Volume 2(4), pages 365-382, April 2026
DOI: 10.65221/0167
eISSN: 3115-5898
Copyright © 2026
Authors retain the copyright of this article
https://reports.afjur.com

AFJUR
African Journals, Universities and Research

African Research Reports

Regular Research Paper

Anti-inflammatory effects of omega-3 fatty acids: Evidence from circulating biomarkers and inflammatory gene-expression studies

Micah Nnabuko Okwah[1,2], Moses Adondua Abah[3,4*], Micheal Abimbola Oladosu[4,5], Captain Tamunotonye Blessing[6], Ahinful Isaac Anku[7], and Ochuele Dominic Agida[3,4]

[1]Department of Internal Medicine, Cardiology unit, Lagos University Teaching Hospital, Lagos State, Nigeria.
[2]Department of Chronic Disease Epidemiology, Yale University, Connecticut, United States of America (USA).
[3]Department of Biochemistry, Faculty of Biosciences, Federal University Wukari, Taraba State, Nigeria.
[4]ResearchHub Nexus Institute, Lagos State, Nigeria.
[5]Department of Biochemistry, Faculty of Basic Medical Sciences, University of Lagos, Lagos State, Nigeria
[6]Department of Plant Science and Biotechnology, Faculty of Science, University of Port-Harcourt, Rivers State, Nigeria.
[7]Department of Chemistry, Faculty of Physical Sciences, New Mexico University, United States of America (USA).

Received 28 December,2025; Accepted 6 April, 2026

Chronic diseases like metabolic syndrome, autoimmune diseases, neurodegenerative pathologies, and cardiovascular diseases are caused by inflammation. Dietary interventions, especially omega-3 PUFAs, have been studied for their ability to regulate inflammation. The biological effects of omega-3 fatty acids, especially EPA and DHA, include absorption into cell membranes, modification of lipid mediators, and control of inflammatory signaling pathways. This review examines gene expression profiles and systemic and molecular indicators to determine omega-3 fatty acid supplementation's anti-inflammatory effects. Human clinical trials show that omega-3 supplementation reduces C-reactive protein (CRP), fibrinogen, and pro-inflammatory cytokines, depending on dose, EPA:DHA ratio, and baseline inflammatory status. Animal and in-vitro studies reveal pathways that modulate eicosanoid production, activate pro-resolving mediators, and suppress transcription factors like NF-κB. Omics studies show that epigenetic and transcriptomic changes mediate these effects. Quality evidence is presented, but limitations in study design, supplementation regimens, and biomarker selection weaken the conclusions. This study highlights data gaps, such as human gene expression data and inter-individual response variability and suggests future research. Overall, omega-3 supplementation may reduce inflammation and provide molecular insights for clinical and public health applications.

Key words: Omega-3 fatty acids, inflammation, biomarkers, gene expression, Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA).

INTRODUCTION

Although inflammation is a basic biological reaction that shields the body from harm and infections, it plays a major role in the development of disease when it persists. Almost all chronic degenerative diseases are associated

---

*Corresponding author. E-mail: alianamiofficial@gmail.com. Tel: +255653253651.

Author(s) agree that this article remain permanently open access under the terms of the Creative Commons Attribution License 4.0 International License

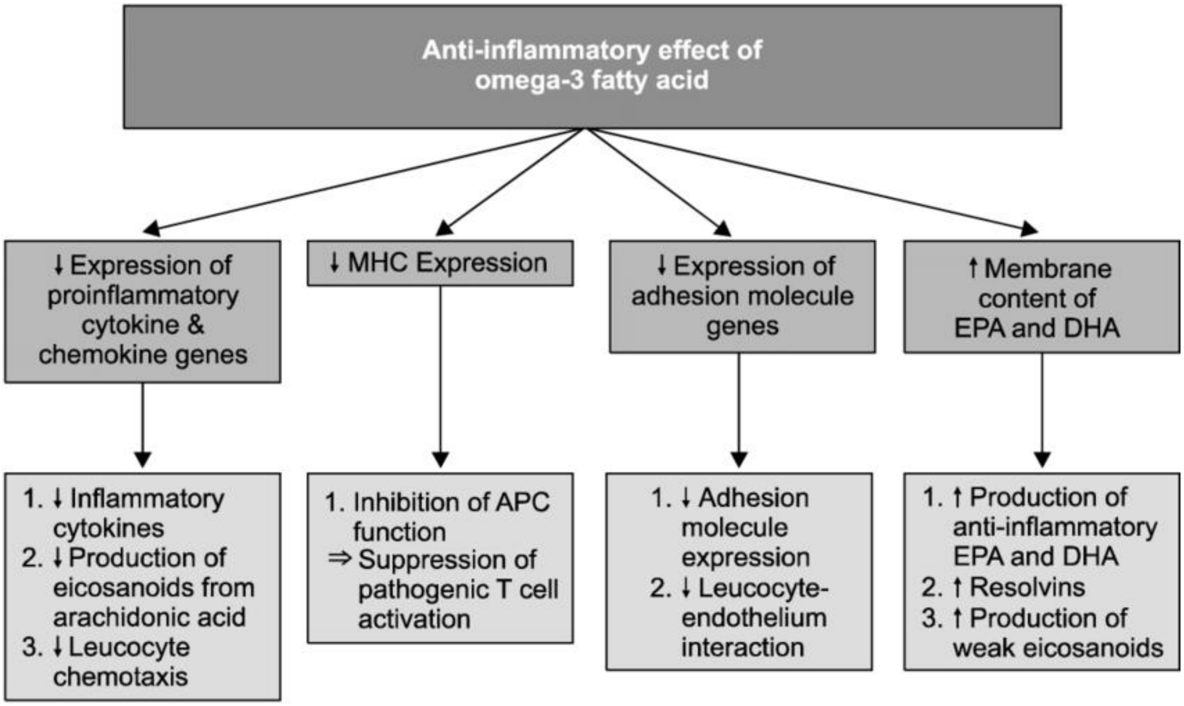

Figure 1. Anti-inflammatory effect of omega-3 fatty acid. APC: antigen-presenting cell, DHA: docosahexaenoic acid, EPA: eicosapentaenoic acid, MHC: major histocompatibility complex.
Source: Kim, 2015.

with low-grade, persistent inflammation (Natto et al., 2019; Pahwa et al., 2023). For instance, autoimmune diseases, type 2 diabetes, Alzheimer's, and atherosclerosis are all facilitated by persistent inflammation (Natto et al., 2019; Pahwa et al., 2023). In addition to reflecting ongoing immune dysregulation, persistent activation of pro-inflammatory pathways mediated by cytokines like interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) and acute-phase proteins like CRP also predicts poor clinical outcomes (Pahwa et al., 2023). Therefore, there is a significant deal of therapeutic and preventive interest in therapies that might safely and effectively reduce this chronic inflammatory state.

Among nutritional strategies to modulate inflammation, omega-3 (n-3) polyunsaturated fatty acids (PUFAs) are among the most studied and promising. These fatty acids are readily obtainable from diet or supplementation, making them scalable and relatively safe adjunct to conventional therapies. The Office of Dietary Supplements (ODS) at the U.S. National Institutes of Health underscores the importance of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) for health maintenance, noting their roles in cardiovascular and immune function (Office of Dietary Supplements (ODS), 2022). Such real-world relevance, combined with their favorable safety profile, has motivated extensive research into how omega-3s influence inflammatory processes. Importantly, emerging evidence suggests that n-3 PUFAs can modulate both acute and chronic inflammatory pathways, highlighting their potential as preventive as well as therapeutic agents in inflammatory conditions (Calder, 2020). The anti-inflammatory benefits of omega-3 supplementation are becoming increasingly supported by clinical data (Figure 1). Omega-3 consumption dramatically lowers CRP and TNF-α levels, according to a meta-analysis of individuals with diabetes and cardiovascular disease (Natto et al., 2019).

Additionally, a comprehensive meta-analysis that combined 32 meta-analyses found that blood CRP, IL-6, and TNF-α were consistently and statistically significantly reduced in a variety of adult populations (Kavyani et al., 2022). These advantages are further supported by randomized trials in specific populations. Omega-3 supplementation reduced CRP and changed the granulocyte-to-lymphocyte ratio in a study of heavy smokers, and high-dose EPA and DHA markedly changed inflammatory markers and metabolic parameters in obese people (Elisia et al., 2022; Borja-Magno et al., 2023).

Mechanistic research helps explain how omega-3s achieve their anti-inflammatory effects. Long-chain PUFAs such as EPA and DHA become incorporated into cellular membranes and displace arachidonic acid (AA), thereby shifting the balance of downstream lipid mediators toward less inflammatory species (Hidalgo et al., 2021). These fatty acids also give rise to specialized pro-resolving mediators (SPMs), including resolvins and protectins, which actively orchestrate the resolution of inflammation (Hong and Lu, 2013). On a transcriptional level, omega-3s modulate key inflammatory pathways: for example, they act via PPAR-γ to suppress NF-κB mediated gene expression, and in macrophages, they may activate the AMPK/SIRT1 axis to further restrain NF-κB signaling (Naeini et al., 2020; Williams-Bey et al., 2014; Kim, 2015). *In vitro*, EPA and DHA reduce expression of inflammatory genes such as IL1β, MAPK, and NFKB in macrophage models, illuminating how their molecular effects could translate to lower systemic inflammation (Williams-Bey et al., 2014; Williams-Bey et al., 2014; Kim, 2015).

This review offers a thorough, current synthesis of the knowledge about how human inflammation is modulated by omega-3 fatty acid supplementation, with a focus on both gene expression effects and biomarker responses. The molecular composition, dietary sources, and distribution of EPA and DHA in human tissues are all discussed. The effects of omega-3 supplementation on oxidative stress parameters, endothelial activation indices, and systemic inflammatory indicators (such CRP, IL-6, and TNF-α) were described by randomized controlled trials, meta-analyses, and systematic reviews. This review also examines mechanistic data from humans, animals, and *in vitro* studies to shed light on how omega-3s impact cell signaling, membrane architecture, and transcriptional networks, including the activation of nuclear receptors (peroxisome proliferator-activated receptors [PPARs]), modulation of NF-κB, and production of pro-resolving lipid mediators. It also examines the emerging field of omega-3 mediated epigenetic and nutrigenomic regulation, such as microRNA modulation and DNA methylation, which may underlie longer-term anti-inflammatory effects. Importantly, this review analyzes sources of variability in response including dose, EPA:DHA ratio, duration, formulation, and baseline inflammatory status and highlight critical gaps in the literature. Finally, research priorities were proposed to guide future clinical and translational studies, aiming to better define the therapeutic potential of omega-3 supplementation for managing chronic inflammation in diverse patient populations.

Omega-3 fatty acids and inflammation

Omega-3 PUFAs are critical dietary modulators of inflammation, exerting effects at molecular, cellular, and systemic levels. The long-chain omega-3s, EPA and DHA, are especially notable for their ability to integrate into cell membranes, influence lipid mediator synthesis, and regulate inflammatory gene expression. These fatty acids have the potential to treat chronic inflammatory disorders since they are linked to decreases in pro-inflammatory cytokines, acute-phase proteins, and endothelial activation markers in humans (Calder, 2010). The types and dietary sources of omega-3 fatty acids, their biological roles, important inflammatory biomarkers, and the molecular mechanisms by which they influence immune response are all covered in this work.

Types and sources (ALA, EPA, DHA; Marine vs. Plant)

Omega-3 (n-3) PUFAs include three main types: alpha-linolenic acid (ALA), EPA, and DHA. ALA (18:3n-3) is primarily found in plant-based sources like flaxseed, chia seeds, and walnuts, whereas EPA (20:5n-3) and DHA (22:6n-3) are abundant in marine foods (fatty fish) and algae-based supplements (Calder, 2012).

Importantly, while humans can convert ALA to EPA and DHA, the conversion rate is quite limited, making EPA and DHA from marine sources more efficient in raising tissue levels of long-chain omega-3s (Calder, 2012). ALA serves as a dietary precursor, but EPA and DHA are the forms most frequently studied for their bioactive and anti-inflammatory properties. Because EPA and DHA are readily incorporated into the phospholipid membranes of cells, especially immune cells, they have a greater functional impact on inflammation compared to ALA (Calder, 2012). This is why many clinical and mechanistic studies focus specifically on EPA and DHA rather than ALA. These sources are shown in Figure 2, which shows current and potential future sources of omega-3 long-chain PUFAs, including marine sources (seafood and microalgae) and genetically engineered plants

Biological functions (Membrane dynamics, lipid metabolism, immune signaling)

Once ingested, EPA and DHA integrate into cell membrane phospholipids, displacing other fatty acids (e.g., AA). This incorporation changes membrane fluidity and microdomain organization (lipid rafts), thereby affecting the function of membrane proteins such as receptors and signaling complexes (Calder, 2012) (Figure 3). These changes can alter how immune cells respond to stimuli. From a signaling standpoint, EPA and DHA bind to nuclear receptors such as PPARs, especially PPAR-γ and PPAR-α. When these receptors are activated, pro-inflammatory programs are suppressed and anti-inflammatory ones are promoted (Oh et al., 2010; Moriyama et al., 2018). Additionally, because EPA and DHA compete with AA in the COX and LOX

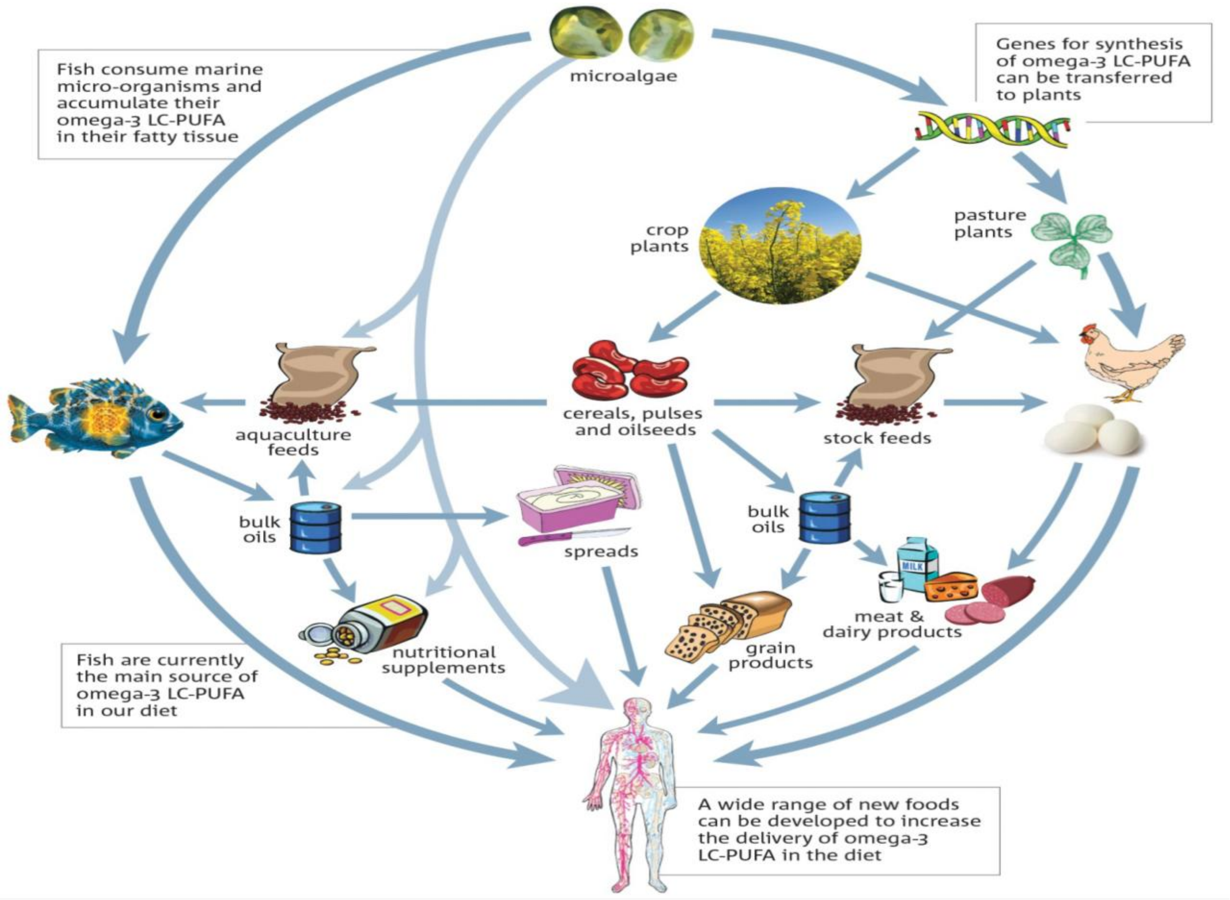

Figure 2. The sources of omega-3 fatty acids. The figure depicts the potential future sources of omega-3 LC-PUFA, with current sources (left) being seafood and microalgae, with possible future sources through genetically engineered plants also indicated at the right.
Source: (Kitessa et al., 2014).

pathways, they limit their availability for conversion to powerful pro-inflammatory eicosanoids (Calder, 2012).

Key inflammatory biomarkers (Systemic, cytokines, endothelial, oxidative stress)

The anti-inflammatory actions of EPA and DHA are often assessed by measuring specific biomarkers. Systemic biomarkers include C-reactive protein (CRP), while cytokines like interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) are direct mediators of inflammation (Calder, 2012). In addition, endothelial activation markers (e.g., ICAM-1, VCAM-1) reflect vascular inflammation and cell adhesion processes, though these are less frequently studied in basic mechanistic work.

On the oxidative stress front, omega-3s modulate redox balance. EPA and DHA can mitigate oxidative stress by reducing reactive oxygen species (ROS) and influencing antioxidant defense systems (such as the production of glutathione peroxidase and catalase) through changes in membrane composition and signaling (Distefano et al., 2024). Because oxidative stress frequently increases inflammatory signals and vice versa, these antioxidant and anti-inflammatory properties are related. To provide context for comprehending how they mediate immunological and inflammatory responses, Table 1 shows the important inflammatory biomarkers and explains their biological roles.

Inflammatory gene expression

The activation or inhibition of immune-related genes in response to stress signals, infections, or metabolic alterations is referred to as inflammatory gene expression. Transcription factors that dictate the

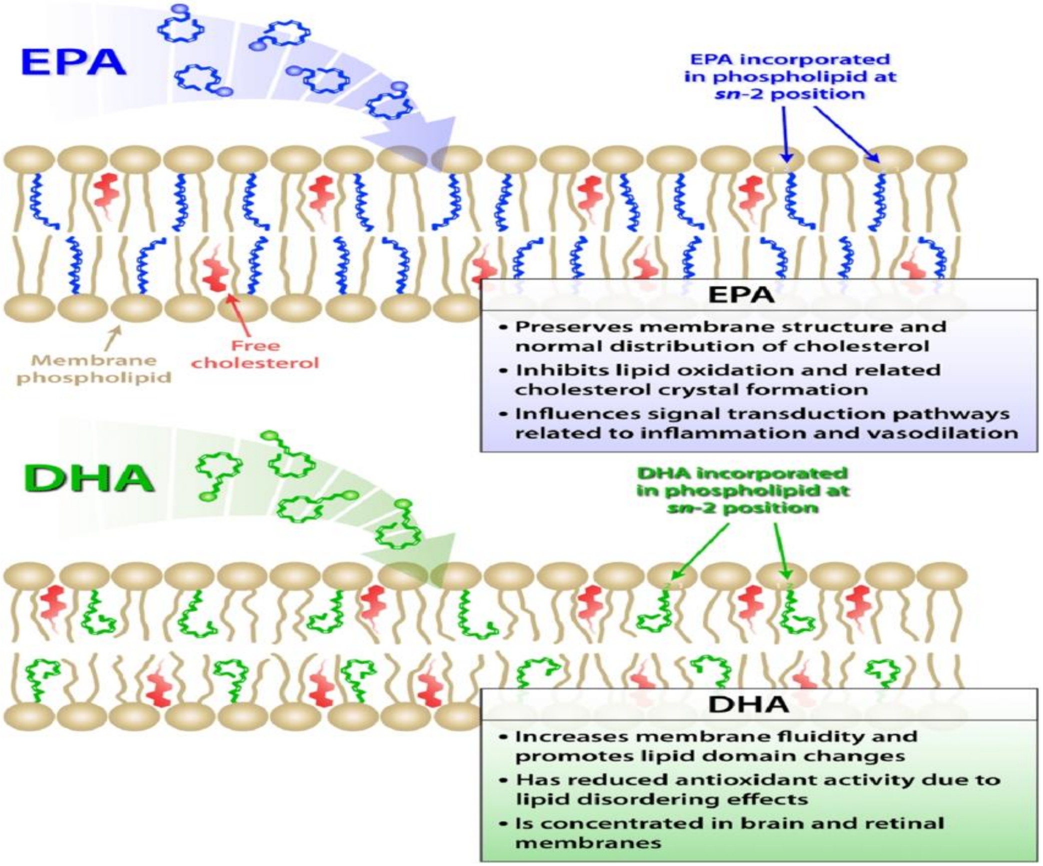

Figure 3. Schematic illustration of the proposed location and contrasting effects of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) on membrane structure.
Source: (Mason et al., 2020).

Table 1. Relevant inflammatory biomarkers and their biological function.

Inflammatory markers	Abbreviations	Functions
Acute-phase protein		
C-reactive protein	CRP	CRP is associated with the formation of cytokines, chemokinesand the acute-phase response

Table 1 Contd.

Cytokines		
Interleukin-6	IL-6	Induces acute-phase response (by inducing CRP), anti-body secretion and differentiation
Interleukin-1a, Interleukin-1b	IL-1a, IL-1b	Proliferation and maturation of lymphocytes, involved in inflammation and acute-phase response
Interleukin-18	IL-18	Involved in the formation of Th1 cells
Tumor necrosis factor-ais a cytokine	TNF-a	Induces adhesion molecules- and cytokine expression, involved in cell death
Adhesion protein		
Soluble intercellular adhesion molecule-1	sICAM-1	Binds monocytes and lymphocytes to the endothelium
Soluble vascular cell adhesion molecule-1	sVCAM-1	Binds monocytes and lymphocytes to the endothelium
sE-selectin	sE-sel	Recruits leukocytes to the inflammatory site
sP-selectin	sP-sel	Recruits leukocytes to the inflammatory site. Induces monocytes and platelet interactions
Chemokines		
Monocyte chemoattractant protein-1	MCP-1	Facilitates migration of leukocytes to the intima
Granulocyte–macrophage colony- stimulating factor	GM–CSF	Growth and differentiation of monocytes
Interleukin-8	IL-8	Facilitates migration of leukocytes to the intima

Adapted from Myhrstad et al., 2011.

synthesis of cytokines, chemokines, and inflammatory enzymes are principally responsible for this regulation (Medzhitov, 2008). These transcriptional regulators coordinate early gene-expression programs that influence the size and duration of the immune response when cells detect inflammatory stimuli (Chen et al., 2017). Nuclear receptors like PPARs and important transcription factor families like NF-κB and AP-1 act as key hubs for regulating these genes. Their detailed mechanisms will be discussed in the later section, but at this stage, it is important to recognize that they integrate cellular signals and maintain immune balance (Lawrence, 2009). Dietary lipids, including omega-3 fatty acids, can influence these transcriptional processes through interactions with membrane receptors and nuclear regulatory proteins (Calder, 2015), as shown in Figure 4.

Mechanisms of anti-inflammatory action of omega-3 fatty acids

Omega-3 PUFAs, particularly EPA and DHA, exert anti-inflammatory effects through multiple complementary mechanisms. As shown in Figure 5, they include incorporation into cell membranes, modification of lipid mediators, production of specific pro-resolving mediators, and control of important inflammatory signaling pathways. Interpreting the clinical and molecular effects of omega-3 supplementation requires an understanding of these pathways.

Membrane incorporation and competition with arachidonic acid (AA)

EPA and DHA integrate into the phospholipid bilayer of cell membranes, altering membrane fluidity, microdomain organization (lipid rafts), and receptor function (Calder, 2015). Omega-3 fatty acids limit the synthesis of pro-inflammatory eicosanoids like prostaglandin E2 (PGE2) and leukotriene B4 (LTB4) by displacing AA from phospholipids, which decreases the substrate availability for cyclooxygenase (COX) and

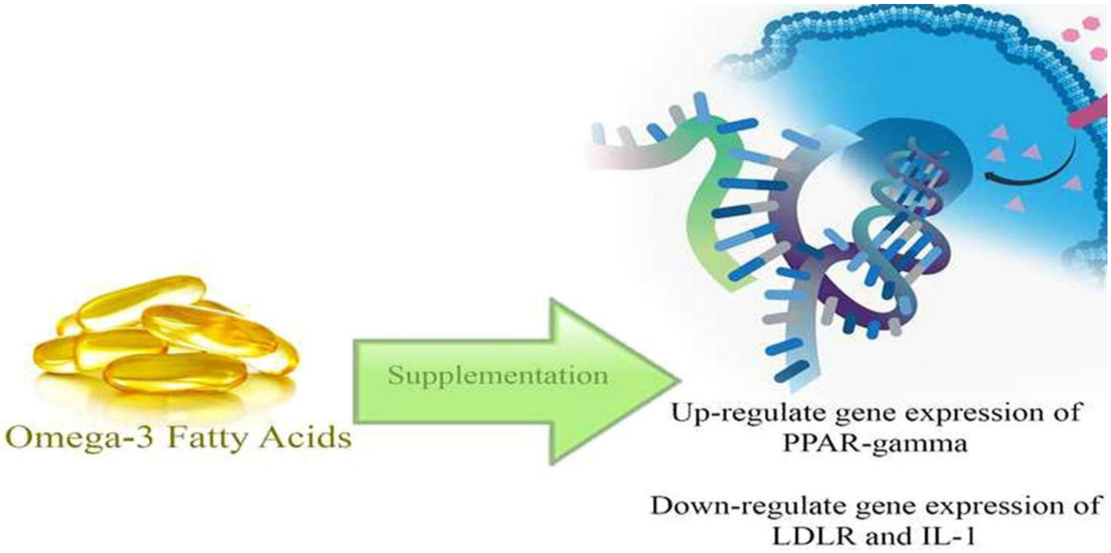

Figure 4. Omega-3 fatty acid supplementation on gene expression of inflammation. The figure illustrates how omega-3 supplementation influences the expression of key inflammation-related genes by upregulating and downregulating certain markers.
Source: (Heshmati, 2021).

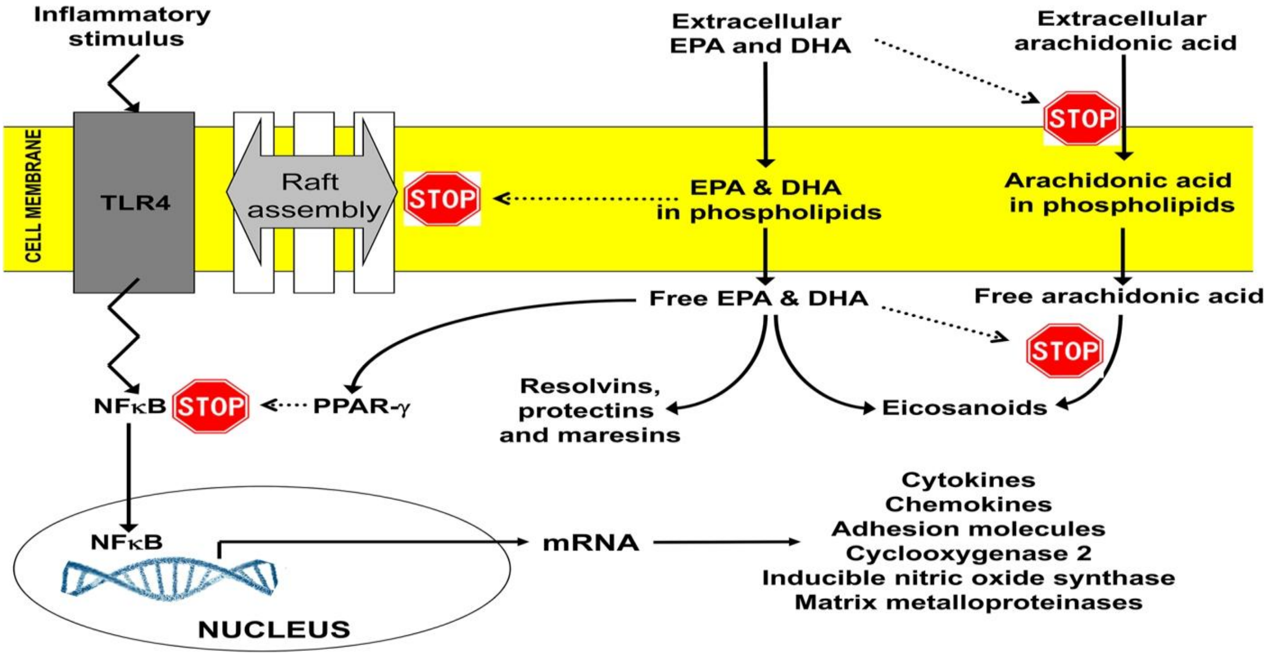

Figure 5. Integrated Mechanisms by Which EPA and DHA Exert Anti-Inflammatory Effects. This figure illustrates the multiple mechanisms by which EPA and DHA exert anti-inflammatory effects, including their incorporation into cell membranes, competition with arachidonic acid, modulation of eicosanoid synthesis, production of specialized pro-resolving mediators, and regulation of key inflammatory signaling pathways such as NF-κB, PPARs, and TLRs.
Source: (Calder, 2020).

Lipoxygenase (LOX) enzymes (Calder, 2015; Serhan, 2014). In clinical settings, this rivalry significantly inflammatory state, which helps to lower vascular and systemic inflammation (Calder, 2015).

Modulation of eicosanoids (EPA vs. AA)

Eicosanoids derived from AA are generally pro-inflammatory, promoting leukocyte recruitment, cytokine production, and endothelial activation (Calder, 2015). In contrast, eicosanoids derived from EPA, including prostaglandin E3 (PGE3) and leukotriene B5 (LTB5), are considerably less potent in eliciting inflammatory responses (Natto et al., 2019; Calder, 2015). Omega-3 PUFAs reduce inflammation while maintaining normal immune function by switching eicosanoid production from AA-derived to EPA-derived species. In patients with metabolic or cardiovascular disorders, clinical research has shown that supplementing EPA-rich formulations lowers circulating levels of AA-derived eicosanoids and related inflammatory biomarkers including CRP and IL-6 (Natto et al., 2019; Kavyani et al., 2022).

Specialized pro-resolving mediators (SPMs: Resolvins, protectins, maresins)

Resolvins, protectins, and maresins are examples of specialized pro-resolving mediators (SPMs) that are derived from EPA and DHA. By reducing neutrophil infiltration, improving macrophage-mediated clearance of cellular debris, and promoting tissue repair, SPMs actively promote resolution of inflammation, in contrast to traditional anti-inflammatory medications that mainly dampen inflammatory signaling (Elisia et al., 2022; Serhan, 2014). Resolvins derived from EPA (RvE series) and DHA (RvD series), as well as protectins and maresins, have been shown in vitro and in vivo to reduce pro-inflammatory cytokine expression and oxidative stress, contributing to the resolution of chronic inflammation without compromising host defense (Elisia et al., 2022; Serhan, 2014).

Regulation of inflammatory signaling (NF-κB, PPARs, TLRs)

Omega-3 PUFAs also modulate intracellular inflammatory signaling. They suppress NF-κB, a master regulator of pro-inflammatory gene expression, leading to reduced transcription of cytokines such as TNF-α, IL-1β, and IL-6 (Natto et al., 2019). Furthermore, omega-3 fatty acids activate PPARs, especially PPAR-γ, which promote anti-inflammatory gene programs and inhibit NF-κB activity (Li et al., 2025). Toll-like receptor (TLR) engagement is also impacted; EPA and DHA reduce TLR-mediated inflammatory pathway activation, reducing innate immune responses in macrophages and other immune cells (Hidalgo et al., 2021). These combination effects at the transcriptional and receptor-signaling levels demonstrate the complex ability of omega-3 PUFAs to lower inflammation both locally and systemically.

Effect of omega-3 supplementation on inflammatory biomarkers

Omega-3 fatty acids, particularly EPA and DHA, are well-recognized for their anti-inflammatory properties, which have been consistently observed across diverse human populations. These long-chain polyunsaturated fatty acids (LC-PUFAs) have been associated with improvements in oxidative stress parameters, attenuation of endothelial activation, cytokine profile regulation, and decreases in systemic inflammatory indicators. People with elevated baseline inflammation, such as those with metabolic syndrome, obesity, type 2 diabetes, cardiovascular disease, and persistent smoking, are especially affected by the anti-inflammatory effects. Table 2 shows the modulatory effects of omega-3 fatty acids on cytokines and other important inflammation mediators, as well as their impact on main classes of inflammatory biomarkers.

Systemic inflammatory markers (CRP, fibrinogen)

CRP is an acute-phase protein commonly used as a marker of systemic inflammation. Evidence from clinical trials and meta-analyses suggests that omega-3 supplementation (EPA and DHA) can modestly reduce CRP levels, particularly in populations with elevated baseline inflammation, such as patients on hemodialysis or cardiovascular disease. Natto et al. (2019), reported that EPA and DHA supplementation in patients with diabetes or cardiovascular disease may reduce CRP, but the effect was inconsistent across studies and not definitively established. Similarly, Calder (Calder, 2020) highlighted studies in hemodialysis patients in which high-dose omega-3 supplementation led to reductions in CRP and fibrinogen, indicating that long-chain PUFAs can attenuate systemic inflammation in populations with significant baseline inflammatory burden. It is believed that incorporating EPA and DHA into cell membranes, altering the composition of lipid rafts, and lowering the synthesis of pro-inflammatory mediators produced from arachidonic acid are the mechanisms underlying the anti-inflammatory benefits. Following omega-3 administration, reductions in fibrinogen, another acute-phase reactant associated with cardiovascular risk, have also been noted. According to Calder (2020) and Kavyani et al. (2022), as fibrinogen encourages platelet aggregation and endothelial dysfunction, reducing fibrinogen may not only indicate a reduction in systemic inflammation but also provide vascular advantages.

Table 2. Effects of omega-3 fatty acids on major inflammatory biomarker classes.

Biomarker class	Representative biomarkers	Primary mechanisms of action	Observed clinical outcomes	Reference
Systemic inflammatory load	CRP, Fibrinogen	Inhibition of hepatic NF-κB signaling	Reduced systemic inflammation	[Natto et al., 2019; Calder, 2020; Borja-Magno et al., 2023]
		Incorporation of EPA/DHA into hepatocyte membranes	Lowered CRP and fibrinogen levels, particularly in metabolic syndrome, diabetes, and CVD patients	
		Modulation of acute-phase response		
Pro-inflammatory Cytokines	IL-6, TNF-α, IL-1β	Suppression of NF-κB and AP-1 transcription factors	Decreased circulating IL-6 and TNF-α	[Kavyani et al., 2022; Elisia et al., 2022; Borja-Magno et al., 2023]
		Downregulation of TLR4 signaling	IL-1β reduction may occur but is less consistent	
		EPA:DHA-dependent attenuation of cytokine secretion	Reduced chronic immune activation in obesity, smoking, and insulin resistance	
Anti-inflammatory cytokines	IL-10	Activation of PPAR-γ and FFA4/GPR120 receptors	Increased IL-10 production in some studies; effect may vary with population and baseline inflammation	[Kavyani et al., 2022; Hidalgo et al., 2021]
		Enhanced immunoregulatory signaling	Promotion of anti-inflammatory regulatory immune responses	
Endothelial activation	ICAM-1, VCAM-1, E-selectin	Inhibition of endothelial NF-κB activation	Improved endothelial function	[Nohé et al., 2003; Eschen et al., 2010 ; Baker et al., 2018 ; Wang et al., 2011]
		Suppression of platelet-activating factor (PAF) synthesis	Reduced expression of ICAM-1 and VCAM-1; E-selectin reduction is less consistently observed	
		Reduced leukocyte–endothelium adhesion	Attenuation of vascular inflammation	
Stress status	Oxidative MDA, Isoprostanes, SOD, GPx	Decreased lipid peroxidation	Lower oxidative burden	[Natto et al., 2019; Calder, 2020; Elisia et al., 2022]
		Enhanced antioxidant enzyme activity (SOD, GPx)	Improved antioxidant defenses, particularly in chronic inflammatory or high oxidative stress conditions; enzyme activity effects may be modest in healthy individuals	

Table 2 Contd.

Stabilization of cellular membranes

All these results suggest that omega-3 fatty acids can influence systemic inflammatory indicators, especially in individuals with high baseline inflammation. However, the effects may differ based on patient characteristics, duration, and dose.

Cytokines (IL-6, TNF-α, IL-1β, IL-10)

Cytokines, including IL-6, TNF-α, IL-1β, and IL-10, are central mediators of inflammation, orchestrating both the initiation and resolution of immune responses. Omega-3 supplementation has been shown to reduce circulating levels of pro-inflammatory cytokines, such as IL-6, TNF-α, and IL-1β. In an open-label randomized crossover trial conducted in heavy smokers, Elisia et al. (2022) observed reductions in TNF-α and IL-6 following EPA and DHA supplementation, accompanied by improvements in the granulocyte-to-lymphocyte ratio. These findings suggest that omega-3s may shift the immune balance toward a less inflammatory phenotype, even in populations experiencing elevated oxidative stress.

Borja-Magno et al. (2023) demonstrated the powerful immunomodulatory effects of long-chain omega-3s on metabolic inflammation by reporting that high-dose EPA and DHA supplementation over a 12-week period dramatically lowered IL-6 and TNF-α levels in obese patients. Additionally, some research has shown increases in the anti-inflammatory cytokine interleukin-10 (IL-10), indicating that omega-3 fatty acids may both improve immunoregulatory pathways and decrease pro-inflammatory signaling (2022). Meta-analyses show that omega-3 supplementation lowers TNF-α and increases antioxidant capacity in type 2 diabetes mellitus; however, effects on IL-6 seem to vary depending on baseline inflammation and supplementation dosage (Natto et al., 2019). All these results highlight how omega-3 fatty acids affect cytokine networks, creating an anti-inflammatory environment that could lead to better therapeutic results.

Endothelial activation markers (ICAM-1, VCAM-1, E-Selectin)

Chronic inflammation induces endothelial activation, characterized by upregulation of adhesion molecules such as ICAM-1, VCAM-1, and E-selectin, which facilitate leukocyte recruitment and vascular inflammation. Omega-3 fatty acids have been shown to attenuate the expression of these molecules, thereby limiting endothelial dysfunction. Hidalgo et al. (2021) demonstrated that EPA and DHA modulate immune and endothelial cell function via FFA1 and FFA4 receptors. *In vitro,* studies further confirm that DHA inhibits NF-κB signaling in endothelial cells, resulting in downregulation of ICAM-1 and VCAM-1 (Calder, 2020). Nohé et al. (2003) found that via lowering endothelial platelet-activating factor production, omega-3s inhibit monocyte adherence to endothelial cells, offering a molecular explanation for their vascular anti-inflammatory actions.

These conclusions are corroborated by clinical research; Eschen et al. (2010) found that patients with chronic heart failure had lower levels of circulating soluble adhesion molecules after taking marine omega-3 supplements, and Baker et al. (2018) noted that omega-3s reduce inflammatory recruitment by attenuating leukocyte-endothelium interactions. Furthermore, Wang et al. (2011) demonstrated a direct biological mechanism by showing in vitro that DHA reduces VCAM-1 expression and NF-κB activation in TNF-α-treated human aortic endothelial cells. All these findings suggest that omega-3 fatty acids prevent vascular inflammation by regulating leukocyte adhesion and endothelial activation, especially during times of increased inflammatory stress.

Oxidative stress markers (MDA, isoprostanes, antioxidant enzymes)

Oxidative stress is closely linked to chronic inflammation, and omega-3 supplementation appears to modulate this pathway favorably. Natto et al., (2019) reported that supplementation reduced malondialdehyde (MDA) and increased activity of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) in patients with diabetes and cardiovascular disease. These benefits are thought to result from the absorption of EPA and DHA into cell membranes, which activates transcriptional processes that strengthen endogenous antioxidant defenses while also

Table 3. Effects of omega-3 supplementation on gene expression

Domain	Key findings
Downregulation of Pro-Inflammatory Genes (COX-2, iNOS, TNF-α, IL-1β)	EPA and DHA reduce expression of pro-inflammatory mediators in immune cells and adipose tissue; modulate NF-κB signaling, eicosanoid synthesis, and inflammasome-related genes [Bouwens et al., 2009; Allam-Ndoul et al., 2016; Lee et al., 2019]. Contributes to systemic anti-inflammatory effects.
Epigenetic and Post-Transcriptional Regulation (DNA Methylation, microRNAs)	Omega-3 PUFAs may influence DNA methylation patterns and miRNA expression, affecting genes linked to inflammation and metabolism [Li et al., 2025]. Evidence mainly from omics and translational studies; human data limited.
Modulation of Lipid Metabolism and Immune Pathways (Fatty-Acid Oxidation, Macrophage Polarization)	Upregulation of fatty-acid oxidation, mitochondrial metabolism, and antioxidant genes; downregulation of pro-inflammatory and lipogenic pathways; possible shift toward anti-inflammatory macrophage phenotypes [Bouwens et al., 2009; Allam-Ndoul et al., 2016; Li et al., 2025]. Supports metabolic–immune reprogramming.
Omics-Level Insights (Transcriptomics, Metabolomics)	Multi-omics studies show coordinated modulation of inflammatory signaling, oxidative stress response, and lipid mediator profiles (SPMs vs eicosanoids) [Allam-Ndoul et al., 2016; Li et al., 2025 ; Bodur et al., 2025]. Suggests system-level reprogramming toward immune-metabolic homeostasis

stabilizing membranes and lowering lipid peroxidation (Calder, 2020). Further research in patients with metabolic syndrome and heavy smokers verified decreases in oxidative stress indicators, highlighting the function of omega-3s in regulating redox status and reducing inflammation-induced cellular damage (Elisia et al., 2022; Borja-Magno et al., 2023).

Effect of omega-3 supplementation on gene expression

Omega-3 LC-PUFAs, EPA and DHA, have been investigated not only for their lipid-lowering or “anti-inflammatory biomarker” effects but also for their capacity to modulate expression of genes involved in inflammation, metabolism, and immune function. These fatty acids can cause significant alterations at the transcriptome (and potentially epigenetic/post-transcriptional) level, according to an increasing amount of human, ex vivo, and omics-level studies. However, the strength of the evidence differs depending on the mechanism and context. The data was examined under four connected themes. The main gene expression alterations linked to omega-3 supplementation are compiled in Table 3, which also highlights how it affects metabolic, inflammatory, and regulatory pathways in the research examined.

Downregulation of pro-inflammatory genes (COX-2, iNOS, TNF-α, IL-1β)

Experiments conducted both in vitro and in vivo have consistently demonstrated that EPA and DHA inhibit the production of inflammatory genes. Human randomized supplementation trials provide one of the most direct sources of evidence. Peripheral blood mononuclear cells (PBMCs) showed significant changes in gene expression in a trial where healthy adults received 1.8 g/day EPA + DHA for 26 weeks: 1,040 genes were differentially expressed compared with control (HOSF oil), many of which belonged to inflammatory or atherogenic pathways (e.g., NF-κB signaling, eicosanoid synthesis, scavenger receptor activity) (Bouwens et al., 2009).

Translational and in vitro studies support and help explain these findings. Human THP-1 macrophages exposed to EPA or DHA (with or without inflammatory stimulation) show reduced expression of pro-inflammatory mediators, including TNF-α and NOS2 (iNOS), relative to untreated cells (Natto et al., 2019). In addition, human adipose tissue (from obese individuals) treated ex vivo with EPA or DHA showed reduced expression of inflammasome-related genes

(NLRP3, IL-1β, IL-18, CASP1), indicating that omega-3s can suppress pro-inflammatory gene programs in metabolically active tissue (Lee et al., 2019). Collectively, these data robustly demonstrate that omega-3 supplementation or exposure in immune/ adipose cells can downregulate classical pro-inflammatory genes. This downregulation likely contributes to systemic anti-inflammatory effects observed in clinical studies.

Epigenetic and post-transcriptional regulation (DNA Methylation, microRNAs)

Recent omics-era research indicates that omega-3 PUFAs may influence non-coding RNA networks and epigenetic marks in addition to transcript-level control, which could result in longer-lasting alterations in gene regulation. According to a thorough analysis of omics-enabled research conducted between 2014 and 2024, omega-3 PUFAs can change genes associated with inflammation and insulin sensitivity by influencing epigenetic processes such as DNA methylation and miRNA expression (Li et al., 202). Direct human intervention data is still few, though. Few well-powered, long-term human studies have consistently shown long-lasting epigenetic reprogramming following supplementation, despite the biological plausibility and some translational evidence supporting the modification of methylation and miRNA by omega-3s. The existing data must therefore be considered preliminary, and epigenetic or miRNA-mediated regulation should be treated as hypothesis-generating rather than established fact.

Modulation of lipid metabolism and immune pathways (Fatty-acid oxidation, macrophage polarization)

Omega-3s also appears to reprogram metabolic and immune-cell gene networks, shifting cellular physiology toward lipid oxidation and anti-inflammatory phenotypes. The omics-review referenced above reported upregulation of genes involved in fatty acid oxidation, mitochondrial metabolism, and antioxidant defense in response to omega-3 intake along with downregulation of pro-inflammatory and lipogenic pathways (Li et al., 2025). Functionally, EPA and DHA inhibited caspase-1 and inflammasome-related gene expression (such as NLRP3, IL-1β, and IL-18) in adipose tissue from obese individuals, indicating a move away from chronic inflammation (Lee et al., 2019). EPA and DHA altered the transcriptome response to LPS stimulation in macrophage models (derived from THP-1) in a dose- and fatty acid-specific manner, impacting not just inflammatory pathways but also genes linked to apoptosis, oxidative stress, and metabolism (Allam-Ndoul et al., 2016). These results lend credence to the theory that omega-3 supplementation may encourage a metabolic–immune reprogramming, including increased lipid oxidation, decreased inflammatory potential, and potentially a shift toward a pro-resolving macrophage phenotype (although there is currently little direct human data on phenotype switching).

Omics-level insights (Transcriptomics, metabolomics)

Large-scale omics studies provide the most comprehensive and integrated evidence of omega-3–induced molecular reprogramming. The review by Li et al. (2025), analyzed 72 studies (multi-omics, lipidomics, transcriptomics, metabolomics) and concluded that omega-3 PUFAs modulate a wide array of pathways: from fatty-acid oxidation and mitochondrial metabolism to inflammatory signaling, oxidative stress response, and immune cell regulation. Furthermore, in human clinical supplementation trials, changes in immune cell gene expression correlate with changes in plasma lipid mediator profiles, favoring specialized pro-resolving lipid mediators (SPMs) over pro-inflammatory eicosanoids. This shift is consistent with a systemic shift away from persistent inflammation and toward resolution (Allam-Ndoul et al., 2016; Bodur et al., 2025). These combined results imply that EPA and DHA may orchestrate coordinated, system-level reprogramming, modifying transcriptomes, lipid mediators, and metabolic pathways in a way that promotes homeostasis, resolution, and enhanced immune-metabolic function, rather than merely temporarily reducing inflammation.

Factors influencing the anti-inflammatory effects of omega-3 supplementation

The effectiveness of omega-3 fatty acids (mostly EPA and DHA) in reducing inflammation varies depending on several factors. Designing supplements techniques for maximum benefit and interpreting inconsistent trial results are made easier with an understanding of these modifiers. Here, the following important factors were taken into consideration: inter-individual variability (baseline inflammation, food background, metabolic/genetic variations), supplement formulation and bioavailability, and dose, duration, and EPA:DHA ratio. Table 4 shows the main factors influencing the anti-inflammatory effects of omega-3 fatty acids and provides practical recommendations to optimize their efficacy.

Dose, duration and EPA: DHA ratio

Numerous meta-analyses demonstrate that the amount

Table 4. Recommended omega 3 fatty acids intake

Recommended Omega-3 products		
Product	**EPH/DHA in one capsule**	**Monthly cost for ~1000 mg/day**
High concentration (starting done one capsule /day)		
Carlson elite EPA gems	1000/16.5 mg	$15
GNC triple strength	734/266 mg	8
Nature Made 1400	683/252 mg	9
Nordic naturals ProOmega (liquid)	1950/975 mg	22
NutriGold triple strength	725/275 mg	11
OmegaVia ultra concentrated	780/260 mg	15
Spring Valley Maximum Care 2000 (Walmart)	645/310 mg	4
Vascepa (Rx only)	(60/40 mg	30
Low concentration (starting done two capsule /day)		
OmegaVia EPA 500	500/21.2 MG	15
Vitacost Super EPA (vitacost.com)	600/150 mg	16

Source: Aiken, 2022.

Table 5. Key factors modulating omega-3 anti-inflammatory effects and practical recommendations.

Factors category	Specific determinants	Effect on Anti-Inflammatory Response	Recommendations	References
Dose and Duration	Total EPA+DHA intake	Higher doses and longer duration → stronger reduction in CRP, IL-6, TNF-α	≥1–2 g/day EPA+DHA for ≥8–12 weeks is usually effective	(Kavyani et al., 2022)
EPA: DHA Ratio	Proportion of EPA vs DHA	May influence cytokine modulation & pro-resolving mediator production	Balanced or DHA-rich formulations may favor specific outcomes	(Calder, 2020)
Supplement formulation	TG, EE, phospholipids	TG and phospholipid forms show higher bioavailability than EE	Choose TG-form or Phospholipid-based supplements; take with fat-containing meals	(Watson, 2019; Calder, 2006)
Stability and Storage	Oxidation status	Oxidized oils have reduced effect; may generate pro-oxidants	Use stabilized formulations, store in cool, dark places	(Watson, 2019)
Baseline Inflammation	High vs low	Higher baseline inflammation → greater measurable reductions in cytokines	Target high-risk populations for anti-inflammatory benefits	(Torres-Vanegas et al., 2025)
Dietary Background	Omega-6 intake, overall PUFA ratio	High omega-6 diet may dampen omega-3 efficacy	Consider reducing omega-6 intake or adjusting diet	(Calder, 2006)

Table 5 Contd.

Genetics and Metabolism	Fatty acid desaturase polymorphisms, absorption	Variability in tissue incorporation and responsiveness	Personalized supplementation, monitor omega-3 index	(Watson, 2019; Calder, 2006)

and duration of omega-3 supplements have a significant impact on the degree of inflammatory biomarker decrease. According to a thorough umbrella meta-analysis, n-3 PUFA therapies significantly lower adult CRP, IL-6, and TNF-α; however, the benefits were more consistent in trials with proper duration and dosage (Kavyani et al., 2022). High-dose EPA+DHA led to the gradual downregulation of pro-inflammatory and immune-activation genes in obese participants in a recent randomized controlled experiment (Borja-Magno et al., 2023). These results imply that while higher-dose and longer-duration regimens provide larger and more consistent reductions, brief, low-dose interventions may not yield significant anti-inflammatory effects. The relative amounts of EPA versus DHA in supplements can modulate efficacy. Some studies hint that different ratios may favor certain anti-inflammatory outcomes though data remain limited and heterogeneous. For instance, supplementation that increased the "omega-3 index" (reflecting erythrocyte EPA+DHA) was associated with reductions in pro-inflammatory markers in physically active individuals (Żebrowska et al., 2021). Meta-analyses that pool studies across variable EPA:DHA ratios may obscure ratio-specific effects. Thus, when designing trials or supplements, researchers and practitioners should consider both total dose and the EPA: DHA composition.

In summary adequate dose, sufficient duration, and attention to EPA:DHA ratio are key determinants of whether omega-3 supplementation produces robust anti-inflammatory effects. Table 5 shows the recommended intake levels for omega-3 fatty acids, providing guidance on appropriate daily amounts based on current nutritional recommendations.

Supplement formulation and bioavailability

Omega-3 fatty acids are delivered in different chemical formulations — triglycerides (TG), ethyl esters (EE), phospholipids (e.g., krill oil), or free fatty acids (FFAs). Bioavailability varies accordingly, for instance, TG-form supplements are generally more readily absorbed and incorporated into membranes than EE-form, which can reduce effective tissue uptake and limit biological effects [39]. A scoping review of omega-3 supplementation and the "omega-3 index" (a measure of EPA+DHA in red blood cells) found that TG-formulations at 1,000 to 1,500 mg/day for 12 weeks or more were consistently effective at raising the index; lower doses or less bioavailable formulations were often ineffective (Dempsey et al., 2023). Taking omega-3 supplements with a meal that contains fat improves absorption and bioavailability (e.g., monounsaturated or polyunsaturated fat) because long-chain PUFA absorption depends on bile-mediated emulsification (Li et al., 2025). Because omega-3 polyunsaturated fatty acids are prone to oxidation, their biological activity is diminished, and pro-oxidant byproducts may be produced. Thus, the anticipated anti-inflammatory effects may be diminished or even reversed by poorly prepared supplements (without antioxidants) or incorrect storage (Li et al., 2025). Therefore, co-ingestion circumstances, storage/stability, supplement formulation, and delivery format are crucial; bad decisions can reduce EPA/DHA's ability to have anti-inflammatory effects.

Inter-individual variability (Baseline inflammation, diet, genetics)

Compared to healthy, low-inflammation populations, the anti-inflammatory effects of omega-3s seem to be more noticeable in people with elevated baseline inflammation (such as obesity, metabolic syndrome, and chronic illness). For instance, marine omega-3 supplementation reduced IL-6 and MCP-1 while increasing pro-resolving mediators and anti-inflammatory cytokines (IL-10) in obese individuals (Torres-Vanegas et al., 2025). On the other hand, reductions in CRP and cytokines are either negligible or not significant in certain trials involving healthy persons or those with low baseline inflammation (Michaeloudes et al., 2023). This implies a "ceiling effect" in which there is less room for additional decrease when baseline inflammation is low and more room for quantifiable benefits when baseline inflammation is higher. The typical dietary ratio of omega-6 to omega-3 fatty acids influences inflammation. High omega-6 (n-6) intake promotes pro-inflammatory eicosanoid production; by contrast, increasing EPA/DHA helps shift balance toward less inflammatory mediators (Bodur et al., 2025).

There is inter-individual variation in how efficiently different people absorb, metabolize, and incorporate omega-3 PUFAs. A review notes that differences in lipid-metabolizing enzyme activity (e.g., desaturases, elongases, CYP450 isoforms) and other metabolic enzymes influence tissue incorporation and conversion, thereby modulating anti-inflammatory outcomes (Michaeloudes et al., 2023). Additionally, erythrocyte omega-3 index or tissue levels can be impacted by variations in gut fat absorption, baseline red blood cell membrane composition, compliance, and concurrent medicines, all of which can affect reactivity (Watson, 2019). In conclusion, the effectiveness of omega-3 supplementation varies greatly among individuals due to genetic, metabolic, nutritional, and disease-state variations, and there is no one-size-fits-all approach.

Safety, limitations, and research gaps

A recent comprehensive meta-analysis of 90 randomized controlled trials found that supplementation with n-3 PUFAs (EPA/DHA) was generally well tolerated but associated with a small increase in minor side-effects including diarrhea, dysgeusia (taste disturbances), and mild bleeding tendency compared to placebo. Throughout these trials, no major or potentially fatal adverse events were reported [Chang et al., 2023). Although very high-dose purified EPA may slightly increase bleeding risk (absolute risk increase ≈ 0.6%), a large systematic review that focused only on bleeding risk across 120,643 patients found no significant increase in overall bleeding events, including intracranial or gastrointestinal bleeding, among those using omega-3s vs. controls (Javaid et al., 2024). Therefore, omega-3s seem to be safe and palatable when taken at standard supplementation levels, with mostly moderate gastrointestinal or taste-related side effects; major adverse reactions are uncommon or unsupported.

Methodological limitations of current studies

Substantial heterogeneity exists across omega-3 trials in dosage, EPA:DHA ratio, formulation (ethyl-ester vs. triglyceride), study duration, and participant characteristics, making cross-study comparisons difficult. Such variability in protocols can obscure dose response relationships and formulation-specific effects (Bernasconi et al., 2021). Additionally, safety reporting is uneven. Rare or delayed dangers (such as bleeding or interactions) may go unnoticed since many trials do not routinely monitor adverse events or long-term results (Nicholls et al., 2020). Studies' outcome measurements vary greatly, ranging from oxidative stress indicators to lipid and inflammatory biomarkers, and sampling frequently uses blood rather than disease-relevant tissues, which restricts the synthesis of molecular and clinical data (Calder, 2025).

Remaining gaps in biomarker and gene expression evidence

There are insufficient long-term, large-scale studies that measure epigenetic endpoints and gene expression. It is unclear whether detected gene-level alterations endure or result in therapeutic improvement because most of the information currently available comes from short-term or small human trials. Since almost all studies use PBMCs or plasma rather than endothelium, adipose tissue, liver, or brain, there is very little tissue-specific data (Calder, 2025).

Due to varied research designs, dose-response thresholds and ideal EPA:DHA ratios are still unknown (Bernasconi et al., 2021). Seldom is inter-individual variability addressed. Factors such as baseline inflammation, genetics, dietary n-6: n-3 ratio, age, and comorbidities can influence responsiveness but are often not considered.

Priorities for future research

Future studies should be long-term, well-powered, and employ gene-expression panels and standardized biomarkers, such as oxidative stress and epigenetic markers. To properly capture inter-individual diversity, research must involve a variety of participant groups. Determining minimal effective regimens requires standardization of omega-3 formulations, dosages, and EPA:DHA ratios. To understand how omega-3s affect cellular pathways and if molecular alterations result in therapeutic advantages, multi-omics and tissue-specific investigations are required (Calder, 2025). Long-term safety monitoring should be included, especially for people who are at risk of bleeding and for high-dose or chronic use (Nicholls et al., 2020).

CONCLUSION

Omega-3 fatty acids consistently improve inflammatory status by lowering key biomarkers such as CRP, pro-Inflammatory cytokines, endothelial activation

Table 6. Summary of key findings on omega-3 anti-inflammatory effects

Domain	Key findings
Systemic markers	Supplementation with EPA and DHA consistently reduces C-reactive protein (CRP) and fibrinogen, indicating lower systemic inflammation. Effects are more pronounced in individuals with higher baseline inflammation and with higher doses (>2–3 g/day) (Natto et al., 2019).
Pro-inflammatory cytokines	TNF-α and IL-6 are generally decreased after omega-3 supplementation. IL-1β reductions are observed in some trials. Anti-inflammatory cytokine IL-10 may increase, suggesting a shift toward immune regulation (Kavyani et al., 2022).
Endothelial activation markers	Markers such as ICAM-1, VCAM-1, and E-selectin are reduced in several trials, suggesting improved vascular health, though findings are somewhat inconsistent (Borja-Magno et al., 2023).
Oxidative stress	Oxidative damage markers (MDA, F2-isoprostanes) are generally reduced after omega-3 supplementation. Antioxidant enzyme activity may increase, reflecting improved redox balance (Elisia et al., 2022).
Gene expression	Omega-3 fatty acids downregulate pro-inflammatory genes (TNF-α, IL-1β, COX-2, iNOS) and upregulate anti-inflammatory and lipid metabolism-related genes (PPAR-γ, PPAR-α). MicroRNAs and epigenetic modifications (DNA methylation) may mediate these effects (Musz et al., 2025).
Specialized pro-resolving mediators (SPMs)	EPA and DHA serve as substrates for resolvins, protectins, and maresins, which actively resolve inflammation by promoting neutrophil clearance, macrophage polarization toward M2, and anti-inflammatory cytokine production (Hong and Lu, 2013).

markers, and oxidative stress indicators. Evidence of gene-level regulation, such as decreased expression of inflammatory genes and advantageous changes in metabolic and immunological pathways, supports these systemic effects. Omega-3s work mechanistically through reduction of inflammatory signaling networks, membrane incorporation, modified eicosanoid synthesis, and specialized pro-resolving mediators. Together, these mechanisms produce a quantifiable anti-inflammatory milieu that may have therapeutic implications for immunological, cardiovascular, and metabolic diseases.

To better understand who benefits most, future research should standardize dosages, formulations, and EPA:DHA ratios while incorporating cutting-edge molecular techniques. When combined with healthy lifestyle choices, omega-3 supplementation is a practical, safe approach that can improve overall inflammation management. Table 6 shows a concise summary of the main findings on the anti-inflammatory effects of omega-3 fatty acids, integrating evidence from gene expression and biomarkers.

ACKNOWLEDGEMENT

The authors thank the researchers who contributed to the success of this research work.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

REFERENCES

Aiken C (2022). How to prescribe omega-3 fatty acids. The Carlat Psychiatry Report. https://www.thecarlatreport.c

Allam-Ndoul, B, Guénard F, Barbier O (2016). Effect of n-3 fatty acids on the expression of inflammatory genes in THP-1 macrophages. Lipids in Health and Disease 15:69. https://doi.org/10.1186/s12944-016-0241-4

Baker E, Yusof, MH, Yaqoob P, Miles EA, Calder PC (2018). Omega-3 fatty acids and leukocyte-endothelium adhesion: Novel anti-atherosclerotic actions. Molecular aspects of medicine 64:169-181. https://doi.org/10.1016/j.mam.2018.08.002

Bernasconi AA, Wiest MM, Lavie CJ, Milani RV, Laukkanen JA (2021). Effect of Omega-3 Dosage on Cardiovascular Outcomes: An Updated Meta-Analysis and Meta-Regression of Interventional Trials. Mayo Clinic proceedings 96(2):304-313. https://doi.org/10.1016/j.mayocp.2020.08.03

Bodur M, Yilmaz B, Ağagündüz D, Ozogul Y (2025). Immunomodulatory Effects of Omega-3 Fatty Acids: Mechanistic Insights and Health Implications. Molecular nutrition and food research 69(10):e202400752. https://doi.org/10.1002/mnfr.202400752

Borja-Magno A, Guevara-Cruz M, Flores-López A, Carrillo-Domínguez S, Granados J (2023). Differential effects of high dose omega-3 fatty acids on metabolism and inflammation in patients with obesity: eicosapentaenoic and docosahexaenoic acid supplementation. Frontiers in nutrition 10:1156995. https://doi.org/10.3389/fnut.2023.1156995

Bouwens M, van de Rest O, Dellschaft N, Bromhaar MG, de Groot LC, Geleijnse JM (2009). Fish-oil supplementation induces antiinflammatory gene expression profiles in human blood mononuclear cells. The American journal of clinical nutrition 90(2):415-424. https://doi.org/10.3945/ajcn.2009.27680

Calder CP (2006). n−3 Polyunsaturated fatty acids, inflammation, and inflammatory diseases 2. The American Journal of Clinical Nutrition 83(6):1505S-1519S. https://doi.org/10.1093/ajcn/83.6.1505S.

Calder PC (2010). Omega-3 fatty acids and inflammatory processes: from molecules to man. Nutrients 2(3):355-374. https://doi.org/10.3390/nu2030355

Calder PC (2012). The role of marine omega-3 (n-3) fatty acids in inflammatory processes, atherosclerosis and plaque stability. Molecular nutrition and food research 56(7):1073–1080. https://doi.org/10.1002/mnfr.201100710.

Calder PC (2015). Marine omega-3 fatty acids and inflammatory processes: Effects, mechanisms and clinical relevance. Biochimica et biophysica acta 1851(4):469-484. https://doi.org/10.1016/j.bbalip.2014.08.010

Calder PC (2020). n-3 PUFA and inflammation: from membrane to nucleus and from bench to bedside. Proceedings of the Nutrition Society 79(4):404-416. doi:10.1017/S0029665120007077

Calder PC (2025). Omega-3 fatty acids and inflammatory processes: from molecules to man. Biochemical Society transactions 45(5):1105-1115. https://doi.org/10.1042/BST20160474.

Chang JP, Tseng PT, Zeng BS, Chang CH, Su H, Chou PH, Su KP (2023). Safety of Supplementation of Omega-3 Polyunsaturated Fatty Acids: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Advances in nutrition 14(6):1326-1336. https://doi.org/10.1016/j.advnut.2023.08.003

Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J (2017). Inflammatory responses and inflammation-associated diseases in organs. Oncotarget 9(6):7204-7218. https://doi.org/10.18632/oncotarget.23208

Dempsey M, Rockwell MS, Wentz LM (2023). The influence of dietary and supplemental omega-3 fatty acids on the omega-3 index: A scoping review. Frontiers in nutrition 0:1072653. https://doi.org/10.3389/fnut.2023.1072653

Distefano A, Orlando L, Giallongo S, Tropea E, Spampinato M, Santisi A (2024). Fish Oil Containing Pro-Resolving Mediators Enhances the Antioxidant System and Ameliorates LPS-Induced Inflammation in Human Bronchial Epithelial Cells. Pharmaceuticals 17(8):1066. https://doi.org/10.3390/ph17081066

Elisia I, Yeung M, Kowalski S, Wong J, Rafiei H, Dyer RA, *et al.* (2022). Omega 3 supplementation reduces C-reactive protein, prostaglandin E2 and the granulocyte/lymphocyte ratio in heavy smokers: An open-label randomized crossover trial. Frontiers in nutrition 9: 1051418. https://doi.org/10.3389/fnut.2022.1051418

Eschen O, Christensen JHLA, Rovere M, Romano P, Sala P, Schmidt EB (2010). Effects of marine n-3 fatty acids on circulating levels of soluble adhesion molecules in patients with chronic heart failure. Cellular and molecular biology 56(1):45-51.

Heshmati J (2021). Effect of omega-3 fatty acid supplementation on gene expression of inflammation, oxidative stress and cardiometabolic parameters: Systematic review and meta-analysis. Journal of Functional Foods 85:104619. https://doi.org/10.1016/j.jff.2021.104619.

Hidalgo MA, Carretta MD, Burgos RA (2021). Long Chain Fatty Acids as Modulators of Immune Cells Function: Contribution of FFA1 and FFA4 Receptors. Frontiers in physiology 12:668330. https://doi.org/10.3389/fphys.2021.668330

Hong S, Lu Y (2013). Omega-3 fatty acid-derived resolvins and protectins in inflammation resolution and leukocyte functions: targeting novel lipid mediator pathways in mitigation of acute kidney injury. Frontiers in immunology 4:13. https://doi.org/10.3389/fimmu.2013.00013

Javaid M, Kadhim K, Bawamia B, Cartlidge T, Farag M, Alkhalil, M (2024). Bleeding Risk in Patients Receiving Omega-3 Polyunsaturated Fatty Acids: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. Journal of the American Heart Association 13(10):e032390. https://doi.org/10.1161/JAHA.123.032390

Kavyani Z, Musazadeh V, Fathi S, Hossein Faghfouri A, Dehghan P, et al. (2022). Efficacy of the omega-3 fatty acids supplementation on inflammatory biomarkers: An umbrella meta-analysis. International immunopharmacology 111:109104. https://doi.org/10.1016/j.intimp.2022.109104

Kim G (2015). Diet and Folk Medicines for Rheumatic Diseases. Journal of Rheumatic Diseases 22(1). DOI:10.4078/jrd.2015.22.1.10

Kitessa SM, Abeywardena M, Wijesundera C, Nichols PD (2014). DHA-containing oilseed: A timely solution for the sustainability issues surrounding fish oil sources of the health-benefitting long-chain omega-3 oils. Nutrients 6(5): 2035–2058. https://doi.org/10.3390/nu6052035

Lawrence T (2009). The nuclear factor NF-kappaB pathway in inflammation. Cold Spring Harbor perspectives in biology 1(6):a001651. https://doi.org/10.1101/cshperspect.a001651

Lee KR, Midgette Y, Shah R (2019). Fish Oil Derived Omega 3 Fatty Acids Suppress Adipose NLRP3 Inflammasome Signaling in Human Obesity, Journal of the Endocrine Society 3(3):504-515. https://doi.org/10.1210/js.2018-00220

Li J, Lin YC, Zuo HL, Huang HY, Zhang T, Bai JW, Huang HD (2025). Dietary omega-3 PUFAs in metabolic disease research: a decade of omics-enabled insights (2014-2024). Nutrients 28:17(11):1836. https://doi.org/10.3390/nu17111836

Li M, Li Z, Fan Y (2025). Omega-3 fatty acids: multi-target mechanisms and therapeutic applications in neurodevelopmental disorders and epilepsy. Frontiers in Nutrition 12:1598588. https://doi.org/10.3389/fnut.2025.1598588

Mason RP, Libby P, Bhatt DL (2020). Emerging Mechanisms of Cardiovascular Protection for the Omega-3 Fatty Acid Eicosapentaenoic Acid. Arteriosclerosis Thrombosis and Vascular Biology 40(5). DOI:10.1161/ATVBAHA.119.313286

Medzhitov R (2008). Origin and physiological roles of inflammation. Nature 454(7203):428-435. https://doi.org/10.1038/nature07201

Michaeloudes C, Christodoulides S, Christodoulou P, Kyriakou TC, Patrikios I, Stephanou A (2023). Variability in the Clinical Effects of the Omega-3 Polyunsaturated Fatty Acids DHA and EPA in Cardiovascular Disease-Possible Causes and Future Considerations. Nutrients 15(22):4830. https://doi.org/10.3390/nu15224830

Moriyama T, Kumon S, Kamiyama T, Karasawa K, Uchida K, Nitta K (2018). The Renoprotective Effects of Docosahexaenoic Acid as an Add-on Therapy in Patients Receiving Eicosapentaenoic Acid as Treatment for IgA Nephropathy: A Pilot Uncontrolled Trial. Internal medicine 57(2):173-179. https://doi.org/10.2169/internalmedicine.9155-17

Musz P, Gabriela RF, W, Sokal-Dembowska A, Jarmakiewicz-Czaja S (2025). Nutrigenomics and Epigenetics in the Dietary Management of Inflammatory Bowel Diseases. Genes 16(11):1368. https://doi.org/10.3390/genes16111368

Myhrstad M, Retterstøl, K, Telle-Hansen V, Ottestad I (2011). Effect of marine n-3 fatty acids on circulating inflammatory markers in healthy subjects and subjects with cardiovascular risk factors. Inflammation Research 60(4):309-319. https://doi.org/10.1007/s00011-010-0302-5

Naeini Z, Toupchian O, Vatannejad A, Sotoudeh G, Teimouri M, Ghorbani M (2020). Effects of DHA-enriched fish oil on gene expression levels of p53 and NF-κB and PPAR-γ activity in PBMCs of patients with T2DM: A randomized, double-blind, clinical trial. Nutrition, metabolism, and cardiovascular diseases 30(3):441-447. https://doi.org/10.1016/j.numecd.2019.10.012

Natto ZS, Yaghmoor W, Alshaeri HK (2019). Omega-3 Fatty Acids Effects on Inflammatory Biomarkers and Lipid Profiles among Diabetic and Cardiovascular Disease Patients: A Systematic Review and Meta-Analysis. Scientific Reports 9:18867. https://doi.org/10.1038/s41598-019-54535-x

Nicholls SJ, Lincoff AM, Garcia M, Bash D, Ballantyne, CM, Barter PJ (2020). Effect of High-Dose Omega-3 Fatty Acids vs Corn Oil on Major Adverse Cardiovascular Events in Patients at High Cardiovascular Risk: The STRENGTH Randomized Clinical Trial. JAMA 324(22):2268-2280. https://doi.org/10.1001/jama.2020.22258

Nohé B, Johannes T, Dieterich HJ (2003). Antiinflammatory effects of omega-3 fatty acids vary at different stages of inflammation. American journal of physiology. Heart and circulatory physiology 285(5):H2248–H2250. https://doi.org/10.1152/ajpheart.01138.2002

Office of Dietary Supplements (ODS). (2022). Omega-3 fatty acids – fact sheet for consumers.

Oh DY, Talukdar S, Bae EJ, Imamura T, Morinaga H, Fan W, et al. (2010). GPR120 is an omega-3 fatty acid receptor mediating potent anti-inflammatory and insulin-sensitizing effects. Cell 142(5):687-698. https://doi.org/10.1016/j.cell.2010.07.041

Pahwa R, Goyal A, Jialal I (2023). Chronic Inflammation. Treasure Island (FL): StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK493173/

Serhan CN (2014). Pro-resolving lipid mediators are leads for resolution physiology. Nature 510(7503):92-101. https://doi.org/10.1038/nature13479

Torres-Vanegas J, Rodríguez-Echevarría R, Campos-Pérez W, Rodríguez-Reyes SC, Reyes-Pérez SD, Pérez-Robles M, Martínez-López E (2025). Effect of a Diet Supplemented with Marine Omega-3 Fatty Acids on Inflammatory Markers in Subjects with Obesity: A Randomized Active Placebo-Controlled Trial. Healthcare 13(2):103. https://doi.org/10.3390/healthcare13020103

Wang TM, Chen CJ, Lee TS, Chao HY, Wu WH, Hsieh SC, et al. (2011). Docosahexaenoic acid attenuates VCAM-1 expression and NF-κB activation in TNF-α-treated human aortic endothelial cells. The Journal of nutritional biochemistry 22(2):187-194. https://doi.org/10.1016/j.jnutbio.2010.01.007

Watson HS (2019). Bioavailability of Omega-3 Fatty Acid Formulations and Their Effect on the Intestinal Microbiota. Doctor of Medicine thesis, University of Leeds, School of Medicine.

Williams-Bey Y, Boularan C, Vural A, Huang NN, Hwang IY, Shan-Shi C, Kehrl JH (2014). Omega-3 free fatty acids suppress macrophage inflammasome activation by inhibiting NF-κB activation and enhancing autophagy. PloS one 9(6):e97957. https://doi.org/10.1371/journal.pone.0097957

Żebrowska A, Hall B, Stolecka-Warzecha A, Stanula A, Sadowska-Krępa E (2021). The Effect of Omega-3 Fatty Acid Supplementation on Serum Adipocytokines, Lipid Profile and Biochemical Markers of Inflammation in Recreational Runners. Nutrients 13(2):456. https://doi.org/10.3390/nu13020456