Jurnal Eduhealth
Volume 16, Number 04 2025 DOI 10.54209/eduhealth.v16i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

The Effectiveness of Omega-3 Fatty Acid Supplementation in the Management of Periodontal Disease in Patients with Type 2 Diabetes Mellitus

Anggun Rafisa[1*], Dewi Marhaeni Diah Herawati[2], Sri Tjahajawati[1], Erli Sarilita[1]
[1]Department of Oral Biology, Faculty of Dentistry, Universitas Padjadjaran, Indonesia. [2]Department of Public Health, Faculty of Medicine, Universitas Padjadjaran, Indonesia

Article Info
Keywords:
Omega-3, polyunsaturated fatty acid, type 2 diabetes mellitus, periodontitis, inflammation

ABSTRACT
Type 2 diabetes mellitus is closely associated with periodontitis through chronic inflammation and impaired tissue healing, resulting in a bidirectional relationship that adversely affects both metabolic control and periodontal health. Omega-3 fatty acids possess anti-inflammatory and pro-resolving properties and have been proposed as adjunctive host-modulatory agents in periodontal therapy for patients with diabates. This systematic review aimed to evaluate the effectiveness of omega-3 fatty acid supplementation, alone or in combination with other adjunctive therapies, on periodontal and systemic outcomes in patients with periodontitis and type 2 diabetes mellitus. This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was conducted in PubMed and Scopus databases for randomized controlled trials published between 2015 and 2025. Eligible studies investigated omega-3 fatty acid supplementation as an adjunct to nonsurgical periodontal therapy in patients with periodontitis and diabetes mellitus. Data were extracted and synthesized descriptively. Six randomized controlled trials met the inclusion criteria. Adjunctive omega-3 fatty acid supplementation consistently demonstrated greater improvements in periodontal parameters, including probing depth, clinical attachment level, and gingival inflammation, compared with nonsurgical periodontal therapy alone. Omega-3–based interventions were associated with significant reductions in inflammatory and cardiometabolic biomarkers, such as interleukins, pentraxin, chemerin, malondialdehyde, and glycated hemoglobin. Combined interventions, particularly omega-3 with low-dose aspirin or omega-3–enriched cranberry juice, yielded the most pronounced periodontal and metabolic benefits.

Corresponding Author:
Anggun Rafisa
Department of Oral Biology, Faculty of Dentistry, Universitas Padjadjaran, Indonesia
anggun.rafisa@unpad.ac.id

INTRODUCTION

Diabetes mellitus (DM) is a major global health problem with a continuously increasing prevalence, exerting substantial impacts on quality of life and healthcare costs [1]. The prevalence of DM in Indonesia is projected to rise significantly in parallel with changes in lifestyle and dietary patterns, increasing from 9.19% in 2020 to 16.09% by 2045 [2]. DM is

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currently classified based on disease-specific pathophysiological mechanisms. Type 2 DM is characterized by insulin resistance accompanied by a relative and progressively inadequate insulin secretion without autoimmune β-cell destruction, often remaining asymptomatic for years and occasionally requiring insulin therapy as the disease advances [3].

DM increases the risk of periodontitis through hyperglycemia-induced excessive inflammation, impaired tissue healing, and disease progression [4, 5]. Evidence indicates that individuals with poorly controlled or untreated DM have a two to threefold increased risk of developing periodontitis [6]. Periodontal inflammation may, in turn, exacerbate insulin resistance, resulting in a complex bidirectional relationship [6, 7]. Periodontitis is linked to impaired glycemic control, heightened insulin resistance, and a greater prevalence of diabetes-related complications, with evidence indicating that periodontal therapy reduces inflammatory burden and improves glycated hemoglobin levels [8, 9].

Current therapeutic approaches for DM primarily focus on glycemic control through synthetic pharmacological agents; however, long-term use is often associated with adverse effects, such as hypoglycemia [10-12]. Fear of injections, concerns regarding improper insulin administration, and pain associated with injections or blood glucose monitoring constitute important barriers to treatment adherence among patients with DM receiving synthetic drug–based therapies [13]. the search for safe and effective natural-based adjunctive therapies for patients with DM has emerged as a promising alternative. Several studies have demonstrated that the integration of complementary and alternative medicine with conventional therapy in patients with DM can enhance clinical effectiveness [14].

Omega-3 fatty acids, owing to their anti-inflammatory and pro-resolving properties, may offer dual benefits for patients with diabetes by improving periodontal parameters while also supporting metabolic control [15, 16]. Adjunctive omega-3 fatty acid therapy in combination with nonsurgical periodontal treatment has been shown to enhance improvements in key clinical parameters, including plaque index, gingival index, probing depth, and clinical attachment level, compared with nonsurgical therapy alone [17, 18]. This systematic review aims to evaluate the effectiveness of omega-3 fatty acid supplementation in the management of periodontitis, with particular emphasis on the heightened vulnerability of individuals with type 2 DM.

METHOD

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed between July and August 2025 using electronic databases, including PubMed and Scopus. Eligible studies were randomized controlled trials (RCTs) published between 2015 and 2025, written in English and investigating omega-3 fatty acid supplementation in patients with periodontitis and DM. The search strategy incorporated a combination of keywords such as “diabetes mellitus,” “omega-3,” “polyunsaturated fatty acid’, “periodontal disease,” “gingivitis,” and “periodontitis.” Studies were excluded if they were literature reviews, books, editorials, letters, notes, errata, conference proceedings, animal studies, observational studies, or otherwise not relevant to the research focus. Studies

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that did not report the variables of interest or did not conform to the predefined study design were also excluded.

The extracted data included the author(s) and year of publication, article title, sample, intervention details, and main findings. Data were tabulated and then subjected to a descriptive analysis. The data were organized in tabular format and analyzed descriptively.

RESULTS AND DISCUSSION

Following the PRISMA guidelines (Figure 1), a total of 1561 records were retrieved from electronic databases, of which 144 duplicate records were removed, leaving 1176 unique articles for further screening. Titles and abstracts were assessed, resulting in the exclusion of 1102 studies that did not meet the inclusion criteria. Subsequently, 74 full-text articles were evaluated for eligibility, and 68 studies were excluded due to irrelevance to the research topic, inappropriate study design, or failure to report the outcomes of interest. Finally, six studies fulfilled all eligibility criteria and were included in the qualitative synthesis of this systematic review.

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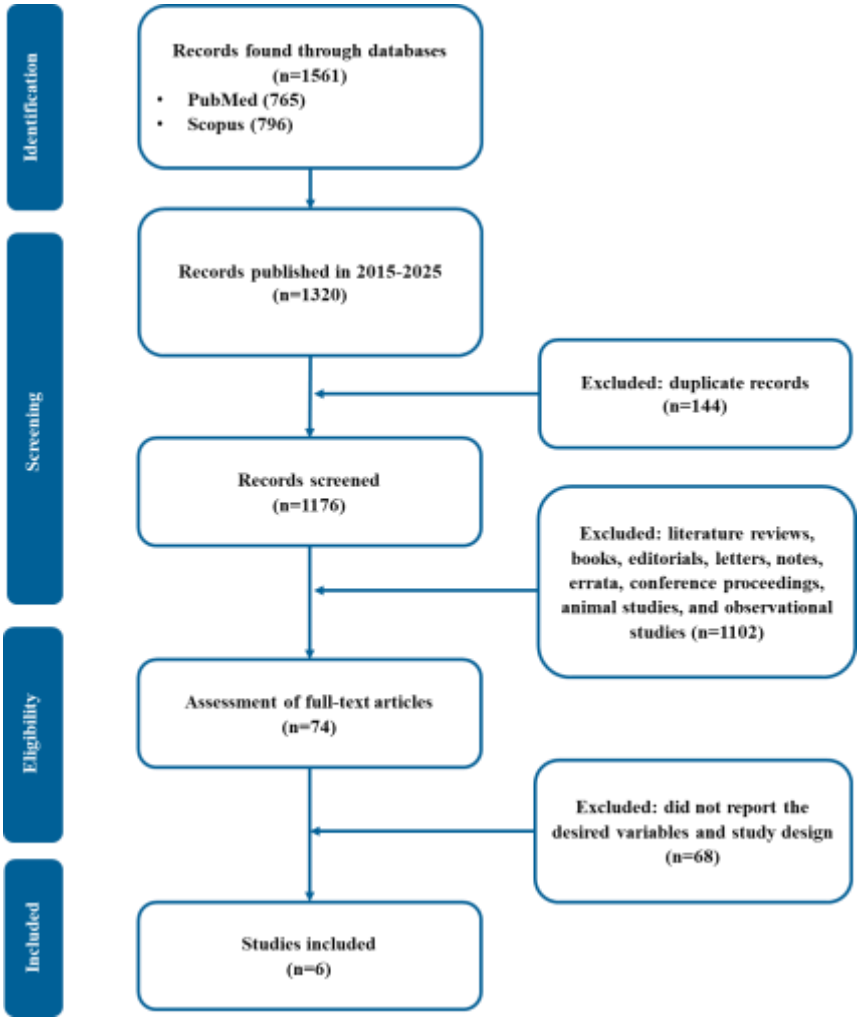

Figure 1. PRISMA-based flow diagram of the study selection process

Across six randomized controlled trials involving patients with periodontitis and type 2 DM (Table 1), adjunctive supplementation with omega-3 fatty acids, either alone or combined with low-dose aspirin or cranberry juice, consistently demonstrated superior clinical and biochemical outcomes compared with nonsurgical periodontal therapy alone. Improvements were observed in key periodontal parameters, including probing depth, clinical attachment level, gingival inflammation, and bleeding indices. In addition, adjunctive omega-3–based interventions were associated with significant reductions in pro-inflammatory and cardiometabolic biomarkers, such as interleukin-1β, IFN-γ, IL-6, IL-8, MCP-3, chemerin, pentraxin, and malondialdehyde, alongside improvements in glycemic control markers including glycated hemoglobin. Notably, combined interventions—particularly omega-3 with low-dose aspirin or omega-3–enriched cranberry juice—produced the most pronounced benefits in both periodontal and systemic outcomes.

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Table 1. Summary the included studies

Authors	Title	Samples	Intervention	Main Findings
dos Santos et al. (2020) [19]	Omega-3 Polyunsaturated Fatty Acids and Low-Dose Aspirin as Adjuncts to Periodontal Debridement in Patients with Periodontitis and Type 2 Diabetes Mellitus: A Randomized Clinical Trial.	Seventy-five patients aged ≥35 years with periodontitis and type 2 diabetes mellitus, randomly allocated into three groups (n = 25 per group).	Control group received periodontal debridement with placebo; Group 1 received omega-3 PUFA (3 g/day fish oil) plus low-dose aspirin (100 mg/day) for 2 months after periodontal debridement; Group 2 received the same omega-3 PUFA and aspirin regimen for 2 months prior to periodontal debridement. Clinical and biochemical evaluations were conducted at baseline, 3 months, and 6 months.	Adjunctive omega-3 and aspirin significantly had greater clinical attachment gain compared with control, accompanied by reductions in pro-inflammatory cytokines (IFN-γ, IL-8, IL-6).
Elwakeel and Hazaa (2015) [20]	Effect of Omega-3 Fatty Acids Combined with Low-Dose Aspirin on Clinical and Biochemical Outcomes in Patients with Chronic Periodontitis and Type 2 Diabetes Mellitus: A Randomized Double-Blind Placebo-Controlled Study	Forty patients aged 24-58 years diagnosed with chronic periodontitis and type 2 diabetes mellitus, randomly assigned into two equal groups (n = 20 per group).	The test group received omega-3 fatty acids combined with low-dose aspirin for six months as an adjunct to closed periodontal debridement, while the control group received a placebo during the same period; clinical and biochemical evaluations were conducted at baseline, 3 months, and 6 months.	Adjunctive omega-3 fatty acids and low-dose aspirin resulted in significantly greater reductions in probing depth, clinical attachment loss, and gingival index compared with placebo at both 3 and 6 months, along with significant decreases in inflammatory biomarkers, including interleukin-1β and monocyte chemoattractant

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Authors	Title	Samples	Intervention	Main Findings
				protein-3 in gingival crevicular fluid.
Ghalwash et al. (2025) [17]	Impact of Adjunctive Omega-3 Supplementation on Clinical Periodontal Parameters and Local and Systemic Chemerin Levels in Patients with Periodontitis and Type 2 Diabetes Mellitus: A Randomized Clinical Trial	Thirty patients aged 30-70 years diagnosed with periodontitis and type 2 diabetes mellitus, randomly allocated into two equal groups (n = 15 per group).	Both groups received nonsurgical periodontal therapy, while the test group additionally received omega-3 fatty acid supplementation at a dose of 1000 mg daily for six months; clinical, biochemical, and metabolic parameters were assessed at baseline, 3 months, and 6 months.	Adjunctive omega-3 supplementation led to significantly greater improvements in clinical periodontal parameters, particularly reductions in probing depth and clinical attachment loss, compared with nonsurgical therapy alone. The omega-3–treated group also exhibited significant reductions in HbA1c levels and marked decreases in both gingival crevicular fluid and serum chemerin concentrations.
Rampally et al. (2019) [21]	Comparison of Low-Dose Aspirin and Omega-3 Fatty Acids as Adjuncts to Nonsurgical Periodontal Therapy in Patients with Type 2 Diabetes Mellitus and Chronic Periodontitis	Forty-two patients aged 30-65 years diagnosed with type 2 diabetes mellitus and chronic periodontitis, equally allocated into three groups (n = 14 per group).	All participants received nonsurgical periodontal therapy. Group I (test group) received low-dose aspirin (75 mg/day) orally for 3 months, Group II (test group) received omega-3 fatty acids (500 mg fish oil) orally twice daily for 3 months, and Group III (control group) received a placebo (empty gelatin capsules) orally twice daily for the	All groups demonstrated significant intragroup improvements in clinical periodontal parameters, including gingival index, probing pocket depth, and clinical attachment level, as well as reductions in glycated

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Authors	Title	Samples	Intervention	Main Findings
			same duration, with clinical and biochemical parameters evaluated at baseline and 3 months post-intervention.	hemoglobin and pentraxin levels following nonsurgical periodontal therapy. Omega-3 fatty acid supplementation resulted in superior outcomes compared with low-dose aspirin and placebo, particularly in reducing pentraxin levels,
Ashrafzadeh et al. (2024) [22]	Beneficial Effects of Cranberry Juice Enriched with Omega-3 Fatty Acids on Inflammatory, Oxidative Stress, and Periodontal Parameters in Patients with Type 2 Diabetes Mellitus and Periodontal Disease: A Randomized Pilot Clinical Trial	Forty-one patients aged 35–67 years with type 2 diabetes mellitus and periodontal disease, randomly assigned into four groups.	Participants were assigned to an 8-week intervention comprising a control group (n = 12) receiving nonsurgical periodontal therapy alone, an omega-3 supplementation group (n = 10) receiving 1 g/day of omega-3, a cranberry juice group (n = 9) receiving 200 mL twice daily, and a cranberry juice enriched with omega-3 group (n = 10) receiving 200 mL twice daily containing 1 g of omega-3, all administered as adjuncts to nonsurgical periodontal therapy. Clinical periodontal parameters and systemic and salivary biomarkers of inflammation and oxidative stress were	The group receiving cranberry juice enriched with omega-3 demonstrated the most pronounced benefits, including significant increases in serum and salivary total antioxidant capacity and reductions in malondialdehyde levels, along with significant decreases in systemic inflammatory markers such as IL-6, TNF-α, and high-sensitivity C-reactive protein compared with baseline and control.

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Authors	Title	Samples	Intervention	Main Findings
			assessed at baseline and after 8 weeks of intervention.	
Javid et al. (2018) [23]	Impact of Cranberry Juice Enriched with Omega-3 Fatty Acids as an Adjunct to Nonsurgical Periodontal Therapy on Metabolic Control and Periodontal Status in Patients with Type 2 Diabetes Mellitus and Periodontal Disease: A Randomized Controlled Trial	Forty-one patients aged 35-70 years diagnosed with type 2 diabetes mellitus for at least 5 years and periodontal disease. Subjects were randomly assigned into four groups.	A control group (n = 12) receiving nonsurgical periodontal therapy alone, an omega-3 supplementation group (n = 10) receiving 1 g of omega-3 twice daily, a cranberry juice group (n = 9) receiving 200 mL twice daily, and a cranberry juice enriched with omega-3 group (n = 10) receiving 200 mL twice daily containing 1 g of omega-3, all administered for 8 weeks alongside nonsurgical periodontal therapy. Clinical periodontal parameters and metabolic outcomes were assessed at baseline and after 8 weeks of intervention	Significant reductions in glycated hemoglobin levels were observed in the omega-3 and omega-3–enriched cranberry juice groups, while a significant increase in high-density lipoprotein cholesterol was detected exclusively in the cranberry juice enriched with omega-3 group compared with baseline and other intervention groups. Probing depth was significantly reduced across all groups following the intervention.

The findings of this review highlight the consistent benefit of omega-3 fatty acids as an adjunctive host-modulatory therapy in the management of periodontitis among patients with type 2 DM. Across studies, omega-3 supplementation enhanced the clinical effects of nonsurgical periodontal therapy, particularly in reducing probing depth and improving clinical attachment levels. These outcomes align with the recognized anti-inflammatory and pro-resolving properties of omega-3–derived lipid mediators, which may attenuate the exaggerated inflammatory response characteristic of diabetic periodontitis [24].

Several studies further demonstrated that the addition of low-dose aspirin to omega-3 supplementation amplified clinical and immunological benefits. Aspirin is known to trigger the formation of aspirin-triggered resolvins, which synergistically enhance inflammation resolution [25, 26]. The trials by dos Santos et al. [19] and Elwakeel and Hazaa [20] reported

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greater clinical attachment gain and deeper reductions in pro-inflammatory cytokines when omega-3 and aspirin were used in combination, suggesting that timing and combination of host-modulatory agents may play a critical role in optimizing periodontal healing in diabetic patients.

Beyond periodontal outcomes, these studies consistently reported improvements in systemic metabolic and inflammatory markers, underscoring the bidirectional relationship between periodontal disease and diabetes. Reductions in glycated hemoglobin, pentraxin, and chemerin levels observed in omega-3–treated groups indicate that periodontal host modulation may positively influence glycemic control and cardiometabolic risk. Improved glycemic control, reflected by reductions in glycated hemoglobin, may be mediated through enhanced insulin sensitivity and decreased insulin resistance [27]. Omega-3 fatty acids modulate cell membrane fluidity and improve insulin receptor signaling, while simultaneously reducing inflammatory cytokines such as IL-6 and TNF-α that interfere with insulin action [28]. Furthermore, attenuation of periodontal inflammation reduces systemic inflammation, thereby diminishing inflammation-induced hyperglycemia and contributing to more stable long-term glycemic regulation [15, 16, 29]. Reductions in pentraxin levels, an acute-phase protein associated with innate immune activation and vascular inflammation, further support the systemic anti-inflammatory effects of omega-3 supplementation. By suppressing hepatic acute-phase responses and limiting cytokine-driven pentraxin synthesis, omega-3 fatty acids may reduce chronic low-grade inflammation commonly observed in patients with diabetes and periodontitis, potentially lowering cardiovascular risk [30, 31]. Similarly, the decline in chemerin levels observed in omega-3–treated groups may reflect improved adipokine regulation and metabolic homeostasis. Chemerin is a pro-inflammatory adipokine implicated in insulin resistance, endothelial dysfunction, and periodontal tissue breakdown [32]. Omega-3 fatty acids have been shown to modulate adipose tissue inflammation, reduce macrophage infiltration, and restore adipokine balance, thereby decreasing circulating chemerin concentrations [33, 34].

Despite the overall consistency of positive findings, heterogeneity across studies should be acknowledged, including variations in omega-3 dosage, duration of intervention, combination therapies, and measured outcomes, all of which may substantially influence both glycemic control and periodontal healing in patients with type 2 DM. Differences in omega-3 dose, treatment duration, and formulation can affect the bioavailability of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) [35], thereby modulating the extent of inflammation resolution, insulin sensitivity, and host immune response that are critical in the pathogenesis of diabetes-associated periodontitis. Moreover, the use of combination therapies, such as omega-3 with low-dose aspirin or antioxidant-rich cranberry juice, may produce synergistic or additive effects on inflammatory and metabolic pathways, complicating direct comparisons across studies [36]. Variability in outcome measures, including clinical periodontal parameters, inflammatory biomarkers, adipokines, and metabolic indices, further contributes to heterogeneity, as diabetes and periodontal disease share complex, bidirectional mechanisms involving chronic inflammation and metabolic dysregulation. In addition, relatively modest sample sizes and limited follow-up periods in

several trials, particularly pilot studies, may restrict the detection of long-term effects on disease progression.

CONCLUSION

The collective evidence supports the adjunctive use of omega-3 fatty acids—alone or in combination with aspirin or antioxidant-rich dietary components—as a promising strategy to improve both periodontal and systemic outcomes in patients with type 2 DM. Future large-scale, well-designed randomized controlled trials with standardized protocols are warranted to clarify optimal dosing regimens, treatment duration, and long-term clinical benefits.

REFERENCES

[1] K. L. Ong *et al.*, "Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021," *The Lancet,* vol. 402, no. 10397, pp. 203-234, 2023.

[2] M. Wahidin *et al.*, "Projection of diabetes morbidity and mortality till 2045 in Indonesia based on risk factors and NCD prevention and control programs," *Scientific Reports,* vol. 14, no. 1, p. 5424, 2024/03/05 2024.

[3] B. L. Mealey and T. W. Oates, "Diabetes mellitus and periodontal diseases," (in eng), *J Periodontol,* vol. 77, no. 8, pp. 1289-303, Aug 2006.

[4] M. Zhao, Y. Xie, W. Gao, C. Li, Q. Ye, and Y. Li, "Diabetes mellitus promotes susceptibility to periodontitis-novel insight into the molecular mechanisms," (in eng), *Front Endocrinol (Lausanne),* vol. 14, p. 1192625, 2023.

[5] A. Mirzaei *et al.*, "Association of hyperglycaemia and periodontitis: an updated systematic review and meta-analysis," (in eng), *J Diabetes Metab Disord,* vol. 20, no. 2, pp. 1327-1336, Dec 2021.

[6] P. M. Preshaw *et al.*, "Periodontitis and diabetes: a two-way relationship," (in eng), *Diabetologia,* vol. 55, no. 1, pp. 21-31, Jan 2012.

[7] I. Păunică *et al.*, "The Bidirectional Relationship between Periodontal Disease and Diabetes Mellitus-A Review," (in eng), *Diagnostics (Basel),* vol. 13, no. 4, Feb 11 2023.

[8] S. Santonocito *et al.*, "Impact of Periodontitis on Glycemic Control and Metabolic Status in Diabetes Patients: Current Knowledge on Early Disease Markers and Therapeutic Perspectives," (in eng), *Mediators Inflamm,* vol. 2022, p. 4955277, 2022.

[9] R. Cao, Q. Li, Q. Wu, M. Yao, Y. Chen, and H. Zhou, "Effect of non-surgical periodontal therapy on glycemic control of type 2 diabetes mellitus: a systematic review and Bayesian network meta-analysis," (in eng), *BMC Oral Health,* vol. 19, no. 1, p. 176, Aug 6 2019.

[10] C. Aloke *et al.*, "Current Advances in the Management of Diabetes Mellitus," (in eng), *Biomedicines,* vol. 10, no. 10, Sep 29 2022.

[11] D. M. Nathan *et al.*, "The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus," (in eng), *N Engl J Med,* vol. 329, no. 14, pp. 977-86, Sep 30 1993.

[12] A. Nakhleh and N. Shehadeh, "Hypoglycemia in diabetes: An update on pathophysiology, treatment, and prevention," (in eng), *World J Diabetes,* vol. 12, no. 12, pp. 2036-2049, Dec 15 2021.
[13] F. Brundisini, M. Vanstone, D. Hulan, D. DeJean, and M. Giacomini, "Type 2 diabetes patients' and providers' differing perspectives on medication nonadherence: a qualitative meta-synthesis," (in eng), *BMC Health Serv Res,* vol. 15, p. 516, Nov 23 2015.
[14] B. McBenedict *et al.*, "The Role of Alternative Medicine in Managing Type 2 Diabetes: A Comprehensive Review," (in eng), *Cureus,* vol. 16, no. 6, p. e61965, Jun 2024.
[15] M. M. van Ravensteijn, M. F. Timmerman, E. A. G. Brouwer, and D. E. Slot, "The effect of omega-3 fatty acids on active periodontal therapy: A systematic review and meta-analysis," *Journal of Clinical Periodontology,* Review vol. 49, no. 10, pp. 1024-1037, 2022.
[16] F. M. Delpino *et al.*, "Omega-3 supplementation and diabetes: A systematic review and meta-analysis," (in eng), *Crit Rev Food Sci Nutr,* vol. 62, no. 16, pp. 4435-4448, 2022.
[17] D. Ghalwash, A. Ammar, A. Hamdy, and A. El-Gawish, "Impact of the Adjunctive Use of Omega-3 in Periodontitis Patients With Diabetes on Local and Systemic Chemerin Levels: A Randomized Clinical Trial," (in eng), *Int J Dent,* vol. 2025, p. 7927250, 2025.
[18] N. C. Castro Dos Santos *et al.*, "Does the use of omega-3 fatty acids as an adjunct to non-surgical periodontal therapy provide additional benefits in the treatment of periodontitis? A systematic review and meta-analysis," (in eng), *J Periodontal Res,* vol. 57, no. 3, pp. 435-447, Jun 2022.
[19] N. C. Castro Dos Santos *et al.*, "Omega-3 PUFA and aspirin as adjuncts to periodontal debridement in patients with periodontitis and type 2 diabetes mellitus: Randomized clinical trial," (in eng), *J Periodontol,* vol. 91, no. 10, pp. 1318-1327, Oct 2020.
[20] N. M. Elwakeel and H. H. Hazaa, "Effect of omega 3 fatty acids plus low-dose aspirin on both clinical and biochemical profiles of patients with chronic periodontitis and type 2 diabetes: a randomized double blind placebo-controlled study," (in eng), *J Periodontal Res,* vol. 50, no. 6, pp. 721-9, Dec 2015.
[21] P. Rampally, R. R. Koduganti, S. N. Ganapathi, V. R. Panthula, and P. J. Surya, "Comparison of effectiveness of low-dose aspirin versus omega-3 fatty acids as adjuvants to nonsurgical periodontal therapy in Type II diabetic patients with chronic periodontitis," (in eng), *J Indian Soc Periodontol,* vol. 23, no. 3, pp. 249-256, May-Jun 2019.
[22] E. Ashrafzadeh, H. Babaei, M. Ravanbakhsh, A. Javid, and L. Maghsoumi-Norouzabad, "Beneficial effects of cranberry juice enriched with omega-3 fatty acids in patients with type 2 diabetic and periodontal disease: A randomized pilot clinical trial," *Journal of Advanced Periodontology and Implant Dentistry,* Article vol. 16, no. 2, pp. 160-172, 2024.
[23] A. Javid *et al.*, "Impact of Cranberry Juice Enriched with Omega-3 Fatty Acids Adjunct with Nonsurgical Periodontal Treatment on Metabolic Control and Periodontal Status in

Type 2 Patients with Diabetes with Periodontal Disease," *Journal of the American College of Nutrition,* Article vol. 37, no. 1, pp. 71-79, 2018.

[24] S. Lamon-Fava, "Associations between omega-3 fatty acid-derived lipid mediators and markers of inflammation in older subjects with low-grade chronic inflammation," (in eng), *Prostaglandins Other Lipid Mediat,* vol. 176, p. 106948, Jan 2025.

[25] P. Wang, C. Zhu, M. Liu, Y. Yuan, and B. Ke, "The inhibiting effect of Aspirin Triggered-Resolvin D1 in non-canonical pyroptosis in rats with acute keratitis," *Experimental Eye Research,* vol. 218, p. 108938, 2022/05/01/ 2022.

[26] N. Chiang and C. N. Serhan, "Aspirin triggers formation of anti-inflammatory mediators: New mechanism for an old drug," (in eng), *Discov Med,* vol. 4, no. 24, pp. 470-5, Dec 2004.

[27] H. M. AbdlWhab, A. Al-Saffar, O. A. Mahdi, and R. B. Alameri, "The impact of insulin resistance and glycaemic control on insulin-like growth factor-1 in patients with type 2 diabetes: a cross-sectional study," (in eng), *Clin Diabetes Endocrinol,* vol. 10, no. 1, p. 36, Nov 23 2024.

[28] S. Sinha, M. Haque, H. Lugova, and S. Kumar, "The Effect of Omega-3 Fatty Acids on Insulin Resistance," (in eng), *Life (Basel),* vol. 13, no. 6, Jun 5 2023.

[29] Y. Guo *et al.*, "Periodontal therapy mitigates inflammation via TNF-α reduction and improves glycolipid metabolism in diabetic patients: a cross-sectional cohort study," (in eng), *Front Endocrinol (Lausanne),* vol. 16, p. 1668695, 2025.

[30] A. Tutor, E. L. O'Keefe, C. J. Lavie, A. Elagizi, R. Milani, and J. O'Keefe, "Omega-3 fatty acids in primary and secondary prevention of cardiovascular diseases," (in eng), *Prog Cardiovasc Dis,* vol. 84, pp. 19-26, May-Jun 2024.

[31] J. R. Nelson, O. Wani, H. T. May, and M. Budoff, "Potential benefits of eicosapentaenoic acid on atherosclerotic plaques," (in eng), *Vascul Pharmacol,* vol. 91, pp. 1-9, Apr 2017.

[32] W. J. S. Pedro *et al.*, "Role of Adipokines Chemerin, Visfatin, and Omentin in Obesity and Their Inflammatory and Metabolic Implications," (in eng), *Biomedicines,* vol. 13, no. 10, Sep 23 2025.

[33] N. S. Kalupahana, K. J. Claycombe, and N. Moustaid-Moussa, "(n-3) Fatty Acids Alleviate Adipose Tissue Inflammation and Insulin Resistance: Mechanistic Insights," *Advances in Nutrition,* vol. 2, no. 4, pp. 304-316, 2011/07/01/ 2011.

[34] J. F. Ferguson, K. Roberts-Lee, C. Borcea, H. M. Smith, Y. Midgette, and R. Shah, "Omega-3 polyunsaturated fatty acids attenuate inflammatory activation and alter differentiation in human adipocytes," (in eng), *J Nutr Biochem,* vol. 64, pp. 45-49, Feb 2019.

[35] T. A. Marsen, M. Pollok, K. Oette, and C. A. Baldamus, "Pharmacokinetics of omega-3-fatty acids during ingestion of fish oil preparations," *Prostaglandins, Leukotrienes and Essential Fatty Acids,* vol. 46, no. 3, pp. 191-196, 1992/07/01/ 1992.

[36] B. He *et al.*, "Combination therapeutics in complex diseases," (in eng), *J Cell Mol Med,* vol. 20, no. 12, pp. 2231-2240, Dec 2016.