International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	SYSTEMIC ISOTRETINOIN AND ORAL HEALTH: SALIVARY, MUCOSAL, AND PERIODONTAL CHANGES AND IMPLICATIONS FOR DENTAL PRACTICE
DOI	https://doi.org/10.31435/ijitss.3(51).2026.6637
RECEIVED	22 June 2026
ACCEPTED	11 September 2026
PUBLISHED	21 September 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

SYSTEMIC ISOTRETINOIN AND ORAL HEALTH: SALIVARY, MUCOSAL, AND PERIODONTAL CHANGES AND IMPLICATIONS FOR DENTAL PRACTICE

Gracjan Koźma (GK) *(Corresponding Author, Email: gracjan.kozma@gmail.com)*
Military Institute of Aviation Medicine, Krasińskiego 54/56, 01-755 Warsaw, Poland
ORCID ID: 0009-0002-8812-6427

Wojciech Sielatycki (WS)
Medical University of Silesia, 40-055 Katowice, Poland
ORCID ID: 0009-0003-8427-1632

Weronika Komar (WK)
Medical University of Silesia, 40-055 Katowice, Poland
ORCID ID: 0009-0007-1034-5730

Marta Sielatycka (MS)
Medical University of Lodz; Al. Kościuszki 4, 90-419 Łódź, Poland
ORCID ID: 0009-0000-3525-9459

Marta Borkowska (MB)
Military Institute of Medicine – National Research Institute, Szaserów 128, 04-141 Warsaw, Poland
ORCID ID: 0009-0002-8105-3384

ABSTRACT
Systemic isotretinoin is widely used for the treatment of severe acne and is frequently associated with mucocutaneous adverse effects. Oral manifestations may include xerostomia, reduced salivary flow, cheilitis, mucosal discomfort, and changes in periodontal parameters, but their clinical significance for dental practice remains incompletely defined. This narrative review summarizes current evidence on salivary, mucosal, and periodontal changes associated with systemic isotretinoin therapy and discusses their implications for dental care. A structured literature search was conducted primarily in PubMed/MEDLINE and supplemented by Google Scholar, Scopus, and Web of Science. Original clinical studies, systematic reviews, and selected mechanistic studies relevant to isotretinoin-associated oral changes were considered. Reduced salivary flow and xerostomia are the most consistently reported oral effects and appear to be largely transient. Cheilitis and oral dryness are common, whereas burning sensations and mucosal ulcerations are reported less frequently. Reduced salivary secretion and, in some studies, decreased buffering capacity may create conditions potentially favorable to dental caries, although a direct causal relationship has not been established. Periodontal findings are heterogeneous. Some longitudinal studies report transient increases in gingival inflammation, bleeding on probing, plaque accumulation, or probing depth, whereas others show little clinical deterioration. Biomarker and microbiological studies suggest additional effects on inflammatory, extracellular-matrix, and antimicrobial pathways, but their clinical significance remains uncertain. Dental management should therefore focus on recognition of oral dryness and mucosal symptoms, individualized caries prevention, plaque control, and periodontal monitoring. Current evidence does not support isotretinoin as a direct cause of periodontitis or routine postponement of necessary dental procedures solely because of isotretinoin therapy.

KEYWORDS
Isotretinoin, Oral Health, Xerostomia, Salivary Flow, Oral Mucosa, Periodontal Health, Dental Caries

CITATION
Koźma, G., Sielatycki, W., Komar, W., Sielatycka, M., & Borkowska, M. (2026). Systemic isotretinoin and oral health: Salivary, mucosal, and periodontal changes and implications for dental practice. *International Journal of Innovative Technologies in Social Science*, 3(51). https://doi.org/10.31435/ijitss.3(51).2026.6637

1. Introduction

Acne vulgaris is a common chronic inflammatory disorder of the pilosebaceous unit, particularly affecting adolescents and young adults. Systemic isotretinoin (13-cis-retinoic acid) remains the most effective pharmacological treatment for severe acne and is recommended particularly in patients with severe disease, scarring, psychosocial burden, or failure of standard topical and systemic therapies (Bettoli et al., 2019; Reynolds et al., 2024). Despite its high efficacy, isotretinoin is associated with a broad spectrum of adverse effects, of which mucocutaneous manifestations are among the most frequent (Bettoli et al., 2019; Kapała et al., 2022).

Dryness of the skin and mucous membranes is a characteristic effect of systemic isotretinoin therapy. Cheilitis is particularly common, while dry or sore mouth and subjective xerostomia are also frequently reported (Bettoli et al., 2019; Kapała et al., 2022). These effects are relevant to dental practice because adequate salivary secretion supports lubrication, buffering, clearance, and microbial homeostasis, while an intact oral mucosal barrier protects tissues against mechanical and chemical irritation. A reduction in salivary flow may therefore have consequences beyond patient discomfort and may potentially influence caries susceptibility, plaque control, and gingival inflammation.

Clinical studies evaluating oral effects of isotretinoin have focused mainly on salivary flow, xerostomia, caries-related parameters, mucosal symptoms, and periodontal status. Although reduced salivary secretion has been reported relatively consistently, periodontal findings are less uniform. Some studies have demonstrated increased gingival bleeding, plaque accumulation, or probing depth during treatment, whereas others have found little clinical deterioration or have reported changes in inflammatory and matrix-remodelling biomarkers that suggest more complex effects on periodontal tissues. Consequently, the oral effects of isotretinoin cannot be explained solely by mucosal dryness or reduced salivary secretion.

These observations have practical implications for dentists, who may encounter patients receiving isotretinoin for several months and presenting with new oral dryness, cheilitis, mucosal discomfort, or changes

in gingival condition. However, the available evidence is derived mainly from relatively small clinical studies, and clear dental management recommendations remain limited. Therefore, this narrative review summarizes current evidence on salivary, mucosal, and periodontal changes associated with systemic isotretinoin therapy and discusses their potential implications for preventive and clinical dental care.

2. Methods

This narrative review was based on a structured literature search conducted primarily in PubMed/MEDLINE and supplemented by Google Scholar. Additional cross-database searches and verification were performed using records indexed in Scopus and Web of Science. Reference lists of key original studies and review articles were also screened, and backward and forward citation searching was used to identify additional relevant publications. The literature search included studies published up to August 31, 2026.

Search terms were combined using Boolean operators and included: “isotretinoin”, “13-cis-retinoic acid”, “retinoic acid”, “oral health”, “saliva”, “salivary flow”, “salivary gland”, “xerostomia”, “hyposalivation”, “oral mucosa”, “cheilitis”, “oral ulceration”, “dental caries”, “DMFT”, “ICDAS”, “periodontal”, “gingivitis”, “periodontitis”, “MMP”, “TIMP”, “dental surgery”, “tooth extraction”, and “wound healing”. Different combinations of these terms were used according to the specific topic being investigated.

Priority was given to human studies evaluating systemic isotretinoin therapy in relation to salivary function, oral symptoms and mucosal changes, caries-related parameters, periodontal outcomes, or oral surgical considerations. Systematic reviews and meta-analyses were included where relevant to summarize the available evidence. Selected experimental studies involving retinoic acid and oral tissues were used only to provide mechanistic context, while broader literature on xerostomia, salivary gland hypofunction, and oral preventive care was considered where necessary to support clinical interpretation.

3. Mechanisms Relevant to Oral Tissues

Isotretinoin is a retinoid with marked effects on cellular differentiation and sebaceous gland activity. Its therapeutic effect in acne is strongly associated with suppression of sebaceous gland function and induction of apoptosis in sebocytes (Bettoli et al., 2019; Nelson et al., 2008). The mucocutaneous dryness observed during treatment is a predictable pharmacological effect and frequently involves the lips and other mucosal surfaces (Bettoli et al., 2019; Kapała et al., 2022). However, the mechanisms underlying individual oral manifestations, particularly reduced salivary secretion, have not been fully established.

Experimental studies indicate that retinoic acid can directly influence oral epithelial differentiation. In cultured human oral keratinocytes, increasing retinoic acid concentrations altered normal epithelial stratification and the expression of keratins and other markers of terminal differentiation (Kautsky et al., 1995). Experimental work on stratified gingival keratinocytes has also demonstrated changes in cell-to-cell and cell-to-matrix adhesion, including disruption of desmosomal and hemidesmosomal structures and reduced expression of several associated proteins (Hatakeyama et al., 2004). These findings provide a possible biological basis for increased epithelial dryness and susceptibility to irritation during retinoid exposure. However, these studies used experimental retinoic acid models and should not be interpreted as direct clinical evidence of isotretinoin-induced mucosal injury.

The oral effects of isotretinoin are therefore likely to reflect several interacting processes rather than a single mechanism. Altered epithelial differentiation may contribute to mucosal and lip changes, while reduced salivary secretion can modify lubrication, buffering, clearance, and other protective functions of saliva. In addition, clinical studies suggest that isotretinoin exposure may influence inflammatory and extracellular-matrix pathways relevant to periodontal tissues. These salivary, mucosal, and periodontal effects are discussed separately in the following sections.

4. Salivary Changes

4.1. Salivary Flow and Xerostomia

Xerostomia and reduced salivary secretion are among the most consistently reported oral effects of systemic isotretinoin therapy. These two findings should be distinguished: xerostomia refers to the subjective sensation of oral dryness, whereas salivary gland hypofunction describes an objectively measurable reduction in salivary secretion (Wolff et al., 2017). Available clinical studies indicate that isotretinoin may be associated with both conditions.

One of the earliest clinical studies evaluating salivary function during isotretinoin therapy used stimulated whole-saliva measurements during treatment and after drug discontinuation (Oikarinen et al., 1995). Stimulated salivary flow was significantly lower during treatment than approximately 3.7 months after treatment discontinuation (1.6 ± 0.7 vs. 2.3 ± 1.2 mL/min; $p = 0.0277$). Salivary pH did not differ significantly between the two measurements. Although this study included only a small number of patients and lacked a pretreatment baseline assessment, it provided early evidence that the effect of isotretinoin on salivary secretion may be reversible.

A subsequent prospective case-control study provided further evidence of impaired salivary function (Erdemir et al., 2017). After six months of isotretinoin treatment at 0.5 mg/kg/day, stimulated salivary flow decreased significantly from 1.30 ± 0.67 to 1.13 ± 0.64 mL/min. No comparable significant change was observed in untreated controls. Another prospective study also observed reduced stimulated salivary flow during eight months of treatment (Alkanhal et al., 2021), although the small sample size and absence of a separate control group limit the strength of these findings. Lower unstimulated salivary flow has also been reported in isotretinoin users in case-control analyses (AlJasser et al., 2022).

Objective functional imaging provides additional evidence of impaired salivary gland function during isotretinoin therapy. In a prospective repeated-measures study of 28 patients receiving isotretinoin at 0.5 mg/kg/day, Tc-99m pertechnetate salivary gland scintigraphy was performed before treatment and after three and six months of therapy. Uptake ratio, maximum accumulation, and ejection fraction decreased significantly in both parotid and submandibular glands at months 3 and 6 compared with pretreatment values, indicating progressive impairment of major salivary gland function during therapy (Örsal et al., 2015). These findings complement studies based on whole salivary flow measurements by providing objective functional assessment at the glandular level.

More recent longitudinal data provide additional information about the time course of these changes. A recent longitudinal study evaluated 24 periodontally healthy patients before treatment, at week 6, at month 5, and after treatment completion (Günay et al., 2026). Unstimulated salivary flow declined early during therapy and subsequently increased after treatment. Subjective oral dryness showed an even more pronounced temporal pattern, increasing from 8.3% at baseline to 66.7% at week 6 and resolving after treatment completion. These findings suggest that salivary symptoms may be particularly noticeable during the early phase of therapy and are largely transient in otherwise healthy young patients.

The overall direction of this evidence is supported by a recent systematic review and meta-analysis (Holanda et al., 2026). Of 577 initially identified records, only two studies fulfilled the criteria for quantitative synthesis, but both demonstrated reduced salivary flow during isotretinoin treatment, resulting in a statistically significant pooled effect. Therefore, reduction in salivary secretion appears to be a reproducible effect of systemic isotretinoin, although the current evidence base remains limited by small samples and methodological heterogeneity.

4.2. Salivary Buffering Capacity and Composition

Evidence regarding changes in salivary properties other than flow rate is more limited. One prospective case-control study observed a significant reduction in salivary buffering capacity after six months of isotretinoin treatment, whereas no significant change was found in the control group (Erdemir et al., 2017). In contrast, another prospective study did not demonstrate a significant change in buffering capacity after treatment (Alkanhal et al., 2021). An earlier follow-up study similarly found no significant difference in salivary pH between measurements performed during and after isotretinoin therapy (Oikarinen et al., 1995).

Isotretinoin exposure has also been associated with changes in salivary proteins involved in extracellular matrix regulation. Increased salivary MMP-9 activity was reported during treatment in an early study (Oikarinen et al., 1995), whereas later case-control studies demonstrated differences in MMP and TIMP concentrations according to isotretinoin exposure and periodontal status (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser et al., 2022). These findings suggest that isotretinoin may affect the biochemical composition of saliva in addition to reducing its volume. However, their clinical significance remains uncertain and is discussed further in the periodontal section.

4.3. Potential Implications for Dental Caries

Saliva contributes to oral health through mechanical clearance, buffering of acids, maintenance of tooth mineral homeostasis, and antimicrobial activity (Lynge Pedersen & Belstrøm, 2019). Consequently, a reduction in salivary flow, particularly when accompanied by impaired buffering capacity, provides a biologically plausible mechanism by which isotretinoin therapy could increase susceptibility to dental caries.

Some clinical observations support this possibility. A prospective case-control study found a significant increase in ICDAS scores during six months of isotretinoin therapy together with reductions in salivary flow and buffering capacity (Erdemir et al., 2017). Importantly, however, changes in salivary parameters were not significantly correlated with changes in ICDAS scores. A small prospective before-after study also reported an increase in DMFT scores and *Streptococcus mutans* levels during therapy, accompanied by decreased salivary flow (Alkanhal et al., 2021). Interpretation of these results requires caution because of the small sample size, the absence of an independent control group in the latter study, and the limitations of DMFT as a measure of short-term caries activity.

Current evidence therefore does not establish systemic isotretinoin as an independent cause of dental caries. Rather, isotretinoin-induced reduction in salivary secretion and, in some patients, buffering capacity may create oral conditions that favor caries development, particularly when additional risk factors such as frequent sugar intake, inadequate oral hygiene, or pre-existing high caries activity are present. This distinction is important when translating the available evidence into preventive recommendations for dental practice.

5. Oral Mucosal Changes

Mucocutaneous adverse effects are among the most common complications of systemic isotretinoin therapy, and the lips and oral mucosa are frequently affected. Cheilitis represents the most characteristic manifestation. In a single-arm meta-analysis of clinical studies, dry lips were reported in 58.2% of patients and cheilitis in 41.5%, while dry or sore mouth occurred in approximately 37.9% (Kapała et al., 2022). These findings indicate that oral and perioral dryness is not an uncommon secondary effect of treatment.

Cheilitis usually presents with dryness, scaling, erythema, fissuring, and occasionally inflammation of the labial commissures. An isotretinoin-specific cheilitis grading scale based on erythema, scale or crust formation, fissuring, and commissural involvement has also been proposed (Ornelas et al., 2016). Although cheilitis is generally mild to moderate, it may cause considerable discomfort and can affect eating, speaking, and daily oral hygiene.

Changes may also involve the intraoral mucosa. A recent prospective study of 60 patients receiving isotretinoin reported xerostomia in 50%, mucosal ulcerations in 16.7%, and gingival changes in 13.3%, in addition to cheilitis in 75% (Alqahtani et al., 2026). Most manifestations were described as mild to moderate and occurred mainly during the early phase of therapy. However, the absence of an untreated control group and limited methodological detail mean that these percentages should not be interpreted as precise population incidence rates.

Transient oral burning has also been reported. In a longitudinal study, oral burning was present in 16.7% of patients at week 6 and subsequently resolved (Günay et al., 2026). This temporal pattern was similar to that observed for subjective oral dryness, suggesting that at least some mucosal symptoms may be most pronounced early during treatment and improve with continued therapy or after its completion.

The biological mechanisms responsible for these manifestations are not fully defined. Experimental studies have shown that retinoic acid can alter oral epithelial differentiation and disrupt desmosomal and hemidesmosomal structures in oral keratinocytes (Hatakeyama et al., 2004; Kautsky et al., 1995). These findings provide a possible explanation for increased epithelial fragility and susceptibility to irritation during retinoid exposure. However, they are based on experimental models and should not be considered direct evidence of clinical mucosal injury caused by systemic isotretinoin.

Overall, the available evidence indicates that cheilitis and oral dryness are the most frequent mucosal manifestations of isotretinoin therapy, while burning sensations and ulcerative lesions appear less common. Most reported changes are mild and transient, but their presence may contribute to discomfort and should be recognized during dental examination.

6. Periodontal Effects

6.1. Clinical Periodontal Changes

The effect of systemic isotretinoin on periodontal tissues remains less clear than its effect on salivary function. Available clinical studies have reported inconsistent findings, ranging from no significant deterioration in periodontal parameters to transient increases in gingival inflammation, bleeding on probing (BOP), plaque accumulation, and probing depth.

A prospective controlled study evaluated periodontal parameters before and after six months of isotretinoin therapy and compared the findings with a healthy control group (Ustaoğlu et al., 2020). No significant deterioration was observed in probing depth (PD), clinical attachment level (CAL), plaque index (PI), gingival index, or BOP during treatment. These findings suggested that isotretinoin did not produce clinically relevant periodontal deterioration in the studied young population over a six-month period. However, the sample was small and consisted mainly of individuals without advanced periodontal disease.

More recent longitudinal studies have identified mild inflammatory changes. One study followed 24 periodontally healthy patients before, during, and after isotretinoin therapy (Günay et al., 2026). BOP increased significantly during treatment and gingivitis was diagnosed in 33.3% of participants at month 5. Importantly, no significant changes were observed in CAL or PI, and no permanent periodontal lesions were identified after treatment completion. These results suggest that isotretinoin therapy may be associated with transient gingival inflammation without evidence of periodontal attachment loss.

A larger prospective study evaluated 80 patients before and after six months of isotretinoin treatment (Erduran et al., 2026). The proportion of patients with positive BOP increased from 18.8% to 48.8%, while mean PI increased from 1.06 to 1.26 and mean PD from 1.25 to 1.73 mm. Although these changes were statistically significant, their clinical magnitude was relatively small, and the study did not evaluate CAL or radiographic bone loss. In addition, the simultaneous increase in plaque accumulation may have contributed to the observed increase in gingival bleeding and PD. Therefore, these findings are better interpreted as evidence of mild or subclinical deterioration in periodontal conditions rather than development of periodontitis.

Overall, current longitudinal evidence suggests that systemic isotretinoin may promote transient gingival inflammatory changes in some patients. However, there is currently no convincing evidence that short-term isotretinoin therapy causes periodontal attachment loss or accelerates periodontitis progression.

6.2. Inflammatory, Oxidative, and Matrix-Remodelling Markers

Clinical periodontal findings should also be considered together with studies evaluating salivary biomarkers and components of the local immune response. Interestingly, these studies do not consistently indicate a pro-inflammatory effect of isotretinoin.

A prospective controlled study found a significant reduction in salivary total antioxidant capacity after six months of isotretinoin treatment despite the absence of significant deterioration in clinical periodontal parameters (Ustaoğlu et al., 2020). Total oxidant status and oxidative stress index did not change significantly. These findings indicate that isotretinoin may modify the biochemical environment of the oral cavity even when measurable periodontal changes are limited.

A series of case-control analyses by AlJasser et al. provides a different perspective. In individuals with gingivitis or stage I periodontitis, isotretinoin use was associated with lower BOP and markedly lower salivary concentrations of matrix metalloproteinases MMP-8 and MMP-9 compared with corresponding non-users (AlJasser, Alaqeely, Al-Hoqail, et al., 2021). Among participants with periodontitis, MMP-8 and MMP-9 concentrations were substantially lower in the isotretinoin group. Because these enzymes participate in extracellular matrix degradation during periodontal inflammation, the findings raise the possibility that retinoid exposure may modify inflammatory and tissue-remodelling pathways. However, the cross-sectional design does not establish that isotretinoin itself caused the observed differences.

A companion analysis showed significantly lower unstimulated salivary flow among isotretinoin users but higher salivary concentrations of tissue inhibitors of metalloproteinases, particularly TIMP-1 and TIMP-2, in several periodontal groups (AlJasser et al., 2022). This combination is noteworthy because reduced salivary secretion could create less favorable local oral conditions, while changes in the MMP/TIMP balance might simultaneously modify inflammatory tissue breakdown.

Systemic retinoid exposure may also influence components of innate antimicrobial defense. A case-control study compared 34 systemic retinoic acid users with 35 healthy controls and evaluated human β-

defensins in saliva, serum, and gingival tissue (Atalay et al., 2023). Salivary hBD-2 levels were significantly lower in retinoid users, including after adjustment for BOP, whereas salivary hBD-1 and hBD-3 and serum and gingival tissue levels of all three defensins did not differ significantly between groups. As hBD-2 contributes to antimicrobial defense at oral epithelial surfaces, this observation provides additional evidence that systemic retinoid exposure may alter selected components of salivary innate immunity. However, the clinical significance of this isolated biomarker difference remains uncertain.

Differences in the subgingival microbial profile have also been reported. In another case-control analysis, isotretinoin users showed lower levels of *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*, but higher levels of *Fusobacterium nucleatum* than non-users (AlJasser, AlAqeely, AlZahrani, et al., 2021). These findings should be interpreted cautiously, as bacterial abundance does not directly reflect periodontal disease progression and the cross-sectional design prevents causal conclusions. Nevertheless, together with the biomarker studies, they suggest that isotretinoin-associated changes in the oral environment are more complex than a uniform increase in periodontal inflammation or dysbiosis.

6.3. Interpretation of the Current Evidence

Taken together, the available evidence does not support a direct destructive effect of systemic isotretinoin on periodontal tissues. Recent longitudinal studies suggest that treatment may be accompanied by mild or transient increases in gingival inflammation and bleeding on probing, but clinically relevant attachment loss has not been demonstrated (Erduran et al., 2026; Günay et al., 2026; Ustaoğlu et al., 2020). Reduced salivary secretion and, in some patients, increased plaque accumulation may contribute to these inflammatory changes.

At the same time, cross-sectional studies have reported differences in MMP-8, MMP-9, TIMP-1, TIMP-2, salivary hBD-2, and the subgingival microbial profile among retinoid users (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser, AlAqeely, AlZahrani, et al., 2021; AlJasser et al., 2022; Atalay et al., 2023). The clinical significance of these findings remains uncertain, and they should not be interpreted as evidence of either periodontal protection or periodontal damage. Overall, current data support periodontal monitoring based on clinical findings rather than isotretinoin exposure alone.

7. Implications for Dental Practice

7.1. Oral Assessment and Preventive Care

Patients receiving systemic isotretinoin do not require a separate dental treatment protocol; however, awareness of the associated oral changes may help identify patients who would benefit from additional preventive measures. During dental history taking, current or recent isotretinoin therapy should be recorded, particularly in patients presenting with new-onset oral dryness, cheilitis, mucosal discomfort, or gingival inflammation.

Clinical assessment should focus on symptoms of xerostomia, mucosal condition, oral hygiene, caries activity, and gingival inflammation. Objective assessment of salivary flow may be considered in patients with persistent or clinically relevant dry-mouth symptoms, as subjective xerostomia does not necessarily correspond directly to the degree of salivary gland hypofunction (Villa et al., 2015; Wolff et al., 2017). Preventive measures should be individualized according to the patient's baseline caries and periodontal risk rather than routinely intensified in every isotretinoin user.

7.2. Management of Xerostomia and Mucosal Symptoms

Management of isotretinoin-associated oral dryness is primarily supportive. Adequate hydration and frequent small amounts of water may provide symptomatic relief. In patients with residual salivary gland function, sugar-free chewing gum or lozenges may stimulate salivary secretion, while saliva substitutes, gels, or oral lubricants can be considered when symptoms persist (Villa et al., 2015; Wolff et al., 2017). Alcohol-containing mouthrinses and other products that increase oral irritation or dryness may be avoided in symptomatic patients.

Because reduced salivary flow may compromise natural protection against demineralization and caries, maintenance of effective oral hygiene and regular use of fluoride toothpaste are particularly important. Additional professional fluoride measures may be considered in patients who develop substantial

hyposalivation or have other caries risk factors (Villa et al., 2015). Frequent consumption of sugar-containing foods and drinks should also be limited.

Cheilitis can usually be managed with regular application of bland lip emollients or barrier preparations. A small study comparing topical tacrolimus with white soft petrolatum in retinoid-induced cheilitis demonstrated improvement with both approaches, although tacrolimus produced faster resolution (Kothari et al., 2024). Because the study included only 26 patients and more intensive pharmacological treatment is rarely required, simple barrier protection remains an appropriate initial approach. Persistent, severe, or atypical mucosal lesions should be evaluated independently rather than automatically attributed to isotretinoin therapy.

7.3. Caries and Periodontal Monitoring

The current evidence does not justify classifying all isotretinoin users as high-caries-risk patients. Nevertheless, patients who develop clinically relevant xerostomia or reduced salivary flow may require closer monitoring because impaired salivary protection can create conditions favorable to caries development (Erdemir et al., 2017; Lynge Pedersen & Belstrøm, 2019). Recall intervals and additional preventive measures should therefore be based on individual findings rather than isotretinoin exposure alone.

A similar approach appears appropriate for periodontal care. Recent longitudinal studies indicate that mild increases in BOP and gingival inflammation may occur during treatment, but there is no convincing evidence of periodontal attachment loss or accelerated periodontitis progression (Erduran et al., 2026; Günay et al., 2026; Ustaoğlu et al., 2020). Particular attention should therefore be paid to plaque control and gingival bleeding, especially in patients with pre-existing periodontal risk factors. Routine periodontal therapy does not need to be modified solely because a patient is receiving isotretinoin.

7.4. Dental Procedures and Wound Healing

Historically, elective surgical procedures were frequently postponed for 6-12 months after isotretinoin therapy because of concerns regarding impaired wound healing and abnormal scarring. Contemporary reviews have questioned the evidence supporting this routine restriction (Spring et al., 2017; Truax et al., 2025). A systematic review and expert consensus found insufficient evidence to justify delaying several types of cutaneous procedures in patients receiving or recently completing isotretinoin (Spring et al., 2017). However, these findings are derived predominantly from dermatological procedures and cannot be directly extrapolated to all dental interventions.

Evidence specific to oral and maxillofacial surgery remains limited. A recent review identified only sparse data regarding procedures such as third-molar extraction and found no convincing evidence that isotretinoin exposure leads to clinically important impairment of oral wound healing (Truax et al., 2025). Consequently, currently available evidence does not support routine postponement of necessary dental procedures solely because of isotretinoin use. Decisions regarding elective oral surgery should instead consider the type and urgency of the procedure, the patient's oral condition, the presence of significant mucosal dryness or inflammation, and other individual risk factors.

Overall, dental management during systemic isotretinoin therapy should focus primarily on recognition and symptomatic management of oral dryness, maintenance of effective caries and periodontal prevention, and individualized monitoring rather than major modification of routine dental care.

8. Discussion

The available evidence indicates that systemic isotretinoin can influence several components of the oral environment, but the strength and clinical significance of these effects differ considerably between outcomes. The most consistent findings concern salivary function and mucocutaneous symptoms, whereas evidence regarding dental caries and periodontal tissues remains more heterogeneous. This distinction is clinically important because statistically detectable changes in oral parameters do not necessarily translate into clinically significant oral disease (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser, AlAqeely, AlZahrani, et al., 2021; AlJasser et al., 2022; Alkanhal et al., 2021; Alqahtani et al., 2026; Erdemir et al., 2017; Erduran et al., 2026; Günay et al., 2026; Holanda et al., 2026; Kapała et al., 2022; Oikarinen et al., 1995; Ustaoğlu et al., 2020).

Reduction in salivary flow represents the most reproducible oral finding associated with isotretinoin therapy. Early observations and later prospective studies demonstrated lower salivary secretion during treatment, while recent longitudinal data indicate that this effect may be particularly evident during the early

phase of therapy and may improve after treatment completion (Erdemir et al., 2017; Günay et al., 2026; Oikarinen et al., 1995). Functional imaging provides complementary evidence: Tc-99m pertechnetate scintigraphy demonstrated progressive reductions in uptake, maximum accumulation, and ejection fraction in both parotid and submandibular glands during six months of isotretinoin therapy (Örsal et al., 2015). A recent systematic review and meta-analysis also supported an overall reduction in salivary flow, although only two studies were suitable for quantitative synthesis (Holanda et al., 2026). The direction of the evidence is therefore relatively consistent, but its certainty remains limited by small samples and methodological heterogeneity.

An important clinical observation is that objective salivary reduction and subjective xerostomia do not necessarily change to the same degree. The decrease in unstimulated salivary flow was relatively modest, whereas the proportion of patients reporting oral dryness increased substantially during the early phase of treatment (Günay et al., 2026). This discrepancy suggests that subjective xerostomia may not directly reflect the magnitude of measurable salivary gland hypofunction. Mucosal hydration, salivary composition, sensory perception, and epithelial changes may also contribute to the sensation of dryness. From a dental perspective, this supports evaluating patient-reported symptoms together with clinical findings rather than relying on a single measure of salivary function.

The available methods for assessing salivary dysfunction should be viewed as complementary rather than interchangeable. Whole-saliva collection provides a clinically accessible measure of overall secretion, whereas gland-specific scintigraphy evaluates uptake, accumulation, and excretory function of the major salivary glands. In the scintigraphic study, functional parameters declined progressively in both parotid and submandibular glands between baseline and months 3 and 6 of isotretinoin therapy, supporting the biological relevance of the reductions observed in conventional salivary-flow studies (Örsal et al., 2015). At the same time, scintigraphy does not establish whether these functional changes persist after treatment because no post-discontinuation examination was performed. Conversely, longitudinal whole-saliva data suggest improvement after treatment completion (Günay et al., 2026). Together, these findings support a treatment-related effect on salivary function while emphasizing that the magnitude, clinical perception, and reversibility of this effect depend on the outcome being measured.

The effects of isotretinoin on salivary properties other than flow are less clearly defined. Reduced buffering capacity was reported in one prospective study, whereas another study did not identify a significant change (Alkanhal et al., 2021; Erdemir et al., 2017). Differences in salivary inflammatory, oxidative, and matrix-remodelling markers have also been described (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser et al., 2022; Oikarinen et al., 1995; Ustaoğlu et al., 2020). These biochemical observations suggest that systemic retinoid exposure may modify the oral environment at several levels, but they currently provide limited guidance for clinical decision-making because their relationship with long-term dental outcomes remains uncertain.

The possible relationship between isotretinoin and dental caries requires particularly cautious interpretation. Saliva contributes to acid neutralization, oral clearance, maintenance of tooth mineral homeostasis, and antimicrobial defense; consequently, reduced salivary secretion provides a biologically plausible pathway toward increased caries susceptibility (Lynge Pedersen & Belstrøm, 2019; Wolff et al., 2017). Some studies have reported increased ICDAS or DMFT scores during isotretinoin treatment (Alkanhal et al., 2021; Erdemir et al., 2017). However, these studies were small, and changes in salivary flow and buffering capacity were not significantly correlated with ICDAS scores in the prospective case-control study (Erdemir et al., 2017). Moreover, DMFT reflects cumulative disease experience and dental treatment and is not an ideal indicator of newly developing lesions over a short observation period. Current evidence therefore supports considering isotretinoin-associated hyposalivation as a potential modifying factor rather than establishing isotretinoin itself as an independent cause of dental caries.

Mucosal manifestations have a clearer association with systemic isotretinoin. Cheilitis and lip dryness are among the most frequently reported adverse effects, while oral dryness, burning sensations, and ulcerative lesions occur less consistently (Alqahtani et al., 2026; Günay et al., 2026; Kapała et al., 2022). The tendency of several symptoms to appear early during therapy and subsequently improve suggests that many manifestations are transient. Experimental studies demonstrating altered oral epithelial differentiation and disruption of cell adhesion structures provide a biologically plausible explanation for increased mucosal fragility during retinoid exposure (Hatakeyama et al., 2004; Kautsky et al., 1995). Nevertheless, these experimental findings should not be interpreted as direct evidence that the same cellular changes occur to a clinically relevant degree in patients receiving conventional isotretinoin doses.

The periodontal findings are more difficult to reconcile. Recent prospective studies have reported increases in bleeding on probing, gingivitis, plaque index, or probing depth during treatment (Erduran et al., 2026; Günay et al., 2026). However, these changes were generally modest and were not accompanied by convincing evidence of periodontal attachment loss. In the longitudinal study with post-treatment follow-up, gingival inflammation increased during therapy without significant deterioration in clinical attachment level, and the observed changes were largely reversible (Günay et al., 2026). Another controlled study found no significant worsening of the main clinical periodontal parameters after six months of treatment (Ustaoğlu et al., 2020). Taken together, these findings suggest that isotretinoin may influence gingival inflammatory status without demonstrating progression to periodontitis.

One plausible explanation is an indirect effect mediated by changes in salivary function and local oral conditions. Reduced salivary secretion may impair lubrication and clearance and may make oral hygiene less comfortable in symptomatic patients. The simultaneous increase in plaque accumulation and gingival bleeding reported in one prospective study is compatible with such an indirect pathway (Erduran et al., 2026). This interpretation may be more clinically plausible than assuming a direct destructive effect of isotretinoin on periodontal tissues, particularly because current longitudinal studies have not demonstrated corresponding attachment loss or radiographic periodontal destruction.

At the same time, biomarker studies do not support a simple uniformly pro-inflammatory model. Lower salivary MMP-8 and MMP-9 levels and higher TIMP concentrations have been reported in isotretinoin users within selected periodontal groups (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser et al., 2022). Differences in the subgingival abundance of several periodontal pathogens have also been observed, while systemic retinoid exposure has been associated with lower salivary hBD-2 concentrations (AlJasser, AlAqeely, AlZahrani, et al., 2021; Atalay et al., 2023). These findings indicate possible effects on extracellular-matrix turnover, innate antimicrobial defense, and the local microbial environment. Their interpretation requires caution, however, because most of these analyses were cross-sectional and several appear to represent companion analyses from the same or substantially overlapping study population. They cannot establish that isotretinoin caused the observed differences or that such changes are clinically protective or harmful.

The apparent discrepancy between clinical inflammatory findings and biomarker observations is therefore not necessarily contradictory. Isotretinoin may simultaneously reduce salivary secretion and alter selected inflammatory or matrix-remodelling pathways (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser et al., 2022; Erduran et al., 2026; Günay et al., 2026). A patient could consequently develop increased gingival bleeding related to plaque accumulation or oral dryness while showing a biochemical profile that does not indicate increased connective-tissue degradation. This possibility provides a useful framework for interpreting the heterogeneous periodontal literature, but it remains a hypothesis that requires confirmation in longitudinal studies combining clinical, salivary, microbiological, and molecular outcomes (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser, AlAqeely, AlZahrani, et al., 2021; AlJasser et al., 2022; Atalay et al., 2023; Erduran et al., 2026; Günay et al., 2026).

The available evidence also has implications for dental procedures. Historical recommendations frequently advised postponing elective interventions for several months after isotretinoin treatment because of concerns regarding impaired wound healing and abnormal scarring. More recent reviews have questioned the evidence supporting a routine isotretinoin-free interval (Spring et al., 2017; Truax et al., 2025). However, most available procedural evidence originates outside dentistry, and direct data regarding oral and maxillofacial surgery remain sparse (Truax et al., 2025). Therefore, the absence of evidence supporting automatic postponement should not be interpreted as evidence that isotretinoin is irrelevant to perioperative assessment. The patient's mucosal condition, salivary symptoms, periodontal status, type and urgency of the procedure, and other individual healing-related risk factors should remain part of an individualized assessment (Spring et al., 2017; Truax et al., 2025).

From a practical perspective, the current evidence favors an individualized preventive approach rather than major modification of routine dental care. Not every patient receiving isotretinoin should automatically be classified as having high caries or periodontal risk. Additional preventive measures are most justified when treatment is accompanied by clinically relevant xerostomia, reduced salivary flow, increased caries activity, poor plaque control, or gingival inflammation. In these patients, attention to fluoride exposure, oral hygiene, dietary habits, salivary symptom management, and periodontal monitoring is reasonable (Villa et al., 2015; Wolff et al., 2017). Conversely, asymptomatic patients with good oral health do not currently require a separate isotretinoin-specific dental protocol.

Several characteristics of the available literature should temper the interpretation of these conclusions. Most clinical studies involve relatively small numbers of young adults and treatment periods of approximately six to eight months (AlJasser et al., 2022; Alkanhal et al., 2021; Erdemir et al., 2017; Erduran et al., 2026; Günay et al., 2026; Oikarinen et al., 1995; Örsal et al., 2015; Ustaoğlu et al., 2020). Patients with established periodontitis, high baseline caries activity, significant systemic comorbidity, or repeated isotretinoin courses are poorly represented. Studies also differ in isotretinoin dose, saliva collection methods, periodontal examination protocols, and follow-up schedules (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser, AlAqeely, AlZahrani, et al., 2021; AlJasser et al., 2022; Alkanhal et al., 2021; Atalay et al., 2023; Erdemir et al., 2017; Erduran et al., 2026; Günay et al., 2026; Holanda et al., 2026; Oikarinen et al., 1995; Örsal et al., 2015; Ustaoğlu et al., 2020). These limitations reduce comparability across studies and may partly account for apparently conflicting findings.

Despite these limitations, the literature supports a coherent overall clinical interpretation. The oral effects of systemic isotretinoin are most clearly expressed as salivary and mucosal changes, particularly reduced salivary flow, xerostomia, and cheilitis (AlJasser et al., 2022; Alkanhal et al., 2021; Alqahtani et al., 2026; Erdemir et al., 2017; Günay et al., 2026; Holanda et al., 2026; Kapała et al., 2022; Oikarinen et al., 1995; Örsal et al., 2015). These effects can plausibly modify the local risk environment for caries and gingival inflammation, but current evidence does not establish isotretinoin as a direct cause of dental caries or periodontitis (Alkanhal et al., 2021; Erdemir et al., 2017; Erduran et al., 2026; Günay et al., 2026; Ustaoğlu et al., 2020). The role of the dentist is therefore primarily to recognize clinically relevant oral adverse effects, control modifiable risk factors, provide symptomatic and preventive care when needed, and avoid unnecessary restrictions unsupported by the available evidence (Spring et al., 2017; Truax et al., 2025; Villa et al., 2015; Wolff et al., 2017).

9. Current Evidence Gaps

The current evidence on oral effects of systemic isotretinoin remains limited by several methodological problems. Most available clinical studies include relatively small samples, short follow-up periods, and young patients with generally good baseline oral and periodontal health (Erdemir et al., 2017; Erduran et al., 2026; Günay et al., 2026; Ustaoğlu et al., 2020). Several studies also lack an untreated control group (Alkanhal et al., 2021; Erduran et al., 2026; Günay et al., 2026), while some of the available biomarker and microbiological data are cross-sectional and therefore cannot establish temporal or causal relationships (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser, AlAqeely, AlZahrani, et al., 2021; AlJasser et al., 2022; Atalay et al., 2023).

Considerable heterogeneity is present in isotretinoin dose, treatment duration, saliva collection methods, definitions of xerostomia and hyposalivation, and periodontal outcome assessment (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser, AlAqeely, AlZahrani, et al., 2021; AlJasser et al., 2022; Alkanhal et al., 2021; Atalay et al., 2023; Erdemir et al., 2017; Erduran et al., 2026; Günay et al., 2026; Holanda et al., 2026; Oikarinen et al., 1995; Ustaoğlu et al., 2020). This limits direct comparison between studies and makes quantitative synthesis difficult. A recent systematic review and meta-analysis evaluating salivary flow identified only two studies suitable for quantitative synthesis, further illustrating the limited and heterogeneous nature of the available evidence (Holanda et al., 2026). In addition, several AlJasser publications use an essentially identical six-group structure and sample size, suggesting that they represent companion analyses from the same or substantially overlapping cohort (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser, AlAqeely, AlZahrani, et al., 2021; AlJasser et al., 2022); this should be considered when interpreting the apparent volume of evidence.

Long-term consequences remain particularly uncertain. Current studies provide little information on patients with established periodontitis, high baseline caries risk, older individuals, or those receiving repeated courses of isotretinoin (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser, AlAqeely, AlZahrani, et al., 2021; AlJasser et al., 2022; Alkanhal et al., 2021; Atalay et al., 2023; Erdemir et al., 2017; Erduran et al., 2026; Günay et al., 2026; Holanda et al., 2026; Ustaoğlu et al., 2020). The clinical relevance of reported changes in salivary biomarkers, including MMPs, TIMPs, oxidative markers, and antimicrobial peptides, also remains unclear because these findings have not been consistently linked with longitudinal periodontal outcomes. Evidence regarding persistent salivary dysfunction, clinically relevant caries development, periodontal attachment loss, and outcomes after oral surgical procedures is similarly insufficient (Erdemir et al., 2017; Erduran et al., 2026; Günay et al., 2026; Holanda et al., 2026; Truax et al., 2025).

Another important limitation is the lack of standardized thresholds for clinically meaningful salivary change. Studies have used stimulated or unstimulated whole saliva, subjective dryness questionnaires, or gland-specific functional imaging, and these measures capture different dimensions of salivary dysfunction (Günay et al., 2026; Örsal et al., 2015; Wolff et al., 2017). Future investigations should therefore report subjective xerostomia and objective salivary outcomes separately and, where possible, relate them to clinically relevant endpoints such as new caries lesions, mucosal symptoms, plaque control, and periodontal inflammation. This would help distinguish statistically significant physiological changes from changes that actually require modification of dental care.

Future prospective studies should therefore include larger controlled cohorts, standardized salivary and periodontal measurements, clearly defined isotretinoin exposure, and post-treatment follow-up. Particular attention should be given to whether observed changes in salivary function and gingival inflammation translate into clinically meaningful long-term dental outcomes.

10. Conclusions

Systemic isotretinoin is associated with several oral changes that may be relevant to dental practice. The most consistent findings are reduced salivary flow, xerostomia, cheilitis, and other manifestations of mucosal dryness (Alqahtani et al., 2026; Erdemir et al., 2017; Günay et al., 2026; Holanda et al., 2026; Kapała et al., 2022; Oikarinen et al., 1995). Available evidence also suggests that reduced salivary secretion may create conditions potentially favorable to caries development, although a direct causal relationship between isotretinoin therapy and dental caries has not been established (Alkanhal et al., 2021; Erdemir et al., 2017; Lynge Pedersen & Belstrøm, 2019).

Periodontal findings are less consistent. Mild and usually transient increases in gingival inflammation and bleeding have been reported (Erduran et al., 2026; Günay et al., 2026), but there is currently no convincing evidence that isotretinoin causes periodontal attachment loss or accelerates periodontitis progression (Erduran et al., 2026; Günay et al., 2026; Ustaoğlu et al., 2020). Biomarker and microbiological studies further suggest that the periodontal response to isotretinoin may involve both unfavorable salivary changes and potentially opposing inflammatory, matrix-remodelling, antimicrobial, and microbial effects (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser, AlAqeely, AlZahrani, et al., 2021; AlJasser et al., 2022; Atalay et al., 2023).

For dental practitioners, the most appropriate approach is therefore individualized monitoring rather than major modification of routine dental care. Patients with clinically significant xerostomia, increased caries activity, or gingival inflammation may benefit from intensified preventive measures and symptomatic management (Villa et al., 2015; Wolff et al., 2017). Current evidence does not support routine postponement of necessary dental procedures solely because a patient is receiving isotretinoin, although evidence specific to oral surgery remains limited (Spring et al., 2017; Truax et al., 2025).

Further well-designed longitudinal studies are required to clarify the long-term clinical significance of these oral changes and to determine whether specific groups of patients require additional dental precautions during isotretinoin therapy.

Table 1. Main clinical studies evaluating oral effects of systemic isotretinoin and related systemic retinoid exposure

Study	Design and participants	Exposure / follow-up	Outcomes assessed	Main findings
Oikarinen et al. (1995)	Follow-up study; SFR/pH assessed in 8 patients, MMP-9 in 17 patients	Oral isotretinoin for ~3 months; assessment during treatment and ~3.7 months after discontinuation	Stimulated SFR, pH, MMP-9 activity	Lower stimulated SFR and higher MMP-9 activity during treatment; salivary pH unchanged
Örsal et al. (2015)	Prospective repeated-measures study; 28 patients	0.5 mg/kg/day for 6 months; baseline, month 3, and month 6	Tc-99m salivary gland scintigraphy; uptake ratio, maximum accumulation, and ejection fraction	Significant progressive reductions in functional parameters of both parotid and submandibular glands during treatment

Study	Design and participants	Exposure / follow-up	Outcomes assessed	Main findings
Erdemir et al. (2017)	Prospective case-control; 45 treated + 45 controls enrolled (22 + 18 completed)	0.5 mg/kg/day for 6 months	Stimulated SFR, buffering capacity, S. mutans, Lactobacillus, ICDAS	Reduced SFR and buffering capacity; increased ICDAS scores; no significant relationship between salivary changes and ICDAS
Ustaoğlu et al. (2020)	Prospective controlled study; 25 treated + 18 controls	Baseline and after 6 months of therapy	PD, CAL, PI, GI, BOP; salivary oxidative stress markers	No significant deterioration in periodontal clinical parameters; salivary total antioxidant capacity decreased
Alkanhal et al. (2021)	Prospective before-after study; 24 patients	0.5 mg/kg/day for 8 months	Stimulated SFR, buffering capacity, S. mutans, Lactobacillus, DMFT	Reduced SFR; increased DMFT and S. mutans; no significant change in buffering capacity
AlJasser et al. (2021), MMP study*	Case-control; 180 participants divided by periodontal status and isotretinoin exposure	Current systemic isotretinoin use	PD, CAL, BOP; salivary MMP-8 and MMP-9	Lower BOP and markedly lower MMP-8/MMP-9 levels in isotretinoin users with periodontal disease
AlJasser et al. (2021), microbiological study*	Case-control; 180 participants	Current systemic isotretinoin use	Subgingival periodontal pathogens	Lower P. gingivalis, T. forsythia and T. denticola; higher F. nucleatum in isotretinoin users
AlJasser et al. (2022), TIMP/SFR study*	Case-control; 180 participants	Current systemic isotretinoin use	Unstimulated SFR, xerostomia, TIMP-1, TIMP-2	Lower SFR and more dry-mouth symptoms; higher TIMP-1/TIMP-2 in several isotretinoin-exposed groups
Atalay et al. (2023)	Case-control; 34 systemic retinoid users + 35 controls	Current systemic retinoic acid exposure	Periodontal parameters; hBD-1, hBD-2 and hBD-3 in saliva, serum and gingival tissue	Lower salivary hBD-2 in retinoid users; no significant differences in other defensins
Günay et al. (2026)	Longitudinal study; 24 periodontally healthy patients	Baseline, week 6, month 5 and post-treatment follow-up	Unstimulated SFR, xerostomia, oral burning, PI, PPD, CAL, BOP, gingivitis, OHIP-14	Transient reduction in SFR and increase in xerostomia, BOP and gingivitis; no significant CAL deterioration; symptoms largely resolved after treatment
Erduran et al. (2026)	Prospective pre-post study; 80 patients	6 months of isotretinoin therapy	BOP, PI, probing depth	Significant increases in BOP, PI and probing depth during treatment
Alqahtani et al. (2026)	Prospective descriptive study; 60 patients	Oral isotretinoin therapy with serial oral examinations	Cheilitis, xerostomia, mucosal ulceration, gingival changes	Cheilitis 75%, xerostomia 50%, mucosal ulcerations 16.7%, gingival changes 13.3%

Abbreviations: BOP, bleeding on probing; CAL, clinical attachment level; DMFT, decayed, missing and filled teeth; GI, gingival index; hBD, human β-defensin; ICDAS, International Caries Detection and Assessment System; MMP, matrix metalloproteinase; OHIP-14, Oral Health Impact Profile-14; PD/PPD, probing depth/probing pocket depth; PI, plaque index; SFR, salivary flow rate; TIMP, tissue inhibitor of metalloproteinases.

Table 2. Practical implications of isotretinoin-associated oral changes for dental practice

Oral finding / concern	Potential clinical relevance	Suggested dental approach
Xerostomia / reduced salivary flow	Oral discomfort, impaired lubrication, and potentially reduced protective salivary functions	Assess symptoms; encourage adequate hydration; consider sugar-free salivary stimulation or saliva substitutes in symptomatic patients (Villa et al., 2015; Wolff et al., 2017)
Reduced buffering capacity	May contribute to a more cariogenic oral environment	Reinforce oral hygiene and fluoride use; assess individual caries risk (Erdemir et al., 2017; Lynge Pedersen & Belstrøm, 2019; Villa et al., 2015)
Potential increase in caries susceptibility	Reduced salivary flow and buffering may favor caries development, although a direct causal relationship has not been established	Individualized caries prevention; closer monitoring in patients with xerostomia or additional caries risk factors (Alkanhal et al., 2021; Erdemir et al., 2017; Lynge Pedersen & Belstrøm, 2019)
Cheilitis and lip dryness	Fissuring, discomfort, irritation	Regular use of bland emollients or barrier preparations; evaluate persistent or severe lesions (Kothari et al., 2024)
Oral mucosal dryness, burning, or ulceration	Discomfort and increased susceptibility to mechanical irritation	Avoid additional mucosal irritants; provide supportive symptomatic care; investigate persistent or atypical lesions independently (Alqahtani et al., 2026; Günay et al., 2026)
Gingival inflammation / increased BOP	Transient gingivitis has been reported during therapy in some patients	Emphasize plaque control; monitor gingival condition, particularly in patients with pre-existing periodontal risk (Erduran et al., 2026; Günay et al., 2026; Ustaoğlu et al., 2020)
Changes in periodontal biomarkers and microbiota	Biological effects are heterogeneous and their clinical significance remains uncertain	No specific treatment modification is currently justified; base periodontal care on clinical findings (AlJasser, Alaqeely, Al-Hoqail, et al., 2021; AlJasser, AlAqeely, AlZahrani, et al., 2021; AlJasser et al., 2022; Atalay et al., 2023)
Periodontitis risk	Current evidence does not demonstrate isotretinoin-induced attachment loss or accelerated periodontitis progression	Routine periodontal management; do not classify patients as having increased periodontitis risk solely because of isotretinoin exposure (Erduran et al., 2026; Günay et al., 2026; Ustaoğlu et al., 2020)
Dental and oral surgical procedures	Evidence of clinically significant impairment of oral wound healing is limited	Necessary dental procedures should not routinely be postponed solely because of isotretinoin use; assess surgical risk individually (Spring et al., 2017; Truax et al., 2025)

REFERENCES

1. AlJasser, R. N., Alaqeely, R. S., Al-Hoqail, I. A., Al-Haddab, M., AlQahtani, S. S., AlKenani, M. E., AlZahrani, A. M., & AlOraini, S. (2021). Association between isotretinoin (Roaccutanne) use and changes in periodontal clinical parameters and MMP-8 and MMP-9 salivary levels. *Frontiers in Bioscience-Landmark, 26*(7), 191–197. https://doi.org/10.52586/4933
2. AlJasser, R., AlAqeely, R., AlKenani, M., AlQahtani, S., AlZahrani, A., & Lambarte, R. (2022). The effect of systemic isotretinoin on salivary tissue inhibitors of metalloproteinases 1 and 2 and salivary flow rate in periodontal disease. *Saudi Journal of Biological Sciences, 29*(1), 148–153. https://doi.org/10.1016/j.sjbs.2021.08.079
3. AlJasser, R., AlAqeely, R., AlZahrani, A., AlKenani, M., AlQahtani, S., AlSarhan, M., AlOtaibi, D., & Lambarte, R. (2021). Antimicrobial effect of isotretinoin therapy on periodontal pathogens: A case-control study. *Antibiotics, 10*(11), 1286. https://doi.org/10.3390/antibiotics10111286
4. Alkanhal, N. A., Aldaij, M. H., Alkanhal, H. A., Al-Haddab, M., & Alfaifi, F. (2021). Dental decay and salivary flow in patients taking systemic isotretinoin: A prospective study. *Journal of Dermatology and Dermatologic Surgery, 25*(2), 80–83. https://doi.org/10.4103/jdds.jdds_122_20
5. Alqahtani, R. M., Alatwi, R. S., Mohammed, M. A. J., Alruwaili, D. N., Alruwaili, A. N., Alqhtani, R. M., & Alanazi, W. Z. (2026). Oral side effects of isotretinoin therapy in acne patients: A prospective study. *Journal of Pharmacy & Bioallied Sciences, 18*(Suppl 1), S165–S167. https://doi.org/10.4103/jpbs.jpbs_1600_25
6. Atalay, N., Balci, N., Toygar, H. U., Yardimci, G., & Gürsoy, U. K. (2023). Serum, saliva, and gingival tissue human β-defensin levels in relation to retinoic acid use. *Journal of Periodontology, 94*(5), 597–605. https://doi.org/10.1002/JPER.22-0466
7. Bettoli, V., Guerra-Tapia, A., Herane, M. I., & Piquero-Martín, J. (2019). Challenges and solutions in oral isotretinoin in acne: Reflections on 35 years of experience. *Clinical, Cosmetic and Investigational Dermatology, 12*, 943–951. https://doi.org/10.2147/CCID.S234231
8. Erdemir, U., Okan, G., Gungor, S., Tekin, B., Yildiz, S. O., & Yildiz, E. (2017). The oral adverse effects of isotretinoin treatment in acne vulgaris patients: A prospective, case-control study. *Nigerian Journal of Clinical Practice, 20*(7), 860–866. https://doi.org/10.4103/1119-3077.183248
9. Erduran, F., Çoşlu, M. D., Karaaslan, S., & Emre, S. (2026). Isotretinoin beyond the skin: A prospective study on its impact on periodontal health. *Dermatology Practical & Conceptual, 16*(2), 6739. https://doi.org/10.5826/dpc.1602a6739
10. Günay, B., Toygar, H., Balevi, A., Gürsoy, M., Gürsoy, U. K., & Balci, N. (2026). Time-dependent effect of isotretinoin use on oral health related quality of life in acne vulgaris patients: A longitudinal study. *Journal of Patient-Reported Outcomes*. Advance online publication. https://doi.org/10.1186/s41687-026-01171-5
11. Hatakeyama, S., Hayashi, S., Yoshida, Y., Otsubo, A., Yoshimoto, K., Oikawa, Y., & Satoh, M. (2004). Retinoic acid disintegrated desmosomes and hemidesmosomes in stratified oral keratinocytes. *Journal of Oral Pathology & Medicine, 33*(10), 622–628. https://doi.org/10.1111/j.1600-0714.2004.00245.x
12. Holanda, P. M. M. de, Barbosa, K. G. N., Santos, A. F. dos, Nóbrega, D. F., Marcelos, P. G. C. L. de, Barbosa, K. L., Menezes, P. L., Islam, N. M., & Panjwani, C. M. B. R. G. (2026). Reduction of salivary flow from anti acne therapy with oral isotretinoin: A systematic review with meta-analysis. *Pediatric Review: International Journal of Pediatric Research, 13*(1), 12–19. https://doi.org/10.17511/ijpr.2026.i01.02
13. Kapała, J., Lewandowska, J., Placek, W., & Owczarczyk-Saczonek, A. (2022). Adverse events in isotretinoin therapy: A single-arm meta-analysis. *International Journal of Environmental Research and Public Health, 19*(11), 6463. https://doi.org/10.3390/ijerph19116463
14. Kautsky, M. B., Fleckman, P., & Dale, B. A. (1995). Retinoic acid regulates oral epithelial differentiation by two mechanisms. *Journal of Investigative Dermatology, 104*(4), 546–553. https://doi.org/10.1111/1523-1747.ep12606058
15. Kothari, R., Pol, D., Asnani, D., Deoghare, S., Kumar, A., & Buccha, Y. (2024). Comparative study between tacrolimus 0.1% ointment versus topical white soft petrolatum jelly in the treatment of oral retinoid-induced cheilitis. *Indian Journal of Dermatology, 69*(2), 202. https://doi.org/10.4103/ijd.ijd_67_23
16. Lynge Pedersen, A. M., & Belstrøm, D. (2019). The role of natural salivary defences in maintaining a healthy oral microbiota. *Journal of Dentistry, 80*(Suppl 1), S3–S12. https://doi.org/10.1016/j.jdent.2018.08.010
17. Nelson, A. M., Zhao, W., Gilliland, K. L., Zaenglein, A. L., Liu, W., & Thiboutot, D. M. (2008). Neutrophil gelatinase-associated lipocalin mediates 13-cis retinoic acid-induced apoptosis of human sebaceous gland cells. *Journal of Clinical Investigation, 118*(4), 1468–1478. https://doi.org/10.1172/JCI33869
18. Oikarinen, K., Salo, T., Kylmäniemi, M., Palatsi, R., Karhunen, T., & Oikarinen, A. (1995). Systemic oral isotretinoin therapy and flow rate, pH, and matrix metalloproteinase-9 activity of stimulated saliva. *Acta Odontologica Scandinavica, 53*(6), 369–371. https://doi.org/10.3109/00016359509006003
19. Ornelas, J., Rosamilia, L., Larsen, L., Foolad, N., Wang, Q., Li, C. S., & Sivamani, R. K. (2016). Objective assessment of isotretinoin-associated cheilitis: Isotretinoin Cheilitis Grading Scale. *Journal of Dermatological Treatment, 27*(2), 153–155. https://doi.org/10.3109/09546634.2015.1086477

20. Örsal, E., Seven, B., Erdem, M. T., Varoğlu, E., Farimaz, H., & Ayan, A. K. (2015). Evaluation of the effect of isotretinoin on salivary gland function by Tc-99m pertechnetate imaging in acne vulgaris patients. *Turkish Journal of Medical Sciences, 45*(3), 674–677. https://doi.org/10.3906/sag-1402-131
21. Reynolds, R. V., Yeung, H., Cheng, C. E., Cook-Bolden, F., Desai, S. R., Druby, K. M., Freeman, E. E., Keri, J. E., Stein Gold, L. F., Tan, J. K. L., Tollefson, M. M., Weiss, J. S., Wu, P. A., Zaenglein, A. L., Han, J. M., & Barbieri, J. S. (2024). Guidelines of care for the management of acne vulgaris. *Journal of the American Academy of Dermatology, 90*(5), 1006.e1–1006.e30. https://doi.org/10.1016/j.jaad.2023.12.017
22. Spring, L. K., Krakowski, A. C., Alam, M., Bhatia, A., Brauer, J., Cohen, J., Del Rosso, J. Q., Diaz, L., Dover, J., Eichenfield, L. F., Gurtner, G. C., Hanke, C. W., Jahnke, M. N., Kelly, K. M., Khetarpal, S., Kinney, M. A., Levy, M. L., Leyden, J., Longaker, M. T., … Zaenglein, A. L. (2017). Isotretinoin and timing of procedural interventions: A systematic review with consensus recommendations. *JAMA Dermatology, 153*(8), 802–809. https://doi.org/10.1001/jamadermatol.2017.2077
23. Truax, L., Hendrixson, M., Naqvi, J., & Trevino, J. (2025). Use of oral retinoids in the perioperative period by surgical specialty: A literature review. *Archives of Dermatological Research, 317*(1), 174. https://doi.org/10.1007/s00403-024-03750-2
24. Ustaoğlu, G., Güler, Ş., & Polat, M. (2020). Effect of isotretinoin on periodontal tissues and oxidative stress markers in the saliva. *Turkderm-Turkish Archives of Dermatology and Venereology, 54*(4), 132–137. https://doi.org/10.4274/turkderm.galenos.2020.99896
25. Villa, A., Connell, C. L., & Abati, S. (2015). Diagnosis and management of xerostomia and hyposalivation. *Therapeutics and Clinical Risk Management, 11*, 45–51. https://doi.org/10.2147/TCRM.S76282
26. Wolff, A., Joshi, R. K., Ekström, J., Aframian, D., Lynge Pedersen, A. M., Proctor, G., Narayana, N., Villa, A., Sia, Y. W., Aliko, A., McGowan, R., Kerr, A. R., Jensen, S. B., Vissink, A., & Dawes, C. (2017). A guide to medications inducing salivary gland dysfunction, xerostomia, and subjective sialorrhea: A systematic review sponsored by the World Workshop on Oral Medicine VI. *Drugs in R&D, 17*(1), 1–28. https://doi.org/10.1007/s40268-016-0153-9