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Review Article

Role of Omega-3 Polyunsaturated Fatty Acids in Human Health: Chemistry, Mechanisms, and Clinical Evidence

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Abstract

Omega-3 polyunsaturated fatty acids (PUFAs) are a structurally distinct class of lipids characterized by a cis double bond at the third carbon from the methyl (ω) terminus. Major nutritionally relevant forms include α -linolenic acid (ALA), eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA). This review synthesizes recent advances in the chemistry, metabolism, and clinical significance of omega-3 PUFAs. Emphasis is placed on their structural features, susceptibility to oxidation, conversion into specialised pro-resolving mediators, and incorporation into biological membranes. These chemical properties are linked to their mechanistic roles in cardiovascular, metabolic, neurological, inflammatory, and developmental health. Emerging aspects such as sustainable omega-3 sources, bioavailability, and the omega-3 index as a biomarker are also discussed. Current clinical evidence highlights that omega-3 PUFAs exert their effects through membrane modulation, receptor signalling, and lipid-mediator pathways. Future research should integrate lipidomics and personalised nutrition approaches to optimise therapeutic applications.

Keywords: Omega-3 fatty acids; EPA; DHA; PUFA; lipid metabolism; clinical health

1. Introduction

Omega-3 PUFAs are essential lipids that humans must obtain from the diet. Chemically, they are long-chain fatty acids with multiple cis double bonds, the first located at the third carbon from the methyl end (n-3 position). The main nutritional species—ALA, EPA, DPA, and DHA differ in chain length and degree of unsaturation, which in turn govern their physical behavior in membranes and their susceptibility to oxidation¹. Classic epidemiological observations in fish-eating populations led to the hypothesis that marine omega-3s confer cardioprotection. Since then, an extensive range of studies has evaluated omega-3 PUFAs in cardiovascular disease (CVD), metabolic syndrome, pregnancy, cognitive decline,

depression, and chronic inflammation¹⁻². Recent evaluations highlight the variety of biological effects and the variability in results from clinical trials, urging the need for a chemistry-focused and individualized strategy³⁻⁵.

This article focuses on the chemistry of omega-3 PUFAs and how it explains their roles in human health; also the structural features and oxidative reactivity, endogenous metabolism to bioactive mediators, dietary and supplemental sources, biomarkers of omega-3 status, and mechanistic links to clinical outcomes across major organ systems. The overall role of omega-3 PUFAs in various physiological and clinical domains is summarized schematically in fig. 1.

Role of Omega-3 Polyunsaturated Fatty Acids in Human Health

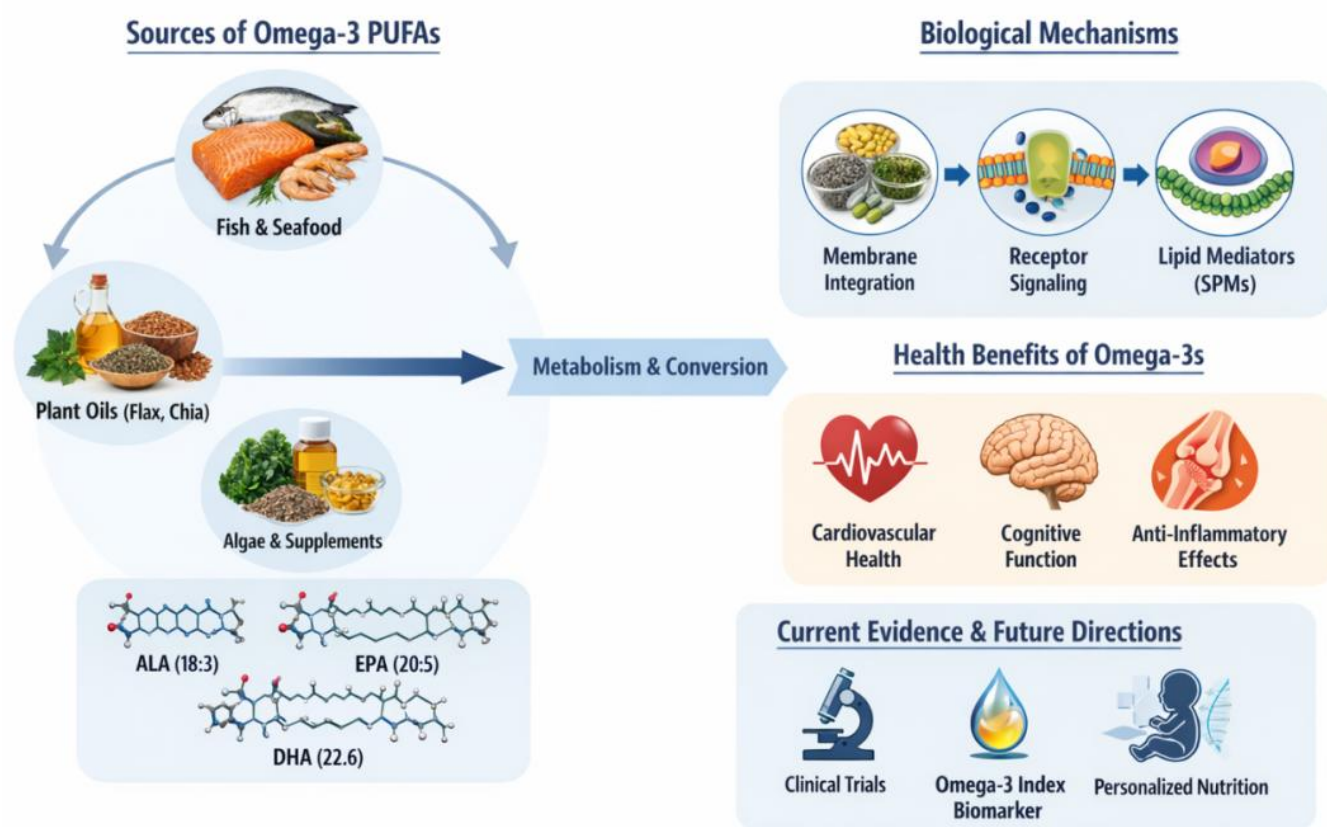


Figure 1: Schematic illustration of the biological mechanisms and clinical effects of omega-3 PUFA, including their roles in cardiovascular, metabolic, neurological, and inflammatory health through modulation of lipid metabolism, inflammatory pathways, and cellular signaling.

2. Chemistry and Metabolism of Omega-3 PUFAs

The chemistry and metabolism of omega-3 PUFAs are defined by their unique structural features, including multiple double bonds that influence their physical properties and reactivity⁶. In the body, shorter-chain precursors undergo endogenous elongation and desaturation to form long-chain omega-3 fatty acids such as EPA and DHA. These fatty acids are then incorporated into cell membranes and various lipid classes, where they play key functional roles. They can also be enzymatically oxidised to produce eicosanoids and specialised pro-resolving mediators, which are important in regulating physiological processes, particularly inflammation.

2.1. Structural features and physical chemistry

Omega-3 PUFAs share several key structural characteristics (Fig. 2) i.e. multiple cis double bonds, often conjugated in a methylene-interrupted pattern ($-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}=\text{CH}-$), which increase molecular flexibility. Chain lengths ranging from 18 carbons (ALA) to 22 carbons (DHA), with increasing unsaturation from ALA (18:3n-3) to DHA (22:6n-3).

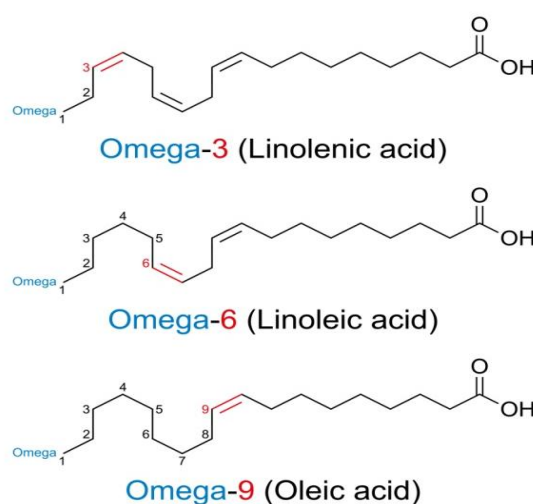


Fig. 2 Chemical structures of major omega-3 PUFAs.

The high degree of unsaturation lowers melting points and increases membrane fluidity. This structural property is central to the ability of DHA to alter membrane packing, influence lipid raft organisation, and modulate protein conformation in neural and retinal tissues⁷. However, the same structural features make omega-3 PUFAs highly prone to auto-oxidation,

initiated by hydrogen abstraction at bis-allylic sites and propagated via peroxy radicals. This gives rise to lipid hydroperoxides and secondary aldehydic products, which have implications for food stability and biological oxidative stress^{3,8}.

2.2. Endogenous elongation and desaturation

In humans, ALA can be elongated and desaturated via $\Delta 6$ -desaturase, elongase, and $\Delta 5$ -desaturase enzymes shared with omega-6 linoleic acid. This pathway converts ALA to EPA, DPA, and, to a limited extent, DHA. Stable isotope and tissue profiling studies show that conversion rates are modest, often below 10 percent for EPA and considerably lower for DHA, especially when linoleic acid intake is high². Consequently, EPA and DHA are considered conditionally essential, particularly for life stages and tissues with high DHA demand (e.g., fetal and infant brain, retina, sperm). Direct intake from marine or microbial sources may be necessary to achieve adequate levels in these compartments⁹.

2.3. Incorporation into membranes and lipid classes

Following intestinal absorption, omega-3 PUFAs are distributed into multiple lipid pools that determine their transport, storage, and biological function. A substantial fraction is esterified into triacylglycerols and incorporated into chylomicrons, enabling delivery to peripheral tissues and storage in adipose tissue. Simultaneously, omega-3 PUFAs are incorporated into membrane phospholipids, particularly phosphatidylcholine and phosphatidylethanolamine, where they influence membrane fluidity, receptor activity, and cellular responses. A smaller proportion is converted into cholesteryl esters within circulating

lipoproteins, contributing to systemic transport and redistribution. The relative partitioning of omega-3 PUFAs among these lipid classes is dynamic and influenced by dietary intake, metabolic status, and tissue-specific demand.

Incorporation of omega-3 PUFAs into membrane phospholipids results in partial displacement of arachidonic acid, leading to measurable changes in membrane composition and biophysical properties such as fluidity, thickness, and lateral organisation. These structural modifications directly affect ion-channel and receptor function, influencing cardiac electrophysiology, neuronal excitability, and neurotransmission. In addition, omega-3 PUFAs disrupt cholesterol-rich lipid rafts, altering the localisation and activity of signalling proteins involved in inflammatory and metabolic pathways.

Furthermore, replacement of arachidonic acid in membrane phospholipids modifies the pool of substrates available for enzymatic reactions. This shift reduces the production of pro-inflammatory eicosanoids while enhancing the generation of specialised pro-resolving mediators (SPMs), thereby promoting resolution of inflammation and tissue repair. In simple terms, omega-3 PUFAs reprogram cellular lipid signalling from a pro-inflammatory to a pro-resolving state.

These membrane-level alterations provide a mechanistic basis for the diverse physiological effects of omega-3 PUFAs, linking their chemical properties to observed benefits in cardiovascular health, metabolic regulation, brain function, and inflammatory conditions (Table 1).

Table 1: Effects of omega-3 PUFA incorporation into membrane phospholipids

Aspect Affected	Membrane-Level Change	Functional / Biological Implication
Ion channels and receptors	Increased membrane fluidity and altered lipid-protein interactions due to displacement of arachidonic acid	Modulation of cardiac electrophysiology, neuronal excitability, neurotransmission, and receptor signalling efficiency
Lipid rafts and signalling platforms	Disruption and reorganisation of cholesterol-rich microdomains	Altered localisation and activity of raft-associated receptors, kinases, and inflammatory signalling pathways
Lipid mediator substrate availability	Reduced arachidonic acid and increased EPA/DHA content in phospholipids	Shift from pro-inflammatory eicosanoid synthesis toward specialised pro-resolving mediator (SPM) production

2.4. Oxidation to eicosanoids and specialised pro-resolving mediators

EPA and DHA serve as substrates for cyclo-oxygenases (COX), lipoxygenases (LOX), and cytochrome P450 enzymes, yielding a range of bioactive lipid mediators.

- i. **Alternative eicosanoids:** 3-series prostaglandins and thromboxanes, and 5-series leukotrienes, which are generally less pro-inflammatory than those derived from arachidonic acid¹⁰

- ii. **Specialised pro-resolving mediators (SPMs):** resolvins (E-series from EPA, D-series from DHA), protectins, and maresins—poly-hydroxylated derivatives with defined stereochemistry and potent pro-resolving actions¹⁰⁻¹²

SPMs actively orchestrate resolution of inflammation by limiting neutrophil recruitment, enhancing efferocytosis, and promoting tissue repair. Human studies show that circulating SPM concentrations are

modulated by dietary omega-3 intake, age, sex, and disease status^{10,13}

3. Sources, Sustainability, and Bioavailability

Omega-3 PUFAs are obtained from a variety of sources, including marine foods such as fish and seafood, which remain the traditional and most direct providers of EPA and DHA. Plant sources contribute mainly α -linolenic acid, which requires metabolic conversion to longer-chain forms. Microalgal and microbial oils offer sustainable and vegetarian alternatives for producing EPA and DHA. The effectiveness of these sources depends on oxidative stability and formulation chemistry, which influence product quality. Ultimately, bioavailability plays a key role in determining how efficiently these fatty acids are absorbed and utilised in the body, with studies showing comparable bioavailability between algal and fish-derived omega-3s¹⁴.

3.1. Marine foods and traditional sources

Fatty fish such as salmon, mackerel, sardines, Hilsa and herring are the primary dietary sources of EPA and DHA.¹⁵⁻¹⁷ Typical servings provide several hundred milligrams to >1 g of EPA+DHA, depending on species and preparation¹⁻².

Fish-oil supplements, produced by concentration and purification of marine oils, offer higher doses and are commonly used in clinical studies. Chemical forms include natural TAGs, re-esterified TAGs, ethyl esters, and phospholipids, each with slightly different digestion and absorption characteristics³.

3.2. Plant sources of omega-3 PUFAs

Plant foods (flaxseed, chia, walnuts, hemp, canola) mainly provide ALA. While ALA has independent health associations and can serve as a precursor to long-chain omega-3s, its conversion is limited, particularly to DHA¹. Rizzo and colleagues (2023) review promising plant-derived sources of PUFAs, including oilseeds and emerging crops that can be bred or engineered for higher ALA or even EPA/DHA content. They argue that diversifying plant sources is vital for meeting global omega-3 needs in a sustainable and culturally flexible manner¹⁸.

3.3. Microalgal and microbial oils

Microalgae and thraustochytrid microorganisms naturally synthesise EPA and DHA. Their oils are now used to produce vegan omega-3 supplements, infant-formula ingredients, and fortified foods. Saini et al. (2021) describe microalgal and microbial sources as chemically comparable to fish oil in EPA/DHA content but with lower contaminant risk and better sustainability profiles³. Recent studies highlight the health benefits of supplementation with microbial omega-3s and discuss the growing market for fish-free EPA and DHA products¹⁹. Biotechnological strategies such as metabolic engineering and controlled fermentation enable tailoring of fatty-acid profiles, potentially optimising EPA:DHA ratios and oxidation stability²⁰.

3.4. Oxidative stability and formulation chemistry

Their high degree of unsaturation makes omega-3 PUFAs vulnerable to oxidation during processing, storage, and digestion. Studies summarise strategies to improve oxidative stability—antioxidant addition, microencapsulation, and protective packaging—emphasising the need to balance shelf-life with bioavailability²¹. Swetha et al. (2024) review sustainable omega-3 production and point out that oxidation control is crucial not only for sensory quality but also for environmental and economic sustainability, as significant energy and resources are required to produce these high-value omega-3 products²².

3.5. Bioavailability

The bioavailability of omega-3 PUFAs is influenced by several interrelated factors, including their chemical form, the food matrix, the amount and type of co-ingested dietary fat, and individual digestive conditions such as pancreatic enzyme activity and bile secretion. These factors collectively determine the efficiency of lipid digestion, micelle formation, and intestinal absorption.

Evidence indicates that omega-3 PUFAs provided in triacylglycerol or phospholipid forms may exhibit higher absorption efficiency than ethyl ester formulations under low-fat dietary conditions. This difference is primarily attributed to variations in enzymatic hydrolysis and micellar incorporation. However, these formulation-dependent differences are substantially minimized when omega-3s are consumed with meals containing adequate dietary fat, which enhances lipid digestion and uptake².

From a clinical perspective, short-term differences in absorption are less important than long-term intake patterns. The incorporation of EPA and DHA into circulating lipids, cell membranes, and erythrocytes occurs gradually over weeks to months and is best reflected by changes in the omega-3 index.

Consequently, consistent and sustained intake of omega-3 PUFAs is the primary determinant of achieving biologically meaningful tissue levels and clinical effects, rather than the specific formulation used in the short term¹.

4. Biomarkers of Omega-3 Status

Biomarkers of omega-3 status are used to assess the levels of EPA and DHA in the body and their potential health implications. The omega-3 index and related measures, such as plasma and red blood cell fatty acid composition, provide reliable indicators of long-term intake. These biomarkers help identify deficiencies and guide dietary or supplemental interventions. At a global level, studies highlight significant variability in omega-3 status, with widespread intake gaps in many populations due to low consumption of marine-based foods²³.

4.1. The omega-3 index and related measures

The omega-3 index—EPA+DHA as a percentage of total fatty acids in erythrocyte membranes—is now widely used as a medium-term biomarker of long-chain omega-3 status⁴⁻⁵. It reflects approximately the last 3–4 months of intake and correlates with tissue levels and several health outcomes.

Dicklin et al. (2024) provide a detailed narrative review of commercially available omega-3 status tests, covering analytical platforms, sample types (red blood cells, whole blood, dried blood spots), reference ranges, and clinical applications in cardiovascular, neurological, ocular, and pregnancy settings⁴. Harris (2025) summarises recent evidence supporting the omega-3 index as both a marker of exposure and an independent risk factor for fatal CVD, suggesting target ranges around 8–11% for optimal protection⁵.

Other measures include plasma phospholipid EPA/DHA, which is more sensitive to short-term changes, and whole-blood omega-3 content, which is analytically convenient but less standardized².

4.2. Global status and intake gaps

Analyses of large population surveys and biomarker-based studies consistently show that omega-3 index values in many regions fall below ranges associated with cardioprotection, reflecting chronically low intakes of EPA and DHA at the population level^{5, 18}. This shortfall is particularly evident in countries and communities with limited fish consumption and restricted availability or affordability of fortified foods and dietary supplements, contributing to increased cardiometabolic risk. Dietary patterns that exclude or minimise marine foods further broaden this gap, as the conversion of α -linolenic acid (ALA) to longer-chain omega-3s is metabolically inefficient in humans. Consequently, vegetarians and vegans frequently exhibit lower circulating EPA and DHA levels and reduced omega-3 index values. Evidence suggests that supplementation with microalgal-derived EPA and DHA can effectively improve omega-3 status in these groups, offering a sustainable and acceptable alternative to fish-based sources²⁴. Such strategies may be particularly important during periods of increased physiological demand, including pregnancy and lactation, when adequate DHA supply is critical for maternal and fetal health⁹.

5. Mechanisms Linking Omega-3 PUFAs to Health

Omega-3 PUFAs influence health through multiple interconnected mechanisms. They exert anti-inflammatory and pro-resolving actions by giving rise to specialised mediators that help limit and resolve inflammation. Their incorporation into cell membranes alters membrane fluidity and receptor function, thereby affecting cellular signalling pathways. In addition, omega-3 PUFAs modulate metabolic and endocrine processes, including lipid metabolism, insulin sensitivity, and hormone regulation. Together, these mechanisms explain their broad physiological and clinical benefits²⁵.

5.1. Anti-inflammatory and pro-resolving actions

Omega-3 PUFAs influence inflammation primarily via following.

- i. **Substrate competition:** EPA and DHA compete with arachidonic acid for COX and LOX enzymes, shifting the eicosanoid profile toward less pro-inflammatory mediators¹⁰.
- ii. **SPM production:** SPMs such as resolvins, protectins, and maresins actively promote resolution, enhancing clearance of inflammatory cells and restoring tissue homeostasis¹²⁻¹³.
- iii. **Receptor and gene regulation:** Omega-3 PUFAs and their metabolites engage G-protein-coupled receptors and nuclear receptors such as PPARs, modulating NF- κ B signalling and expression of cytokine genes²⁶.

These biochemical pathways underpin observed improvements in inflammatory markers and clinical symptoms across diseases ranging from rheumatoid arthritis to depression and metabolic syndrome²⁷⁻²⁸.

5.2. Membrane structure and signalling

DHA-rich phospholipids strongly increase membrane fluidity and influence:

- i. Ion-channel kinetics in cardiomyocytes and neurons.
- ii. GPCR function and downstream signalling cascades.
- iii. Synaptic vesicle dynamics and neurotransmitter release¹.

This membrane-centric chemistry is central to purported roles of omega-3s in neurodevelopment, cognitive ageing, and mood regulation, as highlighted in neurobiological reviews of dementia and depression^{7, 26, 29}.

5.3. Metabolic and endocrine effects

As ligands for PPAR α/γ and other transcription factors, omega-3 PUFAs modulate genes involved in:

- i. Hepatic VLDL-TG synthesis and secretion.
- ii. Fatty-acid oxidation in liver and muscle.
- iii. Insulin signalling and adipokine production^{2, 27}.

Xiao et al. (2022) demonstrate in a systematic review that n-3 PUFAs improve cardiovascular risk factors—particularly triglycerides and blood pressure—in patients with type 2 diabetes, although direct glycaemic effects are modest²⁷.

6. Clinical Evidence in Major Health Domains

Current evidence on the clinical effects of omega-3 PUFAs across major metabolic, developmental, neurological, and psychiatric conditions is summarized in table 2, with emphasis on linking observed clinical outcomes to underlying biochemical mechanisms. It highlights that many observed benefits of omega-3 supplementation arise from modulation of lipid metabolism, membrane composition, and inflammation-resolving pathways rather than direct disease-specific endpoints. A recent study highlights the beneficial role

of omega-3 PUFAs in neurological health. A longitudinal cohort study by Lee et al.³⁰ reported that long-term omega-3 supplementation was associated with improved memory and overall cognitive performance, indicating its potential in supporting brain function and delaying cognitive decline. These findings strengthen the growing evidence for omega-3 fatty acids in managing neurological and age-related cognitive conditions.

Across cardiometabolic disorders, omega-3 PUFAs primarily act as adjuncts by improving dyslipidaemia

and vascular function. In pregnancy and early life, the structural role of DHA in neural and retinal membranes underpins developmental benefits. For cognitive decline and dementia, maintenance of DHA-rich neuronal membranes and specialised pro-resolving mediator production appear central³¹. Mental health outcomes, particularly in depression, are closely linked to anti-inflammatory and pro-resolving mechanisms, with EPA-rich formulations showing greater efficacy. Collectively, the table underscores the importance of disease context, timing of intervention, and inflammatory status in determining clinical responsiveness to omega-3 PUFAs.

Table 2: Clinical effects of omega-3 PUFAs, key outcomes, and underlying mechanisms.

Disease / Condition	Main Findings	Mechanism-Focused Interpretation	Ref.
Type 2 Diabetes & Metabolic Syndrome	Omega-3 supplementation improves triglyceride levels and blood pressure, with minimal effects on fasting glucose or HbA1c.	Regulation of hepatic lipid metabolism (↓ VLDL synthesis) and reduction of low-grade inflammation via omega-3–derived lipid mediators rather than direct insulin sensitisation.	27
Cardiometabolic Risk (Adjunct Therapy)	Omega-3 PUFAs contribute to reduction in cardiovascular risk when used alongside standard therapy but are insufficient as standalone glycaemic treatments.	Membrane incorporation alters eicosanoid balance and enhances specialised pro-resolving mediator (SPM) production, improving vascular tone and inflammatory status.	32
Pregnancy & Fetal Brain Development	DHA is essential for fetal brain and retinal development; supplementation shows modest improvements in cognitive outcomes, though findings remain heterogeneous.	Structural incorporation of DHA into neuronal membranes supports neurogenesis, synaptogenesis, and photoreceptor function.	24
Pregnancy & Maternal DHA Intake	Adequate maternal DHA intake supports neurodevelopment and visual acuity; EPA+DHA intake up to 5 g/day is considered safe.	Preferential placental transfer and accumulation of DHA in fetal neural tissues enhances membrane fluidity and signalling processes.	9
Cognitive Decline & Mild Cognitive Impairment	Omega-3 supplementation provides small but meaningful cognitive benefits, particularly when initiated early.	Maintenance of DHA-rich synaptic membranes enhances neuroplasticity and preserves neuronal function.	29
Alzheimer's Disease & Dementia	Omega-3 PUFAs exhibit neuroprotective effects and may delay disease onset or progression, with reduced efficacy in late-stage disease.	Modulation of amyloid-β metabolism, resolution of neuroinflammation via SPMs, and improved microvascular function.	7
Cognitive Ageing (Epidemiology vs Trials)	Observational studies show stronger associations than intervention trials, indicating variability in clinical response.	Differences in baseline omega-3 status, metabolism, and disease stage influence membrane composition and mediator production.	33
Depression & Mental Health	EPA-rich omega-3 supplementation improves depressive symptoms in a dose-dependent manner, particularly in clinical populations.	Anti-inflammatory and pro-resolving actions modulate neuroimmune pathways and neurotransmitter systems.	28
Inflammation-Associated Depression	Greater clinical benefits observed in patients with elevated inflammatory markers and when used as adjunct therapy.	SPM-mediated resolution of neuroinflammation and modulation of cytokine-driven depressive pathways.	26

7. Future Directions

7.1. Integrative lipidomics and SPM profiling

There is increasing recognition that the commonly used metric of total EPA and DHA intake or status is insufficient to capture the complexity of omega-3 PUFAs biology. Future research should employ high-resolution and quantitative lipidomics to distinguish individual omega-3 species across specific lipid classes, including

phospholipids, triglycerides, and cholesteryl esters. Particular emphasis should be placed on profiling oxidation products and specialised pro-resolving mediators (SPMs), which play critical roles in inflammation resolution and tissue homeostasis. Longitudinal studies examining dynamic lipidomic changes in response to diet, pharmacological interventions, and disease states will further refine mechanistic understanding. Integration of lipidomics

with clinical phenotyping will enable stronger causal links between discrete lipid mediators and health outcomes. Such precision-based approaches are expected to improve interpretation of clinical trials and support personalised omega-3 interventions. Ultimately, integrative lipidomics and SPM profiling will be essential for translating omega-3 PUFA chemistry into targeted and effective clinical applications¹⁰.

7.2. Personalised omega-3 nutrition

Personalised omega-3 nutrition is becoming increasingly practical with advances in biomarker-based assessment. Routine measurement of the omega-3 index provides a quantitative indicator of tissue EPA and DHA status and can be used to guide individualised dosing, monitor adherence, and assess therapeutic response. Recent evidence supports incorporating omega-3 status into cardiovascular and mental-health risk stratification frameworks rather than relying on uniform intake recommendations⁴⁻⁵. Integration of omega-3 index data with genetic variability in fatty-acid metabolism, particularly desaturase (FADS) polymorphisms, may further explain inter-individual differences in response to supplementation. Combining status assessment with inflammatory biomarkers and dietary patterns offers a systems-level approach to precision nutrition. Such strategies hold promise for optimizing clinical efficacy while minimizing unnecessary supplementation and improving long-term health outcomes.

7.3. Sustainable production and food-system integration

Meeting global omega-3 requirements in a sustainable manner necessitates a decisive shift away from exclusive reliance on marine fisheries toward diversified production platforms. Microalgal and microbial fermentation systems offer scalable and environmentally responsible sources of long-chain omega-3 fatty acids, particularly EPA and DHA. In parallel, the development of oilseed crops enriched in α -linolenic acid and engineered to accumulate long-chain omega-3s presents a promising agricultural strategy. Integrating omega-3 fortification into widely consumed staple foods can further improve population-level intake without altering dietary habits³⁴. Within this framework, chemistry plays a pivotal role in ensuring the success of sustainable omega-3 ingredients. Optimization of oxidative stability is essential to preserve bioactivity and shelf life during processing and storage. Equally important are sensory quality and matrix compatibility, which determine consumer acceptance. Advances in formulation science and processing technologies will therefore be critical for embedding sustainable omega-3s effectively within modern food systems.

8. Conclusion

Omega-3 PUFAs represent a chemically and biologically unique class of lipids whose health benefits arise from their structural features and dynamic metabolism. Their susceptibility to oxidation, controlled incorporation into

membrane phospholipids, and conversion into specialised pro-resolving mediators collectively underpin diverse physiological actions. Accumulating evidence supports their protective roles in cardiovascular, metabolic, neurological, inflammatory, and developmental processes, although responses vary with dose, formulation, and individual status. Advances in sustainable sourcing from plant and microbial systems address ecological concerns associated with marine-derived omega-3s. The omega-3 index has emerged as a robust biomarker to guide personalised nutrition and therapeutic strategies. Integration of modern lipidomics and SPM profiling is refining mechanistic understanding and clinical interpretation. Future research should prioritise harmonized methodologies, long-term outcome studies, and precision-based approaches. Such efforts will strengthen the rational, effective, and sustainable use of omega-3 PUFAs in clinical and public-health practice.

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