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# Omega-3 Fatty Acids as Adjunctive Therapy in Periodontitis: A Scoping Review of Immune Modulation and Periodontal Tissue Regeneration

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**ABSTRACT**

Periodontitis is a chronic inflammatory disease characterized by the progressive destruction of tooth-supporting tissues. It has also been reported to be associated with systemic conditions, such as diabetes mellitus and cardiovascular disease. Although scaling and root planing and other non-surgical periodontal therapies remain the mainstays of treatment, clinical outcomes may be limited by persistent inflammation and residual subgingival deposits. This has led to the exploration and investigation of adjuvant approaches. Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), possess well-established anti-inflammatory and immunomodulatory properties. These compounds can enhance periodontal repair by modulating host immune responses and supporting tissue regeneration. As dietary supplements, the compounds are generally safe, affordable, and easily accessible. Therefore, this scoping review aims to map and synthesise evidence regarding the use of omega-3 fatty acids as adjunctive therapy in periodontitis, particularly in immune modulation and periodontal tissue regeneration. The study procedures were carried out in accordance with PRISMA-ScR guidelines Although clinical evidence remains limited, current studies suggest beneficial effects when omega-3 supplementation is combined with conventional periodontal therapy.

**Keywords:** Fatty Acids, Omega-3; Periodontitis; Dietary Supplements; Tissue Regeneration.

**ABSTRAK**

Periodontitis merupakan penyakit inflamasi kronis yang ditandai dengan kerusakan progresif pada jaringan pendukung gigi dan telah dikaitkan dengan kondisi sistemik seperti diabetes melitus dan penyakit kardiovaskular. Pendekatan terapi adjuvan terus diteliti karena, meskipun skeling dan penghalusan akar serta terapi periodontal non-bedah lainnya masih menjadi tatalaksana utama, hasil klinis dapat terbatas akibat inflamasi persisten dan sisa deposit subgingiva. Asam lemak omega-3, khususnya eikosapentaenoat (EPA) dan dokosaheksaenoat (DHA), memiliki sifat antiinflamasi dan imunomodulator yang telah terbukti dengan baik. Asam lemak omega-3 dapat meningkatkan perbaikan jaringan periodontal melalui modulasi respons imun inang dan mendukung regenerasi jaringan. Sebagai suplemen makanan, omega-3 umumnya aman, terjangkau, dan mudah diperoleh. Scoping review ini, yang dilakukan sesuai pedoman PRISMA-ScR, bertujuan untuk memetakan dan mensintesis bukti mengenai penggunaan asam lemak omega-3 sebagai terapi tambahan pada periodontitis, khususnya dalam modulasi imun dan regenerasi jaringan periodontal. Meskipun bukti klinis masih terbatas, studi yang ada menunjukkan efek yang bermanfaat apabila suplementasi omega-3 dikombinasikan dengan terapi periodontal konvensional.

**Kata kunci:** Asam Lemak Omega-3; Periodontitis; Suplemen Makanan; Regenerasi Jaringan

## 1. Introduction

The hallmark of periodontitis is the persistent inflammation of the tissues that surround and support tooth, leading to gradual collapse and falling out of tooth. In 2018, a report from Indonesian National Basic Health Research (Riset Kesehatan Dasar/Riskesdas) discovered a prevalence of 67.8% among those aged 15 and up, indicating that the country's disease burden is still substantial [1]. Several systemic condition, such as diabetes mellitus and cardiovascular disease, have been associated with periodontitis, in addition to its negative impacts on oral health. Persistent periodontal inflammation may contribute to systemic complications through multiple pathways, such as an increased systemic inflammatory load, translocation of periodontal pathogens into the circulation, and impairment of oral health–related quality of life (OHRQoL).

Mechanical non-surgical periodontal therapy represents the conventional approach for managing periodontitis and is primarily directed at removing etiological agents from the root surfaces [2]. Scaling and root planing, carried out with hand instruments and/or ultrasonic equipment, have been demonstrated to result in measurable improvements in clinical parameters [3]. However, in anatomically difficult-to-access areas, residual calculus may remain, and bacterial colonization can persist on the root surface [4]. A range of therapeutic agents has been explored as adjunctive options in the management of periodontitis, including omega-3 fatty acids administered as dietary supplements [5].

A growing interest in omega-3 polyunsaturated fatty acids (PUFAs) as key nutritional components for host-modulation strategies in non-surgical periodontal therapy has been stimulated by the identification of novel pro-resolving lipid mediators by Serhan [6]. Many of these mediators originate from the metabolic conversion of the principal omega-3 PUFAs, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are the principal omega-3 PUFAs. Several studies have demonstrated that these compounds, in particular EPA and DHA, have anti-inflammatory and immunomodulatory properties. The compounds also have the potential to play a role in the management of the course of periodontal disease [7]. In addition, omega-3 supplementation has been reported as a safe, affordable, and clinically advantageous adjunct that can enhance the outcomes of conventional periodontal treatment [8,9].

An examination of current developments in the application of omega-3 fatty acids is presented in this study. Particular attention is given to the potential of these acids to control immunological responses and stimulate the regeneration of periodontal tissue. The results are expected to encourage the integration of omega-3 into evidence-based dental practice in Indonesia as an adjunctive therapy in periodontal treatment protocols. This is primarily due to their multifunctional therapeutic potential, current underutilization, and minimal adverse effects.

## 2. Methods

The current literature about the use of omega-3 fatty acids as supplemental agents in the treatment of periodontitis was mapped out in a thorough and organized fashion for the aim of this study using a scoping review technique. The used methodological approach was PRISMA-ScR, which stands for Preferred Reporting Items for Systematic Reviews and Meta-Analyses: Extension for Scoping Reviews. The protocol for this scoping review was registered in Open Science Framework (OSF; Registration ID: D7JWH; DOI: 10.17605/OSF.IO/D7JWH). Included studies examined how omega-3 fatty acids, namely EPA and DHA, affected periodontal inflammation, immunological regulation, and periodontal tissue regeneration, which included in this review comprised both clinical and preclinical investigations that were published in English. These investigations included randomized controlled trials, observational studies, and experimental studies. Those that did not contain omega-3 supplementation or those that did not pertain to periodontitis were not considered appropriate for inclusion.

A systematic literature search was performed across PubMed, Scopus, ScienceDirect, and Google Scholar. The search strategy combined relevant terms, including “omega-3 fatty acids”, “EPA”, “DHA”, “periodontitis”, “periodontal therapy”, “immune modulation”, and “tissue regeneration”. After a preliminary screening of titles and abstracts, all found records were subjected to a full-text review according to the established inclusion and exclusion criteria. Following the guidelines of a scoping review, the studies were selected and described descriptively.

**3. Results and Discussions**

Lang described periodontitis as a chronic, multifactorial inflammatory disorder associated with microbial dysbiosis and the accumulation of dental plaque biofilm [10]. Although biofilm formation initially triggers gingival inflammation, periodontitis is clinically defined by 3 hallmark features, namely destruction of the tooth-supporting tissues, formation of periodontal pockets, and gingival bleeding. Chapple noted that gingivitis represents a reversible condition, in which periodontal health can be restored with appropriate intervention. Meanwhile, periodontitis is typically irreversible and progressive, necessitating long-term supportive periodontal care [11].

The disease arises from inflammation of periodontal supporting structures initiated by plaque accumulation and pocket development, accompanied by suppurative exudate, collagen degradation, and alveolar bone loss. Periodontal pathogens constitute the primary etiological factors, however, systemic and behavioral risk factors such as smoking, diabetes mellitus, and psychological stress can further accelerate disease progression. In periodontitis, elevated bacterial burden and enhanced local production of inflammatory mediators facilitate the translocation of microorganisms and pro-inflammatory cytokines into the systemic circulation, thereby influencing overall systemic health [12]. The occurrence of bacteremia has been shown to correlate with disease severity, while periodontal risk factors are known to modulate immune-inflammatory responses and affect the remodeling of both hard and soft periodontal tissues

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Increasing plaque buildup is positively linked to the onset and maintenance of chronic periodontal disease, according to studies in both humans and animals. Page reported that plaque control can reverse the inflammatory process. Microorganisms, particularly bacteria, can induce periodontal inflammation directly through enzymatic activity and bacterial products. However, the primary issue is not the bacteria, but rather the indirect inflammatory pathways triggered by bacterial challenge. Inflammation leads to the release of mediators, such as cytokines, which contribute to periodontal tissue destruction. This indirect pathway includes inflammation-induced enzymatic release that provides peptides serving as nutrients for periodontal pathogens, thereby perpetuating disease progression [13].

Root surface debridement, particularly biofilm removal, is essential for the resolution of periodontal inflammation [14]. The effectiveness of hand-instrument root surface instrumentation has been well documented. However, complete biofilm elimination is not always achieved with non-surgical periodontal therapy alone. Clinical resolution of inflammation and prognosis depend on the individual host's immune status. Systematic periodontal treatment is applied to all forms of periodontitis. However, the duration of each treatment phase varies according to the patient’s condition [10]. A comprehensive periodontal treatment program can incorporate both non-surgical and surgical interventions. Instrumentation techniques include hand instruments, sonic and ultrasonic systems, and air-polishing methods. Mechanical disruption of biofilm integrity is a prerequisite for adjunctive periodontal therapies. Despite mechanical intervention, bacterial endotoxins and pathogenic substances can diffuse into gingival tissues, triggering immune-inflammatory responses. According to Sanz, biofilm removal alone is insufficient for managing periodontitis, particularly in advanced stages. Consequently, several adjunctive therapies have been proposed to support biofilm control or to reduce local and systemic inflammation. In light of increasing concerns about antimicrobial resistance, the use of antibiotics in periodontal therapy must be restricted to carefully selected patients, such as those presenting with highly active disease or distinct microbiological characteristics. As an alternative approach, host-modulation strategies using dietary supplements, including omega-3 fatty acids or probiotics, have shown favorable adjunctive effects in supporting periodontal treatment outcomes [14]

The presence of the first double bond at the third carbon from the methyl terminus of fatty acid chain distinguishes omega-3 fatty acids from other essential PUFAs. One of the types of PUFAs is omega-3 fatty acids. The 3 primary components that constitute this category are alpha-linolenic acid (ALA), EPA, and DHA. Metabolic conversion of ALA into EPA and DHA is possible, but it is very slow in humans. Estimates put the rate at less than 15% for EPA and less than 5% for DHA [15]. The major way to get enough EPA and DHA in the diet is to eat foods that are made from animals. The majority of omega-3 fatty acids we consume come from plants and seafood [9]. ALA is abundant in plant-based foods, such as walnuts, chia seeds, flaxseed, and canola oil [16]. Meanwhile, marine items are rich in EPA and DHA, including oily fish (salmon, tuna, sardines, mackerel, etc.), fish oil, and krill oil supplements. People who do not eat a lot of seafood or who have certain

medical conditions have increase the need for omega-3 supplements, such as fish oil and algal oil pills. Omega-3 fatty acids play an essential role in maintaining the integrity of cell membranes, controlling inflammation, and the proper functioning of the central nervous system, according to biological perspectives [17]. During embryonic neurodevelopment and cognitive functioning, DHA is an essential structural component of neuronal and retinal membranes. In addition to its function as a precursor, EPA is included in the synthesis of some mediators that promote resolution, including the anti-inflammatory resolvins and protectins. Aside from lowering triglyceride levels and increasing HDL levels, omega-3 fatty acids also stabilize cell membranes, lessen the likelihood of cardiac arrhythmias, and generally improve cardiovascular health. Eating omega-3 fatty acids has been associated with a lower risk of several chronic diseases, including hypertension, atherosclerosis, arthritis, and mood disorders [18].

To make specific pro-resolving mediators (SPMs), the human body uses cyclooxygenase (COX) and lipoxygenase (LOX) pathways to enzymatically convert EPA and DHA. SPMs included resolvins (RvE1, RvD1), protectins, and maresins [19]. This group of bioactive lipid mediators can actively limit the recruitment of neutrophils to sites of inflammation, inhibit the production of cytokines that promote inflammation, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), and stimulate macrophages to engulf dead cells and tissue debris. Omega-3-derived steroid peptides (SPMs) enhance the active resolution of inflammation and expedite tissue repair, thereby contributing to tissue homeostasis and the prevention of chronic inflammatory disorders. The primary goal of NSAIDs, or nonsteroidal anti-inflammatory drugs, is to suppress inflammatory pathways.

Dietary PUFAs are incorporated into cellular phospholipid membranes, serving as substrates for lipid mediator synthesis involved in cell signaling, gene regulation, and inflammatory control, while also maintaining membrane stability and fluidity (20). The 2 major PUFA families are the n-6 and n-3 series. Contemporary diets tend to be enriched in n-6 fatty acids, particularly linoleic acid derived from soybean, corn, and sunflower oils, which is metabolized into arachidonic acid, while intake of n-3 PUFAs is often insufficient. Long-chain n-3 PUFAs (LCn3PUFAs) are regarded as essential nutrients due to the limited capacity for endogenous synthesis in humans. Among the lipid mediators implicated in chronic inflammatory conditions such as periodontitis, resolvins derived from EPA and DHA exhibit particularly strong anti-inflammatory activity. Consequently, maintaining an adequate and balanced intake of omega-3 fatty acids and PUFAs can confer protective effects against chronic inflammatory and metabolic diseases [20].

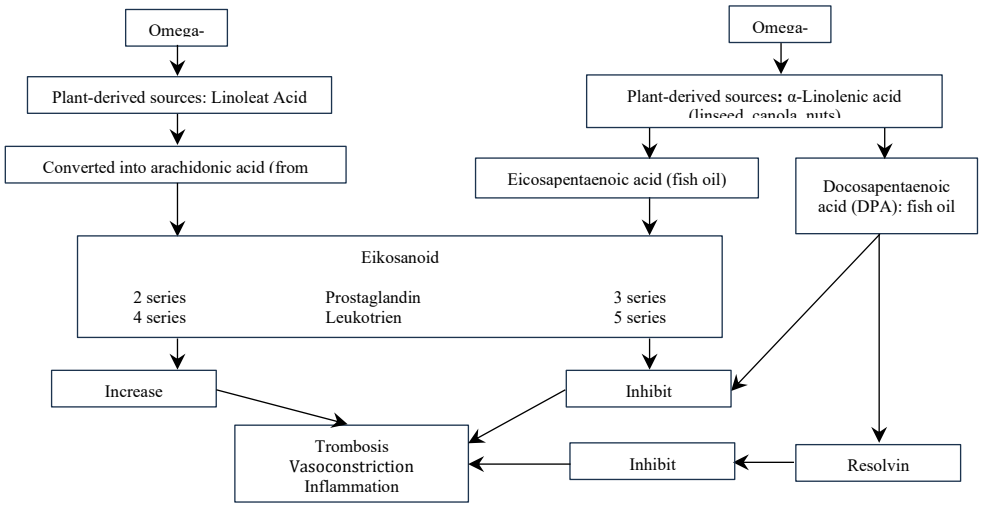


**Figure 1**. Physiological Pathways of PUFAs

Studies have shown that EPA and DHA, 2 types of omega-3 fatty acids, can aid in the repair of periodontal tissue. These fatty acids affect alveolar bone and soft tissues like gingiva and periodontal ligament. Experimental studies by Neprelyuk demonstrated that omega-3 supplementation attenuates chronic inflammatory responses while enhancing fibroblast activity involved in collagen synthesis and extracellular matrix formation [21]. In addition, the immunological environment is optimal for periodontal wound healing when omega-3 fatty acids promote macrophage polarization toward the pro-regenerative M2 phenotype.

Another mechanism by which angiogenesis is enhanced is the increased expression of vascular endothelial growth factor (VEGF), a process mediated by the conversion of EPA and DHA into resolvins and protectins, respectively. In addition, study has shown that growth factors such as basic fibroblast growthfactor (bFGF) and bone morphogenetic protein-2 (BMP-2) can be used in combination with omega-3 fatty acids to enhance periodontal regeneration therapy by promoting neovascularization and bone formation [22]. Taking all of these interactions into consideration, it appears that omega-3 fatty acids facilitate periodontal bone regeneration by increasing an environment that is biologically ideal for the healing process.

Omega-3 fatty acids have a supportive role as an adjuvant in periodontal care, according to clinical evidence. Postmenopausal women's periodontal inflammation and systemic antioxidant enzyme status were both enhanced by combining scaling and root planing (SRP) with omega-3 fatty acid supplements, according to Elgendy's study [23]. Omega-3 supplementation was also associated with a marked reduction in inflammatory biomarkers, such as matrix metalloproteinases and receptor activator of nuclear factor kappa-B ligand (RANKL), according to studies conducted by El-Sharkawy et al. and Mafi [24,25]. In a study by Cumpston including individuals with advanced periodontitis (stages III and IV), patients who underwent SRP and received omega-3 supplementation exhibited significant reductions in clinical inflammatory indices. Omega-3 group had significantly reduced levels of pro-inflammatory cytokines and chemokines, including interleukin-8 (IL-8) and interleukin-17 (IL-17), according to salivary experiments [26].

Despite these results, existing studies were limited by variability in omega-3 dosages, heterogeneity in diagnostic criteria for periodontitis, differences in study design, and diverse patient populations. However, Tur reported that long-term omega-3 supplementation was associated with a low risk profile, with theoretical safety concerns deemed minimal, even among patients receiving antiplatelet or anticoagulant therapy. In addition, it has not yet been fully determined how omega-3 supplementation affects periodontal health over the long run, although the majority of the study that is now available points to positive results in the short term. In subsequent study, the determination of effective dose regimens, the evaluation of long-term efficacy and safety, and the explanation of the molecular mechanisms that underlie periodontal advantages of EPA and DHA must be given the highest priority. To further prove the therapeutic value of omega-3 fatty acids as supplementary medicines in periodontal therapy [27], it is necessary to conduct randomized controlled trials on a large scale with extended follow-up periods.

## 3. Conclusion

In conclusion, omega-3 fatty acids demonstrate considerable potential as adjunctive agents in the management of periodontitis due to their anti-inflammatory, immunomodulatory, and pro-resolving properties. The results from this scoping review show that supplementation with EPA and DHA can enhance the outcomes of conventional periodontal therapy, particularly scaling and root planing, by reducing inflammatory mediators, improving host immune responses, and promoting periodontal tissue regeneration. One of the primary strengths identified in the reviewed studies is the consistent evidence supporting the role of omega-3 in modulating the host inflammatory response, including the reduction of pro-inflammatory cytokines and the stimulation of specialized pro-resolving mediators. In addition, omega-3 fatty acids are widely accessible, cost-effective, and generally safe, making it a practical adjunct in clinical settings. However, despite these results, the available evidence remains limited due to heterogeneity in study design, variations in dosage and duration of supplementation, and differences in study populations. Therefore, further well-designed randomized controlled trials with standardized protocols and long-term follow-up are necessary to establish definitive clinical recommendations and to better understand the long-term benefits of omega-3 supplementation in periodontal therapy.

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## 5. Conflict of Interest

Regarding this research, the writers have stated that they have no competing interests.

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