Therapeutic Capacity of Natural Sialagogues to Decrease Xerostomia: A Review

Sadman Bin Mujib Chowdhury[1], Sharon Caroline Furtado *[1], B V Basavaraj[1]

Department of Pharmaceutics, Faculty of Pharmacy, MS Ramaiah University of Applied Sciences, Gnanagangothri Campus, Bengaluru, 560054, India

Abstract

Xerostomia, more commonly known as dry mouth, is one of the many diseases that is both common and troubling and is marked by reduced salivary secretion which makes talking, chewing, and swallowing more difficult, and also increases the chances of developing infections in the mouth. It is particularly challenging to manage because of its origins, which range from systemic diseases, like Sjögren's syndromes, to medication and radiation. Management of this condition posed significant challenges due to the intricate nature of saliva. Natural products are considered safer alternatives to synthetic due to their lower side effects, accessibility, affordability and overall holistic benefits. The focus of this review is to explore the state of xerostomia management and the research surrounding natural sialgogues in order to steer the development of new, treatment strategies inspired by nature for this prevalent oral health problem.

Keywords: Xerostomia, Dry mouth, salivary secretion, natural therapeutics

Introduction

Dry mouth, also referred to as xerostomia, describes a health condition associated with underlying disease processes or the adverse effects of received treatment. It is the consequence of diminished flow of saliva in the mouth. The absence of saliva can lead to extreme discomfort, makes one more prone to infections, and can lead to a deterioration in one's quality of life. Saliva is regarded as a protector for one's dental health. Other than water, human saliva also contains proteins and various types of electrolytes. Saliva fulfills a variety of functions such as lubricating tissues, aiding speech, taste and swallowing, and most importantly, protecting the teeth from caries infection (1).

Physiology of Saliva

Salivary constituents include water, enzymes, proteins, glycoproteins, small organic molecules, and electrolytes. Saliva production occurs via the nervous system in response to cholinergic stimulation, activating muscarinic receptors in the salivary glands. An adult produces about 1.0 liters - 1.5 liters of saliva per day. Salivary glands produce about .04 milliliters of saliva per minute at rest; with activity, salivary glands can produce saliva at a rate of about 2.0 milliliters every minute. Physiological functions of saliva summarized in Table 1.

Table 1 Functions of Saliva

Function	Description
Digestion	Begins enzymatic digestion of carbohydrates (e.g. by amylase) and fats (e.g. by lipase).
Lubrication	Moistens food to aid in chewing and swallowing; keeps oral tissues hydrated.
pH Regulation	Maintains a neutral pH in the mouth to protect tooth enamel and support oral microbiome balance.
Antimicrobial Defense	Contains antibacterial, antifungal, and antiviral agents.
Local Immunity	Includes secretory IgA antibodies to support immune protection in the mouth.
Speech Facilitation	Helps enable clear articulation by maintaining moisture in the mouth and throat.
Taste Perception	Dissolves food molecules, allowing them to interact with taste receptors.
Oral Comfort	Provides overall moisture and comfort in the oral cavity.

Depending on the individual, as we age, there may be a decline in amylases (ptyalin) and an increase in mucin leading to thicker saliva. There are a lot of factors that would be known to, or unknown to a person that may have already impacted their flow of saliva. Whether it be medication, chronic illness, or dehydration, this may present as dryness within the mouth and have a cascading effect on a host of undesirable implications (2).

Table 2 Common Oral Complications and Symptoms Associated with Xerostomia (3)

Category	Signs and Symptoms
Functional Limitations	• Swallowing difficulty (dysphagia) • Impaired mastication • Speech articulation issues • Altered or diminished taste sensation
Structural Effects & Outcomes	• Oral burning sensation • Unpleasant breath odor (halitosis) • Dryness of the oral mucosa • Tongue inflammation (glossitis) • Chapped or peeling lips • Fungal infection (oral candidiasis) • Tooth decay and increased caries risk

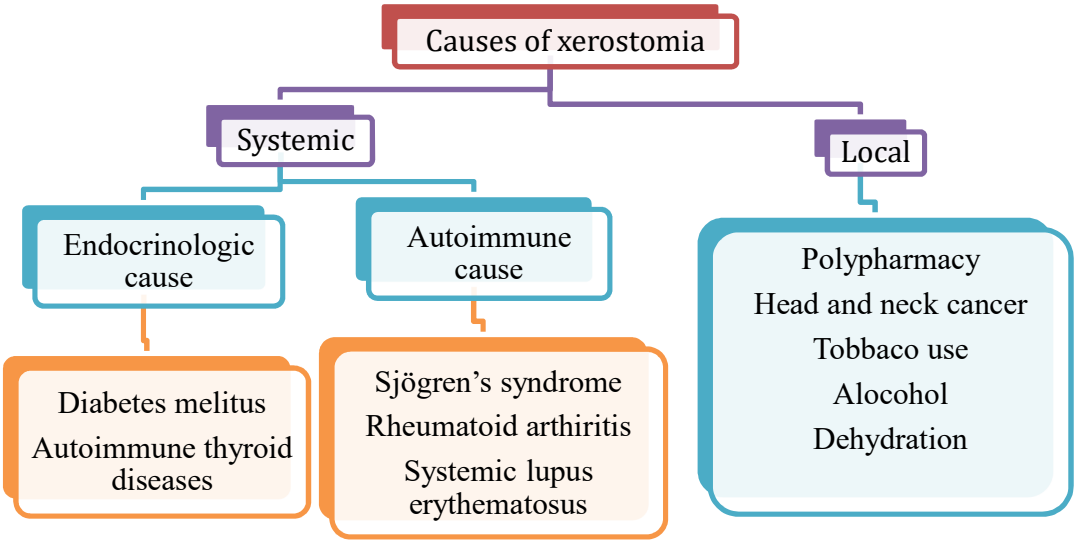

Figure 1 Systemic and Local causes of Xerostomia (4)

Harnessing Natural Remedies for Xerostomia Relief

The following sections provide a summary of the pertinent research, which may be divided into two main categories: (i) *in vivo* studies and (ii) Clinical trials.

Natural Therapeutics for Xerostomia: Evidence from In Vivo Studies

The table 4 summarizes natural products that have been studied for xerostomia and the outcomes of in vivo studies carried out.

Table 3 *In vivo* studies evaluating the efficacy of various natural products in relieving the symptoms of xerostomia

Natural Product	Product Form	Study on	Outcome/Results	Reference
Apigenin	Pure compound	Ovariectomized (OVX) mice	Restored salivary flow, normalized water intake, increased AQP5 expression via ERα pathway.	5
Ixeris dentata	IXD Extract sublingual spray	Sprague-Dawley rats	↑ AQP5 expression, ↑ calcium signaling, improved salivation.	6
Ixeris dentata	IXD ethanolic extract	Sprague-Dawley rats	↓ ER stress (GRP78, CHOP), ↑ antioxidant enzymes, improved gland structure and secretion.	7

Ixeris dentata	IXD methanolic suspended in H2O	Young and aged Sprague-Dawley rat	↑ Saliva flow, acinar cells, AQP5, IP3R; ↓ oxidative & ER stress; improved salivary function.	8
Lycium barbarum polysaccharide (LBP)	LBP powder (>95% purity)	Non-obese diabetic (NOD) mice	↑ Salivary flow, ↓ lymphocytic infiltration, ↑ Tregs, ↓ Th17 and Tfh; safe long-term use.	9
Chinese herbs	Perfusate (5 g/L aqueous extract)	Wistar rats (isolated submandibular glands)	15/20 herbs enhanced salivary secretion when combined with muscarinic agonist; variable secretion patterns.	10

Apigenin

Apigenin is a flavonoid that is naturally occurring in many fruits, vegetables and herbs, including celery, parsley and chamomile. Apigenin is known for its anti-inflammatory and antioxidant properties, and many possible therapeutic applications, such as neuroprotection, and anti-cancer activity. Wei *et al*. (2022) examined apigenin as a possible treatment for xerostomia. The authors studied four herbal compounds - apigenin, dauricine, protopine, and lentinan - to study their ability to up-regulate AQP5 gene transcription in human salivary gland (HSG) cells; AQP5 is an important marker of salivary secretion. Apigenin was the most significant of these compounds as it markedly increased AQP5 transcription and expression even compared to estradiol, which is a common positive control (5).

Ixeris dentata extract

Bhattarai *et al* (2017) investigated a different mechanism by researching how *Ixeris dentata* (IXD) activates aquaporin-5 (AQP5) expression and improves intracellular calcium signaling measured in diabetic rats. The rats were administered a sublingual spray of IXD extract in a single dose of (10 mg/kg) to then observe its effect on salivary secretion. The experiment indicated that IXD extract had a remarkable influence on the expression of AQP5 which is an important water transport protein in the salivary gland and that it activates calcium signaling pathways that are advantageous to support specific calcium signaling to improve salivation and intracellular fluid secretion. Although the trial showed positive results in improving gland function and enhancing salivation - it failed to completely restore the histopathological changes to the salivary glands resulting from diabetes (6). Bhattarai *et al*. (2018) assessed the control of endoplasmic reticulum (ER) stress in salivary glands to analyze how *Ixeris dentata* (IXD) extract could mitigate xerostomia related to diabetes. Often times salivary secretion is diminished in diabetes from deranged cellular functions and poor protein folding. The authors demonstrate that IXD extract can reduce ER stress by modifying important ER stress proteins such as GRP78 and CHOP, allowing for protein folding and improved gland function. The IXD extract also fortified antioxidant defense, reducing oxidative stress and improving overall gland morphology. They found significant restoration of salivary flow, as evaluated *in vivo*,

and important proteins for secretion such as amylase were expressed more often. The authors concluded that IXD extract may serve as a novel treatment for xerostomia in diabetes patients by regulating oxidative stress and ER stress (7). Bhattarai et al. (2018) investigated the effects of *Ixeris dentata* (IXD) extract as a natural therapeutic for age-related dry mouth, an increasing problem in old age due to decreased saliva production, oxidative damage, and increased protein processing dysfunction in the salivary glands. Young (approximately 30 days old) and aged (approximately 18 months old) Sprague-Dawley rats were treated with oral IXD extract at 25, 50, and 100 mg/kg over 8 weeks. Treatment with IXD extract significantly improved saliva flow and stimulated a greater number of acinar cells (salivary secretion cells) in aged rats, which decline with age. IXD treatment also enhanced features of healthy salivary glycoproteins (α-amylase and aquaporin-5 (AQP5) and inositol triphosphate receptors (IP3Rs)) which represent important protein within aging glands that are reduced in salivary gland tissues in aging animals. Subsequent research by the same group investigated the effect of *Ixeris dentata* (IXD) for dry mouth due to diabetes. The extract was tested both alone and together with a probiotic called *Lactobacillus gasseri*. The combination approach had a more substantial effect; for instance, both treatments produced greater salivary flow and amylase activity, but when IXD was paired with *Lactobacillus*, AQP5 and NHE1 expression increased while cellular stress decreased. Particularly, oxidative stress and ER stress were evidently reduced because this was associated with increased antioxidant enzyme activities (e.g., superoxide dismutase (SOD) activity, glutathione (GSH) activity, and glutathione peroxidase (GPx). They identified bioactive constituents in IXD (e.g., Ixerin F and 8-epiisolipidiol-3-β-D-glucopyranoside) that would be likely antioxidants or saliva-stimulating character; taken overall, the research suggests IXD and IXD in combination with beneficial microbes offer a multi-targeted approach to the management of xerostomia that occurs as part of aging and with metabolic diseases (8).

Lycium barbarum Polysaccharide

Wang *et al*. (2021) sought out the therapeutic utility of *Lycium barbarum* polysaccharide (LBP) in a mouse model of primary Sjögren's syndrome (pSS), a chronic autoimmune disorder that results in immune cell infiltration to exocrine glands resulting in symptoms such as dryness in the oral cavity and ocular surface. Results indicated both the high and low-dosage groups of LBP significantly increased salivary flow rates and improved salivary gland function when compared to the control group. The results support the potential of LBP as a natural therapy with managing symptoms of pSS and other autoimmune origins of dry mouth and immune dysregulation (9).

Chinese Herbs

Murakami et al. (2009) investigated the mechanisms by which traditional Chinese herbs may stimulate salivary secretion, offering potential treatments for xerostomia caused by aging, medications, autoimmune disorders, or radiation therapy. Using an isolated and perfused rat submandibular gland model, the researchers evaluated 20 commonly used Chinese herbs—both alone and in combination with carbamylcholine (CCh), a salivary stimulant. The results showed that 15 of the 20 herbs significantly enhanced salivary secretion when combined with CCh, displaying various secretion patterns. Herbs like Maimendong, Tianmendong, and Chishao promoted sustained secretion, while Huangqi and Taizishen triggered sharp, short-term increases. Notably, Danshen and Gancao

stimulated secretion even without CCh, suggesting a direct secretory or neuromodulatory effect (10).

Natural Therapeutics for Xerostomia: Evidence from Clinical Trials

Several natural therapeutics were also investigated using clinical trials and a summary of the same is provided in table 5.

Table 4 Clinical trials testing effectiveness of various natural products in relieving the symptoms of xerostomia

Intervention	Population	Method & Duration	Findings & notes	Reference
Green Tea Gargling	Postmenopausal women (n=40)	Green tea infusion gargle vs. water	Salivary flow increased significantly more with green tea. Catechins stimulate CNS & salivary glands. Affordable & natural remedy.	11
Green Tea Catechin Lozenges	Xerostomia patients, incl. Sjögren's (n=60)	8-week catechin lozenge vs. placebo	3.8× unstimulated & 2.1× stimulated saliva increase in treatment group. Safe and well-tolerated; however, no subjective quality of life improvement seen.	12
Malic Acid Spray (1%)	cGVHD patients with xerostomia (n=28)	2 weeks, 4x/day malic acid spray vs. placebo	Significant DMQ improvement; salivary flow increased from 0.15 to 0.24 mL/min. Xylitol added to reduce erosion; safe but small sample size.	13
Coconut Oil	Head/neck cancer survivors (n=30)	2 weeks topical application	Subjective relief reported: no significant QoL improvement. Safe and inexpensive, but further research needed.	14
Thyme Honey	Head/neck cancer radiation patients (n=72)	Rinse during/after radiation	Reduced dry mouth severity; improved QoL and less pain/swallowing difficulty. Safe, natural supportive therapy.	15
Lemon Mouthwash	Hemodialysis patients (n=44)	1 week per concentration (2.5–20%) crossover	Increased salivary flow; 10% best for flow, 2.5% best tolerated. Recommend rinsing with water after use to protect enamel.	16
Citric Acid (3%) Mouthwash	Drug-induced xerostomia (n=54)	30 days, 4x/day citric acid vs. artificial saliva vs. water	Immediate & longer relief than water, but no increase in unstimulated saliva. Safe short-term, no adverse effects.	17

Olive Oil, Betaine, Xylitol Mouthwashes	Polypharmacy induced dry mouth(n=39)	2 weeks (1 week on the test products + 1 week on their usual care) Spray/gel application	Symptom relief without saliva increase; improved comfort. Calming/moisturizing effect; good QoL improvement.	18
Ginger herbal spray	Type 2 diabetics (n=20)	Oral spray with ginger extract; within-subject control; single use with baseline, placebo, and treatment measures	Significantly increased salivary flow and improved dry mouth symptoms; well tolerated; needs further study.	19
Aloe Vera & Ginger Mouthwash	Diabetics with dry mouth(n=105)	20 mL mouthwash, 3x/day for 2 weeks	Both improved symptoms, ginger more effective; self-reported data; promising natural treatments.	20
Lemon & Aloe Vera + Honey Mouthwash	Xerostomia patients (n=30)	5-day mouthwash use	Both improved dryness, lemon more effective. Natural remedies; lemon stronger but aloe vera + honey also beneficial.	21
Licorice Mouthwash	Hemodialysis patients (n=44)	Randomized controlled trial; licorice mouthwash used 3 times daily for 5 days	90.9% showed increased saliva production and significant reduction in dry mouth symptoms; control group showed little to no improvement. Safe, effective, easy to use, improves oral comfort and quality of life.	22
Oriza Tablet	Drug-induced xerostomia (n=60)	4 weeks tablet vs. placebo	Improvement in unstimulated and stimulated salivary flow & symptoms. Addresses xerostomia from antimuscarinic drugs.	23
Lycopene-Enriched Olive Oil	60 individuals with dry mouth (elderly, polypharmacy common)	Randomized; 12 weeks; spray 3x daily	Improved speech, lip dryness, saliva feeling; salivary flow up; well tolerated; placebo effect present.).	24
Mastic Resin	41 individuals with low unstimulated saliva flow	Exposure to 4 stimuli (no, chew, acid, mastic scent); salivary and	Mastic scent boosted saliva flow, mucins, and reduced dryness; non-invasive olfactory method.	25

		subjective assessments		
Fermented Lingonberry Juice (FLJ)	25 adults	10 mL mouthwash daily for 6 months + follow-ups	Increased saliva, better buffering, less dryness; some lasting effect; no side effects.	26
Linseed (Salinum®)	20 post-radiotherapy patients	Compared linseed gel vs. synthetic saliva	Linseed gel better tolerated, longer relief, reduced plaque/inflammation; efficient at lower dose.	27
Vitamin C/E Complex	45 head & neck cancer patients on radiotherapy	Vitamins C (500 mg) + E (100 IU), BID during therapy	Reduced dry mouth symptoms at 6 months post-treatment; improved oral moisture; no effect on survival or tumor outcomes. Suggests antioxidants may help preserve salivary gland function during radiation; treatment is safe.	28
Malva sylvestris & Alcea digitata	62 radiation therapy patients with xerostomia	Herbal vs. Hypozalix for 4 weeks, symptoms assessed	Herbal group showed greater reduction in dry mouth severity and VAS scores; no side effects reported. Traditional herbal blend found more effective than artificial saliva; improved patient quality of life.	29

Green Tea

Tampubolon et al. (2020) studied the effect of green tea gargling on salivary flow in postmenopausal women with xerostomia, a condition linked to estrogen deficiency. The controlled experimental study involved 40 women aged 45–65 with low salivary flow rates (<0.2 ml/min). Participants were divided into two groups: one gargled green tea infusion (3g in 20ml hot water), while the control group used distilled water. Saliva was collected using the spitting method before and during gargling.

Both groups showed increased salivary flow post-intervention, but the green tea group had a significantly greater improvement (mean increase: 0.28175 ml/min) compared to the control group (mean increase: 0.03335 ml/min), with results statistically significant ($p < 0.05$). The enhancement in salivary secretion was attributed to catechins in green tea, which stimulate the central nervous system and salivary glands. (11).

De Rossi et al. (2014) conducted a randomized, double-blind, placebo-controlled phase II clinical trial to evaluate the effectiveness of a green tea catechin-based lozenge (MighTeaFlow) in patients with xerostomia, including those with Sjögren's syndrome. The study involved 60 participants with objectively reduced salivary flow and dry mouth symptoms. Over an eight-week period, one group received the catechin lozenge, while the other received a placebo identical in appearance and taste.

Results showed that by week eight, the catechin group experienced a significant increase in salivary output—3.8-fold in unstimulated flow and 2.1-fold in stimulated flow compared to baseline—while the placebo group showed no meaningful change (12).

Malic Acid

Bardellini et al. (2019) evaluated the safety and effectiveness of a 1% malic acid spray (SalivAktive®), combined with xylitol, for managing xerostomia in patients with chronic graft-versus-host disease (cGVHD), a population prone to salivary dysfunction. Given concerns about acid-induced oral erosion, xylitol—a non-cariogenic sweetener—was added to the formulation to mitigate dental risks. In this randomized, double-blind, placebo-controlled trial, 28 cGVHD patients with dry mouth used either the malic acid spray or a saline placebo four times daily for two weeks. Results showed significant improvement in the treatment group: salivary flow increased from 0.15 to 0.24 mL/min, and DMQ scores rose from 1.3 to 3.5 ($p < 0.05$) (13).

Coconut oil

Quimby et al. (2020) conducted a pilot study to assess coconut oil as a potential treatment for xerostomia in head and neck cancer survivors who had undergone radiation therapy. Thirty participants used coconut oil over a two-week period and recorded their usage and experiences in personal logs. Quality of life was assessed using the Xerostomia-related Quality of Life Scale (XeQOLS) before and after the trial. Coconut oil was found to be safe, inexpensive, and easy to use, with no reported adverse effects. Participants used it an average of three times daily, and 41.4% continued its use after the study ended (14).

Thyme honey

Charalambous et al. (2017) conducted a randomized controlled trial to evaluate the effectiveness of thyme honey in managing xerostomia in head and neck cancer patients undergoing radiation therapy. Seventy-two patients were divided into two groups: one gargled with thyme honey, the other with saline, following the same protocol during and after treatment. Results showed that the thyme honey group had significantly reduced dry mouth symptoms, improved quality of life, and reported less pain and difficulty swallowing compared to the control group. These improvements were statistically significant (15).

Lemon

Yu and Fang (2025) conducted a double-blind crossover study with 44 hemodialysis patients to evaluate the effects of lemon mouthwash at varying concentrations (2.5%, 10%, 15%, and 20%) on dry mouth and salivary production. Each concentration was used for one week, with a one-week washout period between treatments. All concentrations significantly increased unstimulated saliva flow and reduced xerostomia severity. The 10% solution produced the greatest salivary flow, while 2.5% and 5% were less abrasive yet still effective (16).

Citric acid

Femiano et al. (2011) conducted a clinical trial to compare the effectiveness of artificial saliva, 3% citric acid, and distilled water in treating drug-induced xerostomia in 54 patients taking at least two xerogenic medications. Participants were randomly assigned to use one of the three mouthwashes (5 mL, four times daily) for 30 days. Outcomes included dry mouth symptom relief, unstimulated salivary flow, and safety. Both artificial saliva and

citric acid provided significantly greater immediate relief than water. At 15 minutes post-rinse, 67% of the artificial saliva group and 50% of the citric acid group reported improvement, compared to 11% in the water group (17).

Olive Oil, Betaine, and Xylitol

Ship et al. (2007) investigated the effectiveness of mouthwashes and oral products containing olive oil, betaine, and xylitol in alleviating symptoms of xerostomia. Although these products did not increase actual saliva production, users reported significant relief from dryness, improved comfort, and reduced difficulty with daily functions like speaking, eating, and swallowing. The symptom relief was attributed to the moisturizing and soothing properties of the ingredients: betaine maintained tissue hydration, xylitol enhanced taste and supported dental health, and olive oil formed a protective barrier in the mouth. The products were easy to use, well-tolerated, and free of side effects (18).

Ginger

Mardani et al. (2017) investigated the effectiveness of a ginger herbal spray in treating xerostomia in patients with type II diabetes, a population commonly affected by reduced salivary flow due to metabolic and systemic factors. In a controlled study involving 20 diabetic participants, each subject acted as their own control and was evaluated at baseline, after placebo (glycerin and water), and after using the ginger spray (a mix of glycerin, ginger extract, and purified water). Salivary flow was measured using the Schirmer test. Results showed a significant increase in salivation—from 12.2 mm at baseline and 13.7 mm with placebo to 22.3 mm after ginger spray use ($p < 0.001$). Participants also reported improved oral moisture, symptom relief, and satisfaction with the treatment. No side effects were observed (27). Badooei *et al.* (2021) studied the effects of ginger and aloe vera mouthwashes on dry mouth for diabetics with a triple-blind clinical trial. Participants who used ginger or aloe vera mouthwash during the 2-week intervention period reported a noticeable change in their symptoms of dry mouth. Many stated improvements in salivation and a decreased effect of having to drink water when eating dry foods and no dry mouth when they first wake up (20).

Lemon and a Combination of Aloe Vera Extract and Honey

Rajaei-Behbahani *et al*. (2022) explored how effective lemon extract and a mixture of aloe vera with honey are in relieving dry mouth. Thirty participants who experienced dry mouth used each of the three test mouthwashes—lemon, aloe vera with honey, and plain water (as a placebo) for five days, with a break in between each to avoid overlap. The results showed that both lemon extract and an aloe vera-honey mix had a beneficial effect on symptoms of dry mouth (21).

Licorice

Khatab (2019) reported the effectiveness of licorice root as a natural herb which has antibacterial, anti-inflammatory and antioxidant action, to relieve dry mouth. The authors concluded that licorice mouthwash is a simple, harmless and effective alternative treatment for xerostomia in hemodialysis patients that may enhance their oral comfort and ultimately their quality of life (22).

Oriza Tablet

Piyawannarat *et al* (2024) studied the effects of a natural product, the Oriza tablet or oral rinse, used to treat xerostomia (dry mouth), due to medication (especially antimuscarinic medications). The study conducted a randomized, placebo-controlled, double-blind study with 60 participants who experienced medication-induced dry mouth. The participants were assigned to take either three Oriza tablets or a placebo tablet during a four-week period. The Oriza group exhibited greater improvement on their subjective markers of thirst, dry throat, and trouble speaking (23).

Lycopene-Enriched Olive Oil

Navarro-Morante *et al*. (2016) conducted a clinical study in 2016 to look into a natural remedy for dry mouth.For 12 weeks, 60 individuals used the spray three times a day after being randomly allocated to either the treatment group or a placebo group. Certain symptoms significantly improved for those who took the lycopene spray by the end of the study. For example, difficulties speaking owing to dryness decreased ($P = 0.03$), the sensation of not having enough saliva improved ($P = 0.03$), and lip dryness decreased ($P = 0.04$) (24).

Mastic resin

Faruque *et al.* (2024) recently concluded a promising clinical trial that supported the salivary stimulating effect of mastic resin scent. In this study, 41 subjects with clinically low unstimulated salivary flow rates (<0.25 mL/min) were exposed to four stimulation conditions: no stimulation (baseline), mechanical stimulation (chewing), gustatory stimulation (acid), and olfactory stimulation (mastic resin volatiles). Pertinent tests included salivary flow rate, spinnbarkeit (viscosity), pH, ionic concentrations, and mucins, notably MUC5B and MUC7 for mucosal lubrication.

The researchers found a statistically significant increase in salivary flow for all stimulation conditions compared to baseline, with mastic resin odor exhibiting impressive stimulations ($P < 0.001$) (25).

Fermented Lingonberry Juice

Pärnänen *et al*. (2022) examined the impact of fermented lingonberry juice (FLJ) mouthwash on important salivary indicators in 25 adult participants over the course of a one-year prospective experiment. All salivary metrics significantly improved during the FLJ use period, according to the data. Saliva pH decreased, resting and stimulated saliva flow rates rose, and buffering capacity returned to normal. Even after stopping the mouthwash, these advantages continued to some degree. FLJ's beneficial effects might be related to its polyphenol-rich makeup, which may modulate the oral microbiota and provide modest salivary gland stimulation. The results support the use of fermented lingonberry juice as a safe, natural way to improve salivary function and relieve xerostomia, especially in people looking for alternatives to pharmaceutical medications, even though the precise processes are yet unknown (26).

Lineseed

Andersson *et al*. (1995) evaluated how linseed extract, a natural mucilage, could help people suffering from dry mouth after undergoing radiation therapy for head and neck

cancers. The study involved 20 patients—9 women and 11 men—who had already tried several saliva substitutes with little to no relief. Researchers compared two products: Salinum®, a linseed-based gel made from the Tadorna variety, and MAS-84, a synthetic saliva substitute containing sodium carboxymethyl cellulose.

The results were promising for both, but Salinum® clearly stood out. Patients reported feeling much more comfortable with the linseed-based formula. It didn't just ease the dryness; it seemed to support better oral function, likely by helping the minor salivary glands. Interestingly, those using Salinum® also showed lower levels of plaque and gum inflammation, suggesting their mouths were healthier—possibly because the product helped protect the tissues or encouraged better hygiene through improved comfort (27).

Vitamin C/E Complex

Chung *et al*. (2016) undertook properly planned clinical research to see if consuming vitamins C and E could help alleviate dry mouth (xerostomia) induced by radiotherapy in patients with head and neck cancer. 45 patients were divided into two groups for the trial. One group took antioxidant supplements with vitamin E (100 IU) and vitamin C (500 mg) twice a day while undergoing radiation therapy, while the other group took a placebo that looked exactly the same. Before treatment and one and six months following radiation therapy, researchers used clinical evaluations, salivary gland function tests, and patient questionnaires to gauge the symptoms of dry mouth. The findings suggest that short-term vitamin C and E supplementation during radiation therapy may improve the function of normal salivary glands and ameliorate the symptoms of dry mouth. Positive benefits regarding antioxidant use may be correlated to supporting laboratory evidence that antioxidants can protect normal cells from damage caused by radiation, while not protecting the cancer cells (28).

Malva sylvestris and Alcea digitata

Ameri *et al.* (2016) studied the utility of a traditional herbal remedy of *Alcea digitata* and *Malva sylvestris* to relieve radiation induced dry mouth (xerostomia) in patients with malignant conditions in the head and neck area in a randomized clinical trial. In total, 62 subjects were randomised to receive either the herbal preparation or hypozalix, which is a common artificial saliva replacement. According to these results, the herbal ingredient may provide a natural, safe, and efficient way to treat dry mouth in cancer patients receiving radiation therapy, thus improving their overall quality of life (29).

Conclusion and Future Perspective

Natural extracts have great potential as a safer and more comprehensive treatment for xerostomia than synthetic drugs. Numerous plant-based substances have shown that they can not only increase salivary flow but also safeguard and promote the health of the salivary glands by having anti-inflammatory, antioxidant, and cellular-protective properties. Preclinical and clinical research has shown promising findings, indicating that these natural remedies may assist people with dry mouth manage their symptoms and enhance their quality of life. The available evidence is still developing in spite of this possibility. Small sample sizes, brief study periods, and variations in dosages and formulations limit the scope of many investigations. These difficulties show how much more research is required to develop precise clinical guidelines and guarantee consistent, trustworthy results. Future

research should concentrate on extensive, carefully monitored clinical trials to confirm these substances' medicinal advantages. Creating standardized formulas will be essential to guaranteeing reproducibility and safety. The investigation of new delivery systems, such as mucoadhesive films, lozenges, sprays, or gels that can improve the efficiency and usability of natural sialagogues also holds great promise. With continued research and innovation, natural extracts could become an integral part of xerostomia management offering effective, well-tolerated, and accessible solutions for patients seeking relief from dry mouth.

References

1. Guggenheimer J, Moore PA. Xerostomia: etiology, recognition and treatment. *J Am Dent Assoc*. 2003;134(1):61–9. doi:10.14219/jada.archive.2003.0018.
2. Astor FC, Hanft KL, Ciocon JO. Xerostomia: a prevalent condition in the elderly. *Ear Nose Throat J*. 1999;78(7):476–9. doi:10.1177/014556139907800707.
3. Kapourani A, Kontogiannopoulos KN, Manioudaki AE, Poulopoulos AK, Tsalikis L, Assimopoulou AN, Barmpalexis P. A review on xerostomia and its various management strategies: the role of advanced polymeric materials in the treatment approaches. *Polymers*. 2022;14(5):850. doi:10.3390/polym14050850.
4. Millsop JW, Wang EA, Fazel N. Etiology, evaluation, and management of xerostomia. *Clin Dermatol*. 2017;35(5):468–76. doi:10.1016/j.clindermatol.2017.06.010.
5. Wei W, Cao T, Pathak JL, Liu X, Mao T, Watanabe N, Li X, Zhang M, Li J. Apigenin, a single active component of herbal extract, alleviates xerostomia via ERα-mediated upregulation of AQP5 activation. *Front Pharmacol*. 2022;13:818116. doi:10.3389/fphar.2022.818116.
6. Bhattarai KR, Lee SW, Kim SH, Kim HR, Chae HJ. Ixeris dentata extract regulates salivary secretion through the activation of aquaporin-5 and prevents diabetes-induced xerostomia. *J Exp Pharmacol*. 2017;9:81–91. doi:10.2147/JEP.S141807.
7. Bhattarai KR, Lee HY, Kim SH, Kim HR, Chae HJ. Ixeris dentata extract increases salivary secretion through the regulation of endoplasmic reticulum stress in a diabetes-induced xerostomia rat model. *Int J Mol Sci*. 2018;19(4):1059. doi:10.3390/ijms19041059.
8. Bhattarai KR, Lee HY, Kim SH, Park JS, Kim HR, Chae HJ. Potential application of Ixeris dentata in the prevention and treatment of aging-induced dry mouth. *Nutrients*. 2018;10(12):1989. doi:10.3390/nu10121989.
9. Wang Y, Xiao J, Duan Y, Miao M, Huang B, Chen J, Cheng G, Zhou X, Jin Y, He J, Li Z. Lycium barbarum polysaccharide ameliorates Sjögren's syndrome in a murine model. *Mol Nutr Food Res*. 2021;65(11):2001118. doi:10.1002/mnfr.202001118.
10. Murakami M, Wei MX, Ding W, Zhang QD. Effects of Chinese herbs on salivary fluid secretion by isolated and perfused rat submandibular glands. *World J Gastroenterol*. 2009;15(31):3908–16. doi:10.3748/wjg.15.3908.

11. Tampubolon K, Lubis W, Saragih A. The improvement of saliva flow rate by gargling green tea stepping in menopause women with xerostomia. *Int J Adv Res*. 2020;8:460–5. doi:10.21474/IJAR01/11873.

12. De Rossi SS, Thoppay J, Dickinson DP, Looney S, Stuart M, Ogbureke KU, Hsu S. A phase II clinical trial of a natural formulation containing tea catechins for xerostomia. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2014;118(4):447–54. doi:10.1016/j.oooo.2014.06.015.

13. Bardellini E, Amadori F, Conti G, Veneri F, Majorana A. Effectiveness of a spray containing 1% malic acid in patients with xerostomia induced by graft-versus-host disease. *Med Oral Patol Oral Cir Bucal*. 2019;24(2):e190. doi:10.4317/medoral.22699.

14. Quimby AE, Hogan D, Khalil D, Hearn M, Nault C, Johnson-Obaseki S. Coconut Oil as a Novel Approach to Managing Radiation-Induced Xerostomia: A Primary Feasibility Study. *Int J Otolaryngol*. 2020;2020:8537643. doi:10.1155/2020/8537643.

15. Charalambous A, Lambrinou E, Katodritis N, Vomvas D, Raftopoulos V, Georgiou M, Paikousis L, Charalambous M. The effectiveness of thyme honey for the management of treatment-induced xerostomia in head and neck cancer patients: A feasibility randomized control trial. *Eur J Oncol Nurs*. 2017;27:1–8. doi:10.1016/j.ejon.2017.01.001.

16. Yu IC, Fang JT. Efficacy of lemon mouthwash in improving dry mouth symptoms and salivary flow in Hemodialysis patients. *J Ren Nutr*. 2025;35(1):163–71. doi:10.1053/j.jrn.2024.07.007.

17. Femiano F, Rullo R, Di Spirito F, Lanza A, Festa VM, Cirillo N. A comparison of salivary substitutes versus a natural sialogogue (citric acid) in patients complaining of dry mouth as an adverse drug reaction: a clinical, randomized controlled study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2011;112(1):e15–e20. doi:10.1016/j.tripleo.2011.01.039.

18. Ship JA, McCutcheon JA, Spivakovsky S, Kerr AR. Safety and effectiveness of topical dry mouth products containing olive oil, betaine, and xylitol in reducing xerostomia for polypharmacy-induced dry mouth. *J Oral Rehabil*. 2007;34(10):724–32. doi:10.1111/j.1365-2842.2006.01718.x.

19. Mardani H, Ghannadi A, Rashnavadi B, Kamali R. The Effect of ginger herbal spray on reducing xerostomia in patients with type II diabetes. *Avicenna J Phytomed*. 2017;7(4):308. doi:10.22038/AJP.2017.8755.

20. Rajaei-Behbahani L, Afshar S, Rajaei-Behbahani S, Sadrzadeh-Afshar MS. The Oral Cavity Moisturizing Effects of Lemon and Aloe Vera Extracts in Patients with Xerostomia: A Comparative Study. *Jorjani Biomed J*. 2022;10(3):51–60. doi:10.29252/jorjanibiomedj.10.3.51.

21. Khatab HE. Effect of licorice mouthwash on xerostomia among hemodialysis patients. *Alexandria Sci Nurs J*. 2019;21(2):17–32. doi:10.21608/asalexu.2019.206592.

22. Piyawannarat S, Sirisreetreelux P, Rattapornsompong W, Tancharoen S, Viseshsindh W. Use of the Oral Sialogogue “Oriza Tablet” in Reducing Drug-Induced Xerostomia

in Patients with Overactive Bladder or Neurogenic Bladder: Randomized Clinical Study. *Nat Prod Commun*. 2024;19(10):1934578X241287065. doi:10.1177/1934578X241287065.

23. Navarro Morante A, Wolff A, Bautista Mendoza GR, López-Jornet P. Natural products for the management of xerostomia: a randomized, double-blinded, placebo-controlled clinical trial. *J Oral Pathol Med*. 2017;46(2):154–60. doi:10.1111/jop.12487.
24. Faruque MR, Potocka W, Nazmi K, Ligtenberg AJ, Bikker FJ, Laine ML. Scent of relief: Mastic resin scent recovers salivation in chronic dry mouth patients. *Biomed Pharmacother*. 2024;178:117245. doi:10.1016/j.biopha.2024.117245.
25. Pärnänen P, Lomu S, Räisänen IT, Tervahartiala T, Sorsa T. Effects of Fermented Lingonberry Juice Mouthwash on Salivary Parameters—A One-Year Prospective Human Intervention Study. *Dent J*. 2022;10(4):69. doi:10.3390/dj10040069.
26. Andersson G, Johansson G, Attström R, Edwardsson S, Glantz PO, Larsson K. Comparison of the effect of the linseed extract Salinum® and a methyl cellulose preparation on the symptoms of dry mouth. *Gerodontology*. 1995;12(1):12–7. doi:10.1111/j.1741-2358.1995.tb00124.x.
27. Chung MK, Kim DH, Ahn YC, Choi JY, Kim EH, Son YI. Randomized trial of vitamin C/E complex for prevention of radiation-induced xerostomia in patients with head and neck cancer. *Otolaryngol Head Neck Surg*. 2016;155(3):423–30. doi:10.1177/0194599816642418.
28. Ameri A, Heydarirad G, Rezaeizadeh H, Choopani R, Ghobadi A, Gachkar L. Evaluation of efficacy of an herbal compound on dry mouth in patients with head and neck cancers: a randomized clinical trial. *Evid Based Complement Alternat Med*. 2016;21(1):30–3. doi:10.1177/2156587215590232.
29. Sardellitti L, Filigheddu E, Serralutzu F, Bortone A, Bandiera E, Milia E. Nonpharmacological Interventions in the Management of Xerostomia: A Review on Topical Treatments, Alternative Medicine, and Innovative Therapies. *Oral*. 2024;4(4):616–38. doi:10.3390/oral4040048

.