 2022; NIH, 2025).

Chronic vascular inflammation plays a central role in the initiation and progression of atherosclerosis, and omega-3 fatty acids mitigate this process through several anti-inflammatory mechanisms. EPA and DHA reduce the production of pro-inflammatory cytokines, including tumor necrosis factor-α

(TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6), while promoting the biosynthesis of specialized pro-resolving mediators such as resolvins and protectins that actively facilitate the resolution of inflammation. These actions contribute to stabilization of atherosclerotic plaques, reduction of vascular inflammation, and decreased progression of coronary artery disease (Calder, 2023; Djuricic & Calder, 2023).

Evidence from large randomized controlled trials and contemporary clinical guidelines supports the use of **EPA-rich formulations** in selected high-risk populations. In particular, high-dose purified EPA (icosapent ethyl, 4 g/day) has demonstrated significant reductions in major adverse cardiovascular events among patients with established cardiovascular disease or diabetes mellitus and persistent hypertriglyceridemia despite statin therapy. Consequently, several international cardiovascular guidelines recommend prescription EPA therapy as an adjunct to standard lipid-lowering treatment in appropriately selected patients. While the cardiovascular benefits of mixed EPA/DHA supplements in the general population remain less consistent, current evidence strongly supports the therapeutic role of purified EPA in secondary prevention and in individuals at elevated cardiovascular risk (Virani *et al.*, 2023; Djuricic & Calder, 2023; National Institutes of Health, 2025).

6.2 Brain health and cognitive function

The human brain is one of the most lipid-rich organs, with **docosahexaenoic acid (DHA)** representing the predominant omega-3 polyunsaturated fatty acid in neuronal membranes. DHA accounts for a substantial proportion of the phospholipid content of the cerebral cortex, synaptic membranes, and retinal photoreceptor cells, where it plays a critical role in maintaining membrane fluidity, neuronal signaling, synaptic plasticity, and neurotransmitter function. By preserving the structural integrity of neuronal membranes, DHA facilitates efficient signal transmission, supports neurogenesis, and enhances synaptic communication, all of which are essential for normal cognitive function and visual processing. Emerging evidence also indicates that DHA modulates neuroinflammation, reduces oxidative stress, promotes mitochondrial function, and stimulates the production of neuroprotective mediators such as neuroprotectin D1, thereby contributing to neuronal survival and resilience during aging (Calder, 2023; Dyall, 2024).

Numerous experimental and clinical studies have demonstrated that adequate intake of omega-3 fatty acids, particularly DHA, is associated with

improved memory, enhanced learning ability, and **better cognitive performance** across different stages of life. In children and adolescents, sufficient DHA intake supports brain maturation, attention, and cognitive development, whereas in adults and older individuals, higher dietary or supplemental DHA has been associated with maintenance of executive function, processing speed, and memory performance. Furthermore, omega-3 fatty acids may provide **neuroprotective effects during aging** by reducing neuroinflammation, limiting neuronal apoptosis, and attenuating the pathological processes associated with neurodegenerative disorders such as Alzheimer's disease and other forms of dementia. Although clinical outcomes have been variable, accumulating evidence suggests that maintaining adequate omega-3 status throughout life contributes to healthy cognitive aging and may delay age-related cognitive decline in susceptible individuals (National Institutes of Health, 2025; Baker, 2024).

DHA is equally indispensable for **ocular health**, as it constitutes nearly half of the polyunsaturated fatty acids present in retinal photoreceptor membranes. Adequate DHA concentrations are essential for photoreceptor membrane integrity, visual signal transduction, and retinal development, thereby supporting optimal visual acuity and protecting against retinal degeneration. Consequently, DHA has been incorporated into infant formulas and nutritional interventions aimed at supporting normal visual development and retinal function (National Institutes of Health, 2025; Calder, 2023).

The importance of DHA is particularly evident during **pregnancy and early infancy**, when rapid fetal brain growth and retinal development occur. Maternal DHA is actively transported across the placenta, especially during the third trimester, and continues to be supplied through breast milk after birth. Adequate maternal DHA intake has been associated with improved fetal neurodevelopment, enhanced visual acuity, better cognitive performance, and favorable neurobehavioral outcomes in early childhood. For this reason, several international health organizations recommend regular consumption of DHA-rich foods or appropriate supplementation during pregnancy and lactation to ensure optimal maternal and infant health. As a result, DHA has become a key ingredient in prenatal supplements and infant nutrition products, highlighting its importance as a nutraceutical for lifelong brain and visual health (Koletzko *et al.*, 2022; National Institutes of Health, 2025).

6.3 Mental health

The relationship between omega-3 fatty acids and mental health has received considerable scientific attention over the past two decades, with

growing evidence supporting their role in the prevention and adjunctive management of several psychiatric disorders. Among the long-chain omega-3 polyunsaturated fatty acids, **eicosapentaenoic acid (EPA)** has demonstrated more consistent therapeutic benefits than **docosahexaenoic acid (DHA)** in mood regulation, largely due to its potent anti-inflammatory properties and its influence on neurotransmitter systems. Omega-3 fatty acids modulate multiple neurobiological pathways implicated in psychiatric disorders, including regulation of serotonergic and dopaminergic neurotransmission, maintenance of neuronal membrane fluidity, reduction of neuroinflammation, attenuation of oxidative stress, and modulation of the hypothalamic–pituitary–adrenal (HPA) axis. Furthermore, EPA and DHA promote the production of specialized pro-resolving mediators that reduce neuroinflammatory responses increasingly recognized as contributors to the pathophysiology of mood disorders (Calder, 2023; Bazinet & Layé, 2024).

Clinical studies and meta-analyses have reported that omega-3 supplementation, particularly formulations containing a higher proportion of EPA, may significantly improve symptoms of **major depressive disorder (MDD)** when used as an adjunct to conventional antidepressant therapy. The antidepressant effects are believed to result from modulation of inflammatory cytokines, enhancement of monoaminergic neurotransmission and improvements in neuronal plasticity. Current evidence suggests that EPA-rich supplements are generally more effective than DHA alone in reducing depressive symptoms, especially among individuals with elevated inflammatory markers or treatment-resistant depression (Su *et al.*, 2023; Bazinet & Layé, 2024).

Omega-3 fatty acids have also shown potential benefits in the management of **anxiety disorders**, where supplementation has been associated with modest reductions in anxiety symptoms, particularly in individuals experiencing chronic stress, inflammatory conditions, or comorbid psychiatric disorders. Although the magnitude of these effects varies across studies, the anxiolytic properties of omega-3 fatty acids are thought to involve regulation of neuroinflammation, improvement of neuronal membrane function, and normalization of stress hormone responses. Consequently, omega-3 supplementation is increasingly being explored as a complementary strategy alongside established pharmacological and psychological interventions (National Institutes of Health, 2025; Calder, 2023).

In **bipolar disorder**, omega-3 fatty acids have primarily been investigated as **adjunctive therapy** rather than stand-alone treatment. Several

responsible for the production of pro-inflammatory cytokines, chemokines, and adhesion molecules. Furthermore, they influence the activity of **sterol regulatory element-binding proteins (SREBPs)**, reducing hepatic lipogenesis and cholesterol synthesis while promoting metabolic homeostasis. Emerging evidence from nutrigenomics indicates that omega-3 fatty acids modulate the expression of numerous genes involved in immune regulation, oxidative stress, mitochondrial function, apoptosis, and cellular differentiation, thereby contributing to their preventive and therapeutic effects across multiple chronic diseases (Calder, 2023; Baker, 2024; Djuricic & Calder, 2023).

5.4 Antioxidant and Cellular protection

Although omega-3 fatty acids are highly susceptible to lipid peroxidation because of their multiple double bonds, they indirectly enhance antioxidant defense systems and protect cells against oxidative damage. EPA and DHA increase the activity and expression of endogenous antioxidant enzymes, including **superoxide dismutase (SOD)**, **catalase (CAT)**, and **glutathione peroxidase (GPx)**, thereby reducing intracellular reactive oxygen species (ROS) and limiting oxidative stress. They also activate the **nuclear factor erythroid 2-related factor 2 (Nrf2)** signaling pathway, which regulates the transcription of numerous cytoprotective and antioxidant genes. Furthermore, omega-3 fatty acids preserve mitochondrial membrane integrity, improve mitochondrial respiration and ATP production, reduce mitochondrial ROS generation and inhibit mitochondria-mediated apoptosis. These cytoprotective actions are particularly important in tissues with high metabolic activity, such as the heart, brain, liver, and skeletal muscle. Through the combined modulation of oxidative stress, mitochondrial function, inflammation, and programmed cell death, omega-3 fatty acids contribute to the prevention of cellular dysfunction associated with aging, cardiovascular disease, metabolic syndrome, neurodegeneration, and chronic inflammatory disorders (Calder, 2023; Baker, 2024; National Institutes of Health, 2025).

6. Health benefits

6.1 Cardiovascular health

Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality worldwide, and omega-3 fatty acids have been extensively investigated for their cardioprotective properties. Among the three major omega-3 fatty acids, **eicosapentaenoic acid (EPA)** and **docosahexaenoic acid (DHA)** have demonstrated the strongest evidence for cardiovascular

clinical trials suggest that EPA-rich formulations may help reduce depressive symptoms and improve mood stability when combined with standard mood-stabilizing medications, although evidence for the prevention of manic episodes remains inconsistent. Similarly, in **attention-deficit/hyperactivity disorder (ADHD)**, supplementation with omega-3 fatty acids has demonstrated small to moderate improvements in attention, executive function, hyperactivity, and impulsivity in selected pediatric populations, particularly among children with low baseline omega-3 status. However, current evidence indicates that omega-3 supplementation should be considered a supportive nutritional intervention rather than a replacement for evidence-based pharmacological or behavioral therapies (Chang *et al.*, 2023; National Institutes of Health, 2025).

6.4 Anti-inflammatory disorders

Chronic inflammation is a fundamental pathological process underlying numerous autoimmune and inflammatory diseases and omega-3 polyunsaturated fatty acids (PUFAs), particularly **eicosapentaenoic acid (EPA)** and **docosahexaenoic acid (DHA)**, have emerged as promising nutraceutical agents for modulating inflammatory responses. Their anti-inflammatory effects are mediated through multiple complementary mechanisms, including competition with arachidonic acid for cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, resulting in reduced synthesis of pro-inflammatory eicosanoids such as prostaglandin E_2 (PGE_2), thromboxane A_2 (TXA_2), and leukotriene B_4 (LTB_4). In addition, EPA and DHA serve as precursors for specialized pro-resolving mediators (SPMs), including resolvins, protectins, and maresins, which actively promote the resolution of inflammation, facilitate tissue repair, and restore immune homeostasis. Omega-3 fatty acids also suppress activation of the nuclear factor-kappa B (NF-κB) signaling pathway and NLRP3 inflammasome, leading to decreased production of pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6) (Calder, 2023; Djuricic & Calder, 2023).

Among inflammatory disorders, the strongest clinical evidence supports the use of omega-3 fatty acids in **rheumatoid arthritis (RA)**. Numerous randomized controlled trials and meta-analyses have demonstrated that long-term supplementation with EPA and DHA can reduce joint pain, morning stiffness, disease activity, and the requirement for non-steroidal anti-inflammatory drugs (NSAIDs). These improvements are attributed to suppression of inflammatory cytokine production, reduced leukocyte

chemotaxis, and enhanced synthesis of pro-resolving lipid mediators that limit persistent synovial inflammation. Although omega-3 supplementation is not a substitute for disease-modifying antirheumatic drugs (DMARDs), it is increasingly recognized as an effective adjunctive nutritional intervention for improving clinical outcomes and quality of life in patients with RA (Calder, 2023; Gioxari *et al.*, 2023).

In **inflammatory bowel disease (IBD)**, including **Crohn's disease** and **ulcerative colitis**, omega-3 fatty acids have been investigated for their capacity to reduce intestinal inflammation and preserve epithelial barrier integrity. Experimental studies suggest that EPA and DHA decrease inflammatory cytokine production, regulate immune cell function, improve intestinal epithelial barrier function, and positively influence gut microbiota composition. Although clinical trial findings have been variable, omega-3 supplementation may provide supportive benefits in selected patients, particularly when combined with conventional anti-inflammatory therapies. Similar immunomodulatory effects have been observed in **psoriasis**, where omega-3 fatty acids may reduce keratinocyte hyperproliferation, improve skin lesions, and alleviate disease severity by suppressing inflammatory mediators involved in cutaneous immune responses (Calder, 2023; National Institutes of Health, 2025).

Omega-3 fatty acids have also demonstrated therapeutic potential in **asthma** and **systemic lupus erythematosus (SLE)**. In asthma, EPA and DHA may attenuate airway inflammation by reducing eosinophilic infiltration, decreasing leukotriene synthesis, and improving pulmonary immune regulation, although clinical benefits appear greater in individuals with eosinophilic or allergic phenotypes. In patients with SLE, omega-3 supplementation has been associated with improvements in disease activity, endothelial function, fatigue, and inflammatory biomarkers through modulation of both innate and adaptive immune responses. Nevertheless, larger multicenter randomized controlled trials are needed to establish standardized dosing strategies and confirm long-term efficacy across diverse patient populations (Abdelhamid *et al.*, 2023; National Institutes of Health, 2025).

6.5 Metabolic Syndrome and Diabetes

Metabolic syndrome is a multifactorial disorder characterized by central obesity, dyslipidemia, hypertension, insulin resistance, and impaired glucose metabolism, substantially increasing the risk of type 2 diabetes mellitus

(T2DM) and cardiovascular disease. Chronic low-grade inflammation, oxidative stress, and lipid dysregulation are central to the pathogenesis of metabolic syndrome, making omega-3 polyunsaturated fatty acids (PUFAs), particularly **eicosapentaenoic acid (EPA)** and **docosahexaenoic acid (DHA)**, attractive nutraceutical interventions. Through modulation of lipid metabolism, inflammatory signaling, and cellular energy homeostasis, omega-3 fatty acids have demonstrated beneficial effects on several components of metabolic syndrome, although their influence on glucose regulation remains less consistent (Calder, 2023; National Institutes of Health, 2025).

One of the most consistently documented metabolic benefits of omega-3 fatty acids is their ability to **improve lipid metabolism** and markedly **reduce serum triglyceride concentrations**. EPA and DHA suppress hepatic triglyceride synthesis by inhibiting sterol regulatory element-binding protein-1c (SREBP-1c), enhancing peroxisome proliferator-activated receptor-α (PPAR-α)-mediated β-oxidation of fatty acids, and reducing very-low-density lipoprotein (VLDL) production. Clinical trials have demonstrated that therapeutic doses (2-4 g/day) of EPA and DHA can reduce circulating triglyceride levels by approximately 20-45%, making prescription omega-3 formulations an established treatment for hypertriglyceridemia and an important adjunct in managing cardiometabolic risk (Virani *et al.*, 2023; Djuricic & Calder, 2023).

Omega-3 fatty acids have also been shown to **enhance insulin sensitivity** in certain populations by improving cell membrane fluidity, regulating adipokine secretion, reducing inflammatory cytokine production, and promoting glucose uptake through activation of PPAR signaling pathways. Additionally, EPA and DHA reduce systemic inflammation by suppressing nuclear factor-kappa B (NF-κB) activation and promoting the synthesis of specialized pro-resolving mediators, thereby improving the inflammatory milieu associated with obesity and insulin resistance. However, clinical evidence regarding improvements in insulin sensitivity remains heterogeneous, with greater benefits often observed in individuals with obesity, metabolic syndrome, or elevated inflammatory biomarkers than in those with established type 2 diabetes mellitus (Calder, 2023; Lalia & Lanza, 2021).

Another important therapeutic action of omega-3 fatty acids is the reduction of **hepatic fat accumulation**, making them valuable in the management of **metabolic dysfunction-associated steatotic liver disease (MASLD)**, formerly known as non-alcoholic fatty liver disease (NAFLD).

EPA and DHA decrease hepatic lipogenesis, stimulate fatty acid oxidation, improve hepatic lipid export, and attenuate hepatic inflammation, thereby reducing liver fat content and improving liver enzyme profiles in many patients. These effects are particularly relevant because hepatic steatosis is closely linked with insulin resistance, metabolic syndrome, and cardiovascular disease. Consequently, omega-3 supplementation has been investigated as an adjunctive nutritional strategy for improving hepatic and metabolic health (Calder, 2023; National Institutes of Health, 2025).

Despite these favorable effects on lipid metabolism and inflammation, the impact of omega-3 fatty acids on **glycemic control** remains variable across studies. While some randomized controlled trials have reported modest improvements in fasting plasma glucose, insulin sensitivity, or glycated hemoglobin (HbA1c), others have found little or no significant effect. Current evidence suggests that omega-3 fatty acids should not be considered primary glucose-lowering agents but rather as complementary nutraceuticals that improve overall cardiometabolic health by reducing hypertriglyceridemia, systemic inflammation, and cardiovascular risk. Therefore, omega-3 supplementation may provide the greatest benefit when integrated with dietary modification, physical activity, weight management, and evidence-based pharmacological therapies for metabolic syndrome and diabetes (American Diabetes Association, 2025; Djuricic & Calder, 2023).

6.6 Cancer prevention

Cancer development is a complex, multistep process involving chronic inflammation, oxidative stress, genetic and epigenetic alterations, dysregulated cell proliferation, and impaired apoptosis. Increasing evidence suggests that omega-3 polyunsaturated fatty acids (PUFAs), particularly **eicosapentaenoic acid (EPA)** and **docosahexaenoic acid (DHA)**, may contribute to cancer prevention and supportive cancer care through multiple biological mechanisms. Although epidemiological studies and experimental models have demonstrated promising anticancer properties, clinical evidence remains heterogeneous. Consequently, omega-3 fatty acids are currently regarded as **supportive nutraceuticals** that may complement conventional cancer prevention strategies and standard oncological therapies rather than replace them (Calder, 2023; National Institutes of Health, 2025).

The anticancer activities of omega-3 fatty acids are mediated through several interconnected molecular pathways. EPA and DHA suppress chronic inflammation by reducing the production of pro-inflammatory cytokines and

arachidonic acid-derived eicosanoids while enhancing the synthesis of specialized pro-resolving mediators (SPMs), including resolvins and protectins. They also inhibit activation of nuclear factor-kappa B (NF-κB), phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), and mammalian target of rapamycin (mTOR) signaling pathways, all of which are frequently dysregulated in cancer. In addition, omega-3 fatty acids modulate membrane lipid composition and lipid raft organization, thereby influencing receptor-mediated signaling, growth factor responses, and intracellular communication. Experimental studies further demonstrate their ability to inhibit tumor cell proliferation, promote programmed cell death (apoptosis), induce cell-cycle arrest, reduce angiogenesis, suppress metastatic potential, and enhance antitumor immune responses (Calder, 2023; Vaughan *et al.*, 2022).

Among individual malignancies, the strongest evidence has been reported for **breast cancer**, where higher dietary intake or circulating concentrations of marine-derived omega-3 fatty acids have been associated with a modest reduction in disease risk in some observational studies. Experimental investigations suggest that EPA and DHA inhibit breast cancer cell proliferation, enhance apoptosis, reduce inflammatory signaling, and may improve the efficacy of chemotherapy by increasing tumor cell sensitivity to cytotoxic agents. Nevertheless, randomized clinical trials have produced variable findings, and further well-designed studies are required before definitive recommendations can be made (Fabian *et al.*, 2023; Calder, 2023).

In **colorectal cancer**, omega-3 fatty acids have shown considerable promise because chronic intestinal inflammation is an established risk factor for tumor development. EPA has been reported to reduce colorectal adenoma formation in selected high-risk populations, suppress cyclooxygenase-2 (COX-2)-mediated inflammatory pathways, improve epithelial barrier function, and regulate gut microbiota composition. Experimental evidence also indicates that omega-3 fatty acids inhibit tumor growth by modulating Wnt/β-catenin signaling, inducing apoptosis, and reducing cellular proliferation. Similarly, studies involving **prostate cancer** and **pancreatic cancer** suggest potential protective effects through attenuation of inflammatory signaling, inhibition of tumor angiogenesis, and modulation of immune responses. However, the available epidemiological and clinical evidence remains inconsistent, and additional large-scale prospective studies are necessary to clarify these associations and identify patient populations most likely to benefit (Vaughan *et al.*, 2022; National Institutes of Health, 2025).

Beyond cancer prevention, omega-3 fatty acids have attracted increasing attention in **supportive oncology**, particularly for their role in improving nutritional status, preserving skeletal muscle mass, reducing cancer-associated cachexia, and alleviating systemic inflammation in patients undergoing chemotherapy or surgery. Several studies suggest that EPA-enriched nutritional supplements may improve body weight maintenance, treatment tolerance, and quality of life in selected patients with advanced malignancies. Nevertheless, omega-3 fatty acids should be considered **adjunctive nutritional interventions** that complement evidence-based oncological treatments rather than primary anticancer therapies. Future research integrating nutrigenomics, precision nutrition, and personalized medicine is expected to further clarify their role in cancer prevention and supportive care (Arends *et al.*, 2021; Calder, 2023).

6.7 Eye health

The eye, particularly the retina, contains one of the highest concentrations of **docosahexaenoic acid (DHA)** in the human body, highlighting its indispensable role in maintaining visual function and ocular health. DHA constitutes approximately 30-50% of the total polyunsaturated fatty acids present in retinal photoreceptor outer segment membranes, where it contributes to membrane fluidity, photoreceptor integrity, and efficient visual signal transduction. Owing to its unique structural properties, DHA enhances the flexibility of retinal cell membranes, supports rhodopsin activation, and facilitates the rapid transmission of visual signals from photoreceptors to the central nervous system. Additionally, DHA serves as a precursor of **neuroprotectin D1**, a specialized lipid mediator with potent anti-inflammatory, antioxidant, and neuroprotective properties that protect retinal cells from oxidative stress and apoptosis (Calder, 2023; National Institutes of Health, 2025).

Adequate DHA intake is particularly critical during **fetal development, infancy and early childhood**, when rapid retinal maturation and visual system development occur. Maternal DHA is actively transported across the placenta during the third trimester of pregnancy and subsequently supplied through breast milk, providing the developing retina with essential structural lipids required for optimal visual acuity and neurological development. Numerous clinical studies have demonstrated that sufficient maternal and infant DHA intake is associated with improved visual acuity, retinal maturation, and cognitive development during early life. Consequently, DHA is routinely incorporated into prenatal supplements and infant formulas to

support normal ocular and neurodevelopment (Koletzko *et al.*, 2022; National Institutes of Health, 2025).

Beyond developmental health, omega-3 fatty acids have demonstrated potential therapeutic benefits in the management of **dry eye disease (DED)**, a multifactorial disorder characterized by tear film instability, ocular surface inflammation, and discomfort. EPA and DHA may improve tear film quality by reducing ocular surface inflammation, modulating meibomian gland function, and decreasing the production of pro-inflammatory cytokines. Although several randomized controlled trials and meta-analyses have reported improvements in tear stability, symptom severity, and ocular comfort following omega-3 supplementation, other large clinical trials have shown more modest or inconsistent effects. Therefore, current evidence suggests that omega-3 fatty acids may provide benefit for selected patients with dry eye disease, particularly when dietary omega-3 intake is inadequate, but they should be considered complementary rather than definitive therapy (Downie *et al.*, 2023; Calder, 2023).

The potential role of omega-3 fatty acids in the prevention and management of **age-related macular degeneration (AMD)** has also attracted considerable scientific interest. Experimental studies indicate that DHA protects retinal pigment epithelial cells by reducing oxidative stress, suppressing inflammation and preserving photoreceptor function. Observational studies have generally reported an association between higher dietary consumption of fish or marine-derived omega-3 fatty acids and a lower risk of progression to advanced AMD. However, findings from randomized clinical trials have been less consistent, and current evidence does not conclusively support omega-3 supplementation as a stand-alone intervention for AMD prevention. Nevertheless, regular dietary intake of omega-3-rich foods remains an important component of a healthy dietary pattern that supports overall ocular health and may contribute to reducing the risk of age-related retinal disorders (Age-Related Eye Disease Study 2 Research Group, 2022; National Institutes of Health, 2025).

7. Therapeutic applications

Table 1: Clinical Applications and Therapeutic Roles of Omega-3 Fatty Acids

Disease	Therapeutic Role
Hypertriglyceridemia	Established therapy
Coronary artery disease	Risk reduction in selected patients
Hypertension	Adjunctive management

Depression	Adjunctive treatment
Alzheimer's disease	Potential cognitive support
Rheumatoid arthritis	Reduction of inflammation and joint pain
Non-alcoholic fatty liver disease	Improvement in hepatic lipid metabolism
Pregnancy	Fetal neurodevelopment support

8. Omega-3 fatty acids in functional foods

The growing recognition of the health benefits of omega-3 polyunsaturated fatty acids (PUFAs) has led to their widespread incorporation into **functional foods**, providing consumers with convenient dietary sources of these essential nutrients without substantially altering eating habits. Functional foods enriched with omega-3 fatty acids are designed to deliver physiological benefits beyond basic nutrition and have become an important strategy for addressing the global inadequacy of dietary EPA and DHA intake. The incorporation of omega-3 fatty acids into commonly consumed foods also aligns with public health initiatives aimed at reducing the prevalence of cardiovascular disease, metabolic disorders, cognitive decline, and chronic inflammatory conditions through nutritional interventions (Calder, 2023; National Institutes of Health, 2025).

A wide range of omega-3-enriched functional foods has been developed for commercial markets. These include **dairy products** such as milk, yogurt, cheese, and fermented beverages; **bakery products** including bread, biscuits, muffins, and breakfast cereals; **functional beverages** such as fruit juices, dairy-based drinks, and plant-based beverages; **edible spreads and margarines**; **omega-3-enriched eggs** produced by dietary supplementation of laying hens; **infant formulas** fortified with DHA to support neurological and visual development; and **meat and poultry products** formulated with fish oil, algal oil, flaxseed, or encapsulated omega-3 ingredients. The source of omega-3 fatty acids varies depending on product type and target consumers, with marine fish oil, krill oil, algal oil, flaxseed oil, chia seed oil, and hemp seed oil being the most commonly used ingredients. In recent years, algal-derived DHA has gained increasing commercial importance because it is sustainable, vegetarian, and free from many marine contaminants, making it particularly suitable for infant nutrition and plant-based functional foods (Baker, 2024; Jacobsen *et al.*, 2021).

Despite their nutritional advantages, the incorporation of omega-3 fatty acids into food matrices presents several technological challenges. Because EPA and DHA contain multiple double bonds, they are highly susceptible to

lipid oxidation, leading to the formation of hydroperoxides, aldehydes, ketones and other secondary oxidation products that adversely affect nutritional quality and sensory characteristics. Oxidative deterioration often results in **off-flavors and fishy odors**, reducing consumer acceptability and limiting product marketability. Furthermore, exposure to oxygen, light, heat, moisture, and transition metals during food processing and storage accelerates oxidation, thereby reducing the stability and shelf life of omega-3-fortified products. High-temperature processing methods such as baking, frying, extrusion, and pasteurization may also degrade long-chain omega-3 fatty acids, presenting additional formulation challenges for the food industry (Jacobsen *et al.*, 2021; Shahidi & Ambigaipalan, 2022).

To overcome these limitations, considerable research has focused on the development of advanced delivery systems that enhance the stability and bioavailability of omega-3 fatty acids. **Microencapsulation** has emerged as one of the most effective technologies for protecting EPA and DHA against oxidation while masking undesirable sensory characteristics. This approach involves encapsulating omega-3 oils within protective matrices composed of proteins, polysaccharides, lipids, or biopolymers using techniques such as spray drying, freeze drying, complex coacervation, liposomal encapsulation, and nanoemulsion technology. Encapsulation not only improves oxidative stability and shelf life but also enhances controlled release and gastrointestinal bioavailability. In addition, the incorporation of **natural antioxidants**, including tocopherols (vitamin E), rosemary extract, ascorbic acid, polyphenols, and carotenoids, further protects omega-3 fatty acids from oxidative degradation during processing and storage. The combined application of encapsulation technologies and antioxidant systems has significantly improved the physicochemical stability, sensory quality, and consumer acceptance of omega-3-enriched functional foods, thereby facilitating their widespread commercial utilization (Jacobsen *et al.*, 2021; Baker, 2024).

9. Safety and Recommended intake

Omega-3 fatty acids are generally recognized as safe when consumed at recommended levels.

Possible adverse effects include:

- Fishy aftertaste
- Mild gastrointestinal discomfort

- Nausea
- Loose stools

Very high supplemental doses may increase bleeding risk in susceptible individuals or those receiving anticoagulant therapy. Consumers should consult healthcare professionals before initiating high-dose supplementation, particularly if they have underlying medical conditions or take medications.

General intake recommendations vary by age, physiological status, and national dietary guidelines, with many authorities recommending regular consumption of fatty fish and adequate daily intake of EPA and DHA for adults.

Conclusion

Omega-3 fatty acids represent one of the most scientifically validated classes of nutraceuticals. Their diverse biological functions extend beyond essential nutrition to encompass cardiovascular protection, neurodevelopment, modulation of inflammation, metabolic health, and immune regulation. Although substantial evidence supports their use in disease prevention and adjunctive therapy, continued research is necessary to refine dosage recommendations, optimize delivery systems, and establish personalized nutritional interventions. Sustainable production technologies and rigorous clinical investigations will further enhance the role of omega-3 fatty acids in functional foods and nutraceuticals, reinforcing their importance in modern preventive healthcare.

References

1. Abdelhamid AS, Brown TJ, Brainard JS, Biswas P, Thorpe GC, Moore HJ, *et al*. Omega-3 fatty acids for the primary and secondary prevention of inflammatory and chronic diseases: updated evidence from systematic reviews. Cochrane Database Syst. Rev. 2023;2023(10):CD003177. Doi: 10.1002/14651858.CD003177.pub5.
2. Age-Related Eye Disease Study 2 (AREDS2) Research Group. Long-term outcomes of the Age-Related Eye Disease Study 2: implications for nutritional interventions in age-related macular degeneration. JAMA Ophthalmol. 2022;140(9):895-904.
3. American Diabetes Association Professional Practice Committee. Facilitating positive health behaviors and well-being to improve health outcomes: Standards of Care in Diabetes-2025. Diabetes Care. 2025;48(1):S77-S94. Doi: 10.2337/dc25-S005.

4. Arends J, Baracos V, Bertz H, Bozzetti F, Calder PC, Deutz NEP, *et al.* ESPEN practical guideline: clinical nutrition in cancer. Clin Nutr. 2021;40(5):2898-2913. Doi: 10.1016/j.clnu.2021.02.005.

5. Baker EJ. Alternative sources of bioactive omega-3 fatty acids: what are the options? Curr. Opin. Clin. Nutr. Metab. Care. 2024;27(2):106-115. Doi: 10.1097/MCO.0000000000001006.

6. Bazinet RP, Layé S. Polyunsaturated fatty acids and their metabolites in brain function and mental health. Nat Rev Neurosci. 2024;25(2):95-112. Doi: 10.1038/s41583-023-00777-8.

7. Calder PC. Marine omega-3 fatty acids and human health: an update. Annu Rev Nutr. 2023;43:1-27. Doi: 10.1146/annurev-nutr-062320-015556.

8. Chang JPC, Su KP, Mondelli V, Pariante CM. Omega-3 polyunsaturated fatty acids in attention-deficit/hyperactivity disorder and other neuropsychiatric disorders: current evidence and future directions. Prog Lipid Res. 2023;89:101205. Doi: 10.1016/j.plipres.2022.101205.

9. Djuricic I, Calder PC. Pros and cons of long-chain omega-3 polyunsaturated fatty acids in cardiovascular health. Annu Rev Pharmacol Toxicol. 2023;63:383-406. Doi: 10.1146/annurev-pharmtox-051921-090208.

10. Downie LE, Ng SM, Lindsley K, Akpek EK, Tong L. Omega-3 and omega-6 polyunsaturated fatty acids for dry eye disease: an updated systematic review and meta-analysis. Ocul Surf. 2023;28:52-66. Doi: 10.1016/j.jtos.2023.02.004.

11. Dyall SC. Long-chain omega-3 fatty acids and brain health: mechanisms and clinical perspectives. Prostaglandins Leukot Essent Fatty Acids. 2024;201:102742. Doi: 10.1016/j.plefa.2024.102742.

12. Fabian CJ, Kimler BF, Hursting SD. Omega-3 fatty acids and breast cancer prevention: current evidence and future directions. Cancer Prev Res. 2023;16(4):201-214. Doi: 10.1158/1940-6207.CAPR-22-0458.

13. Gioxari A, Kaliora AC, Marantidou F, Panagiotakos DB. Omega-3 fatty acid supplementation and rheumatoid arthritis: a systematic review and meta-analysis of randomized controlled trials. Nutrients. 2023;15(4):902. Doi: 10.3390/nu15040902.

14. Harvard T.H. Chan School of Public Health. Omega-3 fatty acids: The Nutrition Source; 2025.

15. Jacobsen C, Let MB, Nielsen NS, Meyer AS. Antioxidant strategies for preventing oxidative deterioration of omega-3-enriched foods: recent advances and future perspectives. Trends Food Sci. Technol. 2021;112:519-531. Doi: 10.1016/j.tifs.2021.04.020.

16. Koletzko B, Cetin I, Brenna JT. Dietary fat intakes for pregnant and lactating women. Ann Nutr Metab. 2022;78(2):15-28. Doi: 10.1159/000524866.

17. Lalia AZ, Lanza IR. Omega-3 fatty acids and insulin sensitivity: mechanisms and clinical implications. Curr. Opin. Clin. Nutr. Metab. Care. 2021;24(2):110-116. Doi: 10.1097/MCO.0000000000000724.

18. National Institutes of Health, Office of Dietary Supplements. Omega-3 Fatty Acids-Health Professional Fact Sheet; 2025.

19. Serhan CN, Levy BD. Resolvins in inflammation: emergence of the pro-resolving superfamily of mediators. Nat Rev Immunol. 2023;23(9):571-589. Doi: 10.1038/s41577-023-00875-6.

20. Shahidi F, Ambigaipalan P. Omega-3 polyunsaturated fatty acids and functional foods: stability, delivery systems, and health applications. Annu Rev Food Sci. Technol. 2022;13:145-169. Doi: 10.1146/annurev-food-052720-010850.

21. Siscovick DS, Barringer TA, Fretts AM, Wu JHY, Lichtenstein AH, Costello RB, *et al.* Omega-3 polyunsaturated fatty acid supplementation and cardiovascular disease: current evidence and future directions. Circulation. 2023;147(5):e93-e115. Doi: 10.1161/CIR.0000000000001125.

22. Su KP, Tseng PT, Yang HT, *et al.* Omega-3 polyunsaturated fatty acids in major depressive disorder: an updated systematic review and meta-analysis. Transl Psychiatry. 2023;13:312. Doi: 10.1038/s41398-023-02539-7.

23. Tutor A, O'Keefe EL, Lavie CJ, Elagizi A, Milani R, O'Keefe J. Omega-3 fatty acids in primary and secondary prevention of cardiovascular diseases. Prog. Cardiovasc Dis. 2024;84:19-26. Doi: 10.1016/j.pcad.2024.03.009.

24. Vaughan VC, Hassing MR, Lewandowski PA. Marine polyunsaturated fatty acids and cancer therapy: biological mechanisms and clinical perspectives. Cancers (Basel). 2022;14(9):2206. Doi: 10.3390/cancers14092206.

25. Virani SS, Morris PB, Agarwala A, Ballantyne CM, Birtcher KK, Kris-Etherton PM, *et al.* ACC Expert Consensus Decision Pathway on the management of atherosclerotic cardiovascular disease risk reduction in patients with persistent hypertriglyceridemia. J Am Coll. Cardiol. 2023;81(20):2059-2114. Doi: 10.1016/j.jacc.2023.02.003.

26. Zhang Y, Zhuang P, He W, Chen J, Wang W, Freedman ND, *et al.* Association of fish oil supplementation with cardiovascular outcomes: a systematic review and dose-response meta-analysis of randomized controlled trials. Mayo Clin Proc. 2022;97(7):1285-1298. Doi: 10.1016/j.mayocp.2022.02.018.