BioNexus Bulletin
Content Available at www.saap.org.in
(An International Online Peer-Reviewed Journal) ISSN (O): 3139-2407

Review Article
OPEN ACCESS

A REVIEW OF OMEGA-3 AND OMEGA-6 POLYUNSATURATED FATTY ACIDS: DIETARY SOURCES, METABOLISM, AND SIGNIFICANCE.

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Article History: Received: 14 Aug 2026, Revised: 05 Oct 2026, Accepted: 21Oct 2026

DOI: https://doi.org/10.37022/bnb.v2i3.994

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Abstract
Omega-3 (ω-3) and omega-6 (ω-6) polyunsaturated fatty acids (PUFAs) are essential dietary nutrients involved in cellular structure, membrane function, lipid metabolism, inflammation, and human health. Linoleic acid (LA) and α-linolenic acid (ALA) serve as precursors for longer-chain fatty acids, including arachidonic acid (AA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). These fatty acids are obtained from plant oils, nuts, seeds, fish, and other dietary sources. Their physiological effects are mediated through membrane incorporation, lipid signaling, and gene regulation. Emerging evidence challenges the association of omega-6 fatty acids with inflammation, highlighting their potential cardiovascular benefits. This review studiesdietary sources, metabolism, physiological significance and Dietary recommendations of omega-3 and omega-6 PUFAs in human health.

Keywords: *Omega-3 fatty acids, omega-6 fatty acids, polyunsaturated fatty acids and linoleic acid.*

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INTRODUCTION

Polyunsaturated fatty acids (PUFAs) are important components of the human diet and play essential roles in maintaining cellular structure, membrane integrity, lipid metabolism, cell signaling, and physiological homeostasis. Based on the position of the first double bond from the methyl end of the carbon chain, PUFAs are broadly classified into omega-3 (ω-3) and omega-6 (ω-6) fatty acids. Among these, α-linolenic acid (ALA; 18:3, n−3) and linoleic acid (LA; 18:2, n−6) are considered essential fatty acids because humans lack the enzymes required to introduce double bonds at the n−3 and n−6 positions and therefore must obtain them through the diet [1].

Linoleic acid and α-linolenic acid serve as precursors for the synthesis of longer-chain PUFAs through a series of desaturation and elongation reactions. LA can be metabolized to γ-linolenic acid and subsequently to arachidonic acid (AA; 20:4, n−6), whereas ALA can undergo conversion to eicosapentaenoic acid (EPA; 20:5, n−3) and docosahexaenoic acid (DHA; 22:6, n−3). However, endogenous conversion of ALA to EPA and particularly DHA is relatively limited, making dietary sources of preformed EPA and DHA nutritionally important. Recent research has also emphasized the importance of metabolic enzymes, including desaturases, in determining tissue availability and biological effects of these fatty acids [2].

Omega-3 and omega-6 PUFAs are widely distributed in foods of both plant and animal origin. Vegetable oils, nuts, seeds, and legumes are important dietary sources of LA, while flaxseed, chia seeds, walnuts, soybean oil, and canola oil provide ALA. Marine fish such as salmon, sardines, mackerel, tuna, and herring are major sources of preformed EPA and DHA. Algae and algal oils also represent important sources of DHA and, in some cases, EPA, providing alternative sources of long-chain omega-3 fatty acids. The quantity and bioavailability of EPA and DHA can vary according to their chemical form, food matrix, dietary composition, and source [3].

Following dietary intake, PUFAs are incorporated into membrane phospholipids and participate in the regulation of membrane fluidity, cellular signaling, and gene expression. They can also serve as substrates for the production of biologically active lipid mediators that influence vascular function, immune responses, inflammation, and tissue homeostasis. EPA and DHA are particularly important because they contribute to the formation of specialized lipid mediators involved in the regulation and resolution of inflammatory responses.

Recent research has continued to investigate the modulatory effects of EPA and DHA in cardiovascular and other noncommunicable diseases [4].

The physiological significance of omega-6 fatty acids has traditionally been discussed in relation to inflammation because AA-derived lipid mediators participate in inflammatory pathways. However, current evidence indicates that dietary LA should not be considered inherently pro-inflammatory. A recent review reported that higher LA intake and circulating LA levels are generally associated with improved cardiometabolic health outcomes, particularly in relation to blood lipid profiles. Thus, the biological effects of omega-6 fatty acids depend on the specific fatty acid, its metabolic products, dietary source, and physiological context [5].

Similarly, the health effects of omega-3 fatty acids cannot be explained simply by the omega-3-to-omega-6 ratio. Individual fatty acid intake, dietary quality, bioavailability, metabolic conversion, tissue distribution, and health status are important determinants of their biological effects. Recent literature has consequently shifted toward evaluating individual PUFAs and their specific metabolic functions rather than considering omega-3 and omega-6 fatty acids as uniformly beneficial or harmful categories [2].

Overall, omega-3 and omega-6 PUFAs are nutritionally important fatty acids with diverse structural, metabolic, and physiological functions. Understanding their dietary sources, metabolic pathways, bioavailability, and biological activities is essential for evaluating their contribution to human health. Therefore, this review focuses on the dietary sources, metabolism, physiological significance, health implications, and emerging nutritional applications of omega-3 and omega-6 PUFAs.

DIETARY SOURCES OF OMEGA-3 AND OMEGA-6 POLYUNSATURATED FATTY ACIDS

Omega-3 and omega-6 polyunsaturated fatty acids are obtained mainly through the diet and are present in a variety of plant and animal foods. Alpha-linolenic acid (ALA), the major essential omega-3 fatty acid, is mainly found in plant sources such as flaxseeds, chia seeds, walnuts, soybean oil and canola oil. The long-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are mainly obtained from fatty fish and seafood, including salmon, sardines, mackerel, herring and tuna. Algae are also an important source of EPA and DHA, particularly for individuals following vegetarian or plant-based diets. The major omega-6 fatty acid, linoleic acid (LA), is widely present in vegetable oils such as sunflower, safflower, corn and soybean oils, as well as in nuts and seeds. Gamma-linolenic acid (GLA) is found in certain seed oils, particularly evening primrose and borage oils, while arachidonic acid (AA) is mainly present in animal-derived foods such as meat, poultry and eggs. Therefore, plant oils, seeds and nuts are important dietary sources of omega-3 and omega-6 fatty acids, whereas fish and seafood are particularly rich sources of the long-chain omega-3 fatty acids EPA and DHA [1,6].

METABOLISM AND BIOSYNTHESIS OF OMEGA-3 AND OMEGA-6 POLYUNSATURATED FATTY ACIDS

Omega-3 and omega-6 polyunsaturated fatty acids are metabolized through a series of desaturation and elongation reactions that convert essential fatty acids into longer-chain fatty acids. In humans, α-linolenic acid (ALA; 18:3 n-3) is the main dietary omega-3 fatty acid and is converted by Δ6-desaturase to stearidonic acid (18:4 n-3), followed by elongation and further desaturation to form eicosapentaenoic acid (EPA; 20:5 n-3). EPA can subsequently be elongated and desaturated to produce docosahexaenoic acid (DHA; 22:6 n-3). However, the conversion of ALA to EPA and DHA is relatively limited in humans, making dietary sources of EPA and DHA important.

Similarly, linoleic acid (LA; 18:2 n-6) is the major dietary omega-6 fatty acid and is converted by Δ6-desaturase to γ-linolenic acid (GLA; 18:3 n-6). GLA is then elongated to dihomo-γ-linolenic acid (DGLA; 20:3 n-6), which can be further desaturated to form arachidonic acid (AA; 20:4 n-6). Arachidonic acid and other long-chain PUFAs can be incorporated into cell membranes and serve as precursors for various bioactive lipid mediators involved in inflammation, immune responses and other physiological processes. Both omega-3 and omega-6 fatty acids use some of the same enzymes for their biosynthesis, particularly desaturases and elongases; therefore, their metabolic pathways are interconnected and may influence the availability of their respective long-chain products [1,7] .

PHYSIOLOGICAL AND HEALTH SIGNIFICANCE

Omega-3 (n-3) and omega-6 (n-6) polyunsaturated fatty acids (PUFAs) are essential components of human nutrition with important structural, metabolic, and regulatory functions. Linoleic acid (LA; 18:2n-6) and α-linolenic acid (ALA; 18:3n-3) are essential fatty acids that must be obtained from the diet, whereas long-chain PUFAs such as arachidonic acid (AA; 20:4n-6), eicosapentaenoic acid (EPA; 20:5n-3), and docosahexaenoic acid (DHA; 22:6n-3) can be obtained from foods and synthesized from their respective precursors to varying degrees. PUFAs are incorporated into membrane phospholipids, where they influence membrane fluidity, permeability, receptor function, cellular signaling, and intercellular communication. Thus, they contribute to the maintenance of cellular structure and metabolic homeostasis [7].

PUFAs also serve as precursors for a wide range of biologically active lipid mediators. AA, EPA, and DHA are metabolized through cyclooxygenase, lipoxygenase, cytochrome P450, and related pathways to produce prostaglandins, thromboxanes, leukotrienes, resolvins, protectins, maresins, and other lipid-derived signaling

molecules. These mediators regulate vascular function, platelet activity, immune responses, inflammation, and tissue homeostasis. In particular, EPA- and DHA-derived specialized pro-resolving mediators contribute to theregulation and resolution of inflammatory responses and help restore tissue homeostasis. The biological effects of PUFAs therefore extend beyond their structural functions and include complex regulation of inflammatory and immune pathways [8].

DHA has particular physiological importance in the nervous system and retina because of its high concentration in neuronal and retinal membranes. It contributes to neuronal membrane organization, synaptic function, neurodevelopment, and visual physiology. EPA and DHA have consequently been investigated in relation to cognitive function, neurological health, mood, and healthy ageing. However, the magnitude of clinical benefits varies according to population characteristics, dietary intake, dose, nutritional status, and the specific health outcome examined. Therefore, although adequate long-chain omega-3 fatty-acid availability is particularly important during periods of rapid neurological and visual development, the evidence for therapeutic supplementation differs among clinical conditions [8].

Omega-3 PUFAs also have important cardiovascular functions. EPA and DHA can influence triglyceride metabolism, endothelial and vascular function, platelet activity, cardiac electrophysiology, and inflammatory signaling. Recent evidence indicates that higher EPA and DHA exposure is generally associated with cardiovascular benefits, although findings from randomized clinical trials vary according to dose, formulation, population characteristics, baseline cardiovascular risk, and the specific clinical endpoint. Importantly, recent evidence suggests that high-dose omega-3 supplementation may increase the risk of atrial fibrillation in some populations, emphasizing the importance of dose and individual clinical characteristics when considering supplementation [9].

Omega-6 PUFAs are equally important for normal physiological function and should not be considered inherently harmful or exclusively pro-inflammatory. LA contributes to membrane structure and serves as a precursor for other omega-6 fatty acids, whereas AA is involved in the synthesis of lipid mediators required for normal immune, vascular, reproductive, and inflammatory processes. Recent evidence indicates that LA is not uniformly associated with adverse inflammatory effects and may have beneficial associations with cardiometabolic health. However, evidence concerning its effects on particular diseases, including some cancers and inflammatory conditions, remains inconclusive [10].

The relationship between omega-3 and omega-6 fatty acids is physiologically important because both families share several enzymes involved in fatty-acid desaturation and elongation and contribute to the production of different classes of lipid mediators. Nevertheless, their biological effects cannot be explained simply by categorizing omega-6 fatty acids as "pro-inflammatory" and omega-3 fatty acids as "anti-inflammatory." Individual fatty acids generate multiple metabolites with distinct biological activities, and their physiological effects depend on the specific fatty acid, metabolic pathway, tissue concentration, dietary context, and physiological state [8,10].

Omega-3 and omega-6 PUFAs also participate in immune regulation and inflammatory processes through their conversion into diverse lipid mediators. Rather than viewing PUFA metabolism as a simple balance between "pro-inflammatory" and "anti-inflammatory" fatty acids, current research emphasizes the complexity of lipid mediator networks and the importance of both the initiation and resolution phases of inflammation. EPA- and DHA-derived specialized pro-resolving mediators are particularly relevant to the resolution of inflammation and restoration of tissue homeostasis [8].

Dietary and circulating omega-6 fatty acids have also been investigated in relation to cardiovascular disease, cancer, and mortality. A 2025 global meta-analysis incorporating 150 cohort publications reported that higher dietary intake and circulating concentrations of omega-6 fatty acids were generally associated with lower risks of cardiovascular disease, cancer incidence, and all-cause mortality in the general population, although associations varied according to individual disease outcomes and cancer types. These findings reinforce the importance of evaluating omega-6 fatty acids according to their individual biological effects, dietary sources, and health outcomes rather than assuming that increased omega-6 intake is inherently detrimental [11].

Overall, omega-3 and omega-6 PUFAs are important regulators of human physiology because they provide structural components of cell membranes, serve as precursors of bioactive lipid mediators, and participate in cardiovascular, neurological, immune, inflammatory, and metabolic processes. Current evidence supports evaluating individual fatty acids according to their dietary sources, intake levels, metabolic pathways, and specific health outcomes rather than relying solely on a generalized omega-6-to-omega-3 ratio. A varied dietary pattern providing adequate essential fatty acids and appropriate sources of long-chain omega-3 fatty acids is therefore important for maintaining normal physiological function and supporting long-term health

DEFICIENCY AND EXCESS OF OMEGA-3 AND OMEGA-6 FATTY ACIDS

Deficiency of omega-3 fatty acids is relatively uncommon but may occur when dietary intake is inadequate or nutritional requirements are increased. Insufficient intake may result in rough or scaly skin, dermatitis, and impaired physiological functions. Inadequate availability of DHA may also affect normal visual and neurological functions, particularly during periods of growth and development.

Excessive intake of omega-3 fatty acids, particularly from high-dose supplements, may cause mild gastrointestinal symptoms such as nausea, diarrhea, heartburn, and an unpleasant taste. High doses may also affect platelet function and increase bleeding risk in certain circumstances, especially when combined with anticoagulant medications. Long-term intake of high-dose omega-3 supplements has also been associated with a slightly increased risk of atrial fibrillation in some high-risk populations.

Omega-6 fatty acid deficiency is rare because linoleic acid (LA) is widely available in vegetable oils, nuts, seeds, and other foods. Severe deficiency may cause dry or scaly skin, impaired wound healing, growth retardation, and altered immune function. Essential fatty acid deficiency is more likely to occur in conditions involving inadequate fat intake, malnutrition, malabsorption, or prolonged specialized nutrition.

Excessive omega-6 intake should not be considered inherently harmful or automatically pro-inflammatory. Linoleic acid is an essential fatty acid required for normal physiological functions. Therefore, adequate intake of both omega-3 and omega-6 fatty acids is important for maintaining normal cellular, immune, cardiovascular, and inflammatory functions.

DIETARY RECOMMENDATIONS

Omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) are essential fatty acids that cannot be synthesized adequately by the human body and therefore must be obtained from food. The ICMR–National Institute of Nutrition (ICMR-NIN) Dietary Guidelines for Indians, 2024 recommend using oils and fats in moderation and choosing a variety of oilseeds, nuts, nutricereals and legumes to meet requirements for essential fatty acids**.**

Omega-3 fatty acids, particularly alpha-linolenic acid (ALA), can be obtained from flaxseeds, chia seeds, walnuts, soybeans, mustard and certain legumes. Fish and fish oils provide the long-chain omega-3 fatty acids EPA and DHA.Omega-6 fatty acids, mainly linoleic acid (LA), are widely available from vegetable oils, nuts, seeds and other plant foods. ICMR-NIN recommends dietary diversity and the use of different oils rather than relying on a single oil.

Overall, Indians should consume adequate amounts of unsaturated fats while limiting saturated and trans fats. WHO recommends that dietary fats should primarily be unsaturated and that total fat intake in adults generally should not exceed 30% of energy intake. A balanced diet containing nuts, seeds, pulses, appropriate vegetable oils and, for non-vegetarians, fish can help provide essential PUFAs [12].

CONCLUSION

Omega-3 and omega-6 polyunsaturated fatty acids are essential dietary nutrients that play important roles in maintaining normal physiological functions. They contribute to cell membrane structure, brain and visual development, immune regulation, cardiovascular health, and inflammatory processes. Omega-3 fatty acids, particularly EPA and DHA, are important for neurological and cardiovascular functions, while omega-6 fatty acids, especially linoleic acid, are essential for normal growth, skin health, and cellular function. Deficiency of either fatty acid family can adversely affect health, although severe deficiency is relatively uncommon. Similarly, excessive intake, particularly through high-dose supplements, may produce undesirable effects. Therefore, the focus should be on consuming adequate amounts of both omega-3 and omega-6 fatty acids through a balanced diet rather than avoiding either group. Dietary sources such as fish, nuts, seeds, and plant oils can help provide these essential fatty acids. Overall, maintaining adequate intake and dietary diversity is important for supporting optimal health and preventing nutritional imbalance.

FUNDING

No external funding was received for this study.

ACKNOWLEDGEMENTS

The authors have no acknowledgements to declare.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

INFORMED CONSENT

Informed consent was obtained from all authors, as applicable. ETHICAL STATEMENT Not applicable.

AUTHOR CONTRIBUTIONS

Dr. A. Shobha Rani, Dr. T. Siva Kumar, and Dr. K. S. Shanthi Sree contributed to data collection and manuscript writing. Prof. G. Savithri contributed to the conceptualization of the study.

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