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The Oral Cavity Moisturizing Effects of Lemon and a Combination of Aloe Vera Extract and Honey in Patients with Xerostomia: A Comparative Study

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Abstract

Background and Objectives: Xerostomia has been defined as the dry mouth sensation due to hyposalivation or change in saliva composition. Many herbal medicines have been used as treatment options. Since the combination of aloe vera extract and honey, and Lemon is suggested as a potent oral moisturizer, limited studies have been done in this field. Therefore, we decided to compare the effects of these two moisturizers in cases of xerostomia.

Material and Methods: a combination of aloe vera extract and honey, lemon extract, and placebo mouthwashes were provided to 30 participants suffering from xerostomia. Each patient used three types of mouthwash in the following order: For the first mouthwash, the patients were asked to express their sensation of dry mouth using VAS on the first, third, and fifth days. This was followed by a one-week rest period in which patients did not use mouthwash. The same process was repeated to measure the second and third mouthwashes.

Results: Lemon and a combination of aloe vera extract and honey were both found to be significantly effective in reducing the dry mouth sensation. However, lemon was significantly more effective in this regard. Placebo was significantly less effective than both extracts and overall had no statistically significant impact on the dry mouth sensation (p<0.001)

Conclusion: Lemon mouthwash was significantly more effective than a combination of aloe vera and honey. Thus, it is recommended to improve dry mouth sensation.

Keywords: Xerostomia [MeSH], Aloe [MeSH]; Wetting agents [MeSH]; Citrus [MeSH]



Highlights

- Healthy saliva is an important factor in maintaining oral health.
- Many treatments have been proposed for dry mouth patients. Lemon and a Combination of Aloe Vera Extract and Honey cab be promising agents in this regard.

Introduction

Saliva plays an essential role in maintaining oral health (1). Given the association between healthy saliva secretion and many aspects of oral function and quality of life, dry mouth sensation should not be considered a minor problem (2). Indeed, saliva significantly impacts the defense against viral, bacterial, and fungal infections, remineralization of tooth enamel and dentin, and the sense of taste (3). Complaints of dry mouth and decreased saliva are more common in the elderly (4). Clinical studies have shown that 25% of the elderly in the general population suffer from dry mouth and related problems without having any other disease. However, there is also evidence of the increasing prevalence of dry mouth in young adults (5).

Saliva is almost entirely composed of water and electrolytes, including immunoglobulins, digestive enzymes, histatins, etc. The autonomic nervous system controls salivary secretion mainly via parasympathetic nerve signals (6). The three major salivary glands (parotid, submandibular, and sublingual) together produce about 90% of the daily saliva volume, varying from 0.5 to 1 liter. In the unstimulated state, the submandibular gland produces about 65% of saliva, which is rich in mucin (lubricant oral mucosa). Under stimulation, the parotid gland secrets 50% of saliva (7).

Salivary dysfunctions can be divided into three aspects: xerostomia, as subjective alteration; hyposalivation, as objective reduction of salivary flow; and changes in salivary composition (8). The leading causes of xerostomia include medication, aging, radiotherapy, chemotherapy, and systemic problems such as rheumatic,

endocrine, neurological, genetic, metabolic, and infectious diseases. A variety of medications can cause dry mouth and hyposalivation. However, regardless of the nature of the medication, taking multiple medications daily can reduce saliva secretion (9). The major medications known to be associated with decreased salivary function include tricyclic antidepressants, antihypertensives, diuretics, and antispasmodics (10).

Another important cause of salivary problems is radiotherapy for head and neck cancers. In these radiotherapies, major salivary glands, which are located near the target tumors and lymphatic chains, often get caught in the radiation field. Thus, one of the consequences of these radiotherapies could be glandular degeneration leading to hyposalivation and dry mouth. The severity of such radiotherapy-induced salivary dysfunctions depends on the radiation dose, the size of irradiated tissue, and the patient's individual response (11).

Qualitative and quantitative salivary problems can significantly reduce a person's quality of life by negatively affecting oral mucous membranes and teeth. Such oral dysfunctions can also cause dysgeusia, dysphasia, dysarthria, atrophic mucosa, and recurrent oral damage (8). The changes in oral microflora and saliva composition may also result in the progression of tooth decay, gingivitis, halitosis, mucositis, oropharyngeal candidiasis, denture mismatch, and bacterial sialadenitis (12).

There are several ways to prevent dry mouth. For many years, patients suffering from this problem have used saliva substitutes or artificial saliva to moisturize the oral mucosa, despite their expense (13). While purified water can also alleviate dry mouth, water tends to create a suitable environment for the growth of pseudomonas (14). Furthermore, previous studies have given conflicting reports regarding the moisturizing effects of water. According to one study, oral care using water accelerates the transmission of bacteria from the mouth to the throat, increasing the risk of associated pneumonia (15). Also, some studies have shown that moisturizing gels are

more effective in protecting the oral cavity, removing dental plaque, and preventing bacterial colonization (16).

Despite its positive effects on oral lesions, using normal saline can cause the oral mucosa to become dry. Although lemon-glycerin swabs have also been shown to be effective in stimulating saliva secretion, the repeated use of these products may cause dry mouth (14). Furthermore, because of the acidity of the compound, they can cause mucosal irritation and accelerate tooth decay (17).

Another treatment option for dry mouth is to use medicinal herbs. Aloe Vera is a medicinal plant commonly used to treat various diseases. The inner gel of this plant contains more than 75 beneficial active ingredients, including vitamins, minerals, enzymes, sugars, anthraquinones, lignin, saponins, sterols, amino acids, and salicylic acid (18). Since about 99% of the aloe vera inner gel is water, it has solid moisturizing effects (19). Furthermore, it contains mucopolysaccharides that help bind moisture to the skin and mucous membranes. According to one study, aloe vera could be as effective as other substances (e.g., saliva substitutes) in reducing the symptoms associated with dry mouth (20).

Because of the presence of glucomannan, mannose-rich polysaccharide, and gibberellin (a growth hormone that binds to the growth factor receptor in fibroblasts and stimulates its activity and proliferation, which in turn increases collagen synthesis) in aloe vera, it also provides wound healing properties upon topical or oral application (as a mouthwash) (21). Glucomannan and Acemannan, contained in aloe vera, also activate macrophages and stimulate the immune system, thus providing antibacterial and antiviral effects (22). Aloe vera is also known to have antiinflammatory effects, inhibit the cyclooxygenase pathway, and reduce prostaglandin E2 (23), and has been recommended to treat disorders such as lichen planus, burning mouth syndrome, and mucositis (24).

A popular home remedy for dry mouth is lemon, known for its sour taste and high citric acid content. Research has shown that the effect of lemon juice on physiological salivary secretion is more potent than that of pilocarpine (25).

Considering the limited number of studies performed on the moisturizing effect of the combination of aloe vera extract and honey and how it fares against other oral moisturizers such as lemon juice, and Due to the lack of a study that compares the effect of these two substances, the present study was aimed to fill this gap in the literature by comparing the oral cavity moisturizing effects of lemon and combination of aloe vera extract and honey in patients with xerostomia in Ahwaz dental school.

Materials and Methods

A double-blind (interventional) cross-sectional clinical trial was performed on 30 volunteers in the oral diseases department of Ahwaz Dental School in 2019-2020. The inclusion criteria were 18-50 years of age and complaints of dry mouth sensation. The exclusion criteria were significant salivary gland damage (for example, due to anticancer medication), radiotherapy or chemotherapy history, allergies, and pregnancy or lactation (research ethics committee code: IR.AJUMS.REC.1398.288).

Bottles containing one of the two types of mouthwash or the placebo (A, B, or C) were tagged by a reliable person outside the research group and placed inside an opaque envelope along with the questionnaires. Each patient received three envelopes containing a bottle (A, B & C) and a questionnaire. The results were analyzed exclusively by a statistics consultant at the end of the research.

The patients were asked to express their sensation of dry mouth using VAS. This scale measures the sensation of dry mouth based on behavioral factors, including the level of discomfort (26). This scale is easy to use and reliable, does not need training, and is sufficiently sensitive and suitable for everyday use (27). On this scale, a score of 10 indicates severe dryness, and 0 indicates no dryness of the mouth (26). For the first mouthwash, the VAS score was recorded on the first day (the day of the visit - before starting

the medication) and at the end of the third and fifth days. Then, the patients were asked not to take the medication for one week (rest period). The VAS scores for the second and third mouthwash were obtained in the same way. The researcher performed the follow-up on the specified days.

The patients were asked to use the mouthwash three times a day, each time swishing 5ml of the mouthwash in the mouth (28) for 40 seconds (29) and then spitting it out.

The mouthwash used in the study was lemon extract (1&1, Iran) and a combination of aloe vera extract and honey syrup (Barij Essence, Iran), and the placebo was purified water (Shahid Ghazi Pharmaceutical, Iran).

Results

Out of 30 patients participating in the study, 43.3% were male, and 56.7% were female. The participant had a mean age of 33.50 years, with the youngest being 21 and the oldest being 48 for the aloe vera extract mouthwash; the average VAS score was 6.93 on the first day, 5.87 on the third day, and 4.57 on the fifth day. Statistical analysis showed that a combination of aloe vera extract and honey mouthwash was significantly effective in moisturizing the oral cavity of patients (Table 1). To compare the dry mouth of patients based on a visual analog scale using a combination of aloe vera extract and honey mouthwash in three evaluation stages (first, third and fifth day), analysis of variance test with repeated measurement was used (Table 2). The results of variance analysis with repeated measurements showed that the effect of a combination of aloe vera extract and honey mouthwash in moisturizing the oral cavity of patients was significantly effective (p=0.001) in the sense that there was a statistically significant difference between the mean VAS scores on the first, third, and fifth days. Due to the significance of the results of the analysis of variance with repeated measurements, the LSD post hoc test was used to compare the level of dry mouth on the first, third, and fifth days. The results of the LSD

test (comparing the set of scores obtained at one stage of measurement with the set obtained at another stage of measurement) showed that the mean VAS scores on the third and fifth days after using the aloe vera extract mouthwash were significantly lower than the corresponding score on the first day (p=0.001). Also, the mean VAS score on the fifth day after using the aloe vera extract mouthwash was significantly lower than the mean VAS score on the third day (p=0.001) (Figure 1).

The average VAS score for the lemon extract mouthwash was 6.97 on the first day, 4.63 on the third day, and 2.83 on the fifth day (Table 1). The lemon mouthwash was also significantly effective in moisturizing the oral cavity (p=0.001), as indicated by the statistically significant difference between the mean VAS scores of the first, third, and fifth days (Table 2). The results of the LSD test for the lemon extract mouthwash showed that the mean VAS scores were significantly lower on the third and fifth days than on the first day (p=0.001) and also considerably lower on the fifth day than on the third day (p=0.001) (Table 1&2, Figure 1).

The mean VAS score for the placebo was 6.93 on the first day, 6.90 on the third day, and 6.83 on the fifth day (Table 1). For the placebo, statistical analysis did not detect any significant difference between the mean VAS scores of the three stages of measurement, indicating that the placebo was not significantly effective in moisturizing the oral cavity of patients (p=0.374) (Table 2 & Figure 1).

The results of ANOVA performed to compare the effect of mouthwash showed that while there was no significant difference between the mean VAS scores of the three types of mouthwash on the first day (p=0.994), there was a significant difference between these scores on the third day and the fifth day (p<0.001).

Due to the significance of the results of the ANOVA test, to compare the mouthwashes used on the third and fifth day, the LSD post hoc test was used. The results of the LSD test (comparing the set of scores obtained for each mouthwash with the group obtained for another mouthwash)

showed that the VAS scores obtained for the lemon extract and the aloe vera extract on the third and fifth day were significantly lower than the corresponding scores for the placebo (p<0.01).

Also, the VAS scores obtained for the lemon extract on the third and fifth days were significantly higher than those for a combination of aloe vera extract and honey (p<0.01) (Table 3).

Table 1. Mean and standard deviation of three stages of dry mouth assessment of patients

Dependent variable	Type of mouthwash	Aloe vera+ Honey	Lemon	Placebo	ANOVA	
					F	p-value
Dry mouth based on a visual analog scale	First day M ± SD	6.93±1.36	6.97±1.	6.93±1.39	0.01	0.994
	Third day M ± SD	5.78±1.76	4.93±1.30	6.90±1.40	17.22**	< 0.001
	Fifth day M ± SD	4.57±1.57	2.83±1.12	6.83±1.56	55.95**	< 0.001

M=Mean, SD=Std. Deviation

Table 2. Analysis of variance test with repeated measures in three stages of measuring dry mouth of patients using a combination of aloe vera extract and honey mouthwash

Dependent variable	Type of mouthwash	Source	SS	df	MS	F	p.value
Dry mouth based on the visual analog scale	Aloe vera+	time	84.29	2	42.14	187.27	< 0.001
	Honey	error	13.71	58	0.234		
	lemon	time	257.69	2	128.84	128.84	< 0.001
		error	27.64	58	0.48		
	Placebo	time	0.16	2	0.08	1.00	0.374
		error	4.51	58	0.08		

SS= Sum of Squares, MS=Mean Square.

Table 3. Pair-by-pair comparisons of dry mouth in three types of mouthwash used on the third and fifth days of evaluation

Dependent variable	Evaluation stage	Mouthwash (I)	Mouthwash (J)	difference of the averages (I-J)	standard error	p.value
Dry mouth based on a visual analog scale	Third day	Aloe vera+ Honey	Lemon	1.23	0.39	0.002
		Aloe vera+ Honey	Placebo	-1.03	0.39	0.009
		Lemon	placebo	-2.27	0.39	< 0.001
	Fifth day	Aloe vera+ Honey	Lemon	1.73	0.38	<0.001
		Aloe vera+ Honey	Placebo	-2.27	0.38	<0.001
		Lemon	Placebo	-4.00	0.38	< 0.001

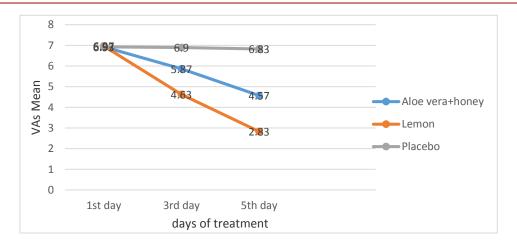


Figure 1. The average of three evaluation stages of patients' dry mouth

Discussion

There are reports showing that the lifetime prevalence of xerostomia in people over 18 years of age can reach as high as 64.8%. Thus, the incidence of this condition is on the rise with the growth and aging of the population. While there is no definite evidence as to which gender is more likely to experience xerostomia (30), some studies have reported a higher prevalence in females (31). Xerostomia is widely known to cause functional problems such as difficulty in chewing and swallowing, speech issues, and decreased taste sensation and also makes the patient prone to gum disease, tooth decay, periodontal disease, bad breath, and plaque formation (30). As a popular treatment for dry mouth, lemon has some local but preventable side effects that make it potentially safer than treatment with muscarinic agonists (such as pilocarpine) (32). Since about 99% of the inner gel of aloe vera leaves is water, it can also serve as a potent oral moisturizer (33).

In this study, the lemon extract and a combination of aloe vera extract and honey both significantly impacted the dry mouth sensation. Still, the former was significantly more effective in this regard than the latter. The placebo used in this study was significantly less effective than both extracts and had no statistically significant impact on the dry mouth sensation.

In this study, 43.3% of the participating patients were male, and 56.7% were female. This slightly higher prevalence among women is consistent with the reports of Badooei et al. (33), Juan Aitken Saavedra et al. (34), and Qapanchi et al. (31) and could be related to the higher prevalence of dry mouth in women their higher sensitivity to this problem, or their higher propensity to participate in studies. On the contrary, Atashi et al. (35) have reported a higher prevalence of xerostomia among men, which may be due to the higher number of men admitted to the ICU in their study.

In the present study, lemon was found to be significantly effective in reducing the dry mouth sensation, which is consistent with the reports of Salum et al. (36), Pandey et al. (28), and Saavedra et al. (34), can be attributed to increased salivation due to the acidification of the oral cavity. However, this finding contradicts the findings of Murugesh et al. (29). This difference could be that they changed the pH of lemon to that of yogurt, which results in reduced salivary stimulation. Also, because of the higher consistency of yogurt and its mild sour taste, which is due to lactic acid (as opposed to the citric acid of lemon), it can cover the surface of the mouth easier and for more extended periods, which leads to more moisture retention in the mucosal surface.

In this study, a combination of aloe vera extract and honey significantly reduced the dry mouth sensation. This finding is consistent with the results of Atashi et al.) (35) and Badooei et al. (33). This can be attributed to aloe vera's surface coverage effect, lubricating effect, pleasant sensation, similarity to saliva in terms of composition, and high water content.

The placebo used in the present study (purified water) had no significant effect on the dry mouth sensation. This is consistent with the reports of Atashi et al. (35) and Badooei et al. (33) and can be related to the placebo's inability to stimulate saliva secretion and provide stable surface coverage.

The results of this study suggest that the lemon extract and a combination of aloe vera extract and honey can both significantly alleviate dry mouth sensation. Still, the lemon extract is considerably more effective in this task.

The administration of sialagogues such as citric acid (lemon) can be considered a valid option only if salivary tissue is present.

Aloe vera syrup (Barij Essence, Iran) used in this study contains a combination of aloe vera extract and honey. Moisturizing effects can be attributed to aloe vera and honey together. Sweet substances of honey can stimulate saliva secretion in the oral cavity and mucus secretion in the airways (37). Aloe vera is mostly water and contains mucopolysaccharides and amino acids that help bind moisture to the mucosa, thereby maintaining surface moisture.

Moisturizing agents like Aloe vera can be used in cases of salivary gland parenchyma damage, such as severe cases of Sjogren's syndrome and mucositis due to cancer treatment, etc.

Conclusion

In other words, according to the results of the present study, lemon seems to be a suitable suggestion in xerostomia patients. Indeed, more research is needed in this field to provide more accurate results.

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Conflict of interest

There is no conflict of interest.

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