



## QUALITY IN SPORT

eISSN 2450-3118 · Open Access · Peer-reviewed

apcz.umk.pl/QS Nicolaus Copernicus University in Toruń



JĘDRAS, Aleksandra, CZEREPAK, Gabriela, POCIASK, Weronika, BEDNARZ, Katarzyna, GRZEGORCZYK, Julia, GLIWA, Katarzyna, CZAJKOWSKA, Weronika, KALICKA, Karolina, OPALA, Krzysztof, and KROWIŃSKI, Jakub. Contemporary Treatment of Oral Manifestations of Sjögren's Syndrome: A Narrative Review. *Quality in Sport*. 2026;73:75023. <https://doi.org/10.12775/QS.2026.73.75023>

### ARTICLE TIMELINE

Received: 05.08.2026. Revised: 25.08.2026. Accepted: 06.09.2026. Published: 14.09.2026.

The journal has been awarded 20 points in the parametric evaluation by the Polish Ministry of Higher Education and Science (Annex to the announcement of 05.01.2024, No. 32553). Unique Journal Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).

Punkty Ministerialne z 2019 – aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych). © The Authors 2026.

OPEN ACCESS · CC BY-NC-SA 4.0 This article is published with open access under the License Open Journal Systems of Nicolaus Copernicus University in Toruń, Poland, and is distributed under the terms of the Creative Commons Attribution Non-commercial Share Alike License (<http://creativecommons.org/licenses/by-nc-sa/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the work is properly cited. The authors declare no conflict of interest regarding the publication of this paper.

## Contemporary Treatment of Oral Manifestations of Sjögren's Syndrome: A Narrative Review

**Aleksandra Jędras**

<https://orcid.org/0009-0007-9146-6357>

University Dental Center in Lublin, Lublin, Poland

**Gabriela Czerepak**

<https://orcid.org/0009-0000-1347-8538>

University Dental Center in Lublin, Lublin, Poland

**Weronika Pociask**

<https://orcid.org/0009-0005-6745-4853>

University Dental Center in Lublin

**Katarzyna Bednarz**

<https://orcid.org/0009-0007-6199-4159>

Specialist Prosthetic Practice Dentist Dorota Janowska in Lublin, Lublin, Poland

**Julia Grzegorzcyk**

<https://orcid.org/0009-0005-2157-9132>

EM-DENT, Lublin, Poland

**Katarzyna Gliwa**

<https://orcid.org/0009-0005-6463-3776>

University Dental Center in Lublin, Lublin, Poland

**Weronika Czajkowska**

<https://orcid.org/0009-0004-5797-7311>

Offices Gallery Dentistry Lublin, Poland

**Karolina Kalicka**

<https://orcid.org/0000-0002-7474-4737>

Smile Institute, Poniatowa, Poland

**Krzysztof Opala**

<https://orcid.org/0009-0002-5378-9001>

EM-DENT, Lublin, Poland

**Jakub Krowiński**

<https://orcid.org/0009-0000-1328-5154>

The Wroclaw Medical University, Wroclaw, Poland

**Abstract**

Background: Oral manifestations of Sjögren's syndrome, particularly xerostomia caused by salivary gland hypofunction, impair oral function, increase the risk of dental and mucosal complications, and reduce quality of life. Symptomatic management remains the mainstay of treatment, although several emerging therapies have recently been investigated.

Aim: To review current evidence on established and emerging treatments for the oral manifestations of Sjögren's syndrome.

Methods: A narrative literature review was conducted using PubMed, Scopus, Web of Science, and Google Scholar. Publications from January 2015 to July 2026 were analyzed to evaluate

conventional management, pharmacological and physical therapies, prevention of oral complications, and systemic immunomodulatory approaches.

Results: Conventional management, including patient education, saliva substitutes, topical fluoride, dietary modification, and preventive dental care, remains the cornerstone of treatment. Pilocarpine and cevimeline are the most effective secretagogues in patients with preserved salivary gland function but are limited by cholinergic adverse effects. Sialendoscopy and intraductal irrigation show the strongest evidence among minimally invasive therapies. Current evidence does not support hydroxychloroquine, conventional immunosuppressants, rituximab, or abatacept for isolated oral dryness. Emerging targeted therapies, including iganalumab, dazodalibep, and nipocalimab, have shown promising preliminary results.

Conclusions: Management should be individualized and multidisciplinary, combining symptomatic relief, preservation of residual salivary gland function, prevention of oral complications, and appropriate treatment of systemic disease. Targeted therapies are promising but require confirmation in larger clinical trials.

**Keywords** Sjögren's syndrome, xerostomia, hyposalivation, treatment

## **1. Introduction**

Sjögren's syndrome is a chronic systemic autoimmune disease characterized by immune-mediated dysfunction of the exocrine glands, particularly the salivary and lacrimal glands. Although its clinical presentation is heterogeneous and may include multiple systemic manifestations, xerostomia and xerophthalmia remain the principal symptoms. The disease predominantly affects women, while its reported prevalence varies according to geographic region, population characteristics, study methodology, and the classification criteria applied (Thurtle et al. 2024).

Xerostomia describes the subjective sensation of oral dryness, whereas hyposalivation refers to an objectively reduced salivary flow. These phenomena frequently coexist but do not always correlate. The perception of dryness may additionally depend on saliva composition, mucosal sensitivity, medication use, hydration, comorbidities, and psychological factors. Saliva contributes to lubrication, speech, mastication, swallowing, taste perception, microbial

homeostasis, acid buffering, enamel remineralization, and mucosal repair. Its quantitative and qualitative deterioration therefore compromises both oral function and the protective mechanisms of the oral cavity (Błochowiak et al. 2016; Serrano et al. 2018; Ngo and Thomson 2021).

Patients with Sjögren's syndrome are at increased risk of many abnormalities. These include rapidly progressing dental caries, particularly cervical and root-surface lesions, oral candidiasis, mucosal atrophy, angular cheilitis, tongue abnormalities, traumatic ulceration, oral burning, dysgeusia, halitosis, dysphagia, and intolerance of removable prostheses (Błochowiak et al. 2016; Serrano et al. 2018). Hyposalivation may also alter oral microbial ecology, although current evidence suggests that reduced salivary flow may be a more important determinant of dysbiosis than the autoimmune diagnosis itself (Saúco et al. 2023).

As oral manifestations of the syndrome affect oral health-related quality of life (Ngo and Thomson 2021; Vujović et al. 2023), treatment outcome evaluation should not be limited to salivary-flow measurements but should also include symptom severity, functional impairment, oral complications, and patient-reported outcomes.

Current management is individualized and multidisciplinary. It combines preservation or stimulation of residual salivary-gland function, replacement of oral moisture, prevention of irreversible dental damage, and early treatment of infections and mucosal complications (Price et al. 2025). Conventional approaches include lifestyle modification, saliva substitutes, topical fluoride, oral lubricants, sugar-free salivary stimulants, and systemic muscarinic agonists. Physical, minimally invasive, immunomodulatory, and targeted biological therapies are increasingly investigated, although many remain supported by preliminary or heterogeneous evidence (Muszyński et al. 2025; Price et al. 2025).

The aim of this narrative review is to critically summarize established and emerging methods for managing oral manifestations of Sjögren's syndrome, with particular attention to xerostomia, salivary-gland hypofunction, oral complications, and the clinical applicability of novel therapies.

## **2. Research materials and methods**

A narrative literature review was conducted using the databases: PubMed, Scopus, Web of Science and Google Scholar. The search included publications from January 2015 to July 2026 and was carried out using the following keywords: "Sjogren's syndrome", "xerostomia", "saliva substitutes", "secretagogues", "physical interventions", "biological therapies" and

“regenerative treatment”. The reference lists of eligible studies were additionally screened for appropriate articles.

### **3. Research results**

#### **3.1. Pathophysiology and oral manifestations**

Salivary gland dysfunction in Sjögren’s syndrome arises from a complex interplay of genetic susceptibility, environmental factors, epithelial-cell dysfunction, and dysregulated innate and adaptive immune responses. Rather than acting as passive targets, salivary gland epithelial cells actively contribute to disease pathogenesis by presenting antigens and producing pro-inflammatory cytokines and chemokines. Persistent glandular inflammation is driven by several interconnected immune pathways, including type I interferon signalling, T-cell activation, B-cell hyperactivity, increased expression of B-cell activating factor (BAFF), and the production of pathogenic autoantibodies (Qi et al. 2024).

Histopathological changes are characterised by focal lymphocytic infiltration, progressive acinar cell loss, ductal abnormalities, fibrosis, adipose tissue replacement, and disruption of glandular innervation and epithelial integrity. Importantly, functional impairment of salivary secretion may occur before extensive structural damage becomes evident. Experimental evidence suggests that defective intracellular calcium signalling, together with reduced expression of inositol 1,4,5-trisphosphate receptors, impairs the secretory capacity of residual acinar cells, contributing to hyposalivation even in the presence of preserved glandular tissue (Teos et al. 2015).

The oral manifestations of Sjögren’s syndrome reflect not only a reduction in salivary volume but also significant alterations in saliva composition. Patients frequently describe saliva as thick, foamy, sticky, or rope-like. Changes in mucin glycosylation and saliva rheology reduce mucosal lubrication, while decreased concentrations of biologically active proteins, including epidermal growth factor, impair epithelial maintenance and wound healing, further compromising oral mucosal health (Chaudhury et al. 2016; Azuma et al. 2018).

Clinically, patients commonly experience persistent thirst, nocturnal oral dryness, difficulty eating dry foods, dysphagia, prolonged chewing, dysgeusia, oral burning, and impaired speech. On examination, characteristic findings include dry, sticky oral mucosa, diminished salivary pooling, a fissured or depapillated tongue, mucosal erythema, angular cheilitis, traumatic ulceration, and irritation associated with denture use (Błochowiak et al. 2016; Serrano et al. 2018; Ngo and Thomson 2021).

The loss of saliva's protective functions—including mechanical cleansing, buffering capacity, antimicrobial activity, and remineralisation—creates a highly cariogenic oral environment. Dental caries often progress rapidly and may involve cervical, root, smooth, incisal, and cuspal surfaces, patterns that are less commonly observed in healthy individuals. Oral candidiasis is also frequently encountered and may present as pseudomembranous or erythematous candidiasis, angular cheilitis, atrophic glossitis, or denture-associated stomatitis. By contrast, the association between Sjögren's syndrome and periodontitis remains less clearly established, with disease severity influenced by confounding factors such as oral hygiene practices, smoking, age, medication use, and access to routine dental care.

Understanding the multifactorial mechanisms underlying oral disease in Sjögren's syndrome has important therapeutic implications. Simply increasing salivary flow is often insufficient, as symptoms may also result from qualitative changes in saliva, mucosal injury, microbial dysbiosis, and irreversible glandular damage. Consequently, effective management requires a comprehensive approach that combines salivary stimulation or replacement with strategies aimed at protecting the oral mucosa, enhancing dental remineralisation, controlling opportunistic infections, and addressing the functional limitations associated with chronic xerostomia.

### **3.2. Conventional management**

Disease management should begin with an assessment of subjective dryness, residual glandular function, oral complications, comorbidities, and medications. Potentially reversible causes, including dehydration, mouth breathing, tobacco exposure, poorly controlled diabetes, and medications with anticholinergic effects, should be addressed whenever possible (Ramos-Casals et al. 2020; Price et al. 2025).

Patient education is fundamental. Regular intake of small amounts of water may provide temporary relief, but sweetened, acidic, carbonated, or caffeinated beverages should be limited because of their cariogenic and erosive potential. Alcohol-containing mouth rinses and strongly flavoured products may aggravate mucosal irritation. Dietary counselling should focus on reducing the frequency of fermentable carbohydrate intake and adapting food consistency without increasing exposure to sugar or dietary acids.

Mechanical and gustatory stimulation may benefit patients with preserved salivary function. Sugar-free chewing gum and lozenges can stimulate salivary reflexes, while xylitol-containing products avoid exposure to sucrose. Acidic stimulants may temporarily increase secretion but should be used cautiously because repeated acid exposure can contribute to dental erosion.

Saliva substitutes are available as sprays, rinses, gels, pastes, lozenges, oils, and adhesive discs. They commonly contain cellulose derivatives, xanthan gum, mucins, glycerol, polyethylene glycol, mineral salts, and lubricating polymers (Assery 2019). Some products additionally contain fluoride, calcium, phosphate, xylitol, enzymes, or antimicrobial proteins. However, no artificial product fully reproduces the rheological, antimicrobial, buffering, and remineralizing functions of natural saliva.

Evidence indicates that saliva substitutes may reduce subjective xerostomia, but differences among products and studies prevent identification of a universally superior formulation (Assery 2019). Patient preference is therefore important. Thin, neutral-tasting sprays may be convenient during the day, whereas viscous gels or adhesive products may provide longer nocturnal relief (Assy et al. 2022; Assy et al. 2023). Preparations should preferably be sugar-free, alcohol-free, non-irritating, and close to neutral pH. Because symptomatic relief does not restore natural dental protection, patients with Sjögren's syndrome should be considered at elevated caries risk. Preventive measures include fluoride toothpaste, interdental cleaning, dietary control, individualized recall intervals, and additional topical fluoride according to caries activity (Vivino et al. 2016; Price et al. 2025). Evidence for specific interventions in Sjögren's syndrome remains limited; a randomized trial of fluoride varnish did not demonstrate statistically significant superiority for its principal outcomes, although this finding should not be interpreted as evidence against fluoridebased prevention (Xin et al. 2016). Conventional interventions are generally safe but provide temporary relief. Their effectiveness should be assessed through oral comfort, sleep, speaking, swallowing, dietary function, mucosal health, caries activity, candidiasis frequency, and quality of life rather than salivary flow alone.

### **3.3. Pharmacological stimulation of salivary secretion**

Systemic secretagogues stimulate residual glandular tissue and are most appropriate for patients with clinically significant xerostomia and measurable decrease in salivary secretion. Their potential benefit should be balanced against systemic cholinergic adverse effects and relevant respiratory, cardiovascular, ophthalmological, gastrointestinal, and urinary comorbidities (Ramos-Casals et al. 2020; Price et al. 2025).

Pilocarpine is a non-selective muscarinic agonist that can increase salivary flow and reduce subjective dryness in some patients (Brito-Zerón et al. 2019; Kapourani et al. 2022). Treatment is commonly initiated at a low dose and increased gradually according to response and tolerability. Excessive sweating is the principal adverse effect, while flushing, headache, nausea, diarrhea, urinary frequency, respiratory secretion, and visual disturbances may also

occur. Pilocarpine is generally contraindicated in uncontrolled asthma and conditions in which miosis is undesirable. Cevimeline has relative functional preference for M1 and M3 muscarinic receptors and is commonly administered at 30 mg three times daily. Clinical studies indicate improvement in xerostomia and salivary secretion, although the available trials are limited and heterogeneous (Brito-Zerón et al. 2019; Oleksak et al. 2021; Karimi et al. 2025). Its adverse effects are similar to those of pilocarpine. There is insufficient direct evidence to establish universal superiority of either drug. Pilocarpine is more widely available, whereas cevimeline may be better tolerated by some patients but is unavailable or unlicensed in many countries. Selection should depend on availability, contraindications, adverse effects, previous response, and patient preference.

Alternative secretagogues, including anethole trithione, bromhexine, N-acetylcysteine, and bethanechol, are supported by substantially weaker evidence and should not be considered equivalent to pilocarpine or cevimeline.

Therapeutic response should be assessed using subjective dryness, water consumption, need for saliva substitutes, speaking, swallowing, nocturnal symptoms, salivary flow, and quality of life. Treatment should be discontinued when no meaningful benefit is obtained at a tolerated dose. Secretagogues do not regenerate destroyed glandular tissue and do not replace fluoride prevention, saliva substitutes, or treatment of oral complications.

### **3.4. Prevention and treatment of oral complications**

Oral care should include regular assessment of dental caries, periodontal status, mucosal lesions, candidiasis, tongue abnormalities, prostheses, pain, dysgeusia, and swallowing difficulties. Follow-up frequency should reflect the severity of hyposalivation, previous caries, recurrent infection, quality of oral hygiene, and the patient's ability to perform self-care.

Oral candidiasis is associated with impaired salivary clearance and reduced antimicrobial activity. Low unstimulated and stimulated salivary-flow rates are important risk factors (Billings et al. 2017; Serrano et al. 2020; Xing et al. 2024). Additional factors include dentures, poor oral hygiene, diabetes, recent antibiotic exposure, corticosteroid treatment, immunosuppression, nutritional deficiencies, and mucosal trauma. The diagnosis should be based on compatible clinical findings because *Candida* may be present as a commensal organism. Microbiological testing is particularly useful in atypical, recurrent, or treatment-resistant cases and when non-albicans species or antifungal resistance are suspected. Localized infection is generally treated with topical agents such as nystatin, miconazole, clotrimazole, or amphotericin B, depending on availability (Quindós et al. 2019; Lu 2021). Sugarfree

formulations are preferable in patients at high caries risk. Systemic fluconazole may be considered for extensive, recurrent, or refractory infection, but drug interactions, hepatic function, cardiac risk, and the possibility of antifungal resistance must be evaluated. Prevention of recurrence requires management of underlying risk factors. Dentures should be cleaned daily, removed at night, and evaluated for instability or traumatic pressure. In denture-associated stomatitis, the prosthesis and the underlying mucosa should be managed simultaneously. Routine long-term antifungal prophylaxis is generally not justified.

Angular cheilitis may have fungal, bacterial, mechanical, or nutritional causes. Treatment should address the identified factors and may include antifungal or antibacterial agents, protective ointments, correction of denture fit, and assessment of iron, folate, or vitamin B12 deficiency.

Persistent erythematous, erosive, white, indurated, or ulcerative lesions should not automatically be attributed to dryness. Oral lichen planus, lichenoid reactions, epithelial dysplasia, autoimmune blistering diseases, and malignancy should be considered. Specialist examination and biopsy may be required (Belkacem Chebil et al. 2019).

Oral burning and dysgeusia are non-specific and may be caused by candidiasis, mucosal dryness, nutritional deficiency, medication use, reflux, diabetes, neuropathy, or primary burning mouth syndrome. Antifungal treatment should not be prescribed solely on the basis of burning symptoms without evidence of infection.

Patients with marked hyposalivation require continuous, individualized caries prevention. Fluoride toothpaste, interdental cleaning, dietary modification, professional fluoride application where indicated, and frequent clinical monitoring remain central (Vivino et al. 2016; Xin et al. 2016; Price et al. 2025). Improvement in salivary secretion after pilocarpine does not eliminate the risk of dental disease and cannot replace preventive care (Hsu et al. 2019).

Periodontal disease should be treated according to established periodontal principles. Removable prostheses require careful adjustment, polished surfaces, effective hygiene, nocturnal removal, and compatible lubricants. Implant treatment is not automatically contraindicated but requires individualized risk assessment and longterm peri-implant maintenance.

### 3.5. Physical and minimally invasive therapies

| <b>Intervention</b>         | <b>Mechanism</b>                                                                               | <b>Evidence summary</b>                                                                                                                  | <b>Recommendation / References</b>                                                                      |
|-----------------------------|------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| Salivary electrostimulation | Low-intensity electrical stimulation activates neural pathways involved in salivary reflex.    | Sham-controlled feasibility trial showed improved Xerostomia Inventory scores and unstimulated salivary flow, but sample size was small. | Promising but investigational (Fedele et al. 2023).                                                     |
| Acupuncture                 | Neuromodulatory approach.                                                                      | Large randomized trial in primary Sjögren's syndrome found no superiority over placebo.                                                  | Not recommended as established treatment (Zhou et al. 2022).                                            |
| Photobiomodulation          | Modulates cellular metabolism, microcirculation, oxidative stress and inflammatory signalling. | Protocols heterogeneous; Sjögren-specific RCTs have not shown consistent benefit versus sham.                                            | Experimental/adjunctive only (Fidelix et al. 2018; Ferrandez-Pujante et al. 2022; Linares et al. 2026). |
| Sialendoscopy               | Endoscopic examination, duct dilation and irrigation.                                          | Controlled studies suggest improved salivary flow and subjective dryness in selected patients with residual glandular function.          | Most direct (though limited) evidence (Karagozoglu et al. 2021).                                        |

|                        |                                                        |                                                            |                                                                    |
|------------------------|--------------------------------------------------------|------------------------------------------------------------|--------------------------------------------------------------------|
| Intraductal irrigation | Saline irrigation of salivary ducts without endoscopy. | Improved stimulated salivary flow and xerostomia outcomes. | Supported by limited evidence; adjunctive option (Du et al. 2022). |
|------------------------|--------------------------------------------------------|------------------------------------------------------------|--------------------------------------------------------------------|

**Table 1.** Summary of evidence for physical and minimally invasive interventions for Sjögren-related xerostomia.

In summary, sialendoscopy and intraductal irrigation currently have the strongest, although still limited, clinical evidence. Electrostimulation requires larger confirmatory trials, while acupuncture and photobiomodulation cannot presently be recommended as routine treatments.

### **3.6. Systemic immunomodulatory and targeted therapies**

Systemic immunomodulatory treatment is primarily intended to control active systemic disease rather than isolated oral dryness. Its effect on salivary function depends on disease duration, baseline secretion, inflammatory activity, autoantibody status, and the extent of irreversible glandular damage. Reduction of systemic disease activity does not necessarily correspond to improvement in patient-reported xerostomia.

Hydroxychloroquine has not demonstrated a consistent clinically meaningful effect on oral dryness or salivary secretion and should not be initiated solely for xerostomia (Wang et al. 2017). Conventional immunosuppressive agents, including glucocorticoids, methotrexate, azathioprine, mycophenolate mofetil, and cyclophosphamide, may be required for systemic manifestations but are not supported as treatments for chronic oral dryness.

Rituximab, a CD20-directed B-cell-depleting antibody, did not significantly improve the principal oral-dryness endpoint in the TRACTISS trial (Bowman et al. 2017). Secondary findings suggested possible stabilization of salivary flow and improvement in glandular ultrasonographic appearance, but these effects did not establish a consistent symptomatic benefit.

Abatacept produced measurable biological effects but failed to demonstrate convincing improvement in stimulated salivary flow or dryness outcomes in a phase III trial (Baer et al. 2021). Neither rituximab nor abatacept should therefore be prescribed solely for oral sicca symptoms.

Newer targeted treatments have produced more encouraging signals. Ianalumab, which targets the BAFF receptor and promotes B-cell depletion, reduced systemic disease activity and was

associated with increased salivary flow at the highest evaluated dose (Bowman et al. 2022). However, improvement in patient-reported dryness was less consistent.

Dazodalibep, an inhibitor of CD40 ligand, improved systemic activity in one patient population and symptom burden in another (St Clair et al. 2024). Numerically greater increases in stimulated salivary flow were reported, but these differences were exploratory and not statistically definitive.

Nipocalimab blocks the neonatal Fc receptor and accelerates degradation of circulating IgG. In anti-Ro-positive patients, high-dose treatment reduced systemic disease activity and produced an encouraging salivary-flow responder signal (Noaiseh et al. 2025). Nevertheless, these findings cannot be generalized to seronegative patients, individuals with predominantly glandular symptoms, or those without residual secretion.

Current evidence therefore does not support hydroxychloroquine, conventional immunosuppressants, rituximab, or abatacept for isolated xerostomia. Ianalumab, dazodalibep, and nipocalimab may influence salivary-gland function in selected patients, but their effects require confirmation in longer and adequately powered trials.

Systemic therapy should be selected according to overall disease activity and organ involvement by an appropriate specialist. Before intensive immunomodulation, active dental infections, candidiasis, and urgent dental conditions should be treated. During therapy, patients should be monitored for infection, ulceration, impaired healing, hematological abnormalities, and adverse mucosal reactions.

Future trials should incorporate oral outcomes as predefined endpoints and stratify patients according to residual salivary flow, disease duration, glandular ultrasonography, histopathology, autoantibody profile, and molecular biomarkers. Until predictors of treatment response are established, targeted systemic therapies should not replace individualized symptomatic management and comprehensive dental prevention.

#### **4. Discussion**

The management of oral manifestations in Sjögren's syndrome remains challenging because reduced salivary secretion results from both reversible functional impairment and irreversible structural damage to the salivary glands. The available evidence indicates that no single intervention adequately addresses all aspects of the disease. Therefore, treatment should combine symptomatic relief, stimulation of residual salivary function, prevention of dental and mucosal complications, and management of systemic disease when clinically indicated.

Conventional symptomatic treatment remains the foundation of oral care. Regular hydration, saliva substitutes, sugar-free chewing gum, oral lubricants, dietary modification, and avoidance of irritating or acidic products may reduce discomfort, but their effects are temporary and they do not restore the biological properties of natural saliva (Assery 2019; Ramos-Casals et al. 2020; Assy et al. 2022; Assy et al. 2023; Price et al. 2025). Product selection should be individualized because no saliva substitute has demonstrated consistent superiority. Patients with severe hyposalivation also require intensive preventive dental care, including fluoride exposure, dietary counselling, plaque control, and frequent clinical monitoring.

Systemic muscarinic agonists, particularly pilocarpine and cevimeline, provide the strongest pharmacological evidence for increasing salivary secretion in patients with preserved glandular function (Brito-Zerón et al. 2019; Oleksak et al. 2021; Kapourani et al. 2022; Karimi et al. 2025). However, their use is limited by adverse effects such as sweating, gastrointestinal symptoms, urinary frequency, and cardiovascular or respiratory precautions. These treatments are unlikely to be effective in patients with advanced glandular destruction and should not replace saliva substitutes or preventive dental care.

Oral candidiasis, rapidly progressing dental caries, mucosal trauma, and denture related complications represent clinically important consequences of salivary-gland hypofunction. Their prevention and treatment should form an integral part of management rather than being considered secondary to xerostomia relief. Antifungal treatment should be based on clinical evidence of infection because *Candida* colonization alone does not confirm active candidiasis (Billings et al. 2017; Quindós et al. 2019; Serrano et al. 2020; Lu 2021; Xing et al. 2024). Recurrent infection requires identification of predisposing factors, including severe hyposalivation, prosthetic contamination, diabetes, antibiotic exposure, and immunosuppressive therapy.

Among physical and minimally invasive approaches, sialendoscopy and intraductal irrigation have demonstrated the most promising improvements in salivary flow and subjective dryness (Karagozoglu et al. 2021; Du et al. 2022). Nevertheless, the available studies included small, selected populations with residual salivary-gland function. Salivary electrostimulation also produced encouraging preliminary results, but larger confirmatory trials are required (Fedele et al. 2023). In contrast, acupuncture and photobiomodulation have not demonstrated consistent superiority over sham treatment in Sjögren-specific randomized trials (Fidelix et al. 2018; Ferrandez-Pujante et al. 2022; Zhou et al. 2022; Linares et al. 2026). These approaches should therefore remain adjunctive or experimental.

Conventional systemic immunomodulatory drugs, hydroxychloroquine, rituximab, and abatacept have not demonstrated consistent clinically meaningful improvement in chronic oral dryness (Bowman et al. 2017; Wang et al. 2017; Baer et al. 2021). Their use should be determined by systemic disease activity rather than isolated xerostomia. Newer targeted therapies, including iganalimumab, dazodalibep, and nipocalimab, have produced promising signals of improved systemic disease activity and, in some studies, salivary secretion (Bowman et al. 2022; St Clair et al. 2024; Noaiseh et al. 2025). However, improvement in objective salivary flow has not always correlated with patient-reported symptom relief. Longer studies are required to determine whether these therapies prevent irreversible glandular damage or reduce dental and mucosal complications.

Future clinical studies should stratify patients according to residual salivary flow, disease duration, salivary-gland ultrasonography, histopathological findings, and molecular biomarkers. Standardized outcomes should combine objective salivary measurements with xerostomia severity, oral function, candidiasis and caries incidence, adverse effects, and oral health-related quality of life.

Overall, current evidence supports an individualized and multidisciplinary treatment strategy. Patients with mild or moderate dysfunction and preserved glandular tissue may benefit from salivary stimulation, whereas those with advanced hypofunction require intensive saliva replacement, mucosal protection, and dental prevention. Emerging targeted therapies may eventually modify glandular disease, but they cannot currently replace established symptomatic and preventive oral care.

## **Conclusions**

Oral manifestations of Sjögren's syndrome require long-term, individualized, and multidisciplinary management. Conventional symptomatic treatment, including saliva substitutes, oral lubricants, dietary modification, fluoride-based prevention, and regular dental follow-up, remains the foundation of care. Pilocarpine and cevimeline may improve salivary secretion in patients with preserved glandular function, although their use is limited by systemic adverse effects. Sialendoscopy, intraductal irrigation, and electrostimulation are promising options for selected patients, but current evidence remains limited. Systemic immunomodulatory therapies should not be used solely for xerostomia. New targeted agents may improve salivary-gland function in some patients, but their longterm influence on oral symptoms, caries, candidiasis, and quality of life requires further investigation. At present, the most effective approach combines symptom relief, preservation of residual salivary function,

prevention of oral complications, and early treatment of infections and dental disease. Future studies should identify predictors of treatment response and determine whether early targeted therapy can prevent irreversible salivary-gland damage.

## **Disclosure**

Author Contributions:

Conceptualization: JG

Methodology: KO

Formal analysis: JG

Investigation: KB, KO

Data curation: KG, JK

Writing – original draft preparation: AJ, WP, KK, KG, GC

Writing – review and editing: GC, WC, KC, KO, JK

Supervision: WP, AJ

Project administration:

All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Acknowledgments: Not applicable.

Conflict of Interest: The authors declare no conflict of interest.

Declaration of the use of generative AI and AI-assisted technologies in the writing process.

During the preparation of this manuscript, the authors used ChatGPT (OpenAI) exclusively for language editing, grammar correction, and translation support. Following the use of this tool, the authors carefully reviewed and edited the manuscript and take full responsibility for the final content of the publication.

## References

- Assery MKA. Efficacy of artificial salivary substitutes in treatment of xerostomia: a systematic review. *J Pharm Bioallied Sci.* 2019;11 Suppl 1:S1–S12. doi:10.4103/JPBS.JPBS\_220\_18.
- Assy Z, Brand HS, Bikker FJ. Preferences of Sjögren's syndrome patients regarding potential new saliva substitutes. *Clin Oral Investig.* 2022;26(10):6331–6339. doi:10.1007/s00784-022-04576-w.
- Assy Z, van Santen JS, Brand HS, Bikker FJ. Use and efficacy of dry-mouth interventions in Sjögren's disease patients and possible association with perceived oral dryness and patients' discomfort. *Clin Oral Investig.* 2023;27(9):5529–5537. doi:10.1007/s00784-023-05172-2.
- Azuma N, Katada Y, Sano H. Deterioration in saliva quality in patients with Sjögren's syndrome: impact of decrease in salivary epidermal growth factor on the severity of intraoral manifestations. *Inflamm Regen.* 2018;38:6. doi:10.1186/s41232-018-0062-0.
- Baer AN, Gottenberg JE, St Clair EW, et al. Efficacy and safety of abatacept in active primary Sjögren's syndrome: results of a phase III, randomised, placebo-controlled trial. *Ann Rheum Dis.* 2021;80(3):339–348. doi:10.1136/annrheumdis-2020-218599.
- Belkacem Chebil R, Oueslati Y, Marzouk M, Ben Fredj F, Oualha L, Douki N. Oral lichen planus and lichenoid lesions in Sjögren's syndrome patients: a prospective study. *Int J Dent.* 2019;2019:1603657. doi:10.1155/2019/1603657.
- Billings M, Dye BA, Iafolla T, Grisius M, Alevizos I. Elucidating the role of hyposalivation and autoimmunity in oral candidiasis. *Oral Dis.* 2017;23(3):387–394. doi:10.1111/odi.12626.
- Błochowiak K, Olewicz-Gawlik A, Polańska A, et al. Oral mucosal manifestations in primary and secondary Sjögren syndrome and dry mouth syndrome. *Postepy Dermatol Alergol.* 2016;33(1):23–27. doi:10.5114/pdia.2016.57764.
- Bowman SJ, Everett CC, O'Dwyer JL, et al. Randomized controlled trial of rituximab and cost-effectiveness analysis in treating fatigue and oral dryness in primary Sjögren's syndrome. *Arthritis Rheumatol.* 2017;69(7):1440–1450. doi:10.1002/art.40093.
- Bowman SJ, Fox R, Dörner T, et al. Safety and efficacy of subcutaneous ivalumab (VAY736) in patients with primary Sjögren's syndrome: a randomised, double-blind, placebo-controlled, phase 2b dose-finding trial. *Lancet.* 2022;399(10320):161–171. doi:10.1016/S0140-6736(21)02251-0.

- Brito-Zerón P, Retamozo S, Kostov B, et al. Efficacy and safety of topical and systemic medications: a systematic literature review informing the EULAR recommendations for the management of Sjögren's syndrome. *RMD Open*. 2019;5(2):e001064. doi:10.1136/rmdopen-2019-001064.
- Chaudhury NMA, Proctor GB, Karlsson NG, Carpenter GH, Flowers SA. Reduced mucin-7 (Muc7) sialylation and altered saliva rheology in Sjögren's syndrome-associated oral dryness. *Mol Cell Proteomics*. 2016;15(3):1048–1059. doi:10.1074/mcp.M115.052993.
- Du H, Fu Z, Zhong Y, et al. A randomized controlled trial to verify the irrigation of salivary glands in relieving xerostomia in patients with Sjögren's syndrome. *Front Immunol*. 2022;13:1039599. doi:10.3389/fimmu.2022.1039599.
- Fedele S, Al-Hamad A, Mercadante V, Porter S, Isenberg D, Poveda-Gallego A, et al. Long-term effectiveness of a novel intra-oral electrostimulator for the treatment of dry mouth in patients with Sjögren's syndrome: a randomised sham-controlled feasibility study—LEONIDAS-1. *J Oral Pathol Med*. 2023;52(7):619–627. doi:10.1111/jop.13452.
- Ferrandez-Pujante A, Pons-Fuster E, López-Jornet P. Efficacy of photobiomodulation in reducing symptomatology and improving the quality of life in patients with xerostomia and hyposalivation: a randomized controlled trial. *J Clin Med*. 2022;11(12):3414. doi:10.3390/jcm11123414.
- Fidelix T, Czapkowski A, Azjen S, Andriolo A, Horvath Neto P, Trevisani V. Low-level laser therapy for xerostomia in primary Sjögren's syndrome: a randomized trial. *Clin Rheumatol*. 2018;37(3):729–736. doi:10.1007/s10067-017-3898-9.
- Hsu CY, Hung KC, Lin MS, et al. The effect of pilocarpine on dental caries in patients with primary Sjögren's syndrome: a database prospective cohort study. *Arthritis Res Ther*. 2019;21:251. doi:10.1186/s13075-019-2031-7.
- Kapourani A, Kontogiannopoulos KN, Barmapalexis P. A review on the role of pilocarpine on the management of xerostomia and the importance of the topical administration systems development. *Pharmaceuticals (Basel)*. 2022;15(6):762. doi:10.3390/ph15060762.
- Karagozoglu KH, Vissink A, Forouzanfar T, et al. Sialendoscopy increases saliva secretion and reduces xerostomia up to 60 weeks in Sjögren's syndrome patients: a randomized controlled study. *Rheumatology (Oxford)*. 2021;60(3):1353–1363. doi:10.1093/rheumatology/keaa284.
- Karimi M, Ahmadi Hajikolaei F, Hoseinpour F, et al. Efficacy of cevimeline on xerostomia in Sjögren's syndrome patients: a systematic review and meta-analysis of randomized

- clinical trials. *Curr Ther Res Clin Exp.* 2025;102:100770. doi:10.1016/j.curtheres.2024.100770.
- Linares MF, dos Santos França TD, Ferreira MCBM, do Nascimento MG, Duarte ALBP, Gueiros LA. Laser acupuncture on the management of xerostomia in Sjögren's disease: a randomized clinical trial. *Oral Dis.* 2026 Apr 20. Online ahead of print. doi:10.1111/odi.70241.
- Lu SY. Oral candidosis: pathophysiology and best practice for diagnosis, classification, and successful management. *J Fungi (Basel).* 2021;7(7):555. doi:10.3390/jof7070555.
- Muszyński D, Kucharski R, Marek-Trzonkowska N, et al. Treatment of xerostomia in Sjögren's syndrome—what effect does it have on the oral microbiome? *Front Cell Infect Microbiol.* 2025;15:1484951. doi:10.3389/fcimb.2025.1484951.
- Ngo DYJ, Thomson WM. An update on the lived experience of dry mouth in Sjögren's syndrome patients. *Front Oral Health.* 2021;2:767568. doi:10.3389/froh.2021.767568.
- Noaiseh G, Sivils KL, Campbell K, et al. Efficacy and safety of nipocalimab in patients with moderate-to-severe Sjögren's disease (DAHLIAS): a randomised, phase 2, placebo-controlled, double-blind trial. *Lancet.* 2025;406(10518):2435–2448. doi:10.1016/S0140-6736(25)01430-8.
- Oleksak P, Novotny M, Patocka J, et al. Neuropharmacology of cevimeline and muscarinic drugs—focus on cognition and neurodegeneration. *Int J Mol Sci.* 2021;22(16):8908. doi:10.3390/ijms22168908.
- Price EJ, Benjamin S, Bombardieri M, et al. British Society for Rheumatology guideline on management of adult and juvenile onset Sjögren disease. *Rheumatology (Oxford).* 2025;64(2):409–439. doi:10.1093/rheumatology/keae152.
- Qi W, Tian J, Wang G, et al. Advances in cellular and molecular pathways of salivary gland damage in Sjögren's syndrome. *Front Immunol.* 2024;15:1405126. doi:10.3389/fimmu.2024.1405126.
- Quindós G, Gil-Alonso S, Marcos-Arias C, et al. Therapeutic tools for oral candidiasis: current and new antifungal drugs. *Med Oral Patol Oral Cir Bucal.* 2019;24(2):e172–e180. doi:10.4317/medoral.22978.
- Ramos-Casals M, Brito-Zerón P, Bombardieri S, et al. EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies. *Ann Rheum Dis.* 2020;79(1):3–18. doi:10.1136/annrheumdis-2019-216114.

- Saúco C, Rus MJ, Nieto MR, et al. Hyposalivation but not Sjögren's syndrome associated with microbial dysbiosis in women. *Front Microbiol.* 2023;14:1240891. doi:10.3389/fmicb.2023.1240891.
- Serrano J, López-Pintor RM, González-Serrano J, Fernández-Castro M, Casañas E, Hernández G. Oral lesions in Sjögren's syndrome: a systematic review. *Med Oral Patol Oral Cir Bucal.* 2018;23(4):e391–e400. doi:10.4317/medoral.22286.
- Serrano J, López-Pintor RM, Ramírez L, et al. Risk factors related to oral candidiasis in patients with primary Sjögren's syndrome. *Med Oral Patol Oral Cir Bucal.* 2020;25(5):e700–e705. doi:10.4317/medoral.23719.
- St Clair EW, Baer AN, Ng WF, et al. CD40 ligand antagonist dazodalibep in Sjögren's disease: a randomized, double-blinded, placebo-controlled, phase 2 trial. *Nat Med.* 2024;30(6):1583–1592. doi:10.1038/s41591-024-03009-3.
- Teos LY, Zhang Y, Cotrim AP, et al. IP3R deficit underlies loss of salivary fluid secretion in Sjögren's syndrome. *Sci Rep.* 2015;5:13953. doi:10.1038/srep13953.
- Thurtle E, Grosjean A, Steenackers M, et al. Epidemiology of Sjögren's: a systematic literature review. *Rheumatol Ther.* 2024;11(1):1–17. doi:10.1007/s40744-023-00611-8.
- Vivino FB, Carsons SE, Foulks G, et al. New treatment guidelines for Sjögren's disease. *Rheum Dis Clin North Am.* 2016;42(3):531–551. doi:10.1016/j.rdc.2016.03.010.
- Vujović S, Desnica J, Stevanović M, et al. Oral health and oral health-related quality of life in patients with primary Sjögren's syndrome. *Medicina (Kaunas).* 2023;59(3):473. doi:10.3390/medicina59030473.
- Wang SQ, Zhang LW, Wei P, Hua H. Is hydroxychloroquine effective in treating primary Sjögren's syndrome: a systematic review and meta-analysis. *BMC Musculoskelet Disord.* 2017;18:186. doi:10.1186/s12891-017-1543-z.
- Xin W, Leung KCM, Lo ECM, Mok MY, Leung MH. A randomized, double-blind, placebo-controlled clinical trial of fluoride varnish in preventing dental caries of Sjögren's syndrome patients. *BMC Oral Health.* 2016;16:102. doi:10.1186/s12903-016-0296-7.
- Xing Y, Shi H, Wang C, Yang Y. Clinical features and risk factors for Sjögren's syndrome patients suffering from oral candidiasis in Shanxi, China. *BMC Oral Health.* 2024;24:812. doi:10.1186/s12903-024-04595-x.
- Zhou X, Xu H, Chen J, et al. Efficacy and safety of acupuncture on symptomatic improvement in primary Sjögren's syndrome: a randomized controlled trial. *Front Med (Lausanne).* 2022;9:878218. doi:10.3389/fmed.2022.878218.