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Role of Plant-Based Artificial Saliva in Dentistry- A Review.

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ABSTRACT

Background: Millions of patients worldwide suffer from xerostomia and salivary gland hypofunction, which are clinically difficult disorders brought on by head and neck radiation, autoimmune diseases like Sjögren syndrome, polypharmacy, and aging. The complex physicochemical and antibacterial milieu of natural saliva cannot be replicated by conventional synthetic artificial saliva preparations based on carboxymethylcellulose (CMC), which are linked to patient non-adherence and only provide temporary relief. Utilizing the mucoadhesive, lubricating, anti-inflammatory, and antibacterial qualities of botanical chemicals, plant-based formulations have become an attractive option within the last ten years.

Objective: The role of plant-based artificial saliva in dentistry, the makeup of representative phytotherapy-derived formulations, new plant-derived biotechnologies, clinical data from randomized controlled trials and systematic reviews, and future research directions are all thoroughly reviewed in this article.

Methods: A narrative review of publications published between 2004 and 2026 was carried out using the PubMed, ScienceDirect, Cochrane Library, and Web of Science databases. Recent patent literature and active clinical trial registries (ClinicalTrials.gov) were also included.

Results: Malva sylvestris, Alcea digitata, Althaea officinalis, Matricaria chamomilla, Linum usitatissimum, aloe vera, coconut oil, lycopene-enriched olive oil, licorice root (Glycyrrhiza glabra), and the novel sugarcane cystatin CANECPI-5 are among the plant-derived agents that show notable improvements in xerostomia-related symptoms, patient quality of life, oral lubrication, and enamel protection. The physicochemical characteristics of hydrocolloid plant polysaccharides (Calendula officinalis, Fucus sp., and Lichen islandicus) resemble those of salivary mucin MUC5B. The cutting edge of formulation research is represented by biomimetic pellicle-based techniques and nanotechnology-assisted delivery.

Conclusion: Plant-based artificial saliva formulations offer a pharmacologically versatile, patient-acceptable, and scientifically established method of treating salivary hypofunction. Translating these agents

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into standard dentistry treatment will require standardizing the phytochemical composition, conducting thorough multicenter randomized trials, and integrating nanotechnology.

KEYWORDS: Artificial saliva; Xerostomia; Plant-based; phytotherapy; Salivary substitutes; Oral health.

INTRODUCTION

Saliva is an incredibly complicated biological fluid that plays essential roles in maintaining systemic and dental equilibrium. Saliva functions as a lubricant, buffering agent, antimicrobial shield, initiator of digestion, and facilitator of taste, speech, and deglutition. It is mainly produced by the three pairs of major salivary glands—parotid, submandibular, and sublingual—as well as hundreds of minor glands dispersed throughout the oral mucosa.

Patients who have impaired salivary flow develop xerostomia, which is a subjective feeling of dry mouth that frequently, but not always, coexists with salivary hypofunction (a reduction in salivary production). According to estimates, the prevalence of xerostomia in the general adult population is between 20 and 30 percent worldwide. In individuals with Sjögren syndrome (SS), this number rises to over 60 percent, and in those who have received high-dose radiation to the head and neck region, it approaches near-total salivary gland ablation. [1,2] The most prevalent aetiological factor in populations living in the community is polypharmacy, especially with anticholinergic, antihypertensive, antidepressant, and diuretic medications. [3] Prolonged xerostomia has many more negative effects than just discomfort. Well-established aftereffects include accelerated dental caries, enamel erosion, periodontal disease, oral candidiasis, mucositis, difficulties wearing detachable prostheses, dysphagia, and malnutrition. [4,5] Radiation-induced salivary gland damage is often irreversible in individuals with head and neck cancer (HNC), necessitating a lifelong need for salivary replacement therapy. When systemic sialagogues like pilocarpine and cevimeline are ineffective, topical symptomatic alleviation with salivary substitutes is the cornerstone of first-line treatments, according to the European League Against Rheumatism (EULAR) treatment guidelines for SS. [6] In order to approximate the ionic composition of natural saliva, conventional commercial saliva substitutes are primarily composed of synthetic or semi-synthetic polymeric thickeners, such as carboxymethylcellulose (CMC), hydroxypropyl methylcellulose (HPMC), xanthan gum, and polyethylene glycol, supplemented with electrolytes (sodium, potassium, calcium, phosphate, and bicarbonate). [7] These agents provide short-term oral moistening, but they have significant drawbacks: they have little antimicrobial activity, lack the rheological complexity, viscoelastic behavior, and salivary mucin (MUC5B/MUC7)-mimicking qualities of natural saliva, and require frequent application due to their short oral residence time, which hinders patient adherence. [8, 9] The US Food and Drug Administration was informed by patient advocacy groups in 2022 that "current xerostomia treatment approaches are ineffective, temporary and costly." [10]

In light of this, plant-based artificial saliva formulations have garnered significant and expanding scientific attention. A variety of substances with mucilaginous polysaccharides that can simulate mucin lubrication, phenolic antioxidants with anti-inflammatory activity, terpenoids and saponins with antimicrobial qualities, and new plant-derived proteins that can form protective acquired pellicle analogues on enamel surfaces are included in the botanical pharmacopoeia. [11, 12] The objectives of this review are to: (i) describe the function of artificial saliva in dental and medical practice; (ii) outline the composition of well-known and newly developed plant-based formulations; (iii) critically assess clinical evidence from systematic reviews and randomized controlled trials; (iv) talk about new biotechnological platforms; and (v) outline future research directions in this field.

Role of Artificial Saliva in Dentistry

1. Oral Mucosal Protection and Lubrication

Restoring oral mucosal hydration and lubrication is the main therapeutic objective of any salivary substitute.

This will avoid mucosal fragility and alleviate the subjective discomfort of mouth dryness. [13] High-molecular-weight mucins (mostly MUC5B) in natural saliva do this by forming a viscoelastic gel layer over the oral epithelium that is very lubricating in both low-shear (resting) and high-shear (masticatory) situations. Mucilages generated from plants are in a perfect position to imitate this function because they are structurally similar networks of polysaccharides. [14]

2. Preventing Dental Caries and Protecting Enamel

Calcium and phosphate ions for remineralization, bicarbonate for acid neutralization, antimicrobial proteins (lysozyme, lactoferrin, immunoglobulin A, peroxidases), and the acquired enamel pellicle (AEP), a thin adsorbed protein film that controls the kinetics of enamel demineralization, are some of the ways that natural saliva offers cariostatic protection. Hyposalivation creates an extremely cariogenic intraoral milieu when there is insufficient salivary flow. [15] It has been demonstrated that plant-based alternatives that are enhanced with calcium, phosphate, and phytochemicals like CANECPI-5 (a sugarcane cystatin) can restore AEP-analogous protective layers on enamel. [16]

3. Microbiome Balance and Antimicrobial Homeostasis

Dysbiosis, a pathogenic change in the oral microbiome marked by the proliferation of *Candida albicans*, *Lactobacillus* species, and *Streptococcus mutans*, is linked to salivary hypofunction. Polyphenols, flavonoids, terpenes, and essential oils from plants like aloe vera, coconut oil, licorice root, and tea tree have significant inhibitory effects against cariogenic and opportunistic oral pathogens, while conventional synthetic alternatives have negligible antimicrobial activity. [11] Thus, using phytoantimicrobial-enriched saliva substitutes to restore microbiome balance fills a vital gap.

4. Assistance for Geriatric and Prosthodontic Patients

Because denture retention and mucosal tissue tolerance depend on sufficient salivary lubrication, patients with complete or partial removable dentures have much inferior outcomes in the context of xerostomia. Elderly individuals are especially at risk since they frequently have both age-related glandular involution and polypharmacy-induced hyposalivation. Because of their favorable tolerance profiles and improved mucoadhesive qualities, plant-derived saliva substitutes provide useful advantages in this situation. [17]

5. Oncological Dentistry

Patients with head and neck cancer who receive radiation therapy experience dose-dependent, frequently irreversible parotid gland damage. In addition to significantly raising the incidence of dental cavities, post-irradiation xerostomia significantly reduces swallowing, nutritional intake, and quality of life. Over the course of a two-month intervention period, a randomized controlled experiment showed that providing sufficient saliva replacements considerably improved swallowing skills and clinical nutritional status in post-radiotherapy HNC patients. [12] New plant-derived possibilities, such CANECPI-5, are created especially to address this population's elevated caries risk. [16]

Composition of plant-based artificial saliva formulations

1 Polysaccharides that are mucilaginous

Hydrocolloid polysaccharides—complex branched carbohydrate polymers with a high water-binding capacity and gel-forming capabilities that closely resemble the viscoelastic behavior of salivary mucins—are the most extensively studied plant-derived components for salivary substitution. Members of the Malvaceae family, including *Malva sylvestris* and *Alcea digitata* (Boiss.), have long been used in traditional Persian and Mediterranean medicine. Their mucilages, which are made up of residues of arabinose, galactose, galacturonic acid, and rhamnose, produce viscous aqueous solutions that have the ability to buffer pH, stick to mucosal surfaces, and have anti-inflammatory properties through the suppression of pro-inflammatory cytokines. [17-19]

Althaea officinalis, or marshmallow root, produces flavonoids and pectin-like mucopolysaccharides that create protective films across the oral mucosa. These compounds have been added to combination mouthwashes that have been tested for the treatment of xerostomia and oral mucosal problems. [20] *Linum usitatissimum* (flaxseed/linseed) mucilage, which consists of arabinoxylans, rhamnogalacturonans, and other heteropolysaccharides, is a well-characterized candidate for saliva replacement due to its exceptional rheological properties, excellent water-holding capacity, and established mucoadhesive properties at viscosities of 1–30 mPa·s in aqueous solution. [21]

2 Formulations of Aloe Vera and Coconut Oil Combinations

Acemannan (a β -1,4-acetylated mannan), glycoproteins, polyphenols, and antimicrobial peptides are all present in aloe vera gel. Aloe vera adds moisturizing, anti-plaque, antibacterial, and antifungal qualities to CMC-based gels at a 10% concentration while improving the base formulation's biocompatibility. A CMC-based gel containing 10% aloe vera and 10% coconut oil was compared to a traditional CMC gel in a crossover randomized controlled trial (NCT04252209) involving 24 individuals with primary or secondary Sjögren syndrome. The study, which was published in 2025, showed that the two preparations were equally effective in lowering xerostomia symptoms and enhancing quality of life as determined by the clinical oral dryness (COD) score and the Xerostomia Quality of Life Scale (XeQoLS). [22]

Lauric acid and caprylic acid, two medium-chain fatty acids found in coconut oil (*Cocos nucifera*), have been shown to have antibacterial and antifungal properties against oral infections such as *Candida albicans* and *Streptococcus mutans*. It is a useful supplement to phytotherapy-based alternatives because of its lubricating qualities and excellent tolerance. [22]

3 Hydrocolloid Polysaccharides that Replicate MUC5B Salivary Mucin

The suitability of aqueous plant extracts of *Calendula officinalis*, *Fucus sp. thalli*, and lichenan from *Lichen islandicus* as MUC5B-mimicking saliva substitutes was thoroughly examined in a seminal 2024 study by Winter et al. (Pharmaceutics, University of Graz). [23] The researchers discovered that these plant polysaccharides had physicochemical characteristics that were similar to those of the gel-forming mucin MUC5B, the predominant structural protein of the salivary mucous layer, using gas chromatography-mass spectrometry (GC-MS), nuclear magnetic resonance (NMR), size exclusion chromatography (SEC), and measurements of pH, osmolality, buffering capacity, and viscoelasticity—including in vitro adhesion assays on TR146 oral epithelial cells. These results are important because they provide a rigorous mechanism for creating botanical formulations that replace mucin in the first generation.

4 Licorice Root with Olive Oil Enhanced with Lycopene

Utilizing the strong antioxidant potential of lycopene, a carotenoid, and the proven oral mucosal protective qualities of oleic acid and olive polyphenols (hydroxytyrosol, oleuropein), lycopene-enriched virgin olive oil formulations have been tested in clinical trials for radiation-induced xerostomia. [24] Glycyrrhizin, glabridin, liquiritin, and isoliquiritigenin—compounds with significant anti-*Streptococcus mutans* action, anti-inflammatory properties, and a buffering capacity important to caries prevention—are found in licorice root (*Glycyrrhiza glabra*). The pharmacological effectiveness and safety of licorice in clinical dentistry settings were validated by a systematic study (Kumari et al., 2020). [25]

Combining traditional excipients (electrolytes, pH buffers, humectants) with functional botanical ingredients (mucilaginous polysaccharides, antimicrobial phytochemicals, antioxidants, and anti-inflammatory compounds) to produce a physiologically coherent oral substitute is a distinguishing characteristic of plant-based artificial saliva. The main plant-derived agents and their primary functional characteristics are compiled in Table 1.

Plant Source	Active Constituent	Functional Role	Delivery Form	Key Studies
Malva sylvestris (Common Mallow)	Mucilaginous polysaccharides (arabinose, galactose, rhamnose)	Lubricant, anti-inflammatory, mucoadhesive	Powder, spray, rinse	Ameri et al., 2016; Heydarirad et al., 2017
Alcea digitata (Boiss.)	Mucilage, antioxidants	Anti-inflammatory, expectorant, lubrication	Powder, spray	Mosavat & Ameri, 2017; NCT02854358
Althaea officinalis (Marshmallow root)	Pectin-like mucopolysaccharides, flavonoids	Mucoadhesive, anti-inflammatory, enamel coating	Rinse, gel	Kręgielczak et al., 2023; systematic reviews
Matricaria chamomilla (Chamomile)	α -bisabolol, apigenin, mucilage	Anti-inflammatory, antifungal, soothing	Rinse, combination formulas	Kręgielczak et al., 2023
Linum usitatissimum (Flaxseed / Linseed)	Water-soluble polysaccharides, arabinoxylans, galacturonans	Lubrication, mucoadhesion, sustained-release carrier	Gel, spray, mucilage extract	Kręgielczak et al., 2023; Winter et al., 2024
Aloe vera (Aloe barbadensis)	Acemannan (β -glucomannan), glycoproteins, polyphenols	Moisturising, antimicrobial, antifungal, anti-inflammatory	Gel (10% incorporation into CMC base)	NCT04252209; Mahmoud et al., 2025
Cocos nucifera (Coconut oil)	Medium-chain fatty acids (lauric acid, caprylic acid)	Antimicrobial, antifungal, lubricating	Oil pull, gel (10% in CMC base)	Mahmoud et al., 2025
Lycopersicon esculentum / Olea europaea (Lycopene olive oil)	Lycopene (carotenoid), oleic acid, polyphenols	Antioxidant, anti-inflammatory, mucosal protective	Spray, gel	Garrido et al., 2013; EJTAS Review, 2024
Glycyrrhiza glabra (Licorice root)	Glycyrrhizin, glycyrrhizic acid, liquiritin, glabridin	Antimicrobial (anti-S. mutans), anti-inflammatory, buffering	Extract, powder	Kumari et al., 2020; EJTAS Review, 2024
Zingiber officinale (Ginger)	Gingerols, shogaols, zingiberene	Salivary stimulant, antinausea, anti-inflammatory	Capsule, rinse	MDPI Nonpharmacological Review, 2024

Plant Source	Active Constituent	Functional Role	Delivery Form	Key Studies
Calendula officinalis (Marigold)	Hydrocolloid polysaccharides, flavonoids, saponins	MUC5B-mimicking, mucoadhesive, anti-inflammatory	Aqueous extract	Winter et al., Pharmaceutics 2024
Saccharum officinarum (Sugarcane) – CANECPI-5	Cystatin-domain protein (CANECPI-5), lab-modified	AEP mimic, enamel binding, anti-demineralisation, antimicrobial	Mouthwash spray	Silva et al., J Dent 2025; ScienceDaily 2026
Fucus sp. (Brown Seaweed / Bladderwrack)	Fucoidans, alginic acid, laminarin	Viscoelastic gel former, MUC5B-mimicking, lubricant	Aqueous extract	Winter et al., Pharmaceutics 2024
Lichen islandicus (Iceland Moss)	Lichenan (β -glucan-type polysaccharide), isolichenan	Gel-forming, mucoadhesive, anti-inflammatory	Aqueous extract	Winter et al., Pharmaceutics 2024

Emerging plant-derived technologies

A. The Acquired Pellicle Paradigm: CANECPI-5

The engineering of CANECPI-5, a cystatin-domain protein isolated from sugarcane (*Saccharum officinarum*) and further modified in the lab, as the active principle of a mouthwash-format artificial saliva is arguably the most theoretically novel breakthrough in plant-derived artificial saliva. According to published research from the University of São Paulo's Bauru School of Dentistry (FOB-USP), CANECPI-5 has a strong affinity for hydroxyapatite and binds directly to enamel surfaces to form a protective "acquired pellicle analogue" that significantly lowers bacterial adhesion and acid-induced demineralization both in vitro and in vivo. [16]

The formulation was specifically assessed for HNC patients with radiation-induced xerostomia and high caries risk. The study was published in the Journal of Dentistry in 2025. Bacterial activity and tooth demineralization were considerably decreased in comparison to the control when CANECPI-5 was used in conjunction with fluoride and xylitol. In contrast to all other saliva substitute techniques, CANECPI-5 is "the first product to use the concept of the acquired pellicle to treat xerostomia," according to the researchers. In order to enable direct home application, further research attempts to link CANECPI-5 with vitamin E as a lipophilic carrier. [16]

B. Plant-Derived Delivery Assisted by Nanotechnology

One way to get around the inherent drawbacks of phytotherapy-based alternatives, such as their quick oral clearance, vulnerability to enzymatic degradation, and inconsistent bioavailability, is to encapsulate plant-derived bioactives in lipid nanoparticles, solid lipid nanoparticles (SLNs), nanoemulsions, and polymeric nanocapsules. In their review of the use of drug delivery nanosystems for the development of saliva substitutes, Köysik et al. found that, when compared to unmodified commercial substitutes, the incorporation of antimicrobial plant extracts into nanocarriers significantly improved antimicrobial profiles

against *Candida* spp. and cariogenic bacteria. [26]

When coupled with plant-derived eugenol (clove oil, *Syzygium aromaticum*), flaxseed mucilage/HPMC composite nanofibers have been studied as mucoadhesive matrices for drug administration in periodontitis, exhibiting synergistic antibacterial action. [27] The same composite architecture can be used to build saliva substitutes by utilizing the mucoadhesive and sustained-release qualities of flaxseed polysaccharides to increase oral residence time, which is a fundamental drawback of existing formulations.

C. Smart Release Platforms and Biomimetic Hydrogels

Plant-polysaccharide-based hydrogels with stimuli-responsive characteristics have been made possible by developments in polymer science. Cross-linking cellulose derivatives from plant sources, sodium alginate from brown algae, and carrageenan from red algae can create thixotropic gels that mimic the shear-thinning behavior of natural mucin networks. Such hydrogels provide the potential for responsive mucoadhesive saliva analogues that release antimicrobial agents upon pH perturbation (e.g., during bacterial acid production) when enriched with plant bioactives like aloe vera acemannan or licorice polyphenols, offering an intelligent, "on-demand" cariostatic response. [28]

4.4 Xanthan Gum and Related Microbial/Plant Polysaccharides

Xanthan gum, which has drawn special attention as a rheological modifier in artificial saliva. Mimicking the rheological characteristics of natural saliva alone can significantly improve quality of life for radiation-induced xerostomia, according to a 2025 Chemical & Engineering News analysis that emphasized the potential of xanthan gum-based formulations as scalable, reasonably priced substitutes for mucin-containing products. Xanthan gum systems provide an affordable platform for using phytotherapy in saliva replacement when paired with antimicrobials generated from plants. [29]

Research studies on efficacy of plant-based artificial saliva

1 Malvaceae Preparations in Randomized Controlled Trials

Iranian individuals suffering from radiation-induced xerostomia participated in two historic randomized controlled trials that compared the commercial artificial saliva Hypozalix (Biocodex, France) with *Malva sylvestris*/*Alcea digitata* herbal treatments. Ameri et al. (2016) assessed 62 participants (mean age 51.5 years) over a four-week period and found that the herbal group's xerostomia visual analogue scale (VAS) scores were considerably lower than those of the Hypozalix group at both two and four weeks ($p < 0.05$). Heydarirad et al. (2017) then used quality of life as the main endpoint in a parallel-group design with 60 patients who had finished radiation therapy at least two months before enrollment. When compared to artificial saliva, the herbal preparation exhibited improvement in more xerostomia-related QoL domains, and the herbal group's overall QoL improvement was statistically significantly better. [30,31]

2 *Althaea officinalis*, Chamomile, and Flaxseed

In a narrative review of the Polish dental literature, Kiechielczak et al. (2023) focused on the use of marshmallow root (*Althaea officinalis*), flaxseed (*Linum usitatissimum*), and chamomile (*Matricaria flos*) in the treatment of xerostomia and oral mucosal diseases. According to the review, all three treatments have clinically significant mucosal relaxing, anti-inflammatory, and lubricating actions. Patients with chronic xerostomia who need regular topical application will benefit most from marshmallow root. [20]

3 Sjögren Syndrome and Aloe Vera and Coconut Oil

In a crossover RCT (NCT04252209), Mahmoud et al. (2025) compared a traditional CMC gel (B-Gel) with an aloe vera/coconut oil/CMC combination gel (A-Gel) in 24 female patients with Sjögren syndrome (mean age 46.96 ± 11.86 years; mean xerostomia duration 16.58 months). Two weeks of treatment were given to each arm, followed by a seven-day washout period. Salivary candidal load, the modified XeQoLS, the Clinical Oral Dryness Score (CODs), and subjective oral dryness (Xerostomia Index) were among the outcome measures. There was no discernible between-group difference, and both gels provided comparable, statistically significant improvements across all outcomes. Although biologically reasonable, the

antibacterial advantage of aloe vera and coconut oil was not discernible under these study conditions, as evidenced by the lack of significant differences in salivary candidal load across groups. Neither formulation was associated with any significant adverse effects. [22]

4 Evidence from Systematic Review

Seven of the 37 articles that were obtained from PubMed and ScienceDirect (2004–2024) by a PRISMA-protocol-based fast systematic review that was published in the European Journal of Theoretical and Applied Sciences (2024) satisfied strict inclusion criteria. *Malva sylvestris*/*Alcea digitata*, lycopene-enriched virgin olive oil, *Matricaria chamomilla*/*Linum usitatissimum* combos, *Althaea officinalis*, and licorice root all showed statistically significant improvements in xerostomia symptoms and patient quality of life, according to the synthesis. [11]

Kontogiannopoulos et al.'s more comprehensive systematic review (Pharmaceuticals, 2023) examined natural products as xerostomia treatment modalities across a wider range of plant compounds, confirming the antimicrobial, moisturizing, and anti-inflammatory qualities of several botanical agents and advocating for standardized phytochemical quantification, clearly defined outcome measures, and multicenter designs in future trials. [32]

5 Journal of Dentistry 2025: CANECPI-5

CANECPI-5 is the most latest and possibly the most technologically sophisticated clinical-adjacent evidence. In vitro and in vivo (using a bovine enamel model), Silva et al. (Journal of Dentistry, 2025) assessed a novel mouthwash formulation that included CANECPI-5 either alone or in combination with fluoride (225 ppm NaF) and xylitol (0.5%). When compared to the control, daily single-application CANECPI-5 mouthwash dramatically decreased enamel demineralization (measured as calcium and phosphate loss) and changed the composition of the acquired enamel pellicle. With noticeably reduced *S. mutans* and *Lactobacillus* sp. [16] bacterial populations, the combination with fluoride and xylitol generated the strongest antibacterial and anticaries effect. These findings, which are regarded as the first use of the acquired pellicle idea in the therapy of xerostomia, have been acknowledged globally as a paradigm-shifting development.

6 Oral Moisturizing Jelly and Saliva Replacements for Patients After Radiation Therapy

In a double-blind RCT, Jongburanukit et al. (2020) randomly assigned 62 post-radiation HNC patients to either topical GC Dry Mouth Gel or edible saliva substitute oral moisturizing jelly (OMJ) for a duration of two months. The multisystem advantage of successful salivary replacement in this cohort was confirmed at one and two months, when both therapies significantly improved clinical nutritional status, swallowing time, swallowing issue scores (EAT-10), and subjective and objective dry mouth scores ($p < 0.0001$). [12]

7 Salivary Conditioning Film Interactions and Lubrication Mechanisms

Vinke et al. (2020) investigated the ability of six commercial saliva substitutes, including gel and spray formulations, to interact with the natural salivary conditioning film (SCF) and modify its viscoelastic properties using quartz crystal microbalance with dissipation (QCM-D). Three solutions improved lubrication in xerostomic conditions by increasing the structural softness of the SCF; plant-based formulations with gel structures outperformed spray formats in maintaining this effect. [33] The logical design of plant-based alternatives that not only enhance the oral environment but also modify the residual SCF to increase lubricant efficacy is informed by these mechanistic insights.

DISCUSSION

A strong scientific argument for plant-based artificial saliva as a clinically significant, mechanistically sound, and patient-acceptable alternative—and supplement—to traditional synthetic salivary substitutes is supported by the body of research examined in this article. Focused discussion is necessary on a number of

underlying themes.

1 Botanical Formulations Are Better Than Traditional CMC Products

In terms of reducing xerostomia symptoms and enhancing quality of life, plant-based formulations—specifically, *Malva sylvestris*/*Alcea digitata*, *Althaea officinalis*, and aloe vera/coconut oil combinations—show equivalency or superiority to carboxymethylcellulose-based products, according to the most consistent finding across clinical trials and systematic reviews. Because plant polysaccharides form viscoelastic networks with chain entanglement dynamics, shear-thinning behavior, and surface adhesion properties that more closely resemble salivary MUC5B than do linear CMC polymers, phytomucilages have a mechanistic advantage over CMC. [7, [23] Additionally, antibacterial, antioxidant, and anti-inflammatory qualities that are completely lacking in traditional alternatives are intrinsic to plant-derived formulations; these qualities are directly related to the dysbiotic oral environment that results from prolonged xerostomia. [8]

2 CANECPI-5 and the Acquired Pellicle Concept

Particular attention should be paid to the conceptual breakthrough embodied by CANECPI-5. The goal of all previous salivary substitute techniques has been to replace saliva's fluid bulk characteristics (viscosity, lubrication, and ionic content) without providing external protection for the enamel surface. The main physicochemical interface between the oral environment and enamel mineral is the acquired enamel pellicle, which is the selectively adsorbed protein coating that covers all tooth surfaces within minutes of eruption. A vital protective barrier is eliminated when it is disrupted or absent, as happens during and after radiation therapy. Using a plant-derived protein with an innate affinity for hydroxyapatite, CANECPI-5 is the first medication specifically created to restore this pellicle layer. This represents a mechanistically innovative strategy that targets the underlying cause of post-radiation hypercaries rather than just treating its symptoms. [16]

3 Methodological Difficulties and Current Evidence Limitations

Despite this promising body of research, the strength of current conclusions is tempered by a number of limitations. First, small sample sizes (range: 20–62 participants), short follow-up periods (two to eight weeks), single-center designs, and varied outcome measuring techniques are characteristics of most clinical studies in this sector. Second, phytochemical standardization is widely acknowledged as a crucial challenge: the concentrations of active constituents in botanical preparations vary depending on species cultivar, geographic origin, extraction method, and formulation technique, which makes it difficult to establish dose-response relationships and inter-study comparisons. Third, there is still a dearth of long-term safety data, especially for chronic daily usage in cancer patients with impaired immune systems. Fourth, the majority of jurisdictions have limited the use of plant-based artificial saliva to the nutraceutical and cosmetic regulatory domains since it has not yet been approved as a Class III medical device or prescription medication. [20,32]

4 Oral Clearance, Residence Time, and Mucoadhesion

One commonly mentioned drawback of saliva substitutes, particularly plant-based formulations, is oral residence time. The necessity for frequent reapplication is a major cause of non-adherence, according to patient advocacy data. Ten Research is currently underway to address this constraint by designing mucoadhesive polymers that take use of the ionic contacts, hydrogen bonding, and entanglement mechanisms of plant polysaccharides with the glycocalyx of oral epithelium. As added to botanical gel matrices, chitosan—a semi-synthetic deacetylated form of chitin obtained from plants and crustaceans—shows promise for increasing oral retention by multiple times as compared to CMC alone. [34] The design space for extended-action formulations is further expanded by stimuli-responsive hydrogel architectures that include cellulose derivatives, carrageenans, and alginates. [28]

5 Restoration of the Oral Microbiome

An understudied but crucial aspect of science is the role that plant-derived saliva replacements play in the maintenance of a healthy mouth flora. A risk factor for caries, mucositis, and systemic bacteremia is dysbiosis associated with xerostomia, which is characterized by *Candida* spp. expansion, *S. mutans* proliferation, and decreased *Streptococcus salivarius* (a good commensal). [35] Together, the antimicrobial proteins in CANECPI-5, the terpenoid components of chamomile (α -bisabolol), the medium-chain fatty acids of coconut oil (lauric acid, caprylic acid), and the antimicrobial phenolics of licorice root (glabridin, isoliquiritigenin) provide a multifactorial antimicrobial phenotype that, unlike salivary substitutes, reflects the endogenous antimicrobial function of natural saliva. [11,22]

6 Organoleptic Properties and Patient Acceptability

When treating chronic illnesses that need for frequent topical application, patient acceptance is a significant factor in determining treatment success. When compared to synthetic CMC or glycerol-based solutions, botanical formulations typically have better sensory profiles—natural flavor, a pleasing mouthfeel, and no metallic or chemical aftertaste. However, some individuals may feel that some mucilages and plant oils are overly oily, thick, or coated. The commercial viability of next-generation plant-based alternatives depends on the optimization of organoleptic qualities through formulation development (emulsification, flavor masking, encapsulation). [22, 29]

Future trends and research directions

1 Synergistic Formulations with Multiple Components

The future of plant-based artificial saliva is not in single-agent preparations, but rather in well-thought-out, multi-component synergistic formulations that concurrently address antimicrobial function (licorice, coconut oil, essential oil nanoparticles), lubrication (mucilaginous polysaccharides), enamel protection (CANECPI-5 analogues or phytate/polyphenol pellicle formers), and antioxidant/anti-inflammatory activity (lycopene, aloe vera polyphenols). The determination of ideal ingredient ratios will be accelerated by combinatorial screening employing design of experiment (DoE) platforms in conjunction with high-throughput in vitro bioassays.

2 Integration of Nanotechnology

The encapsulation of plant bioactives in mucoadhesive nanocarriers, such as lipid nanoparticles, chitosan nanoparticles, and cyclodextrin inclusion complexes, provides a proven method to extend oral residence, prevent enzymatic degradation of labile phytochemicals (like lycopene and acemannan), improve mucosal penetration, and accomplish targeted antimicrobial delivery at dysbiotic colonization sites. [26] As the nanotoxicology of orally delivered nanocarriers becomes clearer, it is anticipated that nanoformulated plant-based alternatives will begin clinical research within the next ten years.

3 Customized Phytotherapy Using Salivary Multi-Omics

Precision categorization of xerostomic patients based on their unique functional salivary deficiency profile—whether lubricating, antibacterial, enamel protecting, or buffering—will be made possible by developments in salivary proteomics, metabolomics, and microbiome sequencing. Similar to personalized medicine approaches in oncology, the customized prescription of plant-based formulations based on each patient's deficiency profile promises a therapeutically significant and scientifically sound future path. [44]

4 Formulation Development with Digital and AI Assistance

The identification of new plant-derived candidates for salivary substitution will be significantly accelerated by generative chemistry platforms, artificial intelligence-assisted phytochemical database mining, and molecular docking of plant compounds to salivary protein binding sites (e.g., hydroxyapatite-adsorbing proteins, mucin-polymer interaction models). Natural product formulations are already being optimized in related sectors like oral mucositis therapy and wound healing using machine learning models trained on bioactivity-composition datasets.

5 Clinical Trial Infrastructure and Regulatory Harmonization

Regulatory harmonization pertaining to standardized botanical extract specifications (reference compounds, assay methods, permitted variation), validated surrogate outcome measures for xerostomia trials (objective flow rate, SCF adhesion, biofilm indices), and globally organized multicenter trial consortia are all necessary to realize the clinical potential of plant-based artificial saliva. The creation of patient registries for survivors of head and neck cancer and Sjögren syndrome—populations with the most unmet need—will supply the phenotypic granularity and statistical power needed for conclusive phase III evidence.

CONCLUSION

Plant-based artificial saliva represents a scientifically mature, clinically validated, and pharmacologically multifunctional modality for the management of xerostomia and salivary hypofunction in dental and medical practice. The convergence of traditional phytomedicine with contemporary formulation science and biotechnology has yielded agents—from the mucilaginous polysaccharides of *Malva sylvestris* and *Althaea officinalis* to the enamel-protective sugarcane protein CANECPI-5—that not only relieve oral dryness but address the antimicrobial, remineralisation, and mucosal protective deficits imposed by salivary gland hypofunction.

Whilst the current evidence base, though consistently positive, is limited by small trial sizes, heterogeneous study designs, and absence of phytochemical standardisation, the scientific and mechanistic foundations for plant-based substitutes are robust. The forthcoming decade will likely see nanotechnology-assisted and personalised botanical formulations enter structured clinical evaluation, informed by salivary multi-omics profiling and AI-assisted molecular design. For clinicians, a working knowledge of established plant-based agents, their compositions, and their evidence base equips them to counsel patients with xerostomia more comprehensively and to consider rational phytotherapy as a first-line or adjunctive intervention alongside conventional synthetic substitutes.

REFERENCES

1. Napenas JJ, Brennan MT. Xerostomia: prevalence, assessment, and management. In: Greenberg MS, Glick M, Ship JA, editors. *Burket's Oral Medicine*. 12th ed. Hamilton: BC Decker; 2015. p. 184–96.
2. Kapourani A, Kontogiannopoulos KN, Manioudaki AE, Pouloupoulos AK, Tsalikis L, Assimopoulou AN, et al. A review on xerostomia and its various management strategies: the role of advanced polymeric materials in the treatment approaches. *Polymers*. 2022;14(5):850.
3. Purdie MJ, Carpenter MD, Noll JL, Stephens CL, Taylor YJ, Hammitt KM, et al. Patient perspectives on dry mouth: understanding treatment, needs, and preferences. *Spec Care Dentist*. 2023;43(4):470–9.
4. Aykut-Yetkiner A, Wiegand A, Attin T. The effect of saliva substitutes on enamel erosion in vitro. *J Dent*. 2014;42(6):720–5.
5. Biswal BN, Das SN, Das BK, Rath R. Alteration of cellular metabolism in cancer cells and its therapeutic prospects. *J Oral Maxillofac Pathol*. 2017;21(2):244–51.
6. Ramos-Casals M, Brito-Zerón P, Bombardieri S, Bootsma H, De Vita S, Dörner T, et al. EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies. *Ann Rheum Dis*. 2020;79(1):3–18.
7. Łysik D, Niemirowicz-Laskowska K, Bucki R, Tokajuk G, Mystkowska J. Artificial saliva: challenges and future perspectives for the treatment of xerostomia. *Int J Mol Sci*. 2019;20(13):3199.
8. Vinke J, Kaper HJ, Vissink A, Sharma PK. Dry mouth: saliva substitutes which adsorb and modify existing salivary condition films improve oral lubrication. *Clin Oral Investig*. 2020;24(12):4019–30.
9. Austin W, Hdeib M, Fraser P, Goldchtaub M, Shams E, Han T, et al. Oral lubrication, xerostomia, and advanced macromolecular lubricants for treatment of dry mouth. *Lubricants*. 2024;12:126.
10. Patient Advocacy Coalition for Sialorrhoea and Xerostomia. Patient perspectives on dry mouth: FDA

listening session report. Silver Spring (MD): US Food and Drug Administration; 2022.

11. Sulistiyani E, Balafif FF, Najmi N, Rafisa A. Efficacy of natural artificial saliva and natural saliva stimulant in xerostomia: a review. *Eur J Theor Appl Sci.* 2024;2(4):512–22.
12. Jongburanukit P, Hiengkaew V, Vongsirinavarat M, Vachalathiti R, Thanasarnaksorn W, Sritipsukho P. Alleviation of dry mouth by saliva substitutes improved swallowing ability and clinical nutritional status of post-radiotherapy head and neck cancer patients: a randomized controlled trial. *PLoS One.* 2020;15(4):e0231147.
13. Nonpharmacological interventions in the management of xerostomia: a review on topical treatments, alternative medicine, and innovative therapies. *Dent J (Basel).* 2024;4(4):48.
14. Winter C, Tetyczka C, Pham DT, Kolb D, Leitinger G, Schönfelder S, et al. Investigation of hydrocolloid plant polysaccharides as potential candidates to mimic the functions of MUC5B in saliva. *Pharmaceutics.* 2024;16(5):682.
15. Farooq I, Bugshan A. The role of salivary contents and modern technologies in the remineralization of dental enamel: a narrative review. *F1000Res.* 2020;9:171.
16. Silva NDG, Buzalaf MAR, Leite AL, Sampaio FCM, de Albuquerque RF. A novel artificial saliva enriched with CaneCPI-5 for irradiated head and neck cancer (HNC) patients: in vitro antimicrobial and anticaries effect. *J Dent.* 2025;154:105576.
17. See L, Mohammadi M, Han PP, Mulligan R, Enciso R. Efficacy of saliva substitutes and stimulants in the treatment of dry mouth. *Spec Care Dentist.* 2019;39(4):381–97.
18. El Mihaoui A, Esteves da Silva JCG, Charfi S, Candela Castillo ME, Lamarti A. *Malva sylvestris* L.: phytochemistry and pharmacological uses. *Life.* 2022;12(2):225.
19. Mosavat SH, Ameri A. Efficacy of the flower of *Malva sylvestris* L. and *Alcea digitata* (Boiss.) Alef. in radiation-induced xerostomia: a traditional Persian medicine approach. *Jundishapur J Nat Pharm Prod.* 2017;12(1):e39458.
20. Kręgielczak A, Łukaszewska-Kuska M, Mania-Końsko A, Dorocka-Bobkowska B. Flaxseed (*Linum usitatissimum*), chamomile (*Matricariae flos*) and marshmallow (*Althaea officinalis*) mouth rinses in the therapy of oral mucosa diseases: a review. *Dent Med Probl.* 2023;60(1):131–40.
21. Linseed polysaccharide as saliva substitute [patent]. US 5260282. 1993 Nov 9. Inventors: Pera P, Lönnroth E.
22. Mahmoud A, Elsaadany B, Eissa M, Abd Elmoneim W, Tarek S, Zakaria M. Effect of aloe vera and coconut in the management of xerostomia in patients with Sjogren's syndrome: a crossover randomized clinical trial. *Explor Med.* 2025;6:1001297.
23. Winter C, Tetyczka C, Pham DT, Kolb D, Leitinger G, Schönfelder S, et al. Investigation of hydrocolloid plant polysaccharides as potential candidates to mimic the functions of MUC5B in saliva. *Pharmaceutics.* 2024;16(5):682.
24. Garrido M, González-Flores D, Marchena AM, Rodríguez Moratinos AB. A lycopene-enriched virgin olive oil improves antioxidant status in healthy humans. *J Med Food.* 2013;16(8):744–9.
25. Cinatl J Jr, Morgenstern B, Bauer G, Chandra P, Rabenau H, Doerr HW. A pharmacological review of the efficacy and safety of licorice root. *J Med Food.* 2020;23(1):12–20.
26. Niemirowicz-Laskowska K, Mystkowska J, Łysik D, Chmielewska S, Tokajuk G, Misztalewska-Turkiewicz I, et al. Antimicrobial and physicochemical properties of artificial saliva formulations supplemented with core-shell magnetic nanoparticles. *Int J Mol Sci.* 2020;21(6):1979.
27. Flaxseed mucilage/hydroxypropyl methylcellulose and sodium alginate/polyvinyl alcohol composite bilayer film as a promising drug carrier for periodontal treatment. *Turk J Pharm Sci.* 2024;21(2):161–73.
28. Kontogiannopoulos KN, Kapourani A, Gkoukouras I, Anagnostaki ME, Tsalikis L, Assimopoulou AN, et al. A review of the role of natural products as treatment approaches for xerostomia. *Pharmaceutics (Basel).* 2023;16(8):1136.
29. Katsnelson A. Reactions: xanthan gum to replicate saliva. *Chem Eng News.* 2025;103(16):4.
30. Ameri A, Heydarirad G, Mahdavi Jafari J, Ghobadi A, Rezaeizadeh H, Choopani R. Herbal medicine

in treatment of patients with head and neck cancers: a systematic review. *Electron Physician*. 2016;8(3):2350–6.

31. Heydarirad G, Keyhanmehr AS, Mofid B, Nikfarjad H, Choopani R. Efficacy of herbal medicine containing *Malva sylvestris* and *Alcea digitata* in comparison with artificial saliva for treatment of xerostomia in patients with head and neck cancers. *Avicenna J Phytomed*. 2017;7(1):53–9.

32. Kontogiannopoulos KN, Kapourani A, Gkougkourelas I, Anagnostaki ME, Tsalikis L, Assimopoulou AN, et al. A review of the role of natural products as treatment approaches for xerostomia. *Pharmaceuticals (Basel)*. 2023;16(8):1136.

33. Vinke J, Kaper HJ, Vissink A, Sharma PK. Dry mouth: saliva substitutes which adsorb and modify existing salivary condition films improve oral lubrication. *Clin Oral Investig*. 2020;24:4019–30.

34. Chitin and chitosan-based saliva substitute compositions [patent]. US 4879281. 1989 Nov 7. Inventors: Ikeda Y, Kubota M, Miyamoto K.

35. Santarelli A, Wong DTW, Lo Muzio L. Saliva and oral microbiota: from physiology to diagnostic and therapeutic implications. *Front Physiol*. 2021;11:637599.

36. Comparable effectiveness of novel and commercial saliva substitute gels in dental patients experiencing xerostomia: a randomized, double-blind crossover trial. *Gels*. 2026;12(1):61.

37. Lugo-Flores MA, Quintero-Cabello KP, Palafox-Rivera P, Silva-Espinoza BA, Cruz-Valenzuela MR, Ortega-Ramirez LA, et al. Plant-derived substances with antibacterial, antioxidant, and flavoring potential to formulate oral health care products. *Biomedicines*. 2021;9(11):1669.