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ORIGINAL RESEARCH

Comparative Mucosal Wetting Capacity of Novel and Commercial Saliva Substitute Formulations: An in vitro Study

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Purpose: This study evaluated the effectiveness of novel, inexpensive saliva substitute formulas (Rangsit University (RSU) preparation) in maintaining mucosal wetness compared with commercial products.

Materials and Methods: In vitro experiments were conducted using swine tongues to assess the wetness of various RSU saliva substitute solutions and gels, with four flavors each (sweet mint, sweet vanilla, sweet-sour mint, and sweet-sour lemon), compared with water, hospital-based mouth rinse from a government dental school, and commercial products (Biotene® mouthwash and GC Dry Mouth Gel®). The wetness was measured at baseline and at 0, 10, 20, 30, 60, and 120 minutes using a digital moisture analyzer.

Results: All saliva substitutes consistently maintained a higher relative wetness than water, particularly beyond 60 minutes ($p < 0.001$). RSU solutions with a sour flavor (sweet-sour mint and sweet-sour lemon) had a similar wetness to commercial saliva substitute mouthwash at all times. These solutions were more effective in maintaining higher relative wetness over time than those without a sour flavor (sweet mint and sweet vanilla) ($p < 0.05$) and provided more wetness than the hospital-based mouth rinse at 120 minutes. The RSU solution formula also provided comparable wetness to RSU gel preparation at every time point. While RSU gel formulas initially provided comparable wetness to water, they maintained significantly higher wetness at 60 minutes ($p = 0.029$) and 120 minutes ($p = 0.002$). These results were similar to those of commercial saliva substitute gel, which maintained stable wetness since application up to 120 minutes ($p = 0.052$).

Conclusion: Our novel saliva substitute formulas show similar effectiveness to commercial products in maintaining mucosal wetness. These inexpensive products could be a viable alternative for patients with dry mouth who cannot afford commercial formulations.

Keywords: artificial saliva, mouth dryness, mouthwash, xerostomia

Introduction

Dry mouth, which is a sign of hyposalivation or a subjective feeling of xerostomia, affects oral health and quality of life.[1–3] Medication, radiotherapy of the head and neck region, and some systemic diseases (eg Sjögren syndrome, diabetes mellitus, HIV infection, and renal disease) are common causes of dry mouth.[4] Sipping water frequently, mechanical stimulation by chewing gum, using a prescribed sialogogue or saliva substitutes according to individual preferences, and maintaining good oral health reduce signs and symptoms of xerostomia and its complications.[5–7]

In addition to diagnosing xerostomia using a questionnaire, hyposalivation can be diagnosed using multiple methods.[8–10] The measurement of salivary flow rate is the gold standard for diagnosing hyposalivation.[10] However, this measurement takes time and must be performed by a healthcare professional using the correct technique. An oral moisture meter (Mucus®; Japan Life Co., Saitama, Japan) has been developed and successfully used to evaluate oral

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dryness.[11,12] The oral moisture meter can quantify the water content of the oral mucosa in seconds. Therefore, this device may aid in the clinical measurement of oral moisture or mucosal wetness in general dentistry. Several studies have demonstrated the usefulness of an oral moisture meter in determining the degree of oral mucosal moisture in patients with dry mouth from various etiologies.[8,11–13]

There are many formulas for saliva substitutes, such as in-house (hospital-based) products or over-the-counter oral lubricants. [5] Gels, sprays, lozenges, tablets, and mouthwashes are commercially available. [5] The outcome of oral mucosal wetness depends on the preparation and ingredients. [14] In Thailand, commercial products are relatively expensive compared with in-house saliva substitutes in the government healthcare sector.

Therefore, this study aimed to evaluate mucosal wetness resulting from four flavors of artificial saliva developed in gel and in solution compared with commercial products in vitro using swine tongues. These novel, inexpensive products are intended to be manufactured as a gel, spray, or mouthwash for patients with dry mouth who are receiving dental treatment in a private dental school or dental clinic and cannot afford commercial saliva substitutes.

Materials and Methods

This experimental study was conducted by the College of Dental Medicine and College of Pharmacy, Rangsit University. The study was approved by the Ethics Review Board of Rangsit University and was conducted in full accordance with the Declaration of Helsinki (COA., No. RSU–ERB2022–078). For studying mucosal wetness in vitro, fresh swine tongue represents the clinical condition of the human mucosal tongue. This study utilized swine tongues obtained from a local market, sourced from animals slaughtered for commercial food production. No live animals were used or harmed specifically for the purposes of this research.

Formulation Preparation

Two variations of saliva substitutes, comprising a solution intended to be formulated as a spray or mouthwash, and a gel, with four flavors for each, have been developed by the College of Pharmacy, Rangsit University (RSU). Sweet mint (SM), sweet vanilla (SV), sweet-sour mint (SSM), and sweet-sour lemon (SSL) were created to serve different taste preferences. The creation of a solution and a gel also aimed to serve different preferences for the method of application. All RSU solutions and gels were made from the same base materials (Supplementary Table 1). All materials were ordinarily used for oral cosmetics or foods.[15]

Regarding the saliva substitute preparation, hydroxyethyl cellulose (0.5% and 3.0%) was dissolved in distilled water. Sodium chloride, potassium chloride, and calcium chloride were added to simulate the ionic content of natural saliva. Potassium sorbate and propylene glycol were used as preservatives and humectants, respectively. Xylitol, citric acid, vanilla tincture, lemon, and peppermint oil were added as flavoring agents. All formulations had pH values measured using a pH meter, which showed a pH of 5.5–7.5. Their viscosity properties were determined using Brookfield's viscometer. The formulations were stable, and there was no phase separation after being observed at 2°C–8°C for 3 months.

We also evaluated drinking water, one hospital-based mouth rinse from a government dental school, one commercial saliva substitute mouthwash (Biotene® mouthwash, Haleon Company, Weybridge, United Kingdom), and one commercial saliva substitute gel (GC Dry Mouth Gel®, GC Corporation, Tokyo, Japan) for comparison.

Swine Tongue Preparation

For studying mucosal wetness in vitro, fresh swine tongues purchased from the centered butcher shop in Pathumthani, which represents the clinical condition of the human mucosal tongue, were stored at 4°C until use. The swine tongues were cleaned with normal saline solution and distilled water and dried with a tissue napkin. The temperature of each swine tongue was measured using a thermometer, and each tongue had a comparable average temperature set at 18°C–20°C at the beginning of the experiment. A coin with a diameter of 18 mm was placed on the mucosal areas and outlined with ink as a landmark for dropping each saliva substitute studied. Each swine tongue had 3–4 experimental sites. From a power of analysis at 80%, 14 sites were chosen for experiments with each formula of saliva substitute and drinking water. Therefore, there were 168 experimental sites with drinking water and 11 formulas of artificial saliva.

Allocation of Saliva Substitutes

Two drops of RSU saliva substitute solution (0.05 mL) were distributed onto the marked area from a 1 mL syringe. The syringe was placed perpendicular to the swine tongue while the sample was being dropped. Artificial RSU salivary gel was placed on the swine tongue using a plastic stick to spread the sample within the experimental site. The amount of gel used was 0.05 mL, which is equivalent to the quantity of the solution. Drinking water, hospital–based mouth rinse, commercial saliva substitute mouthwash, and commercial saliva substitute gel were dispensed using the same pattern as RSU saliva substitutes.

Measurement of Mucosal Wetness

A Digital Moisture Analyzer/Oral Moisture Checking Device (Mucus®, product number: 441244; Life Co., Ltd., Saitama, Japan) was used to measure mucosal wetness according to the manufacturer's instructions. The device sensor was covered with a sterile polyethylene disposable bag (thickness, 12 μm) and pressed to the tongue mucosa at 200 g of pressure until a beeping sound was heard (approximately 3 seconds) at room temperature. Mucosal wetness was measured three times in the marked region, where each formula of saliva substitute was dropped, and the median value was used for analysis per the manufacturer's instructions. Regarding the interpretation of oral dryness in individuals, values ≥ 29.6% are considered normal, values of 28.0–29.5% are borderline, and values ≤ 27.9% are low.[11] One investigator calibrated the method according to the manufacturer's recommendation until there was no intra-observer variation and independently measured the oral mucosal moisture value from all 168 experimental sites to avoid interpersonal variation. The wetness measurement intervals for each experimental site were before the application (pre), at baseline immediately after dropping the experimental saliva substitute (time: 0 minutes), and 10, 20, 30, 60, and 120 minutes after application. During each interval, the evaporation of the saliva substitute and water was controlled and minimized by a plastic lid on the swine tongue throughout the study.

Statistical Analysis

The data were analyzed using statistical software (SPSS Statistics for Windows, V.25.0, IBM Corp., Armonk, NY, USA). The normality of the data distribution was assessed using the Shapiro–Wilk test. Where appropriate, the differences in relative wetness between a specific saliva substitute formulation at each time point were analyzed by analysis of variance or the independent *t*–test. The differences in relative wetness between baseline and different times after application were analyzed by repeated measured analysis of variance with post–hoc analysis by the paired *t*–test, respectively. A p value < 0.05 indicates a statistically significant difference.

Results

The measured wetness of the various saliva substitute formulas is shown in Table 1. The mean wetness of all specimens before application of the saliva substitute (pre) and water was significant ($p = 0.034$). Therefore, to compare the wetness resulting from testing various saliva substitute formulas, the relative wetness to pre-application at each site of every swine tongue was calculated by dividing the wetness value at each time point by the initial wetness value before application. The relative wetness results show how much the wetness changed at each time point compared with the initial wetness without any saliva substitute or water application. Consequently, a value > 1 indicates an increase in wetness (Table 2).

The SSM and SSL formulas showed a similar relative wetness. Similarly, the mean relative wetness of SM was comparable to that of SV at every time point. However, there were significant differences in relative wetness between RSU solutions with or without a sour flavor ($p < 0.05$). SSM and SSL appeared to be more effective in maintaining higher relative wetness over time than SM and SV. Therefore, RSU solutions were grouped by whether they had a sour flavor or not into two groups.

Figure 1 shows the relative wetness of water and each saliva substitute (SSM plus SSL and SM plus SV groups) in solution formulas over time. Saliva substitutes in the solution formula began to show more wetness than water at 20 minutes, and beyond 60 minutes, all solution formulas provided significantly more wetness than water ($p < 0.001$). When we compared each solution formula, the RSU solution without a sour flavor was not different in wetness compared

Table 1 The Measured Wetness of Drinking Water, Saliva Substitutes in Solution, and Gel Formula

Time (Minutes)	Wetness (%) (Mean ± SD)										
	Water	Solution Formula						Gel Formula				
		RSU Sweet Mint	RSU Sweet Vanilla	RSU Sweet-Sour Mint	RSU Sweet-Sour Lemon	Hospital-based Mouth Rinse	Commercial Saliva Substitute Mouthwash	RSU Sweet Mint	RSU Sweet Vanilla	RSU Sweet-Sour Mint	RSU Sweet-Sour Lemon	Commercial Saliva Substitute Gel
Pre	11.5 ± 2.3	13.1 ± 5.0	11.04 ± 2.5	12.09 ± 6.7	10.3 ± 3.6	14.7 ± 6.7	8.7 ± 2.4	11.2 ± 3.9	11.1 ± 5.1	11.4 ± 4.6	12.2 ± 4.5	15.1 ± 8.5
0	38.5 ± 1.6	28.9 ± 1.6	29.2 ± 1.4	30.6 ± 1.9	31.1 ± 1.9	30.2 ± 1.8	29.8 ± 1.9	30.5 ± 1.9	31.2 ± 1.4	31.4 ± 1.9	31.4 ± 1.3	31.6 ± 1.4
10	34.0 ± 1.8	29.2 ± 1.9	29.8 ± 2.2	30.8 ± 1.4	30.7 ± 1.8	30.4 ± 1.3	28.7 ± 1.6	29.9 ± 2.2	30.0 ± 3.6	30.1 ± 2.5	29.7 ± 2.0	31.0 ± 1.8
20	31.7 ± 1.4	28.7 ± 2.5	29.1 ± 2.8	30.5 ± 1.8	30.0 ± 2.3	31.0 ± 2.4	30.0 ± 2.3	30.3 ± 2.9	29.3 ± 2.3	29.9 ± 1.6	30.3 ± 1.6	31.8 ± 1.3
30	29.6 ± 1.4	27.5 ± 1.7	28.8 ± 1.3	30.9 ± 0.5	28.3 ± 3.7	31.2 ± 2.0	28.5 ± 2.2	32.4 ± 1.2	29.9 ± 1.8	29.6 ± 0.8	28.6 ± 3.3	31.9 ± 1.6
60	24.2 ± 1.5	30.3 ± 1.7	29.2 ± 2.2	31.6 ± 2.1	29.0 ± 2.7	30.0 ± 2.2	28.8 ± 2.2	30.7 ± 1.9	30.8 ± 1.2	30.7 ± 1.9	30.4 ± 2.1	30.0 ± 1.4
120	22.1 ± 1.6	31.9 ± 1.4	30.6 ± 1.7	30.8 ± 1.6	30.5 ± 1.7	28.4 ± 1.9	27.2 ± 2.4	30.5 ± 1.2	30.8 ± 0.9	29.8 ± 1.0	31.2 ± 1.3	30.7 ± 2.0

Notes: Pre = The initial wetness without any saliva substitute or water application.
Abbreviations: SD, standard deviation; RSU, Rangsit University.

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Table 2 Relative Wetness of Water and Each Form of Saliva Substitute

Time (Minutes)		Wetness Ratio (mean ± SD)					*p** (0–5)	*p*** (0 vs 1–5)	*p*** (1 vs. 4)
		Formula							
	Water (0)	RSU Solution (1)	Hospital-Based Mouth Rinse (2)	Commercial Saliva Substitute Mouthwash (3)	RSU Gel (4)	Commercial Saliva Substitute Gel (5)			
0	3.36 ± 1.9	3.07 ± 1.0	2.50 ± 1.1	3.71 ± 1.2	2.86 ± 1.0	2.76 ± 1.4	0.053	0.013	0.823
10	2.92 ± 1.7#	3.04 ± 1.1	2.52 ± 1.1	3.55 ± 1.1	2.77 ± 1.0	2.66 ± 1.3	0.436	0.692	0.473
20	2.75 ± 1.6#	3.00 ± 1.0	2.51 ± 1.0	3.67 ± 1.0	2.77 ± 1.0	2.76 ± 1.4	0.251	0.518	0.726
30	2.58 ± 1.4#	2.94 ± 1.0	2.52 ± 1.0	3.51 ± 1.0	2.80 ± 1.0	2.78 ± 1.4	0.182	0.106	0.766
60	2.11 ± 0.9#	3.00 ± 1.0	2.41 ± 1.0	3.57 ± 1.1	2.82 ± 1.0	2.62 ± 1.4	< 0.001	< 0.001	0.760
120	1.88 ± 0.8#	3.04 ± 1.0#	2.33 ± 1.0#	3.34 ± 0.9#	2.81 ± 0.9	2.61 ± 1.2	< 0.001	< 0.001	0.334
*p****	<0.001	<0.001	0.012	0.019	0.073	0.052	-	-	-

Notes: *ANOVA; **t-test; ***repeated measures ANOVA; #$p < 0.01$ by the paired *t*-test versus 0 minutes.
Abbreviations: SD, standard deviation; RSU, Rangsit University.

with hospital–based mouth rinse ($p > 0.05$) and significantly inferior to commercial saliva substitute mouthwash ($p < 0.05$). However, the RSU solution with a sour flavor had a similar wetness to that of commercial saliva substitute mouthwash at all times and provided significantly more wetness than the hospital–based mouth rinse at 120 minutes ($p = 0.02$).

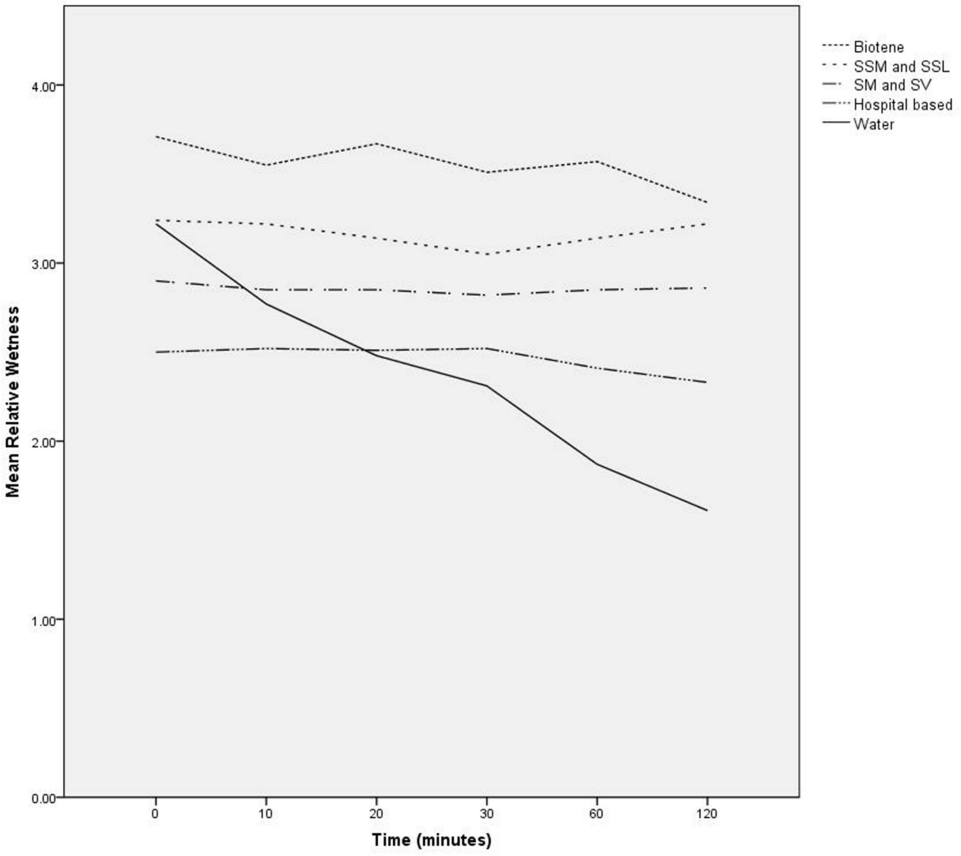

Figure 1 Relative wetness of saliva substitute in solution formulas and water at baseline and at 10, 20, 30, 60, and 120 minutes.
Abbreviations: SSM, sweet-sour mint; SSL, sweet-sour lemon; SM, sweet mint; SV, sweet vanilla.

Regarding the RSU gel (Figure 2), the highest wetness was observed for the SM gel. However, there was no significant difference in wetness between the RSU gel formulas of the four flavors. We then compared mean wetness between RSU gel formulas and commercial saliva substitute gel and water. While the RSU gel initially showed comparable wetness to water, it showed significantly higher wetness than water at 60 minutes ($p = 0.029$) and beyond 60 minutes ($p = 0.002$). The RSU gel formula results were similar to those of commercial saliva substitute gel, which maintained stable wetness up to 120 minutes ($p = 0.052$).

Table 2 shows the comparison of the relative wetness between water, RSU solutions and gel formulas, hospital–based mouth rinse, and commercial products over time. Initially, there was no significant difference in wetness between water and various saliva substitutes ($p = 0.053$). Except for the commercial saliva substitute mouthwash, water appeared to be slightly wetter than artificial saliva at 0 minutes ($p = 0.013$). However, over time, all saliva substitute consistently showed higher relative wetness than water, particularly beyond 60 minutes ($p < 0.001$). The mean relative wetness of the RSU solution formula (3.02 ± 0.05) was not significantly different from that of the RSU gel preparation at all combined time points (2.81 ± 0.03, $p = 0.695$).

The relative wetness of drinking water decreased over time. Beyond 10 minutes, the relative wetness of water was significantly decreased compared with 0 minutes and gradually decreased every 10 minutes ($p < 0.01$). At 60 minutes, the relative wetness of water was significantly decreased by one–third and was almost decreased by half at 120 minutes compared with 0 minutes ($p < 0.01$). In contrast, the RSU saliva substitute solution was as effective in retaining wetness as the hospital–based mouth rinse and commercial saliva substitute mouthwash; however, they significantly decreased at 120 minutes compared with 0 minutes ($p < 0.001$, $p = 0.012$, and $p = 0.019$, respectively). Notably, commercial saliva substitute mouthwash showed the most consistent and prolonged effect, followed by RSU and hospital–based saliva

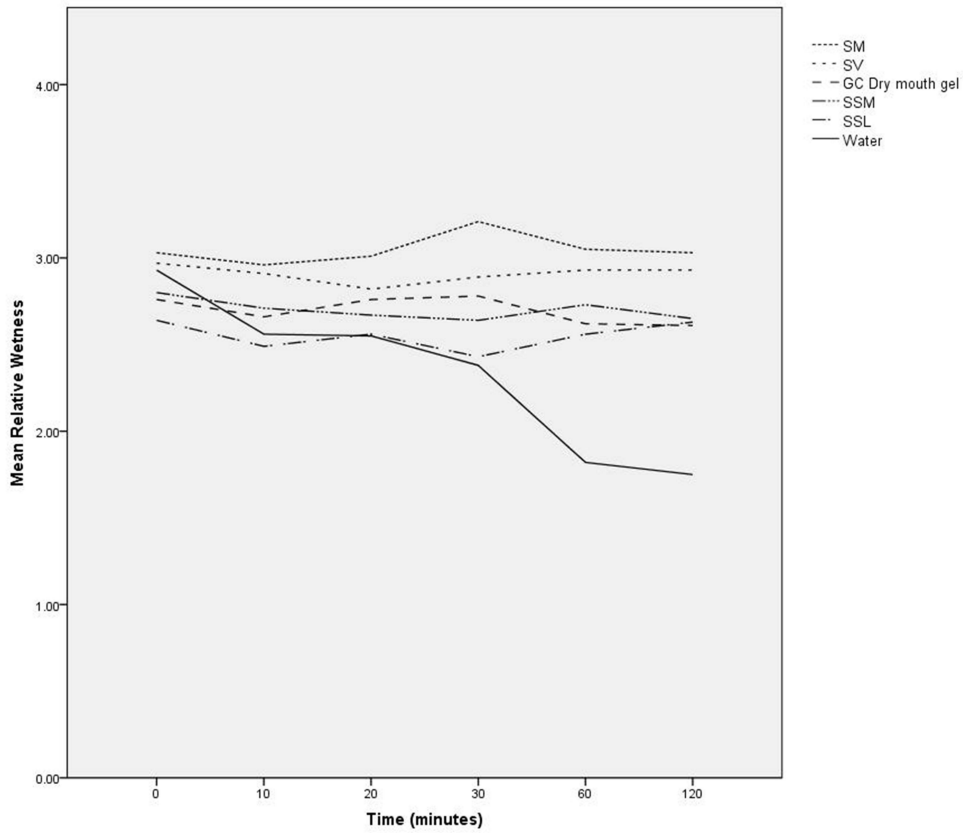

Figure 2 Relative wetness of saliva substitute in gel formulas and water at baseline and at 10, 20, 30, 60, and 120 minutes.
Abbreviations: SSM, sweet-sour mint; SSL, sweet-sour lemon; SM, sweet mint; SV, sweet vanilla.

substitute solutions. Interestingly, saliva substitutes in gel formulas (both RSU gel and commercial saliva substitute gel) maintained wetness without significantly decreasing by 120 minutes ($p = 0.073$ and $p = 0.052$, respectively).

Discussion

The effectiveness of various novel saliva substitute formulas in maintaining mucosal wetness was investigated in this study. The swine tongue was used as the experimental model to mimic the oral mucosa. The wetness of the tongues was measured by the oral moisture-checking device (Mucus®) at different time points after each saliva substitute was applied. The oral moisture-checking device (Mucus®) effectively measures mucosal wetness and has been previously validated for its utility in diagnosing dry mouth.[11,12] Fukushima et al demonstrated the device's effectiveness in distinguishing between individuals with and without dry mouth, showing high sensitivity and specificity in detecting oral dryness.[11] Also, a study on dehydrated patients showed a significant correlation between the severity of dehydration and oral moisture levels as measured by this oral moisture-checking device.[12]

Except at the beginning of application, saliva substitute formulas, which are characterized by higher viscosity than water,[7] consistently maintained higher relative wetness than water, which was particularly significant beyond 60 minutes. This study is consistent with a previous study, which showed the superior effectiveness of saliva substitutes for water in patients with dry mouths.[16–18] Saliva substitutes showed almost threefold relative wetness compared with pre-application at all time points. This outcome indicates that all saliva substitutes effectively increased wetness upon application and up to 120 minutes after application, which is similar to results in previous studies.[19,20] Furthermore, the wetness levels from all novel saliva substitute applications reached moisture levels similar to those of patients without dry mouth.[11]

In this study, the wetness of the water significantly gradually decreased every 10 minutes. At 60 minutes, the wetness of water was decreased by one-third and was almost decreased by half at 120 minutes compared with 0 minutes. Although water can evaporate into the surrounding air, a plastic cover controlled and minimized this evaporation in this study. The nature of the water itself could explain our results. Similar to the human tongue, swallowing and speaking flushes water to the esophagus, which decreases water on the tongue, making it feel drier, especially in patients with a dry mouth.[21] Femiano et al suggested sipping water every 1 hour for patients with dry mouths.[22] They showed no significant symptomatological improvement after 1 hour of water intake. The results of our study are consistent with this suggestion.

Similar to previous reports,[20,23,24] saliva substitute solution in this study, commercial saliva substitute mouthwash showed the most consistent and prolonged effect in maintaining wetness, followed by RSU and hospital-based saliva substitute solutions. Each solution significantly changed from the beginning of the application to 120 minutes, which is consistent with Donath et al's study.[19] SSM and SSL maintained wetness over time and were equivalent to commercial saliva substitute mouthwash and appeared more effective based on their consistently higher relative wetness than SM and SV across all time points. The RSU solution without a sour flavor was not different in wetness compared with hospital–based mouth rinse and was significantly inferior to commercial saliva substitute mouthwash. These findings suggest that SSM and SSL formulas are more effective than SM and SV formulas in maintaining a long-lasting sensation of wetness in the mouth. Sour flavoring from citric acid or lemon oil may be a beneficial addition to saliva substitute solutions in terms of providing a longer-lasting beneficial effect in relief of the dry mouth feeling compared with plain salivary substitutes.[22] Mizuhashi et al reported that the effectiveness of moisturizing gels varied according to their flavor.[25] The acidity of citric acid or from Japanese apricot moisturizing gels is effective for continuously increasing saliva secretion in individuals with oral dryness.[25] Further research on the specific ingredients or compositions of saliva substitute solutions would allow for a more complete interpretation. Additionally, further investigation to understand the particular components could help explain the observed differences in effectiveness behind this sustained effect and lead to more success in retaining moisture between the RSU solutions with and without sour flavor.

In this study, RSU gel initially showed similar wetness to water, but showed a higher wetness than water at 60 minutes and longer. At 120 minutes, the wetness resulting from the RSU gel was not different from the commercial gel and remained stable, which is similar to a previous report.[20] Similar to the commercial products, a saliva substitute of the RSU gel formula provided more stable wetness at 120 minutes than the RSU solution formula.

In this study, we investigated the equivalent quantity of solution and gel spread as a thin film over the experimental site. Therefore, the observed wetness could reflect the effectiveness of each preparation on the tongue mucosa. The

detected differences in effectiveness between the solution and gel formulas could be because of several properties, such as the ingredients and delivery mechanism.[7] The specific ingredients and their concentrations differed between each saliva substitute gel and solution formula. Some ingredients might be more effective in gel form, while others might work better in a solution format. Sprays from a solution might deliver a broader or more uniform coating, while gels might create a more concentrated area of wetness.[7] Assy et al examined the criteria for new saliva substitutes according to the preferences of patients with Sjögren's syndrome.[26] They reported that the ideal saliva substitute had a thin, watery consistency in spray form, with a neutral flavor, and provided prolonged alleviation of a dry mouth. Additionally, this substitute should preferably not contain artificial sweeteners or alcohol, should not have a bitter taste, and should not cause discoloration of the teeth. Further studies on our novel saliva substitute formulas and clinical investigation in patients with dry mouth need to be performed.

A strength of our findings is that relative wetness was used for the analysis of saliva substitutes. The wetness measurement also did not affect the obtained results, because a single researcher performed the measurements to avoid interobserver variation. Although useful results were obtained from this investigation, the study has some limitations. This was an in vitro study of the swine tongue. Clinical research related to novel saliva substitutes in patients with dry mouth needs to be performed to confirm the applicability of our findings irrespective of the natural salivary flow or mechanical movement of the oral cavity.

Conclusion

All novel substitutes offered increased wetness upon application, similar to commercial products from this in vitro study. The RSU solution with a sour flavor was similar to commercial saliva substitute mouthwash, and the RSU gel was identical to commercial saliva substitute gel. By 120 minutes, all saliva substitutes were more effective than water in maintaining mucosal wetness. RSU saliva substitutes in gel formulas showed promise in maintaining constant wetness and were superior to RSU solutions up to 120 minutes. These findings suggest that these inexpensive formulations could be a viable alternative for patients with dry mouth who cannot afford relatively more expensive commercial products.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Cannon I, Robinson-Barella A, McLellan G, Ramsay SE. From drugs to dry mouth: a systematic review exploring oral and psychological health conditions associated with dry mouth in older adults with polypharmacy. *Drugs Aging*. 2023;40(4):307–316. doi:10.1007/s40266-023-01017-5
2. Molek M, Florenly F, Lister INE, Wahab TA, Lister C, Fioni F. Xerostomia and hyposalivation in association with oral candidiasis: a systematic review and meta-analysis. *Evid Based Dent*. 2022. doi:10.1038/s41432-021-0210-2
3. Khongsirisombat N, Kiattavorncharoen S, Thanakun S. Increased oral dryness and negative oral health-related quality of life in older people with overweight or obesity. *Dent J*. 2022;10(12):231. doi:10.3390/dj10120231
4. Thomson W. Dry mouth and older people. *Aust Dent J*. 2015;60(S1):54–63. doi:10.1111/adj.12284
5. Assery MKA. Efficacy of artificial salivary substitutes in treatment of xerostomia: a systematic review. *J Pharm Bioallied Sci*. 2019;11(Suppl 1):s1–s12. doi:10.4103/jpbs.jpbs_220_18
6. Ito K, Izumi N, Funayama S, et al. Characteristics of medication-induced xerostomia and effect of treatment. *PLoS One*. 2023;18(1):e0280224. doi:10.1371/journal.pone.0280224
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. doi:10.3390/ijms20133199

8. Sakamoto M, Araki J, Moriyama M, et al. The utility of oral moisture measurement for the diagnosis of Sjögren's syndrome: its potential application as a diagnostic criterion. *J Oral Maxillofac Surg Med Pathol*. 2024;36(5):743–748. doi:10.1016/j.ajoms.2024.02.007
9. Goto T, Kishimoto T, Iwawaki Y, et al. Reliability of screening methods to diagnose oral dryness and evaluate saliva secretion. *Dent J*. 2020;8(3):102. doi:10.3390/dj8030102
10. Navazesh M, Kumar S. Measuring salivary flow: challenges and opportunities. *J Am Dent Assoc*. 2008;139(suppl 2):35S–40S. doi:10.14219/jada.archive.2008.0353
11. Fukushima Y, Yoda T, Araki R, et al. Evaluation of oral wetness using an improved moisture–checking device for the diagnosis of dry mouth. *Oral Sc Int*. 2017;14(2):33–36. doi:10.1016/S1348-8643(17)30017-4
12. Fukushima Y, Sano Y, Isozaki Y, et al. A pilot clinical evaluation of oral mucosal dryness in dehydrated patients using a moisture-checking device. *Clin Exp Dent Res*. 2019;5(2):116–120. doi:10.1002/cre2.145
13. Okamoto A, Miyachi H, Tanaka K, Chikazu D, Miyaoka H. Relationship between xerostomia and psychotropic drugs in patients with schizophrenia: evaluation using an oral moisture meter. *J Clin Pharm Ther*. 2016;41(6):684–688. doi:10.1111/jcpt.12449
14. 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(11):4019–4030. doi:10.1007/s00784-020-03272-x
15. Yazicioglu O, Ucuncu MK, Guven K. Ingredients in commercially available mouthwashes. *Int Dent J*. 2024;74(2):223–241. doi:10.1016/j.identj.2023.08.004
16. Jose A, Singh ML, Magnuson B, Farag A, Varghese R, Papas A. A randomized controlled study to evaluate an experimental moisturizing mouthwash formulation in participants experiencing dry mouth symptoms. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2018;126(3):231–239.e5. doi:10.1016/j.oooo.2018.05.007
17. Jose A, Siddiqi M, Cronin M, Dilauro TS, Bosma ML. A randomized clinical trial in subjects with dry mouth evaluating subjective perceptions of an experimental oral gel, an oral rinse and a mouth spray compared to water. *Am J Dent*. 2016;29(1):58–64.
18. Jose A, Atassi M, Shneyer L, Cronin M. A randomized clinical trial to measure mouth moisturization and dry mouth relief in dry mouth subjects using dry mouth products. *J Clin Dent*. 2017;28:32–38.
19. Donath F, Tonner F, Chavda R, Gatignol J-P, Bouyrie J. Randomized trial of the efficacy and safety of a new oral spray for drug–induced xerostomia. *Clin Exp Dent Res*. 2016;2(2):112–120. doi:10.1002/cre2.29
20. Barbe AG, Ludwar L, Hamacher S, Noack MJ. Efficacy of a newly developed mouth gel for xerostomia relief—A randomized double-blind trial. *Oral Dis*. 2019;25(6):1519–1529. doi:10.1111/odi.13105
21. Mizuhashi F, Takahashi M, Mizuhashi R, Toya S, Morita O, Koide K. Influence of swallowing saliva repeatedly on oral moisture. *J Prosthodont Res*. 2010;54(3):128–132. doi:10.1016/j.jpor.2009.12.002
22. 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
23. Barbe AG, Schmidt-Park Y, Hamacher S, Derman SHM, Noack MJ. Efficacy of GUM® hydral versus biotène® oralbalance mouthwashes plus gels on symptoms of medication-induced xerostomia: a randomized, double-blind, crossover study. *Clin Oral Investig*. 2018;22(1):169—180. doi:10.1007/s00784-017-2096-0
24. Salom M, Hachulla E, Bertolus C, Deschaumes C, Simoneau G, Mouly S. Efficacy and safety of a new oral saliva equivalent in the management of xerostomia: a national, multicenter, randomized study. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2015;119(3):301–309. doi:10.1016/j.oooo.2014.12.005
25. Mizuhashi F, Koide K, Toya S. Effectiveness of oral moisturizing gel and flavor on oral moisture and saliva volume: a clinical study. *J Prosthet Dent*. 2021;125(5):767–771. doi:10.1016/j.prosdent.2020.02.031
26. Assy Z, Bikker FJ, Mashhour E, Asadi M, Brand HS. Preferences of Sjögren's syndrome patients regarding potential new saliva substitutes. *Clin Oral Investig*. 2022;26(10):6245–6252. doi:10.1007/s00784-022-04576-w