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THERAPEUTIC POTENTIAL OF OMEGA-3 FATTY ACIDS IN PERIODONTAL DISEASE - A NARRATIVE REVIEW

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ABSTRACT

Aim: This narrative review critically examines the clinical and mechanistic evidence regarding the use of omega-3 polyunsaturated fatty acids (PUFAs) as adjuncts in periodontal therapy. The objective is to assess the consistency of reported outcomes, evaluate the quality of available randomized controlled trials (RCTs), and identify methodological limitations that hinder firm clinical recommendations.

Methods: A structured literature search was conducted in PubMed, Scopus, and Embase for peer-reviewed studies published between January 2010 and April 2025. Search terms included "omega-3 fatty acids", "PUFA", "EPA", "DHA", "periodontitis", "host modulation", and related terms. Inclusion criteria comprised clinical trials, systematic reviews, and relevant experimental studies with full-text availability. No meta-analysis was performed due to heterogeneity in study design and outcomes.

Results: Omega-3 fatty acids, particularly EPA and DHA, may contribute to periodontal therapy by modulating inflammation, enhancing the production of specialized pro-resolving mediators (SPMs), and reducing levels of pro-inflammatory cytokines. Some RCTs report improvements in probing pocket depth (PPD), clinical attachment level (CAL), and salivary biomarkers when omega-3s are used adjunctively with scaling and root planing (SRP). However, variability in dosage, source, treatment duration, and outcome measures limits comparability. Few studies assessed SPM levels or reported effect sizes and confidence intervals. Evidence on co-administration with low-dose acetylsalicylic acid (ASA) is inconclusive.

Conclusions: Although mechanistically plausible and supported by selected clinical trials, the adjunctive use of

omega-3 fatty acids in periodontitis lacks sufficient high-quality, consistent evidence to justify clinical recommendations. Standardized RCTs with robust design, biochemical monitoring, and long-term follow-up are needed. Omega-3s remain a promising component of integrative care but should not yet replace established therapeutic protocols.

Keywords: omega-3 fatty acids, periodontitis, host modulation, scaling and root planing, specialized pro-resolving mediators, polyunsaturated fatty acids, resolvins, inflammation resolution

INTRODUCTION

Periodontitis is a chronic, multifactorial inflammatory disease characterized by progressive loss of clinical attachment and destruction of periodontal supporting structures. According to the 2017 World Workshop classification, it affects nearly half of the global adult population and represents a major cause of tooth loss worldwide [1]. The disease typically begins with the accumulation of dysbiotic bacterial biofilm, which triggers a host-mediated inflammatory response in the gingival tissues.

While gingival inflammation may resolve with adequate oral hygiene in healthy individuals, susceptible hosts may develop a persistent and exaggerated immune-inflammatory reaction. This pathological response leads to progressive periodontal tissue breakdown and, if left untreated, eventual tooth loss [2,3]. Contemporary models of pathogenesis, including the immunological framework proposed by Chapple et al. (2018), emphasize that dysbiosis is not solely microbial in origin but reflects a dysfunctional interaction between microbial communities and the host immune system (Hajishengallis, Chavakis, & Lambris, 2020).

Modern periodontal therapy is structured in sequential phases. The first phase is based on non-surgical mechanical debridement through professional plaque removal and subgingival instrumentation, aimed at disrupting the biofilm and reducing bacterial load. Surgical intervention is reserved for sites that do not respond adequately to initial therapy. Adjunctive strategies may be incorporated into both non-surgical and surgical phases to enhance therapeutic outcomes and improve long-term disease control [4].

Among the adjunctive approaches under investigation, omega-3 polyunsaturated fatty acids (n-3 PUFAs) have received increasing scientific attention as agents of host modulation. These compounds are thought to regulate the inflammatory response and promote resolution mechanisms through lipid mediators such as resolvins and protectins (Calder, 2007; Bannenberg & Serhan, 2010; Hasturk et al., 2006). Despite this potential, the European Federation of Periodontology currently does not recommend the routine use of omega-3 fatty acids as adjuncts to subgingival instrumentation in stages I to III periodontitis, citing insufficient clinical evidence for efficacy [5,6].

Several randomized controlled trials (RCTs) and observational studies have been conducted in the past decade, some reporting improvements in clinical parameters such as probing depth, clinical attachment level, and bleeding on probing following omega-3 supplementation (Ali et al., 2024; Prasanth et al., 2024; Stańdo-Retecka et al., 2023). However, existing systematic reviews on this topic show inconsistency in conclusions. While some reviews indicate potential benefits (Chee et al., 2016), others point to heterogeneity in study designs, dosages, durations, and outcome measures, which limit the strength of recommendations and raise concerns about bias and reproducibility (Panezai & van Dyke, 2023; Panezai & Van Dyke, 2022). Furthermore, recent clinical trials published after these reviews may significantly influence the current body of evidence.

Given the evolving nature of the evidence base and the growing interest in host-modulatory approaches to periodontal treatment, a comprehensive and up-to-date critical evaluation is warranted. This review addresses the question: To what extent do omega-3 fatty acids improve clinical outcomes in the treatment of periodontitis, and what is the quality and consistency of the available evidence supporting their use as host-modulating agents?

AIM

This review critically examines recent clinical and mechanistic studies on the use of omega-3 fatty acids in the treatment of periodontitis, with particular focus on their role as host-modulating agents. It aims to identify the consistency of reported clinical outcomes, assess the strength and quality of current evidence, and define existing limitations and gaps that preclude conclusive recommendations.

METHODS

This narrative review aimed to critically evaluate clinical and experimental evidence regarding the adjunctive use of omega-3 polyunsaturated fatty acids (PUFAs) in periodontal therapy. A structured literature search was conducted in PubMed, Scopus, and Embase databases for English-language peer-reviewed articles published between January 2010 and April 2025. The search strategy employed combinations of the following terms: "omega-3 fatty acids", "PUFA", "EPA", "DHA", "periodontitis", "periodontal disease", "host modulation", "scaling and root planing", "inflammation resolution", and "specialized pro-resolving mediators", using Boolean operators

(AND, OR, NOT).

Eligible studies included randomized controlled trials, systematic reviews, and preclinical investigations reporting clinical or mechanistic outcomes relevant to periodontal treatment. Exclusion criteria were: lack of clinical endpoints, studies not related to periodontal or oral inflammatory diseases, and non-peer-reviewed literature.

Given the methodological heterogeneity among the included studies, no meta-analysis was performed. Risk of bias was not formally assessed. Instead, this review focuses on identifying mechanistic patterns, recurring clinical outcomes, and unresolved questions in the current body of evidence regarding omega-3 fatty acids as host-modulating agents in periodontitis management.

FINDINGS AND DISCUSSION

1. THE ROLE OF THE IMMUNE-INFLAMMATORY RESPONSE IN THE PATHOGENESIS OF PERIODONTITIS

The pathogenesis of periodontitis is initiated by a nonspecific epithelial response within the gingival sulcus to the accumulation of bacterial biofilm. During the initial phase, pro-inflammatory cytokines and adhesion molecules, such as intercellular adhesion molecule-1 (ICAM-1), are expressed, leading to increased vascular permeability. This facilitates the transmigration of leukocytes into the connective tissue, a process mediated by the complement system, cytokines, and leukotrienes. The early inflammatory response in gingival tissues is characterised by a dense neutrophilic infiltrate, typical of an acute inflammatory reaction. Neutrophils employ both anaerobic and aerobic antimicrobial mechanisms; however, the production of reactive oxygen species (ROS) during the oxidative burst contributes to collateral damage of surrounding host tissues [1,7].

As the inflammatory process progresses, macrophages are recruited to the site of infection. These cells exhibit potent phagocytic and cytotoxic capabilities and play a critical role in bridging the innate and adaptive immune responses through antigen presentation to Th (helper, CD4) lymphocytes. Moreover, macrophages secrete a variety of pro-inflammatory cytokines that further amplify the local immune response. These mediators activate surrounding resident cells, such as fibroblasts, keratinocytes, epithelial and endothelial cells, osteoblasts, and osteoclasts, which, in turn, release additional inflammatory mediators, thereby sustaining and further intensifying the inflammatory cascade [7,8].

In the majority of cases, the protective aspects of the host immune response are sufficient to limit the destructive potential of neutrophils and cell-mediated immunity, thereby preventing tissue damage and facilitating a return to homeostasis. However, under unfavorable conditions, in predisposed individuals, ongoing tissue destruction and persistent bacterial challenge, the regulatory capacity of the host immune system may become compromised. As a result, the inflammation driven by the host response progresses to chronic periodontitis, characterized by irreversible and progressive loss of periodontal tissues. Thus, the immune-inflammatory response, while initially protective, becomes a key driver of tissue breakdown in the chronic phase of periodontitis [9].

2. APPLICATION OF HOST MODULATING THERAPY IN THE TREATMENT OF PERIODONTITIS

Host Modulating Therapy (HMT) represents a therapeutic approach aimed at modifying the host's immune-inflammatory response to reduce tissue inflammation or destruction and promote periodontal stability. First introduced in the 1980s and extensively detailed by R.C. Williams in 1990, this approach targets the dysregulated host response that contributes to the pathogenesis and progression of periodontitis. HMT may be applied either locally or systemically, depending on the pharmacological agent and the clinical context [5,10].

In clinical practice, HMT is most frequently employed as an adjunct to conventional non-surgical periodontal therapy, namely, scaling and root planing (SRP), during the second phase of treatment. Its primary aim is to enhance therapeutic efficacy and improve the predictability of clinical outcomes, particularly in cases demonstrating a suboptimal response to mechanical debridement alone [4].

Since the introduction of the HMT concept, a broad spectrum of pharmacological agents has been investigated for their modulatory potential. These include sub-antimicrobial doses of tetracyclines (e.g., doxycycline), bisphosphonates, statins, probiotics, metformin, non-steroidal anti-inflammatory drugs (NSAIDs, such as aspirin), and omega-3 polyunsaturated fatty acids. More recently, interest has extended to synthetic and biologic agents commonly used in the management of autoimmune diseases, such as rheumatoid arthritis, due to their potential impact on periodontal disease modulation.

While several of HMT agents have demonstrated efficacy in modulating periodontal disease activity, their clinical application is often limited by concerns related to bacterial resistance, adverse effects, or insufficient long-term data. As a result, the further identification of safe, effective, and targeted host-modulating agents remains an active area of periodontal research and clinical interest [11].

3. THE ROLE AND METABOLISM OF POLYUNSATURATED FATTY ACIDS IN THE HUMAN BODY

Omega-3 and omega-6 fatty acids are essential polyunsaturated fatty acids (PUFAs) of significant physiological importance. As fundamental constituents of cell membranes, they are incorporated into phospholipid bilayers, influencing membrane fluidity, signal transduction, and inflammatory responses. Due to the absence of desaturase enzymes capable of introducing double bonds beyond the Δ9 position in the fatty acid chain, these lipids are classified as essential and must be acquired exogenously, primarily and ideally through the diet, and secondarily via supplementation.

Arachidonic acid (AA), a major representative of the omega-6 fatty acid family, is synthesized from dietary linoleic acid, which is abundant in sunflower, corn, and soybean oils. In contrast, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the principal long-chain omega-3 fatty acids, are derived from the metabolic conversion of α-linolenic acid, found in oily marine fish, flaxseed oil, canola oil, and green leafy vegetables [12].

AA, EPA, and DHA further serve as substrates for a shared set of enzymes, including cyclooxygenases (COX), lipoxygenases (LOX), and cytochrome P450 epoxygenases (CYP450), which catalyze the biosynthesis of a range of bioactive lipid mediators. Due to their reliance on common enzymatic pathways, these fatty acids compete for incorporation into downstream metabolic processes, thereby influencing the balance between pro-inflammatory and pro-resolving mediators.

The Western diet, typically characterized by a high omega-6 to omega-3 ratio, promotes disproportionate incorporation of AA into membrane phospholipids, reportedly 20 to 25 times greater than that of EPA or DHA. Consequently, it has been demonstrated that the phospholipid bilayers of neutrophils, monocytes, and lymphocytes are composed of approximately 20% AA, whereas EPA and DHA contribute only about 1% and 2.5%, respectively. This imbalance may affect the inflammatory profile and immune function of the host [13].

4. IMMUNOMODULATORY EFFECTS OF OMEGA-3 FATTY ACIDS

The metabolic conversion of arachidonic acid (AA) predominantly yields pro-inflammatory mediators, including prostaglandins (PGs), thromboxanes (Txs), and leukotrienes (LTs). In contrast, anti-inflammatory derivatives such as lipoxins, members of the specialized pro-resolving mediators (SPMs) family, are synthesized in comparatively limited quantities [14].

Cyclooxygenase-2 (COX-2), however, exhibits substrate flexibility and is capable of utilizing a broader spectrum of fatty acids as substrates. Elevated intake of omega-3 fatty acids, particularly EPA and DHA, competitively reduces the incorporation of AA in membrane phospholipids of immune and inflammatory cells. Consequently, the biosynthesis of AA-derived pro-inflammatory eicosanoids is attenuated, while alternative products such as EPA-derived eicosanoids, endocannabinoids, and SPMs, including E- and D-series resolvins, protectins, and maresins, are upregulated.

Moreover, the enzymatic conversion of EPA by COX and lipoxygenases (LOX) generates lipid mediators with significantly lower pro-inflammatory potency compared to those derived from AA. These EPA-derived eicosanoids contribute to a more controlled and less destructive inflammatory response [12].

Thus, omega-3 fatty acids, and their increased dietary intake, exert their immunomodulatory effects on multiple levels: (1) by reducing the availability of AA for conversion into pro-inflammatory mediators, (2) by serving as alternative substrates for enzymatic pathways that generate inflammation-resolving molecules, and (3) by directly modulating immune cell function. Additionally, EPA has been shown to inhibit neutrophil infiltration at inflammatory sites, thereby attenuating tissue damage and promoting the resolution of inflammation [15].

5. THE ROLE OF SPECIALIZED PRO-RESOLVING MEDIATORS (SPMS) IN INFLAMMATION RESOLUTION

Specialized pro-resolving mediators (SPMs) are a class of bioactive, endogenously derived lipid molecules generated from the enzymatic metabolism of AA, EPA, and DHA. This family includes lipoxins (LXs), resolvins (Rvs), protectins (PDs), and maresins (MaRs). These mediators are synthesized during the resolution phase of acute inflammation and function as agonists of G protein-coupled receptors (GPCRs), orchestrating active pro-resolving processes. Their biological activity includes suppressing further recruitment of leukocytes to the inflammatory site and promoting efferocytosis, the clearance of apoptotic cells and cellular debris by macrophages [16].

The identification and characterization of SPMs have fundamentally altered the understanding of inflammation resolution, which is now recognized as an active, highly regulated biological process rather than a passive decline of inflammation. Chronic inflammation is increasingly viewed as a result of defective or inadequate resolution of

the acute inflammatory response. SPMs, through stereospecific interaction with their receptors, help regulate the immune response and reestablish tissue homeostasis. Several factors influence the efficacy of SPM-driven resolution pathways, including the density and affinity of SPM receptors, the efficiency of enzymatic biosynthesis, intracellular signal transduction dynamics, and dietary intake of polyunsaturated fatty acids (PUFAs), which serve as essential precursors [17].

A deeper understanding of the role of the host immune-inflammatory response in the pathogenesis of periodontitis, along with the function of SPMs derived from fatty acid metabolism in orchestrating resolution, has opened new therapeutic avenues for the management of chronic inflammatory diseases, including periodontitis.

6. OSTEOPROTECTIVE EFFECTS OF OMEGA-3 FATTY ACIDS AND SPECIALIZED PRO-RESOLVING MEDIATORS (SPMS)

Chronic periodontitis is characterized by progressive bone loss, primarily driven by an imbalance between bone-resorbing osteoclasts and bone-forming osteoblasts. A pivotal pathway in osteoclastogenesis involves the receptor activator of nuclear factor kappa B (RANK) and its ligand RANKL. The expression of RANKL is modulated by pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-1 (IL-1), and is observed in multiple cell types, including osteoblasts, fibroblasts, and T lymphocytes, all present in the periodontal tissues [18].

Both EPA and DHA not only exert protective effects on existing osteoblasts but also promote osteoblastogenesis. Furthermore, they indirectly inhibit osteoclast differentiation by modulating signaling pathways involved in the synthesis of pro-inflammatory mediators such as IL-1, IL-6, and TNF-α. DHA alone exhibits potent antiosteoclastic activity by downregulating the expression of multiple genes directly involved in osteoclastogenesis. It also suppresses RANK expression, inhibits osteoclast migration and adhesion, and promotes their apoptosis. Collectively, these mechanisms contribute to a reduction in overall osteoclast numbers, thereby shifting the balance toward bone formation [12, 19].

The osteoprotective effects of SPMs, bioactive lipid mediators derived from polyunsaturated fatty acids (PUFAs), are even more pronounced. Among these, resolvin E1 (RvE1) has been most extensively studied and shown to significantly attenuate inflammatory bone resorption in periodontal lesions while enhancing bone regeneration [20].

A scoping review by Rovai et al. investigated the role of SPMs in craniofacial and alveolar bone regeneration, emphasizing their dual function in resolving inflammation and promoting osteogenesis. Meta-analytic findings from the review indicated that SPM treatment resulted in a 14.85% increase in newly formed bone relative to controls. Additionally, the residual bone defect area was reduced by 0.35 mm^2, and the linear distance between the defect margin and the alveolar crest decreased by 0.53 mm [21].

7. ANTIMICROBIAL PROPERTIES OF OMEGA-3 FATTY ACIDS

Beyond their well-documented anti-inflammatory effects, omega-3 polyunsaturated fatty acids (PUFAs) have demonstrated promising antimicrobial activity, particularly against oral pathogens associated with periodontal disease. In a study by Huang and Ebersole, EPA and DHA significantly suppressed the growth of key periodontal and cariogenic pathogens, including *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, *Prevotella intermedia*, *Streptococcus mutans*, and *Candida albicans* [22]. Similarly, Abdullatif et al. reported antimicrobial efficacy of these fatty acids against *Aggregatibacter actinomycetemcomitans* [23]. Supporting these observations, Ribeiro-Vidal et al., using an in vitro model of mature multispecies biofilm, demonstrated that both EPA and DHA markedly reduced bacterial viability and biomass, including reductions in periodontal pathogens [24].

Although the antimicrobial potential of omega-3 PUFAs is increasingly recognized, the underlying mechanisms remain to be fully elucidated. Current hypotheses suggest that EPA and DHA integrate into microbial cell membranes, increasing membrane fluidity and permeability, thereby disrupting membrane integrity and ultimately leading to bacterial cell death. Additionally, the presence of multiple unsaturated bonds within their structure may confer direct cytotoxic effects on bacterial membranes [12].

Despite the promising findings, further research is required to fully elucidate the molecular mechanisms of the antimicrobial action of omega-3 fatty acids and to optimize their potential as adjunctive agents in the prevention and management of periodontitis.

8. CLINICAL EVIDENCE FOR THE USE OF OMEGA-3 FATTY ACIDS IN THE MANAGEMENT OF PERIODONTITIS

In recent years, multiple randomized controlled trials (RCTs) have explored the use of omega-3 polyunsaturated fatty acids (PUFAs) as adjuncts in periodontal therapy. Although many of these studies suggest clinical benefit, the consistency and strength of evidence vary. This section summarizes and critically evaluates the main clinical trials.

Ali et al. (2024) conducted an RCT to evaluate the effect of combined eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) supplementation on probing pocket depth (PPD) and bleeding on probing (BoP) in patients with chronic periodontitis. Thirty patients received 1000 mg of omega-3 fatty acids daily for 180 days in addition to scaling and root planing (SRP). The intervention group showed significant reductions in PPD (from 5.4 ± 0.7 mm to 3.0 ± 0.4 mm) and BoP (from 71.2% to 28.3%), compared to the SRP-only control group [25].

Prasanth et al. (2024) administered plant-based omega-3 (500 mg twice daily) combined with SRP. Significant improvements were observed in clinical attachment loss (CAL), PPD, and gingival bleeding index (GBI). IL-1β levels in saliva were also significantly reduced in the intervention group [26].

Similar improvements were reported by Stańdo-Retecka et al. (2023), Kujur et al. (2020), and El-Sharkawy et al. (2010), while Stańdo et al. (2020) noted improvement only in CAL, not in PPD. Salian et al. (2024) found no significant differences in PPD and did not assess CAL [27–33].

The results of these studies are summarized in the following table:

Table 1. Summary of Key Randomized Controlled Trials (RCTs) on Omega-3 Fatty Acids in Periodontal Therapy

Author, Year	Design and Duration	Participants	Intervention	Control	Key Parameters	Main Findings
Ali et al., 2024	RCT, 6 months	30	EPA + DHA 1000 mg/ day + SRP	SRP	PPD, BoP	Significant reduction in PPD and BoP
Prasanth et al., 2024	RCT, 3 months	40	Plant-derived omega-3, 500 mg × 2/day + SRP	SRP	CAL, PPD, GBI, IL-1β	Improved CAL and PPD, reduced IL-1β levels
Stańdo-Retecka et al., 2023	RCT, 8 weeks	60	High-dose omega-3 + SRP	SRP	CAL, microbiota	Marked CAL improvement, microbiota shift
Kujur et al., 2020	RCT, 6 weeks	50	Fish oil + SRP	Placebo + SRP	PPD, CAL	Improved clinical indicators
El-Sharkawy et al., 2010	RCT, 6 months	80	Omega-3 + ASA + SRP	SRP	PPD, CAL	Enhanced SRP effect, reduced inflammation

Abbreviations: PPD — probing pocket depth; CAL — clinical attachment level; BoP — bleeding on probing; GBI — gingival bleeding index; IL-1β — interleukin-1 beta; SRP — scaling and root planing; ASA — acetylsalicylic acid

While the outcomes summarized above suggest potential benefit, the strength of these conclusions depends heavily on the methodological quality and consistency of the trials. A critical appraisal is presented in Table 2.

Table 2. Methodological Quality and Limitations of Selected RCTs on Omega-3 Fatty Acids in Periodontal Treatment

Author, Year	Sample Size	Blinding	Duration	Risk of Bias	Key Limitations	Overall Strength

Ali et al., 2024	30	Not stated	6 months	High	Small sample, lack of blinding, no placebo control	Low
Prasanth et al., 2024	40	Single	3 months	Moderate	No placebo group, short follow-up duration	Moderate
Stańdo-Retecka et al., 2023	60	Double	8 weeks	Low	Limited immunological analysis, microbiota endpoints unclear	Moderate–High
Kujur et al., 2020	50	Not stated	6 weeks	High	Minimal reporting on randomization and masking procedures	Low
El-Sharkawy et al., 2010	80	Double	6 months	Moderate	Baseline imbalance between groups not addressed	Moderate

Abbreviations: RCT — randomized controlled trial

Although the overall trend favors omega-3 supplementation as an adjunct to SRP, the evidence base is limited by small sample sizes, heterogeneity of designs, lack of blinding in several studies, and inconsistent outcome measures. These limitations must be acknowledged when interpreting the therapeutic relevance of omega-3 fatty acids in periodontal care.

The next section addresses the combined use of omega-3 fatty acids and acetylsalicylic acid, which has been investigated as a means to potentiate anti-inflammatory effects via specialized pro-resolving mediators.

8.1 The Combined Use of Omega-3 Fatty Acids and Acetylsalicylic Acid (ASA) in Periodontal Therapy

The adjunctive use of omega-3 polyunsaturated fatty acids (PUFAs) in combination with low-dose acetylsalicylic acid (ASA) has emerged as a potential therapeutic strategy in the management of periodontal disease. This approach aims to enhance the anti-inflammatory effects of omega-3 fatty acids by leveraging ASA's pharmacological inhibition of cyclooxygenase (COX), which leads to reduced synthesis of pro-inflammatory prostaglandins. Furthermore, ASA facilitates the conversion of omega-3 fatty acids into specialized pro-resolving mediators (SPMs), such as resolvins and protectins, which play key roles in resolving inflammation and promoting periodontal tissue regeneration.

Several randomized controlled trials have investigated the clinical efficacy of this combination. Studies by Castro et al. (2020), Elkhouli et al. (2011), and El-Sharkawy et al. (2010) demonstrated significant improvements in probing pocket depth (PPD) and clinical attachment loss (CAL) when omega-3 fatty acids were administered alongside low-dose ASA as an adjunct to scaling and root planing (SRP) [34-36]. Similarly, Naqvi et al. (2014) and Farhad et al. (2014) reported statistically significant reductions in PPD after six months of adjunctive therapy using omega-3 fatty acids combined with ASA [37, 38].

However, more recent findings have introduced some uncertainty. Araujo et al. (2025) conducted a rigorous RCT in which patients received 900 mg of omega-3 fatty acids and 100 mg of ASA daily, in addition to SRP. While improvements in both clinical and immunological periodontal parameters were observed, these changes did not reach statistical significance when compared to the control group, which received SRP alone [39].

Despite encouraging outcomes from some studies, the overall evidence base remains insufficient to draw definitive conclusions regarding the efficacy of this combination therapy. Inconsistencies in study design, dosing regimens, and treatment durations highlight the need for further large-scale, long-term randomized controlled trials to clarify the therapeutic value of the ASA and omega-3 fatty acids combination.

9. OMEGA-3 FATTY ACIDS AS A COMPONENT OF A HOLISTIC HEALTH STRATEGY

Contemporary medical practice emphasizes the importance of a holistic approach to patient care, recognizing that therapeutic interventions should be evaluated not only for their localized efficacy but also for their systemic impact on the patient's overall well-being. Within this framework, omega-3 polyunsaturated fatty acids (PUFAs) have garnered attention as a multifunctional therapeutic agent. In addition to their documented role in the management of periodontal inflammation, omega-3 fatty acids exert systemic anti-inflammatory effects, rendering them a valuable adjunct in the broader context of chronic disease prevention and management [15].

The cardiovascular benefits of omega-3 fatty acids are particularly well-established. The landmark Diet and Reinfarction Trial (DART), a randomized controlled trial conducted in 1997 involving 2,033 male participants, demonstrated that consuming oily fish rich in omega-3 fatty acids at least twice weekly as part of secondary prevention post-myocardial infarction was associated with a 29% reduction in all-cause mortality [40]. Beyond cardioprotection, the anti-inflammatory properties of omega-3s have shown clinical utility in rheumatology, particularly in the treatment of rheumatoid arthritis. Supplementation has been associated with reductions in joint pain, swelling, and morning stiffness. Emerging evidence also suggests a potential role for omega-3 fatty acids in the management of neurodegenerative disorders such as Alzheimer's disease, with ongoing studies exploring their effects on cognitive function and mental health outcomes [15].

Omega-3 fatty acids, primarily found in fatty fish and certain plant oils, are a fundamental component of the Mediterranean diet, widely regarded as one of the healthiest dietary patterns. Beyond their cardiovascular and anti-inflammatory benefits, this dietary model has also been associated with improved metabolic regulation, contributing to reduced risk of type 2 diabetes and obesity. Thus, omega-3 fatty acids play a multifaceted role in promoting systemic health, supporting their use not only in the treatment of periodontal disease but also as a preventive strategy against a wide range of chronic conditions [41, 42].

CONCLUSIONS

1. Current evidence suggests that omega-3 polyunsaturated fatty acids (PUFAs), particularly EPA and DHA, may offer modest benefits as adjuncts to scaling and root planing (SRP) in periodontal therapy. Several randomized controlled trials (RCTs) report improvements in clinical parameters such as probing pocket depth (PPD) and clinical attachment level (CAL), along with reductions in inflammatory markers. In some studies, the combination of omega-3 fatty acids with low-dose acetylsalicylic acid (ASA) has shown potential for synergistic anti-inflammatory effects.
2. However, these findings are limited by methodological heterogeneity, including variations in study design, dosing regimens, duration of intervention, and outcome measures. Small sample sizes and short follow-up periods further limit the generalizability of results. Importantly, neither the European Federation of Periodontology (EFP) nor the American Academy of Periodontology (AAP) currently endorse omega-3 supplementation in evidence-based treatment guidelines.
3. Given the low certainty of current evidence, omega-3 supplementation cannot yet be recommended as a standard adjunct in periodontitis management. High-quality, placebo-controlled RCTs with standardized protocols, appropriate follow-up durations, and validated biomarkers are needed to clarify its clinical relevance. Future research should also further explore the role of specialized pro-resolving mediators (SPMs), derived from omega-3 PUFAs, in inflammation resolution and tissue regeneration, as well as their potential antimicrobial properties.

AUTHOR CONTRIBUTIONS

Conceptualization: Barbara Lipka, Rafał Wiench; Literature search and data curation: Barbara Lipka, Jakub Fiegler-Rudol, Aleksandra Nasiek; Methodology: Barbara Lipka, Jakub Fiegler-Rudol, Natalia Stefanik; Writing - original draft preparation: Jakub Fiegler-Rudol, Michał Lipka, Wojciech Tokarczyk, Michał Piotrowski, Artur Los; Writing - review and editing: Barbara Lipka, Aleksandra Nasiek; Supervision: Dariusz Skaba, Rafał Wiench.

All authors have read and agreed with the final version of the manuscript.

ARTIFICIAL INTELLIGENCE DISCLOSURE

Artificial intelligence tools (e.g., ChatGPT, OpenAI) were used to assist with language editing, structural refinement, and the formulation of selected textual segments (e.g., background synthesis, objectives, conclusions). All AI-assisted content was critically reviewed, fact-checked, and finalized by the authors.

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The authors declare no conflicts of interest.

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