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Impact Of GLP-1 Receptor Agonists On Oral Health: An Integrative Review

Letícia Pitelli Bertazzi, Kauany Rodrigues Dos Santos,
Gestter Willian Lattarin Tessarin
(University Center North Of São Paulo (UNORTE), São José Do Rio Preto,SP, Brazil).

Abstract:
Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have emerged as key therapeutic agents in the management of type 2 diabetes mellitus and obesity due to their multifactorial metabolic effects. Beyond glycemic control, these agents modulate inflammatory pathways, energy balance, and tissue homeostasis, raising increasing interest in their potential implications for oral health. This narrative review aimed to analyze current evidence regarding the impact of GLP-1–based therapies on the oral environment, periodontal disease, and peri-implant outcomes.The findings indicate that GLP-1RAs may exert both beneficial and adverse effects within the oral cavity. Potential benefits include anti-inflammatory activity, modulation of immune responses, and promotion of osteogenic pathways relevant to periodontal stability and bone regeneration. Conversely, therapy-related adverse effects—such as xerostomia, gastrointestinal disturbances, and altered dietary patterns—may negatively impact salivary function and microbial homeostasis, potentially increasing susceptibility to dysbiosis. Preclinical evidence supports a role for GLP-1 signaling in attenuating periodontal inflammation, enhancing osteoblast differentiation, and improving bone remodeling, particularly in metabolically compromised conditions. However, clinical data remain limited and heterogeneous, preventing definitive conclusions regarding their impact on periodontal outcomes and implant success. In summary, GLP-1RAs represent a clinically relevant systemic factor in dental practice. Their net effect on oral health appears to be context-dependent, influenced by metabolic status, treatment phase, and patient-specific factors. Further well-designed clinical studies are required to clarify their role in periodontal therapy and implant dentistry.

Key Word: *GLP-1 receptor agonists; Periodontitis; Oral microbiome; Bone metabolism; Osseointegration*

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I. Introduction

Over the past decades, glucagon-like peptide-1 (GLP-1) has transitioned from being recognized merely as an incretin hormone to becoming a central regulator of metabolic homeostasis. Initially described for its role in enhancing glucose-dependent insulin secretion, GLP-1 is now understood as a multifunctional peptide that modulates appetite, energy balance, gastrointestinal motility, and systemic metabolic processes. This expanded understanding has positioned GLP-1 as a cornerstone in contemporary therapeutic strategies targeting type 2 diabetes mellitus (T2DM), obesity, and cardiometabolic disorders [1,2].

The concept underlying incretin biology dates back to the early twentieth century, when researchers first hypothesized that the gastrointestinal tract could secrete factors capable of influencing pancreatic function. Following the discovery of secretin and gastrin, experimental observations demonstrated that intestinal extracts could reduce glycemia by stimulating insulin secretion—an effect later termed the "incretin effect." With the subsequent identification of insulin and the development of reliable plasma insulin assays, attention shifted toward isolating the specific gut-derived mediators responsible for this phenomenon. Among these, GLP-1, derived from post-translational processing of the proglucagon gene, emerged as a key physiological regulator [3].

Physiologically, GLP-1 contributes to postprandial glycemic control by enhancing insulin secretion in a glucose-dependent manner, suppressing glucagon release, delaying gastric emptying, and promoting satiety. These mechanisms collectively improve glycemic stability while minimizing the risk of hypoglycemia. However, the clinical application of native GLP-1 was initially limited due to its extremely short half-life—approximately two minutes—resulting from rapid degradation by the enzyme dipeptidyl peptidase-4 (DPP-4). This pharmacokinetic constraint stimulated the development of long-acting GLP-1 receptor agonists (GLP-1RAs) designed to mimic endogenous activity while offering greater therapeutic durability [1,6,7].

The introduction of synthetic GLP-1RAs marked a transformative period in metabolic medicine. Early agents such as exenatide demonstrated proof of concept but were limited by gastrointestinal adverse effects and structural divergence from native GLP-1. Subsequent analogues, including liraglutide, dulaglutide, and semaglutide, achieved enhanced molecular stability, prolonged duration of action, and improved tolerability profiles. More recently, dual and triple incretin receptor agonists—such as tirzepatide and retatrutide—have

expanded the therapeutic paradigm by targeting multiple metabolic pathways simultaneously, producing substantial reductions in body weight and cardiometabolic risk markers [1,6].

Beyond glycemic regulation, accumulating clinical evidence indicates that GLP-1RAs exert cardioprotective, renoprotective, and anti-inflammatory effects. Large-scale outcome trials have demonstrated reductions in major adverse cardiovascular events, progression of chronic kidney disease, and improvements in obesity-related comorbidities. These findings have significantly broadened the clinical indications for GLP-1-based therapies, reinforcing their role as multifunctional agents within chronic disease management. The rapid expansion in scientific publications over the past decade reflects this growing academic and clinical interest [8].

Given the widespread and increasing use of GLP-1 receptor agonists in populations frequently affected by chronic inflammatory and metabolic conditions, understanding their systemic effects—including potential implications for oral tissues—has become increasingly relevant. As obesity, diabetes, and chronic inflammation are closely linked to oral diseases such as periodontitis and dental caries, the systemic metabolic modulation induced by GLP-1-based therapies may carry important consequences for oral health. Exploring these interactions represents an emerging and clinically significant field of investigation.

II. Material And Methods

This study is a narrative bibliographic literature review based on the selection and analysis of scientific articles related to glucagon-like peptide-1 receptor agonists (GLP-1RAs), periodontal disease, oral microbiology, and bone metabolism. The literature search was conducted using multiple electronic databases, including PubMed, Scopus, Google Scholar, and Embase. The search strategy employed specific descriptors such as GLP-1 receptor agonists, periodontitis, oral microbiome, alveolar bone, osseointegration, and inflammation, combined using Boolean operators.

Articles included in the review were full-text publications available in English and published in peer-reviewed journals. Both experimental (in vitro and in vivo), clinical, and review studies were considered. The selection process involved a critical evaluation of each article, focusing on relevance to the proposed topic, methodological quality, and contribution to the understanding of metabolic–periodontal interactions. This structured approach supported the development of an integrated narrative on the systemic and oral implications of GLP-1–based therapies.

III. Result

Physiological Effects of GLP-1 Receptor Agonists with Potential Impact on the Oral Environment

GLP-1 receptor agonists (GLP-1RAs) are widely prescribed for type 2 diabetes and obesity management due to their multifaceted systemic actions, including glucose regulation, appetite suppression, and metabolic modulation. Although their main mechanisms focus on metabolic outcomes, emerging research indicates that these agents may also influence physiological processes relevant to the oral cavity, such as salivary gland function and local inflammatory responses. These effects are supported by both mechanistic studies and clinical observations documenting oral symptoms among GLP-1RA users [9].

One of the most commonly reported oral adverse experiences with GLP-1RA therapy is xerostomia (dry mouth), often attributed to alterations in salivary gland responsiveness. Reviews suggest that prolonged activation of GLP-1 receptors within salivary glands—particularly with agents like semaglutide—may disrupt normal signaling pathways, including cAMP and β-arrestin mediation, leading to reduced exocytosis and salivary secretion. Clinical pharmacovigilance databases have noted disproportionate reports of dry mouth with semaglutide relative to other GLP-1RAs, although causal relationships require further clinical confirmation. [9,10].

Xerostomia is clinically relevant because saliva plays a central protective role in oral homeostasis. It buffers acids, facilitates remineralization of enamel, and has antimicrobial properties that maintain microbial balance. Reduced salivary flow is strongly associated with increased risk for dental caries and opportunistic infections, as low saliva levels impede the neutralization of acids and clearance of pathogenic biofilms [11].

Beyond salivary effects, GLP-1RAs may indirectly influence oral health through gastrointestinal side effects such as nausea, vomiting, and delayed gastric emptying [12]. Persistent vomiting or gastroesophageal reflux can expose dental enamel to acidic gastric contents, promoting erosion and weakening tooth structure. Moreover, nausea and decreased appetite associated with GLP-1RA use can lead to changes in diet and hydration patterns, which might contribute to hyposalivation and altered oral microbial ecology. [13].

Conversely, evidence also suggests potential *beneficial* impacts of GLP-1 pathways on periodontal tissues. Experimental and clinical studies have demonstrated that GLP-1RAs can exert anti-inflammatory and osteoprotective effects in periodontal models, reducing inflammatory cytokine expression and inhibiting alveolar bone resorption. These findings imply that GLP-1 signaling may help modulate host inflammatory responses in periodontal disease, although more research in human oral contexts is needed to validate these outcomes [10, 14].

Taken together, while the primary physiological actions of GLP-1 receptor agonists are systemic and metabolic, there is growing evidence that these agents may also affect the oral environment through both adverse and potentially protective pathways. Recognizing these multifactorial impacts is crucial for clinicians to anticipate, monitor, and manage oral health outcomes in patients undergoing GLP-1RA therapy.

Salivary Changes, Dysbiosis, and Oral Microbial Imbalance in Metabolic Disorders

The human oral cavity hosts one of the most complex microbial ecosystems in the body, comprising more than 700 identified species distributed across multiple genera and major bacterial phyla. While a substantial proportion of these microorganisms has been taxonomically characterized, a significant fraction remains uncultivated and known only through molecular signatures. This vast microbial diversity reflects the oral cavity's unique ecological niches, including the tongue, gingival sulcus, dental surfaces, and saliva, each providing distinct environmental conditions for microbial colonization [15, 16]. As the initial segment of the digestive tract, the oral environment serves as a critical interface between external exposures and systemic physiology, influencing nutrient processing, immune surveillance, and inflammatory regulation [17].

Rather than being defined solely by the presence of specific pathogens, oral health is increasingly understood within an ecological framework. In this model, disease arises from dysbiosis—a disruption in the balance between commensal and pathogenic species—rather than from isolated microbial agents. A stable microbiome maintains dynamic equilibrium with host tissues, contributing to immune modulation and mucosal integrity. When this balance is disturbed by environmental or systemic stressors, including dietary changes, metabolic disorders, or inflammatory conditions, microbial composition and function may shift toward a pro-inflammatory state, facilitating tissue destruction and disease progression [18].

Dietary patterns represent one of the most influential modulators of oral microbial composition [15]. Comparative analyses across distinct populations have demonstrated that macronutrient intake, food processing patterns, and lifestyle factors significantly alter the relative abundance of key microbial taxa. Shifts in diet can modify microbial metabolic capabilities, including urease activity and vitamin synthesis pathways, thereby affecting local pH regulation and biofilm dynamics [19]. Importantly, these dietary influences extend beyond localized effects, as changes in oral microbial communities have been associated with broader metabolic phenotypes, including obesity, type 2 diabetes, and metabolic syndrome. Such findings highlight the bidirectional relationship between metabolic health and oral ecological balance [20, 21].

Saliva plays a central regulatory role in maintaining microbial homeostasis. Beyond its mechanical cleansing function, saliva contains antimicrobial peptides, immunoglobulins, enzymes, cytokines, and buffering agents that collectively shape the oral microenvironment [22]. Variations in salivary flow rate, composition, and circadian rhythm can significantly influence microbial distribution and inflammatory signaling. Emerging research indicates that salivary cytokines, including IL-1β, IL-6, and IL-8, exhibit temporal oscillations that may correlate with fluctuations in microbial abundance. These dynamic interactions suggest that saliva functions not only as a protective fluid but also as a biological mediator linking local and systemic inflammatory states [23]. The intricate interplay between oral microbiota and host immunity becomes particularly evident in inflammatory and neoplastic conditions such as oral squamous cell carcinoma (OSCC). Alterations in microbial composition have been associated with changes in immune-related mediators, including cytokines such as IL-2 and IL-10, which regulate cellular and humoral immune responses [24]. IL-2 primarily promotes T-cell activation and cytotoxic immune activity, whereas IL-10 exerts anti-inflammatory effects and contributes to immune tolerance. Imbalances in these cytokine networks may reflect or contribute to pathological processes within the oral cavity [25]. The simultaneous evaluation of salivary microbiota and systemic immune markers underscores the concept that oral ecological disruption and immune dysregulation are tightly interconnected phenomena.

Despite significant advances in microbial profiling techniques, important gaps remain in understanding how systemic metabolic disturbances influence oral dysbiosis. Evidence increasingly links metabolic disorders—including obesity and type 2 diabetes—to alterations in oral microbial communities and salivary biomarker profiles [23]. These associations suggest that metabolic inflammation and insulin resistance may reshape the oral ecosystem, potentially increasing susceptibility to periodontal disease and other inflammatory conditions [26]. However, the precise mechanisms through which systemic metabolic modulation translates into oral microbial imbalance remain incompletely elucidated. In this context, therapies that substantially alter metabolic and inflammatory pathways—such as GLP-1 receptor agonists—may theoretically influence oral microbial ecology through indirect mechanisms [9]]. By improving glycemic control, modulating systemic inflammation, and inducing weight loss, GLP-1–based treatments could potentially reduce pro-inflammatory signaling that contributes to periodontal tissue breakdown. Conversely, gastrointestinal adverse effects, altered dietary intake, and changes in hydration status associated with these agents may impact salivary flow and oral environmental stability, thereby influencing microbial composition. Although direct evidence linking GLP-1 signaling to oral microbiota modulation is currently limited, the convergence of metabolic regulation, immune modulation, and microbial ecology provides a biologically plausible framework for future investigation [27].

Understanding these complex interactions is essential for advancing a more integrated perspective on oral-systemic health. Further longitudinal and mechanistic studies are needed to clarify whether metabolic therapies such as GLP-1 receptor agonists act as protective modulators of oral inflammation, indirect contributors to dysbiosis, or both, depending on individual host and environmental factors.

GLP-1 Signaling, DPP-4 Activity, and Periodontal Inflammation

Periodontitis is a chronic inflammatory disease that compromises the supporting structures of the teeth, including the gingiva, periodontal ligament, and alveolar bone, and remains one of the leading causes of tooth loss worldwide. Beyond its local destructive effects, periodontitis is increasingly recognized as a condition with systemic implications. Its pathogenesis is driven by microbial dysbiosis that triggers a sustained and dysregulated host immune response, resulting in excessive production of pro-inflammatory mediators, oxidative stress, and progressive connective tissue and bone destruction. Importantly, periodontitis exhibits strong associations with cardiometabolic disorders, particularly obesity and type 2 diabetes mellitus (T2DM), highlighting the interconnected nature of oral and systemic inflammatory networks [28,29].

The bidirectional relationship between periodontitis and T2DM is well established [30]. Chronic hyperglycemia promotes the formation of advanced glycation end-products (AGEs), enhances oxidative stress, and amplifies inflammatory cytokine production within periodontal tissues. In turn, periodontal inflammation contributes to systemic inflammatory burden, potentially worsening insulin resistance and glycemic dysregulation. Obesity further compounds this interaction through lipotoxicity, adipokine imbalance, and chronic low-grade inflammation. These shared pathogenic mechanisms suggest that metabolic and periodontal diseases are not isolated entities, but rather interconnected manifestations of systemic inflammatory dysregulation [31]. Within this framework, the incretin hormone glucagon-like peptide-1 (GLP-1) emerges as a critical regulatory node. Beyond its established role in glucose metabolism, GLP-1 exerts anti-inflammatory, antioxidant, and tissue-regenerative effects. GLP-1 receptor agonists (GLP-1 RAs), widely used in the management of T2DM and obesity, have demonstrated the capacity to reduce systemic inflammatory markers, attenuate oxidative stress, and promote tissue repair [1]. Given that diabetes and obesity share disruptions in GLP-1 signaling pathways, these therapies may offer translational relevance in modulating inflammatory conditions such as periodontitis [14].

A central mechanistic link connecting periodontal inflammation and GLP-1 biology involves dipeptidyl peptidase-4 (DPP-4), the enzyme responsible for rapid GLP-1 degradation [32]. Notably, certain periodontopathogenic bacteria—particularly *Porphyromonas gingivalis*—exhibit DPP-4–like enzymatic activity. These bacterial proteases contribute not only to nutrient acquisition within the asaccharolytic subgingival environment but may also interfere with host incretin signaling by degrading GLP-1 [32, 33]. Elevated DPP-4 activity has been detected in saliva and gingival crevicular fluid of patients with periodontitis, correlating with disease severity. In parallel, host immune and stromal cells upregulate DPP-4 expression during inflammatory responses, reinforcing the enzyme's role at the host–pathogen interface. This convergence suggests a bidirectional axis in which periodontal dysbiosis may impair GLP-1–mediated metabolic regulation, while systemic metabolic dysfunction may exacerbate periodontal inflammation [34, 35]. Preclinical investigations provide further support for the therapeutic relevance of GLP-1 signaling in periodontal disease. In experimental periodontitis models, liraglutide has demonstrated anti-inflammatory and bone-preserving effects, mediated in part through activation of antioxidant pathways such as Nrf2/HO-1 and suppression of NF-κB signaling [36]. GLP-1 receptor activation has also been shown to enhance osteoblast differentiation and mineralization in stem cells derived from dental pulp and periodontal ligament, even under hyperglycemic conditions. Mechanistically, pathways involving Wnt/β-catenin signaling, Runx2 transcriptional regulation, and modulation of inflammatory microRNAs have been implicated [37]. These findings suggest that GLP-1 RAs may exert dual benefits—attenuating inflammatory tissue destruction while simultaneously promoting regenerative processes [38].

Additionally, combined therapeutic approaches have demonstrated synergistic potential. Agents such as exendin-4, when paired with stromal cell–derived factor-1 (SDF-1) [37], enhanced periodontal ligament stem cell proliferation and osteogenic differentiation in vivo. Other adjunctive compounds, including curcumin and omega-3 fatty acids, have been shown to modulate inflammatory signaling and microbial virulence, further supporting the concept of integrated metabolic–periodontal therapy [39]. The structural similarities between bacterial and human DPP-4 enzymes raise intriguing possibilities for repurposing DPP-4 inhibitors as dual-action agents capable of targeting both systemic glycemic regulation and periodontal pathogenicity [40].

Clinical observations further reinforce this interconnected model. Periodontitis is more prevalent in individuals with obesity and T2DM, and severe obesity has been associated with altered incretin profiles, including reduced GLP-1 levels and elevated glucagon and glucose-dependent insulinotropic peptide (GIP). Interestingly, periodontal therapy has been reported to partially restore GLP-1 and GIP levels, even in non-diabetic populations, suggesting that local inflammatory control may positively influence systemic incretin dynamics [20]. However, persistent elevation of systemic inflammatory markers in obese individuals indicates that periodontal intervention alone may be insufficient without concurrent metabolic management [27].

Collectively, current evidence delineates a complex, interdependent network linking periodontal inflammation, microbial proteolytic activity, metabolic dysregulation, and incretin signaling. GLP-1 and its receptor agonists occupy a strategic position within this network, with the potential to modulate oxidative stress, inflammatory cascades, bone metabolism, and immune responses [1]. While mechanistic and experimental data are promising, robust longitudinal clinical trials are still required to determine whether GLP-1–based therapies translate into measurable improvements in periodontal outcomes. Understanding this intricate interplay not only broadens the conceptualization of periodontitis as a systemic inflammatory condition but also opens avenues for developing dual-benefit therapeutic strategies that simultaneously address cardiometabolic dysfunction and periodontal disease.

GLP-1 Receptor Agonists, Bone Metabolism, and Alveolar Tissue Repair

Bone homeostasis is a dynamic process maintained through the continuous balance between bone formation and bone resorption. This physiological equilibrium is primarily regulated by the coordinated activity of osteoblasts, responsible for bone formation, and osteoclasts, which mediate bone resorption. Central to this regulatory system is the receptor activator of nuclear factor-κB ligand (RANKL)/receptor activator of nuclear factor-κB (RANK)/osteoprotegerin (OPG) signaling axis. RANKL promotes the differentiation and activation of osteoclast precursors, whereas OPG acts as a decoy receptor that binds RANKL and prevents osteoclastogenesis. Disruption of this balance can lead to alterations in bone density, impaired regeneration, and increased susceptibility to skeletal complications [41, 42].

Metabolic disorders such as diabetes mellitus and obesity have been associated with disturbances in bone metabolism. Chronic hyperglycemia, systemic inflammation, and oxidative stress contribute to reduced bone mineral density and increased risk of fractures in diabetic individuals [6]. These systemic alterations are also relevant to the oral environment, where bone metabolism plays a crucial role in maintaining alveolar bone integrity and supporting periodontal structures. Consequently, metabolic dysregulation may negatively influence periodontal stability, alveolar bone remodeling, and tissue repair following dental procedures [9]. Within this metabolic–skeletal interface, GLP-1 signaling has emerged as a potential modulator of bone biology. GLP-1 receptor agonists (GLP-1RAs), widely used in the treatment of type 2 diabetes and obesity, have demonstrated pleiotropic effects beyond glycemic control, including anti-inflammatory, metabolic, and tissue-regenerative properties. Increasing experimental evidence suggests that activation of GLP-1 receptors may influence bone turnover through multiple molecular pathways [27].

One of the proposed mechanisms involves the stimulation of osteoblast differentiation and activity. GLP-1 signaling has been associated with the upregulation of key osteogenic markers, including runt-related transcription factor 2 (RUNX2), alkaline phosphatase (ALP), type I collagen (COL1), and osteocalcin (OC), which are essential regulators of bone matrix formation and mineralization. Additionally, GLP-1 receptor activation can stimulate intracellular signaling cascades such as phosphatidylinositol-3 kinase (PI3K), mitogen-activated protein kinase (MAPK), ERK1/2, p38, and c-Jun N-terminal kinase pathways. These signaling networks ultimately promote transcriptional events that support osteoblast maturation and bone formation [37, 43]. Another important mechanism involves modulation of the Wnt/β-catenin signaling pathway, a critical regulator of osteogenesis. GLP-1 signaling has been shown to stimulate elements of this pathway, including LRP5/6 and β-catenin, thereby enhancing osteoblast differentiation and bone formation. Simultaneously, GLP-1 activity appears to reduce the expression of sclerostin, a protein produced by osteocytes that inhibits Wnt signaling and suppresses bone formation [37, 44]. Downregulation of sclerostin may therefore facilitate osteogenic activity and contribute to improved bone remodeling.

Beyond promoting bone formation, GLP-1 receptor agonists may also influence bone resorption. Experimental studies have reported reductions in biochemical markers associated with osteoclast activity, such as C-terminal cross-linked telopeptide of type I collagen (CTX-1) and urinary deoxypyridinoline levels. In addition, GLP-1 signaling has been associated with calcitonin-mediated pathways that further suppress osteoclast function [45, 46]. These combined mechanisms suggest that GLP-1RAs may contribute to a favorable balance between bone formation and resorption. Another relevant aspect of GLP-1 activity involves the regulation of mesenchymal stem cell differentiation. Experimental evidence indicates that GLP-1 receptor activation can promote the differentiation of mesenchymal stem cells into osteoblasts while simultaneously inhibiting their differentiation into adipocytes. This shift in cellular fate supports osteogenic activity and may enhance bone regenerative potential, particularly under conditions of metabolic stress [47, 48].

Although most mechanistic evidence has been derived from experimental and animal models, these findings have important implications for oral and maxillofacial tissues. Alveolar bone undergoes constant remodeling in response to mechanical forces, inflammatory stimuli, and systemic metabolic conditions [49]. In patients with metabolic disorders, impaired bone turnover and chronic inflammation may compromise alveolar bone integrity and delay tissue repair following periodontal therapy, tooth extraction, or implant placement [50]. By improving glycemic control, reducing systemic inflammation, and potentially modulating osteogenic

pathways, GLP-1 receptor agonists may contribute indirectly to more favorable conditions for alveolar bone maintenance and tissue regeneration. However, clinical evidence evaluating the direct effects of GLP-1RAs on alveolar bone remodeling and oral surgical outcomes remains limited. Furthermore, the significant weight loss associated with these therapies may influence bone density in some patients, highlighting the complexity of their overall skeletal impact [27, 44].

Taken together, current evidence suggests that GLP-1 signaling occupies a strategic position at the intersection of metabolic regulation, inflammation, and bone remodeling. While preclinical studies indicate promising osteogenic and anti-resorptive effects, further clinical research is required to determine whether these mechanisms translate into measurable improvements in alveolar bone healing and regenerative outcomes within the context of dental practice.

IV. Discussion

Clinical Implications of GLP-1–Based Therapies in Oral Surgery and Implant Dentistry

The widespread adoption of GLP-1–based therapies for T2DM and obesity has direct relevance for contemporary dental practice, particularly in oral surgery and implant dentistry [8], where outcomes depend heavily on metabolic control, inflammatory burden, and bone remodeling capacity [30]. Periodontitis, obesity, and insulin resistance form a bidirectional triad linked by chronic low-grade systemic inflammation, characterized by sustained elevations of mediators such as IL-1β, IL-6, and TNF-α, accompanied by higher levels of systemic markers including CRP and PGE2 [20,51]. These inflammatory pathways help explain why patients with obesity and diabetes frequently exhibit more severe periodontal breakdown, altered immune responses, and impaired healing, which are clinically consequential when planning extractions, regenerative procedures, and implant placement [52, 50].

Within this pathophysiological background, GLP-1RAs have been proposed as potential "dual-benefit" agents: beyond improving glycemic control and promoting weight loss, they may support periodontal and peri-implant tissue stability through anti-inflammatory and osteoprotective mechanisms [10, 27]. Nevertheless, current evidence remains largely preclinical or observational, and any purported oral benefits must be interpreted cautiously until confirmed by robust human trials with prespecified periodontal and peri-implant endpoints.

From a clinical perspective, dentists should recognize that GLP-1RA users may present with therapy-related conditions capable of modifying oral-surgery risk and postoperative recovery [2]. Gastrointestinal adverse effects—particularly nausea, early satiety, vomiting, and delayed gastric emptying—may indirectly influence the oral environment by altering hydration and dietary patterns and, in patients with reflux or vomiting, increasing exposure of enamel and oral tissues to acidic contentes [53, 54]. In parallel, xerostomia has been described in association with GLP-1RA therapy and is clinically important because salivary hypofunction compromises antimicrobial defense, buffering capacity, and biofilm control, increasing susceptibility to caries activity, mucosal discomfort, and opportunistic infection [22]. Therefore, perioperative dental management in these patients benefits from a comprehensive medication history (agent, dose, timing, and recent dose changes) and proactive preventive counseling—hydration strategies, salivary stimulation measures, and intensified caries prevention—particularly during dose-escalation phases when adverse effects may be more pronounced [53, 55]. These considerations do not replace conventional periodontal or surgical protocols; rather, they represent supportive measures aimed at stabilizing the oral environment and reducing avoidable complications.

In periodontal and peri-implant contexts, GLP-1RAs are biologically plausible modulators of tissue healing because they intersect with immune–bone pathways relevant to regeneration [29, 38]. Preclinical evidence suggests that GLP-1RAs may attenuate inflammatory signaling in gingival tissues and shift immune profiles toward a more reparative phenotype, including reductions in proinflammatory macrophage polarization, thereby creating conditions that could favor periodontal wound healing and bone preservation [36, 56]. Experimental data also support osteogenic effects relevant to implant dentistry, including enhanced osteogenic differentiation of alveolar bone marrow–derived mesenchymal stem cells and improved bone-implant integration in diabetic animal models [36, 48]. Such findings are consistent with broader mechanistic frameworks in which GLP-1 signaling interacts with pathways linked to bone formation and remodeling and, therefore, may be particularly relevant in metabolically compromised patients in whom osseointegration is at higher risk [44, 50]. Translational strategies have also explored localized delivery systems designed to maintain adequate peri-implant concentrations of GLP-1 analogs. Sustained-release carriers based on PLGA—sometimes combined with chitosan to optimize release characteristics—have been investigated to enhance peri-implant osteogenesis in diabetic models without necessarily altering systemic glycemia, supporting the concept that local adjunctive approaches might one day complement implant therapy in selected high-risk patients [57,58]. Human evidence, however, is still scarce; limited clinical observations have suggested that peri-implant marginal bone changes may differ between hypoglycemic drug classes, with some data indicating comparatively lower marginal bone loss among patients receiving GLP-1–based therapy than among those using other agents across follow-up intervals [59, 60]. Yet the heterogeneity of medications, co-therapies, baseline glycemic control, periodontal status, and outcome definitions precludes definitive conclusions.

Microbial and ecological considerations further complicate the clinical picture. While direct studies assessing the oral microbiome before and after GLP-1RA therapy remain limited, indirect effects are plausible. By improving glucose homeostasis and reducing systemic and local inflammatory pressure, GLP-1RAs could theoretically alter the nutrient and immune landscape that shapes dysbiosis in periodontitis and peri-implant disease [27, 61]. In addition, mechanistic links between periodontal pathogens and incretin biology—such as DPP-4–like activity described in key periopathogens—raise the possibility that increased GLP-1 availability may partially counteract microbial strategies that intersect with host metabolic signaling [6, 32]. Conversely, GI adverse events, reduced intake, and dehydration risk may promote hyposalivation and destabilize oral ecology, potentially increasing susceptibility to dysbiosis if preventive measures are not implemented. Thus, the net clinical impact of GLP-1RAs on peri-implant disease risk is likely to be context-dependent, varying with host factors, therapy phase, and oral-hygiene behaviors [22, 53].

Taken together, GLP-1–based therapies are increasingly relevant exposures in oral surgery and implant dentistry, primarily because they modify the systemic inflammatory and metabolic conditions that strongly influence periodontal stability, bone healing, and osseointegration [8]. At present, the most defensible clinical stance is not to treat GLP-1RAs as "dental therapeutics," but to incorporate their systemic and adverse-effect profiles into individualized planning, prevention, and maintenance strategies—especially in patients with obesity, insulin resistance, and active periodontal disease [62, 63]. Future research should prioritize well-designed randomized human trials that prespecify periodontal and peri-implant endpoints (e.g., bleeding on probing, probing depth, clinical attachment level, and radiographic bone changes), integrate biomarkers (such as GCF MMP panels and RANKL/OPG), and adjust analyses for HbA1c and weight change to distinguish systemic mediation from direct local tissue effects. Parallel investigation into tissue-level GLP-1 receptor expression in gingiva and periodontal ligament, as well as translational studies of local delivery platforms, will be essential to determine whether GLP-1–based strategies can reliably enhance surgical and implant outcomes beyond what is achieved through optimized metabolic control and standard periodontal therapy.

Ultimately, the growing use of GLP-1–based therapies in patients with metabolic disorders introduces a new systemic variable that dental professionals must consider when planning oral surgical and implant procedures. Although current evidence suggests that GLP-1 receptor agonists may positively influence inflammatory regulation, bone metabolism, and tissue repair, most findings remain derived from preclinical models or limited observational data. Consequently, their role in improving periodontal healing, peri-implant stability, and long-term implant success cannot yet be definitively established. As the prevalence of GLP-1RA use continues to increase worldwide, understanding how these therapies interact with oral tissues and surgical outcomes will become increasingly important. Integrating metabolic management with dental care may ultimately represent a key strategy in optimizing periodontal and implant therapy outcomes, highlighting the need for interdisciplinary collaboration and well-designed clinical research in this emerging field.

V. Conclusion

GLP-1 receptor agonists represent an increasingly important systemic variable in patients undergoing dental, periodontal, and implant-related treatments. Current evidence suggests that these agents may exert dual and context-dependent effects on oral health. On one hand, their ability to improve glycemic control, reduce systemic inflammation, and modulate bone metabolism provides a biologically plausible framework for beneficial impacts on periodontal stability, tissue repair, and osseointegration. On the other hand, therapy-related adverse effects—particularly xerostomia, gastrointestinal disturbances, and altered nutritional and hydration patterns—may compromise salivary function and oral ecological balance, potentially increasing the risk of dysbiosis and oral disease.

At present, the available evidence remains largely preclinical or observational, and direct clinical benefits of GLP-1RAs on periodontal and peri-implant outcomes have not been conclusively established. Therefore, these agents should not be considered dental therapeutics per se, but rather systemic modifiers that must be integrated into individualized clinical planning. From a practical standpoint, dental professionals should incorporate detailed medication histories and adopt preventive strategies aimed at mitigating therapy-related oral risks, particularly in patients with obesity, insulin resistance, and active periodontal disease.

Future research should prioritize controlled clinical trials with standardized periodontal and peri-implant endpoints, as well as mechanistic studies exploring GLP-1 receptor expression and local tissue effects. Advancing this knowledge will be essential to determine whether GLP-1–based therapies can be leveraged not only for metabolic control but also as adjunctive modulators of oral health and regenerative outcomes.

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