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The Roles of Polyunsaturated Fatty Acids (PUFAs) in Oral Health and the Management of Oral Diseases: A Narrative Review

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ABSTRACT

Polyunsaturated fatty acids (PUFAs) are essential fatty acids that have gained increasing attention because of their potential contributions to oral health and oral disease management. This narrative review provides an overview of PUFAs, discusses their biological roles in maintaining oral health, and summarizes current evidence regarding their therapeutic applications in oral diseases. Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), exhibit anti-inflammatory, immunomodulatory, antioxidative, tissue-reparative, and microbiome-modulating properties that may support oral tissue homeostasis. Evidence suggests that these biological activities contribute to the reduction of periodontal inflammation, modulation of immune responses, attenuation of oxidative stress, promotion of tissue repair, and maintenance of oral microbial balance. Clinical studies have demonstrated the potential benefits of PUFAs in the management of recurrent aphthous stomatitis, oral mucositis, oral submucous fibrosis, periodontal diseases, oral cancer, and systemic conditions that affect oral health, such as Sjögren's syndrome. In addition, omega-3 fatty acids have shown promise as adjunctive therapies capable of improving clinical outcomes when combined with conventional treatment approaches. Despite encouraging findings, challenges related to bioavailability, optimal dosage, long-term efficacy, and standardized treatment protocols remain. Overall, current evidence supports the potential role of PUFAs as dietary and therapeutic agents for promoting oral health and improving the management of oral diseases, although further high-quality clinical studies are required to strengthen the evidence base and facilitate clinical translation.

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I. INTRODUCTION

Oral diseases remain a major global public health challenge, affecting approximately 3.5 billion people worldwide and disproportionately impacting vulnerable populations, including children, older adults, and socioeconomically disadvantaged groups.[1-3] The most prevalent oral conditions include dental caries, periodontal disease, tooth loss, and oral cancers, all of which contribute substantially to disability and economic burden worldwide.[3-5] Dental caries and periodontal disease are among the most common oral diseases globally, affecting more than 2 billion people and approximately 14% of adults, respectively.[5, 6] The burden of oral diseases has increased considerably over recent decades, driven largely by population growth and aging, with disability-adjusted life years (DALYs) attributable to oral conditions increasing by 64% between 1990 and 2015.[7, 8] Despite improvements in some regions, substantial disparities persist, particularly in low- and middle-income countries (LMICs), where access to dental care

remains limited.[5, 9, 10]

Nutrition plays a fundamental role in oral health by influencing the development and maintenance of craniofacial, dental, and periodontal structures. Both undernutrition and overnutrition can adversely affect oral health outcomes.[11, 12] Oral health and nutrition exhibit a bidirectional relationship, whereby poor oral health can impair dietary intake, while inadequate nutrition can exacerbate oral diseases such as dental caries and periodontal disease.[13-15]

Among nutritional factors, polyunsaturated fatty acids (PUFAs), particularly omega-3 fatty acids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have attracted increasing attention because of their anti-inflammatory and antibacterial properties.[16, 17] Beyond oral health, PUFAs contribute to systemic health through the regulation of lipid metabolism, immune function, and inflammatory responses, which may indirectly support oral health.[18-20] Consequently, omega-3 PUFAs are increasingly being explored as adjunctive therapies to enhance the outcomes of conventional treatments for inflammatory oral diseases.[17] Increased recognition of their health benefits, together with concerns regarding insufficient dietary intake, has further stimulated interest in PUFA supplementation for both systemic and oral health.[21, 22] Therefore, this narrative review aims to provide an overview of polyunsaturated fatty acids (PUFAs), discuss their biological roles in maintaining oral health, and summarize current evidence regarding their potential applications in the management of oral diseases.

II. OVERVIEW OF PUFAs

PUFAs are fatty acids characterized by the presence of more than one double bond in their structure. These double bonds are typically arranged in a cis configuration and separated by a single –CH_2– group.[23, 24] PUFAs are classified into two major families: omega-3 (n-3) and omega-6 (n-6) fatty acids. Omega-3 fatty acids include alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), with ALA serving as a plant-derived precursor for EPA and DHA.[24, 25] Omega-6 fatty acids include linoleic acid (LA) and arachidonic acid (AA), with LA acting as a precursor for AA.[24, 26] Both omega-3 and omega-6 fatty acids are considered essential fatty acids because they cannot be synthesized by humans and therefore must be obtained through dietary intake.[26, 27]

Dietary sources of omega-3 fatty acids include both marine and plant-based foods. Fatty fish, shellfish, and marine algae are the primary sources of EPA and DHA.[28-30] Plant-derived sources such as flaxseed, walnuts, and canola oil are rich in ALA.[29, 31] In addition, omega-3-enriched eggs produced from flaxseed-fed hens provide significant amounts of ALA and DHA.[29] Omega-6 fatty acids are commonly found in vegetable oils, including sunflower and soybean oils, as well as nuts, seeds, and animal-derived products.[27, 32]

Evidence indicates that many populations do not achieve the recommended intake of long-chain omega-3 PUFAs, particularly EPA and DHA. A study among the Australian population found that seafood contributes approximately 71% of long-chain omega-3 intake, although overall consumption remains below recommended levels.[32, 33] Similarly, among pregnant women in New Zealand, only 30.9% meet the recommended daily intake of 200 mg DHA.[33]

Omega-3 supplements are commonly derived from fish oil or microalgae and provide concentrated sources of EPA and DHA.[28, 30, 34] Microalgae-based supplements have gained increasing attention because of sustainability considerations and concerns regarding contamination in fish-derived products.[30] Omega-3 supplementation has been associated with cardiovascular health benefits, anti-inflammatory effects, and support of cognitive function.[25, 35, 36] In addition, omega-3 supplements have been used in therapeutic settings for conditions such as diabetes, inflammatory bowel disease, and colorectal cancer.[36, 37] Although PUFA supplementation has demonstrated various health benefits, maintaining an appropriate balance between omega-6 and omega-3 fatty acids remains important. Excessive consumption of omega-6 relative to omega-3 fatty acids may contribute to inflammation and other health risks, highlighting the importance of an appropriate omega-6 ratio.[36, 38]

III. BIOLOGICAL ROLES OF PUFAs IN ORAL HEALTH

Polyunsaturated fatty acids (PUFAs), particularly omega-3 (n-3) fatty acids, play important roles in oral health through their anti-inflammatory, immunomodulatory, antioxidative, tissue-reparative, and microbiome-modulating properties. Omega-3 fatty acids reduce the production of pro-inflammatory cytokines such as interleukin-1, interleukin-6, and tumor necrosis factor while promoting the synthesis of anti-inflammatory mediators, including resolvins.[39-41] These effects are particularly relevant in periodontal inflammation and chronic inflammatory conditions such as periodontitis.[41-43] Omega-3 supplementation has also been shown to reduce alveolar bone loss and tissue destruction in periodontitis models through modulation of inflammatory responses and suppression of matrix metalloproteinases (MMP-2 and MMP-9), which are involved in periodontal tissue breakdown.[44, 45]

In addition to their anti-inflammatory effects, PUFAs modulate immune responses through their influence on the production of eicosanoids, prostaglandins, and leukotrienes. Omega-3-derived mediators, including prostaglandin E3 (PGE3) and leukotriene B5 (LTB5), exhibit anti-inflammatory and immunoregulatory properties that are beneficial for periodontal health.[40, 43]

Omega-3 fatty acids also help counteract oxidative stress, which is recognized as an important factor in the progression of periodontal disease. Their antioxidant properties contribute to reducing damage associated with free radicals and lipid peroxidation.[24, 46] Evidence also suggests that diets rich in omega-3 fatty acids positively influence the oral microbiome. Omega-3 fatty acids may reduce dysbiosis and promote microbial eubiosis, thereby supporting periodontal health and reducing the risk of oral diseases.[47-49]

The biological properties of omega-3 fatty acids have led to growing interest in their application in oral healthcare. Their ability to reduce inflammation, support bone preservation, and modulate immune responses has highlighted their potential as adjunctive approaches in periodontal disease management.[43, 46] Furthermore, dietary patterns rich in omega-3 fatty acids, vitamins, and polyphenols have been recommended to reduce gingival inflammation and improve oral health outcomes.[47, 49]

Despite these promising findings, optimal dosages, long-term efficacy, and standardized supplementation protocols for omega-3 fatty acids in oral health remain unclear. Further clinical studies are needed to evaluate their effectiveness and to investigate potential synergistic effects with other bioactive compounds, including vitamin D and melatonin.[43]

IV. THERAPEUTIC APPLICATIONS OF PUFAs IN ORAL DISEASES

PUFAs have demonstrated considerable potential in the management of oral diseases. Their therapeutic applications have been investigated in a variety of oral conditions, including oral mucosal lesions, periodontal diseases, oral cancer, and systemic disorders that affect oral health. Several studies have further demonstrated the potential benefits of omega-3 supplementation in patients with recurrent aphthous stomatitis (RAS). Daily supplementation with 1000 mg of omega-3 PUFAs for 3–6 months was associated with significant reductions in pain intensity, ulcer size, ulcer severity, and recurrence rates compared with placebo.[50] Patients receiving omega-3 supplementation also reported improvements in oral health-related quality of life.[51, 52] These benefits are thought to be related to the anti-inflammatory and wound-healing properties of omega-3 fatty acids, which may reduce inflammatory mediator production and facilitate ulcer resolution.[17, 53] Furthermore, omega-3 supplementation was generally well tolerated, with no significant adverse effects reported.[50, 51, 53]

In oral submucous fibrosis (OSMF), omega-3 supplementation has shown promise as an adjunctive therapy because of its anti-inflammatory properties. When combined with standard intralesional treatment consisting of dexamethasone and hyaluronidase, omega-3 polyunsaturated fatty acids have been associated with improvements in several OSMF clinical outcomes, including burning sensation, mouth opening, tongue protrusion, and cheek flexibility.[53-55] Comparative studies have further shown that omega-3 supplementation provides clinical benefits comparable to those achieved with spirulina, with no statistically significant differences observed between the two adjunctive treatment approaches.[55]

Periodontal diseases represent one of the most extensively investigated applications of PUFAs in oral healthcare. Supplementation with omega-3 PUFAs has been associated with reductions in periodontal inflammation and tissue destruction, as well as improvements in clinical parameters including bleeding on probing (BOP), probing depth (PD), and clinical attachment level (CAL).[56, 57] Evidence from animal studies also suggests that omega-3 fatty acids may reduce bone resorption and promote bone formation.[17] In addition, the dietary balance between omega-6 and omega-3 PUFAs appears to be important for periodontal health, as a high omega-6 ratio has been associated with increased periodontal disease events.[58, 59] While omega-6 fatty acids such as AA may contribute to inflammatory responses, omega-3 fatty acids may counteract these effects.[56, 60]

Clinically, omega-3 PUFAs have been used as adjuncts to scaling and root planing (SRP), demonstrating additional benefits in reducing inflammation and improving clinical attachment levels compared with SRP alone.[57, 61] Furthermore, local application of omega-3 PUFAs combined with aspirin during periodontal surgery has shown potential to enhance tissue regeneration and CAL gain.[62] Nevertheless, clinical outcomes remain variable, and some studies have reported no significant improvements following omega-3 supplementation. These inconsistencies may be influenced by differences in dosage, treatment duration, individual patient characteristics, and baseline PUFA status across populations.[61, 63, 64]

Potential applications of omega-3 PUFAs have also been reported in oral cancer. Higher erythrocyte levels of EPA and DHA have been associated with a lower risk of oral cancer, with adjusted odds ratios of 0.52 and 0.19, respectively, and the protective association appears to be more pronounced among non-smokers and non-drinkers.[65] Higher dietary intake and erythrocyte levels of DHA and other omega-3 fatty acids have also been linked to improved overall survival in oral cancer patients.[66] These benefits may be related to the anti-inflammatory and pro-resolving properties of EPA and DHA, including the generation of lipid mediators that regulate leukocyte activity and promote the resolution of inflammation, as well as interactions with genetic and molecular pathways involved in inflammation, oxidative stress, and tumor apoptosis.[67, 68] Nutritional interventions using EPA-enriched formulas have shown potential to modulate inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6), while combined EPA and DHA supplementation has been associated with improvements in body weight and nutritional status among cancer patients, although further studies are needed to clarify their specific effects on oral cancer outcomes and establish optimal supplementation strategies.[69, 70]

Omega-3 fatty acids have also demonstrated potential benefits in the management of oral mucositis, a painful complication commonly associated with chemotherapy and radiotherapy. Clinical studies have reported reductions in mucositis severity, pain scores, and recovery time among patients receiving omega-3 supplementation, particularly in severe cases.[71-73] Improvements in quality of life and oral function, including mouth opening and tongue movement, have also been observed.[53, 73] The beneficial effects of omega-3 fatty acids have been attributed to their anti-inflammatory and wound-healing properties.[53, 73, 74] Both topical and systemic administration have shown promise; topical omega-3 nanoemulgel has been reported to reduce inflammation and microbial dysbiosis in radiation-induced mucositis, while oral supplementation has been associated with reduced mucosal damage and enhanced recovery.[71, 73]

Beyond oral diseases, omega-3 PUFAs may provide benefits in systemic conditions that affect oral health. In Sjögren's syndrome, omega-3 supplementation has been suggested to alleviate symptoms such as dry mouth, although stronger evidence is still needed.[75] Omega-3 supplementation has also been proposed to improve oral health indirectly through modulation of the oral–gut microbiota axis, reduction of systemic inflammation, and promotion of overall health.[76]

Despite their therapeutic promise, several challenges remain. PUFAs are characterized by low solubility and susceptibility to rapid oxidation, which may limit their bioavailability and therapeutic efficacy. Advanced delivery systems, including nanoemulsions and liposomes, are being explored to improve stability and absorption.[77] Furthermore, additional large-scale, high-quality clinical studies are needed to establish optimal dosages, evaluate long-term efficacy, and develop standardized treatment protocols for oral diseases.[17, 43, 53]

V. CONCLUSION

Polyunsaturated fatty acids, particularly omega-3 fatty acids, play important roles in maintaining oral health through their anti-inflammatory, immunomodulatory, antioxidative, tissue-reparative, and microbiome-modulating properties, which contribute to the regulation of inflammatory responses, protection against oxidative damage, promotion of tissue healing, and maintenance of oral microbial homeostasis. Current evidence indicates that PUFAs may provide therapeutic benefits in a variety of oral conditions, including recurrent aphthous stomatitis, oral mucositis, oral submucous fibrosis, periodontal diseases, and oral cancer, while also offering potential advantages in systemic conditions that influence oral health. Their use as adjunctive therapies alongside conventional treatment approaches has shown promising clinical outcomes. Nevertheless, limitations related to bioavailability, heterogeneity of study designs, and the lack of standardized supplementation protocols continue to restrict broader clinical implementation. Further well-designed clinical trials are needed to determine optimal dosing strategies, evaluate long-term effectiveness, and clarify the role of PUFAs in evidence-based oral healthcare.

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VII. DISCLOSURE

The author reports no conflicts of interest in this work.

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