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The Role of Omega-3 Fatty Acids in Inflammation and Immune Function

Mugo Moses H.

School of Natural and Applied Sciences Kampala International University Uganda

ABSTRACT

Omega-3 fatty acids (ω-3 FAs) are essential polyunsaturated fats with well-established roles in human health, particularly in modulating inflammation and supporting immune function. Among the most studied ω-3 FAs are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are primarily derived from marine sources such as fish oil. These fatty acids exert potent anti-inflammatory effects by influencing the production of pro-inflammatory mediators, including cytokines, eicosanoids, and prostaglandins. Additionally, ω-3 FAs promote the resolution of inflammation by generating specialized pro-resolving lipid mediators like resolvins, protectins, and maresins. Their immunomodulatory effects are evident in the regulation of innate and adaptive immune responses. EPA and DHA enhance the phagocytic capacity of macrophages, improve T-cell function, and modulate B-cell activity. This review critically examines the molecular mechanisms by which ω-3 FAs influence inflammation and immune function, highlighting their therapeutic potential in inflammatory diseases, autoimmune disorders, and chronic conditions like cardiovascular disease and cancer. Lastly, recommendations for optimal intake of ω-3 FAs and potential areas for future research are discussed.

Keywords: Omega-3 fatty acids**;** Inflammation**;** Immune function**;** Eicosapentaenoic acid (EPA)**;** Docosahexaenoic acid (DHA)

INTRODUCTION

Omega-3 fatty acids are crucial components of cell membranes and precursors to bioactive lipid mediators that play significant roles in maintaining immune homeostasis and resolving inflammation[1–4]. Unlike omega-6 fatty acids, which are more commonly associated with pro-inflammatory effects, ω-3 FAs are predominantly anti-inflammatory and immunomodulatory. The balance between ω-6 and ω-3 FAs is vital for maintaining the body's inflammatory state[5]. This review explores the dual impact of ω-3 FAs on inflammation and immune function, providing an overview of their mechanisms of action, clinical implications, and recommendations for dietary intake.

Omega-3 Fatty Acids: Structure and Sources

Omega-3 FAs are polyunsaturated fatty acids (PUFAs) characterized by the presence of a double bond at the third carbon atom from the methyl end[6–9]. The three main types of ω-3 FAs include:

I. Alpha-linolenic acid (ALA), found in plant oils such as flaxseed, chia seeds, and walnuts,

II. Eicosapentaenoic acid (EPA), primarily obtained from fish and marine sources,

III. Docosahexaenoic acid (DHA), also found in marine oils.

EPA and DHA are the most bioactive forms of ω-3 FAs, with the strongest influence on inflammatory and immune pathways.

Mechanisms of Action in Inflammation

Modulation of Eicosanoids and Pro-inflammatory Mediators: Eicosanoids, including prostaglandins and leukotrienes, are lipid mediators derived from arachidonic acid (ω-6 FA) and EPA (ω-3 FA). While arachidonic acid metabolites are largely pro-inflammatory, EPA-derived eicosanoids are less inflammatory. Omega-3 FAs reduce the production of pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α, while simultaneously promoting anti-inflammatory cytokines like IL-10 [10, 11].

Specialized Pro-resolving Lipid Mediators (SPMs): SPMs such as resolvins, protectins, and maresins are metabolites of EPA and DHA that actively resolve inflammation by halting neutrophil infiltration, promoting macrophage-mediated clearance of apoptotic cells, and fostering tissue repair. These molecules play pivotal roles in transitioning inflammation from the initiation

phase to the resolution phase, mitigating chronic inflammation and tissue damage[12, 13].

Omega-3 Fatty Acids and Immune Function

Effects on Innate Immunity: Innate immunity, the body's first line of defense, is greatly influenced by ω-3 FAs. EPA and DHA enhance macrophage activity, improving their ability to clear pathogens and apoptotic cells. They also regulate the activation of neutrophils and natural killer (NK) cells, which are essential for immediate immune responses. Omega-3 FAs reduce the excessive production of reactive oxygen species (ROS) by neutrophils, thereby preventing oxidative stress-mediated tissue damage during inflammation[14].

Effects on Adaptive Immunity: In the adaptive immune system, ω-3 FAs modulate T-cell proliferation and differentiation, promoting the development of regulatory T cells (Tregs) while suppressing Th1 and Th17 inflammatory responses. This shift toward an anti-inflammatory T-cell profile can be beneficial in autoimmune diseases such as rheumatoid arthritis and multiple sclerosis. Additionally, ω-3 FAs influence B-cell function by reducing antibody production, further contributing to immune regulation[14, 15].

Clinical Implications of Omega-3 Fatty Acids

Cardiovascular Health: Omega-3 FAs have long been recognized for their cardioprotective effects, partly due to their anti-inflammatory properties. They reduce the risk of atherosclerosis by inhibiting the formation of foam cells and preventing endothelial dysfunction. Clinical studies have demonstrated that supplementation with ω-3 FAs can lower serum triglycerides, reduce blood pressure, and decrease the risk of myocardial infarction and stroke[16, 17].

Autoimmune and Inflammatory Diseases: The immunomodulatory effects of ω-3 FAs have been extensively studied in autoimmune diseases. In rheumatoid arthritis, ω-3 FA supplementation has been shown to reduce joint inflammation, improve mobility, and decrease the reliance on non-steroidal anti-inflammatory drugs (NSAIDs). Similarly, ω-3 FAs have been beneficial in managing inflammatory bowel diseases (IBD) such as Crohn's disease and ulcerative colitis, where they help maintain remission and reduce flare-ups[18].

Cancer: Omega-3 FAs may also have anti-tumor properties. EPA and DHA have been shown to modulate cancer cell proliferation, apoptosis, and angiogenesis. In prostate cancer, ω-3 FAs can reduce tumor growth and metastasis by inhibiting inflammatory pathways, although more clinical trials are needed to confirm these findings [19, 20].

CONCLUSION

Omega-3 fatty acids play a critical role in modulating inflammation and supporting immune function. Their ability to influence both innate and adaptive immune responses makes them valuable in the prevention and management of chronic inflammatory and autoimmune diseases. While dietary intake of ω-3 FAs should be encouraged, supplementation may be necessary in some cases. Ongoing research is expected to further elucidate the therapeutic potential of ω-3 FAs, paving the way for targeted interventions in inflammatory and immune-mediated conditions.

Recommended Actions

Dietary Intake: For optimal health benefits, the American Heart Association recommends consuming at least two servings of fatty fish (rich in EPA and DHA) per week, equivalent to about 500 mg/day of combined EPA and DHA. In cases of high triglycerides, supplementation up to 2-4 grams of ω-3 FAs per day may be beneficial.

Supplementation Guidelines: For individuals who do not consume adequate ω-3 FAs through their diet, supplementation with fish oil or algae-derived ω-3 supplements is advisable. It is essential to consult a healthcare provider before initiating high-dose ω-3 FA supplementation, especially in individuals taking anticoagulants, as ω-3 FAs can have blood-thinning effects.

Future Research

Further research is needed to better understand the specific molecular pathways through which ω-3 FAs exert their effects in various disease states. Randomized controlled trials should explore the long-term benefits of ω-3 FAs in autoimmune diseases, cancer, and metabolic disorders. Additionally, the role of genetic variations in individual responses to ω-3 FAs warrants investigation, as personalized nutrition may enhance therapeutic outcomes.

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