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Effect of lozenge surface texture, taste and acidity on salivary flow rate: A cross-over preclinical trial in healthy subjects

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Xerostomia, Lozenge, Dry mouth, Saliva stimulation, Salivary flow

Abstract

Dry mouth is a multifaceted condition which is caused by reduced salivary secretion. This study aimed to evaluate and compare the effects of different lozenge surface textures, tastes and acidity levels on stimulated salivary secretion for increased oral moistening in participants without hyposalivation. This randomized, double-blind, clinical crossover trial with before and after comparison involved 33 healthy volunteers. Five lozenges, including a baseline control (C), apple (A), sour (S), sour apple (SA) and granular pectin (P) were tested on five different days with all the subjects. Salivary flow, pH value, and subjective feeling (visual analog scale) were measured before and after consuming the lozenge each day. Throughout all trial days the unstimulated whole salivary flow (UWSF) averaged 0.65 $\pm$ 0.26 ml/min. Lozenges S, SA, and P showed higher stimulated whole salivary flow (SWSF) than C ($P < 0.001$) by more than 0.5 ml/min. Lozenge P, with a rough surface, demonstrated the highest difference between UWSF and SWSF, 2.41 $\pm$ 0.69 ml/min. The stimulated saliva with the lozenges containing acidifiers (S, SA and P) was more than 1.4 pH units lower compared to lozenges C and A ($P < 0.001$). Subjects reported the strongest subjective feeling of increased saliva with lozenges SA and P. Overall lozenges SA and P provided the best objective results in enhancing salivary flow rate and subjective feeling of increased salivary flow.

Introduction

Dry mouth is a multifaceted condition with various nomenclatures utilized in literature to describe it. Xerostomia is merely the subjective sensation of dry mouth, whereas hyposalivation describes reduced salivary production (Sreebny & Valdini, 1988; Davies, 1997; Meyer-Lueckel & Kielbassa, 2002; Saleh et al., 2015). Furthermore, asialia is used if salivation cannot be detected (Saleh et al., 2015). The complexity of dry mouth is that not all patients with xerostomia (subjective) suffer from hyposalivation (objective), and conversely, not all patients with hyposalivation suffer from xerostomia (Guggenheimer & Moore, 2003; Sreebny & Vissink, 2010). The prevalence of dry mouth increases with age (Taubert et al., 2007; Thomson, 2015; Filippi & Waltimo, 2020). The most common cause is the intake of xerogenic medications or functional degeneration of the salivary glands (ionising radiation, radiotherapy in the head and neck region). Other causes can be local (acute/chronic diseases of the salivary glands, malignancy, etc.) or systemic diseases (rheumatological, chronic inflammatory, endocrine, genetic, metabolic, and infectious diseases) (Kielbassa et al., 2006; Saleh et al., 2015).
Despite extensive salivary diagnostics, the cause is not always traceable. This is relevant because a causal treatment (therapy of the underlying disease or changing medication) promises the best treatment success. If a causal therapy is not possible in patients with dry mouth, the literature recommends salivary stimulation (Sreebny, 1989; Närhi et al., 1999; Jedel, 2005; Strietzel et al., 2007; Femiano et al., 2011; Alajbeg et al., 2012). There are various known options to that end, such as mechanical stimulation, gustatory stimulation, electrical stimulation, acupuncture, pharmacological stimulation, and topical use of pharmacological solutions (Bernardi et al., 2002; Frydrych et al., 2002). In addition, the treatment of hyposalivation often focuses on providing palliative care rather than a curative approach (Kielbassa et al., 2006; Tschoppe et al., 2010). This is due to the greatly reduced or even absent residual activity of the large salivary glands. This leaves symptomatic treatment as the last available option. Lozenges can be used for salivary stimulation as well as symptomatic treatment (Björnström et al., 1990; Gravenmade & Vissink, 1993; Dawes, 2008). Not only do they work as a mechanical stimulation (mastication by sucking the lozenge), but they can also lead to a gustatory stimulation. This puts lozenges in a unique spot compared to chewing gums, as they do not dissolve and thereby do not have the salivary substitute properties of the lozenges. After salivary stimulation, a symptomatic therapy with salivary substitutes or, if necessary, household remedies can be performed. The advantage of lozenges over chewing gum is that the lozenge melts. Therefore, the lozenge plays an important role in treating dry mouth, as it not only stimulates saliva but also can replace saliva to a certain extent. It is important to note, that this will only work when there are remaining salivary gland cells that can be stimulated. Patients with dry mouth and no remaining salivary flow may encounter challenges in consuming a lozenge (Sreebny & Vissink, 2010).
In cases of dry mouth, patients are often recommended to chew sugar-free chewing gum. However, for denture wearers and patients with severe dry mouth, this can lead to the gum sticking to teeth or dentures. The advantage of lozenges is that they are easily available and can be consumed anywhere, making them readily accessible to patients.
One of the main causes of dry mouth is the insufficient production of saliva by the salivary glands. One way to counteract this is to stimulate salivary production with lozenges. To determine which characteristic of a lozenge can stimulate this function the most, this study was conducted. It aimed to evaluate and compare the effects of different lozenge surface textures,

tastes and acidity levels on stimulating salivary production for increased oral moistening in healthy volunteers as part of a preliminary investigation and screening process for later experiments in patients suffering from reduced salivary flow rate. In addition to assessing salivary flow rates, pH measurements were conducted and data on sex, age, height, weight, BMI, stress levels and subjective dry mouth assessments (Xerostomia Inventory) were collected. This preclinical trial was intentionally conducted exclusively with healthy volunteers due to the high sensitivity of mucous membranes in the mouths of individuals experiencing dry mouth (Millsop et al., 2017). It is imperative that the lozenges are initially well-received by healthy test subjects to mitigate potential discomfort for patients with dry mouth. Based on the mentioned context, the following lozenges for salivary stimulation were developed. Our primary goal was to investigate the impact of incorporating flavor (A: apple), acid (S: sour), or both components (SA: sour-apple) into an isomalt-based lozenge on the enhancement of salivary flow rate (subjective and objective). Additionally, a comparison of the impact of the lozenge surface was pursued by adding granular pectin to the lozenge SA, resulting in the creation of lozenge P (P: pectin).

Materials and methods

This clinical crossover trial was reviewed and approved by the Ethics Committee of Northwestern and Central Switzerland (Approval Number: 2020-01942) and conducted at the University Center for Dental Medicine Basel (UZB; University of Basel, Basel, Switzerland) in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. All the participants have signed and approved an informed consent. It was designed as a randomized double-blind clinical crossover trial with before and after comparison (subjects as well as investigators were blinded). In order to detect a difference in SFRdiff of 0.15 ml/min, with 80% power and a 5% significance level in a paired t-test for the given repeated measure design, a minimum of 28 subjects were required. Voluntary participants were recruited through posters displayed at the University Center for Dental Medicine Basel. For this study 33 suitable subjects were selected who were willing to participate, systemically healthy, and without allergies. These subjects were older than 18 years of age, non-smokers, not pregnant, and not currently using any medication (excluding contraceptives). To account for the impact of BMI and stress on salivary production, prior to the trials, all subjects were provided with a medical history form containing specific questions about sex, age, height, weight, body mass index (BMI), as well as their perceived stress levels and any instances of experiencing dry mouth (Guggenheimer & Moore, 2003). They also got a Xerostomia Inventory (XI) containing eleven specific questions about xerostomia and related oral symptoms.

Lozenge composition

The five lozenges used in this study were manufactured by Ricola (Ricola; Laufen, Switzerland). The lozenge Control (C) (isomalt + steviol glycosides + cooling aroma) was used as a baseline. Each of the other four lozenges had distinct characteristics. Lozenge Apple (A) (baseline + apple flavor), Sour (S) (baseline + malic acid + citric acid), Sour Apple (SA) (baseline + malic acid + citric acid + apple flavor), and granular Pectin (P) (baseline + malic acid + citric acid + apple flavor + pectin) were compared with the Control C.

Apple flavor was chosen as gustatory stimulation. The use of citric acid (E330) improves dry mouth, but caution should be exercised regarding the risk of erosion on the remaining teeth and irritation of the oral mucosa (Femiano et al., 2011). Malic acid (E296) has a lower erosive potential on teeth, which is why this acid was used in addition to citric acid in the tested lozenges (Meurman et al., 1990). Pectine, a natural polysaccharide extensively applied in food manufacturing, was used in powder form as abrasive coating to roughen the surface of the lozenge (Einhorn-Stoll, 2018; Cerri et al., 2023).

Test procedure

In order to eliminate the influence of circadian rhythm, the subjects were specifically instructed to appear at the same time of day (09:00 am) on all five days. They were not allowed to smoke or consume any alcoholic or caffeinated product 24 h before the examination. Furthermore, the subjects were not allowed to eat, drink, practice oral hygiene (including chewing gum/sweets) or use lip balm for 90 minutes prior to the examination.
On each trial day, the salivary flow rate was determined twice (Fig. 1): first unstimulated without lozenge (UWSF) and then stimulated with lozenge (SWSF). The subjects were instructed to sit still and upright with a slight forward inclination of their upper body during the measurements, ensuring minimal distractions. In the initial measurement (“A”), the subjects were asked to swallow all their saliva at the first acoustic signal (T0(A)). From this moment on, the subjects were asked to spit into the collection tube (“A”) every 30 seconds (at the sound of the acoustic signal) for 5 minutes.

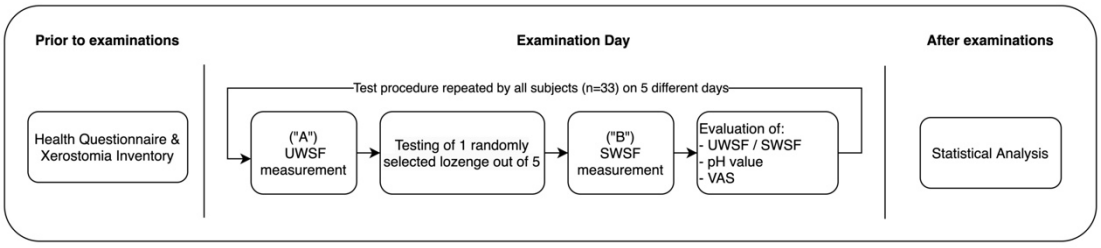

Figure 1. Flowchart displaying the test procedure. UWSF: unstimulated whole salivary flow; SWSF: stimulated whole salivary flow; VAS: visual analog scale.

For the second measurement (“B”), the subjects were directed to suck the before randomly selected lozenge for 1 minute. After that, a new signal (T0(B)) sounded, at which the subjects were asked to swallow the entire saliva (without the lozenge). From this point on, the procedure was the same as for the first measurement. Strict attention was paid to ensure that the lozenge was not swallowed or fell into the collection tube. Had such event occurred, the lozenge would have been promptly extracted from the tube using sterile tweezers and the subject would have resumed sucking on it for the remaining duration. To mitigate any potential “period effect” bias in the evaluation of the results, the lozenges were tested in a randomized order across all subjects. During the trial, every subject received a numbered envelope that was returned to them each trial day. Within the envelope, there were 5 individually wrapped lozenges, each labeled with a numerical code. On each trial day, the subjects randomly selected one lozenge from the envelope. Furthermore, to prevent potential bias associated with

testing multiple lozenges on the same day, only one measurement of UWSF and one measurement of SWSF were taken each day.
To quantify the extent of the increase in salivary flow rate between UWSF and SWSF, the metric called SFRdiff (salivary flow rate difference) was introduced, defined as the difference between SWSF and UWSF. The purpose of this metric is to compare and identify which lozenge induced the most significant augmentation in salivary flow rate.

Determination of the salivary flow rate

The amount of saliva was determined by weight in grams using a Semi-micro balance 1502ZX (Mettler Toledo; Columbus, Ohio, USA). 1 milliliter of saliva equals 1 gram (Gravenmade & Vissink, 1993). To determine the amount of saliva, each collection tube 50ml (Sarstedt; Nümbrecht, Germany) was already weighed (empty) before the trials. After the sialometry, the tubes were weighed again and the initial weight was subtracted resulting in the total amount of the saliva in grams. The UWSF and SWSF (ml/min) were then determined by dividing this number by five (5 minutes measuring time) and were then recorded on the questionnaires that were filled out by the subjects on the same trial day.

Determination of the pH value

Like the salivary flow rate, the pH value was also evaluated immediately after the trial was conducted. The pH value was determined using a pH-meter FiveEasy Plus FP20-Micro-Kit (Mettler Toledo; Columbus, Ohio, USA). First the UWSF was measured, then the SWSF. After each pH measurement, the measuring electrode was cleaned with deionized water. Prior to each day of the experiment, the pH-meter was calibrated accordingly. The pH values were then recorded on the questionnaires that were filled out by the subjects on the same trial day.
Determination of the subjective feeling (VAS)
After every trial day, the subjects filled out a questionnaire in which they indicated their subjective sensations of the lozenge using a visual analog scale (VAS) with the following questions: does the lozenge give the sensation of more saliva, does the lozenge taste sour, does the lozenge have a pleasant taste, does the lozenge have a rough surface, would you consume such a lozenge again, would you recommend this lozenge for dry mouth. The VAS all had a length of exactly 10 centimeters. After sucking the lozenge, the subjects had to make a cross on the line. A ruler was used to measure the distance between the starting point of the line and the center of the cross. The length was measured to the nearest millimeter and then recorded as a number.

Statistical analysis

The differences between UWSF and SWSF (SFRdiff) were calculated by subtracting UWSF from SWSF values. As verified by graphical tools (quantile comparison plots, standardized residuals versus fitted values), SFRdiff values were analyzed on the original scale. Therefore, mean (SD) values and the corresponding p-values (F-test) were indicated. For the evaluation of the VAS scales median (IQR) values were presented with the corresponding p-values from the nonparametric significance test (Kruskal-Wallis). Comparing SFRdiff between lozenges, linear mixed-effects models were calculated to receive estimates for the difference in mean values with

95% confidence intervals and the corresponding p-values. Pairwise comparisons were provided by applying the Tukey contrast. All regression models were adjusted with the cofactors, including sex, age, BMI, and pH value of SWSF. Potential significant interactions for gender or age were preliminarily analyzed, and potential nonlinearities for age and pH value were analyzed. A p-value <0.05 was considered significant. All analyses were performed using the statistical program R version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 39 subjects were assessed for eligibility; 4 subjects did not meet the inclusion criteria and an additional 2 subjects declined to participate. Consequently, a total of 33 subjects provided informed consent and underwent randomization. Each subject tested all five lozenges. The recruitment process for the trial is presented in the CONSORT flow diagram (Fig.2). The average age of the subjects was 25.9 ±7.3 years. Among the subjects, 18 (55%) were identified as females, while 15 (45%) were males. The subjects exhibited a mean BMI of 22.3 ±2.7. A total of 7 subjects (21%) reported experiencing stress. The total points achieved in the Xerostomia Inventory (XI) averaged 19.6 ±5.3 (Table 1). The anamnestic factors such as height, weight, and BMI had a significant association with sex, whereas factors such as stress and total points in the XI did not show a high significance level.

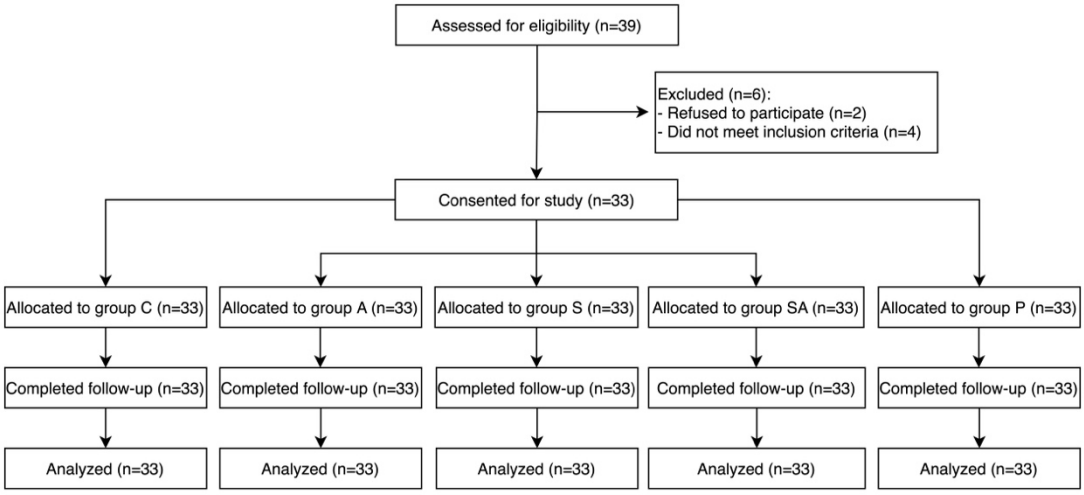

Figure 2. CONSORT flow diagram of subject inclusion.

The average unstimulated whole salivary flow (UWSF) across all trial days and subjects was 0.65 ±0.26 ml/min, and the stimulated whole salivary flow (SWSF) averaged 2.66 ± 0.77 ml/min (Tab. II). Among the lozenges, C exhibited the lowest difference between UWSF and SWSF (SFRdiff) with a mean SFRdiff of 1.57 ± 0.46 ml/min (p<0.001) across all subjects (Fig. 3). The largest SFRdiff was measured in group P with 2.41 ± 0.69 ml/min (p<0.001) followed by group SA with 2.17 ± 0.73 ml/min (*P* < 0.001) (Table 2).

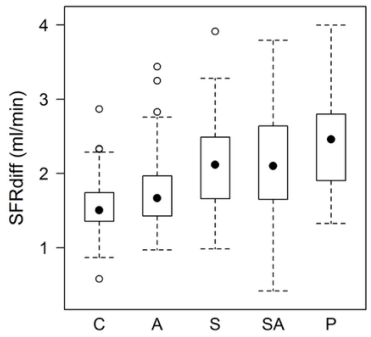

Figure 3. Boxplot: SFRdiff in ml/min of the five lozenges. C: control; A: apple; S: sour; SA: sour apple; P: pectin; SFRdiff: stimulated whole salivary flow – unstimulated whole salivary flow.

Adding apple flavor A to the control C led to an increased SWSF of +0.23 ml/min ($P = 0.029$). The largest increase in SWSF occurred in group P, where the SWSF showed a gain of +0.86 ml/min ($P < 0.001$). The lozenges S, SA and P showed a by >0.5 ml/min higher SWSF than C ($P < 0.001$). Under current conditions, UWSF pH values between 6.38 and 8.47 could be measured. The average UWSF pH value was 7.05 ± 0.28. No SWSF below the pH value of 6.0 was measured for A and C (Fig. 4). Only SA, P, and S exhibited pH values below the critical pH threshold of 5.5, as defined in the methods section.

Table 1. Main characteristics of the study population. Mean (SD, standard deviation) are indicated. *P*-values are derived from t-tests.

	Female (*N* = 18)	**Male (*N* = 15)**	**Total (*N* = 33)**	***P*-value**
Age (years)	23.7 (1.8)	28.5 (10.2)	25.9 (7.3)	0.062
Height (cm)	167.2 (8.3)	182.5 (5.6)	174.2 (10.5)	<0.001
Weight (kg)	59.6 (6.5)	77.9 (11.0)	67.9 (12.7)	<0.001
BMI	21.4 (2.5)	23.3 (2.5)	22.3 (2.7)	0.031
Stress yes in % (n)	33.3 (6)	6.7 (1)	21.2 (7)	0.095
Total Points in Xerostomia Inventory (11 – 55)	20.9 (4.8)	18.1 (5.6)	19.6 (5.3)	0.129
UWSF (ml/min)	0.60 (0.28)	0.70 (0.22)	0.65 (0.26)	0.012

Note. UWSF: unstimulated whole salivary flow.

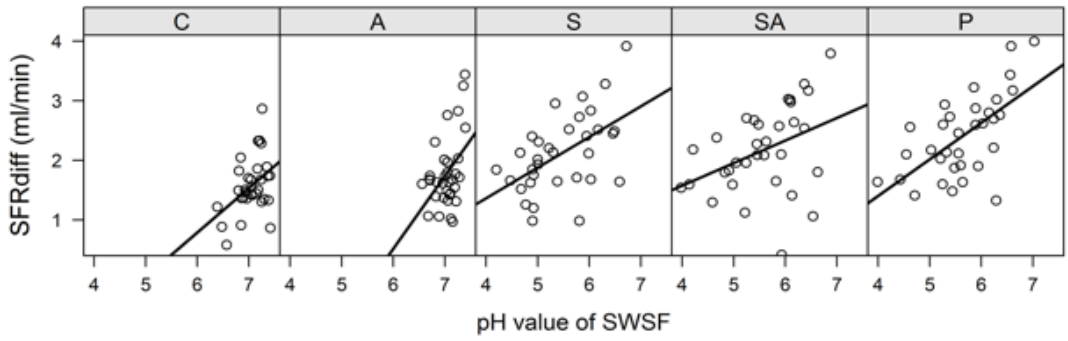

Figure 4. pH values of the SWSF in correlation to the SFRdiff (ml/min) of the five lozenges. C: control; A: apple; S: sour; SA: sour apple; P: pectin; SWSF: stimulated whole salivary flow; SFRdiff: SWSF – UWSF.

If a higher SFRdiff was achieved through lozenge consumption, a less pronounced decrease of the SWSF pH value was observed. Conversely, when a smaller SFRdiff was observed, the pH value exhibited a greater decline.

Table 2. Overview of the UWSF and SWSF evaluation results as well as the SFRdiff and the pH-values of UWSF and SWSF. Mean and standard deviation are indicated. Overall *P*-values for UWSF/SWSF, SFRdiff and pH are derived from F-tests.

	C	A	S	SA	P	Total	*P*-value
UWSF (ml/min)	0.63 (0.26)	0.64 (0.25)	0.70 (0.28)	0.62 (0.26)	0.64 (0.24)	0.65 (0.26)	0.794
SWSF (ml/min)	2.20 (0.61)	2.43 (0.68)	2.81 (0.77)	2.79 (0.78)	3.06 (0.74)	2.66 (0.77)	<0.001
SFRdiff (ml/min)	1.57 (0.46)	1.78 (0.60)	2.11 (0.66)	2.17 (0.73)	2.41 (0.69)	2.01 (0.69)	<0.001
pH UWSF	7.03 (0.27)	7.07 (0.24)	7.08 (0.33)	7.05 (0.27)	7.02 (0.28)	7.05 (0.28)	0.983
pH SWSF	7.05 (0.26)	7.04 (0.22)	5.46 (0.68)	5.56 (0.75)	5.65 (0.70)	6.15 (0.93)	<0.001

Note. C: control; A: apple; S: sour; SA: sour apple; P: pectin; UWSF: unstimulated whole salivary flow; SWSF: stimulated whole salivary flow; SFRdiff: SWSF – UWSF.

The evaluation of the VAS (VAS 0: does not apply; VAS 10: applies), which was filled out by the subjects after every examination, yielded the results summarized in Table 3. The subjects had the strongest subjective feeling of increased salivation with P and SA, but there was no significant difference between the lozenges ($P = 0.102$). Only the lozenges containing acidifiers, S, SA, and P, were considered to be sour. The most pleasant-tasting lozenge was SA with a VAS of 8.8 (IQR 7.0, 9.8) and only lozenge P was considered having a rough surface with a comparatively high VAS of 6.9 (IQR 5.0, 8.8; $P < 0.001$). Subjects would most likely consume SA again, and they would also most likely recommend SA to patients with dry mouth.

Discussion

This study could successfully demonstrate that the taste, acidity level and surface texture of lozenges can play a significant role in their ability to stimulate salivary production. Even introducing flavor to a previously mostly tasteless lozenge resulted in an enhanced SWSF. These

findings illustrate the influence of gustatory factors on salivary flow rates. Additionally, the inclusion of acid (in the form of lozenges S, SA and P) prominently increased salivary flow compared to the control group in healthy volunteers. However, it also correspondingly reduced the pH value of the SWSF saliva. Notably, altering the lozenge's surface from smooth to rough effectively augmented SWSF maintaining a constant pH level. Nevertheless, subjects favored the smooth surface of lozenge SA over the rough surface of lozenge P. The study employed a crossover design, enabling all 33 subjects to be tested with all five lozenges. Crossover studies provide the advantage of obtaining significant findings even with a smaller study population. Before conduction a trial in patients suffering from dry mouth, this study with healthy subjects was conducted. This allowed the evaluation of whether and to what extent a positive effect on dry mouth could be expected from these lozenges. Our subjects had a minimum 24-hour break between two different lozenges to reduce the carry-over effect.

Table 3. Tabular view of the visual analog scales results (0 – 10) on the subjective perception of the lozenges indicated as medians and interquartile ranges (IQR). P-values are derived from Kruskal-Wallis tests.

	Control (C)	Apple (A)	Sour (S)	Sour apple (SA)	Pectin (P)	*P*-value
1. Does the lozenge make you feel more salivated?	7.9 (6.9, 9.6)	8.2 (7.0, 9.9)	8.8 (7.0, 9.8)	9.0 (8.0, 9.9)	9.3 (8.4, 9.9)	0.102
2. Does the lozenge have a sour taste?	0.2 (0.0, 0.9)	1.0 (0.0, 2.2)	3.9 (1.3, 5.9)	4.1 (2.0, 6.1)	3.1 (1.2, 6.4)	<0.001
3. Does the lozenge have a pleasant taste?	5.8 (3.2, 7.0)	7.2 (6.0, 8.9)	6.9 (5.8, 7.9)	8.8 (7.0, 9.8)	8.2 (7.1, 9.6)	<0.001
4. Does the lozenge have a rough surface?	0.3 (0.1, 1.6)	0.5 (0.0, 2.0)	1.1 (0.1, 2.2)	0.3 (0.0, 1.1)	6.9 (5.0, 8.8)	<0.001
5. Would you consume such a lozenge again?	5.9 (2.2, 7.1)	7.0 (5.8, 9.1)	6.1 (5.0, 7.9)	9.1 (7.1, 10.0)	7.8 (6.9, 9.4)	<0.001
6. Would you recommend this lozenge to somebody suffering from dry mouth?	6.8 (5.1, 7.8)	7.7 (6.8, 9.2)	7.8 (6.1, 8.0)	8.6 (7.8, 9.6)	7.8 (6.9, 9.3)	0.005

Note. C: control; A: apple; S: sour; SA: sour apple; P: pectin; UWSF: unstimulated whole salivary flow.

Limits for physiological salivary flow rates are difficult to define because it is strongly dependent on intraindividual (time of day and hydration) and interindividual (sex, age, body weight, and size of salivary glands) variations (Sreebny, 2000; Sreebny & Vissink, 2010). Ericsson and Hardwick defined salivary flow rate values, which are still often used as reference values in Switzerland today (Ericsson & Hardwick, 1978). A UWSF ranging from 0.25–0.35 ml/min is considered within the physiological range, while values below 0.1 ml/min are categorized as very low. For SWSF, a physiological range of 1–3 ml/min is established, and values below 0.7 ml/min are classified as very low. In this study, the mean UWSF averaged 0.65 ml/min, which is considered relatively high. The subjects in this study were rather young (mean age: 25.9).

Changes in salivary flow rates depending on people's age have been discussed in earlier publications (Affoo et al., 2015; Xu et al., 2018). They reported that people of higher age have significantly lower (p<0.001) UWSF and SWSF than young people. The procedure for collecting UWSF samples can also impact the obtained measured values (Navazesh,1993, Navazesh & Kumar, 2008). In a prior study by Bergdahl and Bergdahl (2000), stress was found to have a significant association with dry mouth in subjects experiencing this condition (Bergdahl & Bergdahl, 2000). In the present study, none of the subjects suffered from dry mouth, which explains the absence of very low UWSF rates. This is also evident in the relatively modest mean score of 19.6 ±5.3 obtained in the Xerostomia inventory. The interpretation signifies that a score of 11 points (minimum) suggests the absence of dry mouth, while a score of 55 points (maximum) indicates an increased likelihood of experiencing dry mouth. For better illustration of the correlation between stress and dry mouth, a study design specifically involving subjects with dry mouth would be more suitable.

The strongest increase in SWSF was observed with P (+0.86 ml/min), which goes in line with the subjective perception of the participants, who also reported the highest sensation of increased saliva with P (VAS median: 9.3). The only difference between P and SA was the surface roughness of the lozenge, which was caused by non-dissolved, granular pectin particles on the surface itself (Einhorn-Stoll, 2018). As established in previous research, salivary production can be stimulated not only through gustatory (such as apple flavor in this case) and chemical stimulation (using malic acid and citric acid) but also through mechanical stimulation (sucking on the lozenge) (Sreebny, 1989; Davies, 1997; Da Mata et al., 2009). It should be noted that citric acid (as well as malic acid) can be a chemical stimulation as well as a gustatory stimulation of salivary flow if it is not tasteless. Since the only difference between SA and P was the surface texture of the lozenge, this result suggests that the additional surface roughness leads to an additional increase in the SWSF. However, patients with dry mouth often suffer from sensitive oral mucous membranes and are more susceptible to sharp edges. Those patients could find rough surfaces unpleasant (Tanasiewicz et al., 2016; Millsop et al., 2017). Considering this aspect, a comprehensible recommendation regarding the surface texture of lozenges for individuals with dry mouth can only be provided after testing the different surface textures on this specific population.

The role of the salivary pH value cannot be underestimated. The use of acids (malic acid and citric acid in this case) leads to increased salivary production but can have adverse effects like erosions on the dentition and irritations of the oral mucosa in the long term (Femiano et al., 2011). As known from other studies, an acidic pH value in the mouth leads to demineralization of enamel and dentin (Harper et al., 2021). The critical pH value for the demineralization of hydroxyapatite (enamel) is around 5.5. The analysis of the SWSF-saliva samples following the consumption of lozenges demonstrated that all lozenges containing malic and citric acid (S, SA, and P) led to a decrease in the pH value of the SWSF saliva. In this study, UWSF pH values between 6.38 and 8.47 could be measured, averaged at 7.05. This is very close to guideline values from previous studies in which a UWSF pH value of 6.5–6.9 is indicated as physiological (Harper et al., 2021). The SWSF usually has a slightly more basic saliva with pH values of 7.0–7.5. The results show that pH values were less sour when the SFRdiff was larger. This might be explained by the fact that the same volume of lozenge was dissolved in more saliva and therefore resulted in less acidifier concentration in the saliva probe. In this study, the SWSF was not measured by paraffin wax chewing gums but by acid-containing lozenges. This also explains

why pH values down to 3.98 were measured. This drop in pH below the earlier mentioned critical limit of 5.5 could pose a risk of dental erosion for patients who still have residual dentition. It would therefore be interesting to test the lozenge on edentulous subjects. For subjects with residual dentition, it would make sense to further develop the lozenge SA and P until the pH value is no longer close to the mentioned limit. In retrospect, it would have been beneficial to measure the pH value of the lozenges itself. This additional step would have provided clearer insights into the pH drop observed in the SWSF values.
Regarding the subjective sensation of the participants, the two lozenges SA and P were the most popular among the subjects. Not only did the subjects have the greatest feeling of more saliva with these two lozenges, but they also found these two the best tasting and would most likely consume these two again or recommend them to others. The greatest difference between the two lozenges was evident in the VAS for surface roughness. SA was not rough at all (VAS 1.00), whereas P was perceived as rough (VAS 6.29).
An acidic taste does not automatically mean an acidic pH value (Kajii et al., 2002; Roper, 2007). One reason for this is that the taste perception of inorganic acids is stronger than that of organic acids. It is important to note that an acidic taste causes more saliva to be produced, thus increasing the SWSF. However, the sour taste also leads to the stimulation of the swallowing reflex (Kajii et al., 2002). Therefore, the saliva gained is reduced again.
All tests were conducted on a group of healthy volunteers, limiting the applicability of the results to individuals with normal salivary gland function. In the case of individuals with dry mouth, salivary gland activity is often impaired, making stimulation less effective or even impossible. Among a group of subjects suffering from dry mouth, the outcomes might diverge. It would be intriguing to explore the potential of the lozenge SA and P not only as salivary stimulants but also as substitutes for saliva in such cases. Therefore, further studies need to be conducted especially on patients with dry mouth in order to evaluate the effectiveness of these lozenges as potential substitutes for saliva in such individuals.

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Zusammenfassung

Einleitung

Mundtrockenheit ist ein komplexes Symptom welches subjektiv und/oder objektiv bestehen kann. Die Prävalenz von Mundtrockenheit steigt mit zunehmendem Alter und ist in erheblichem Masse von der Restfunktion der Speicheldrüsen abhängig. In dieser klinischen Crossover-Studie ging es darum, den speichelstimulierenden Effekt von verschiedenen Bonboneigenschaften zu vergleichen.

Material und Methode

In dieser randomisierten, doppelblinden Crossover-Studie wurde das Ziel verfolgt, die speichelstimulierenden Effekte verschiedener Lutschbonbons zu untersuchen. In die vorliegende Studie wurden insgesamt 33 freiwillige gesunde Erwachsene einbezogen. Die Studie wurde durch die Ethikkommission Nordwest- und Zentralschweiz genehmigt und gemäss der 1964 Deklaration von Helsinki durchgeführt. Die Lutschbonbons wurden durch die Firma Ricola AG hergestellt. Die Kontrollgruppe erhielt ein Bonbon ohne Geschmacks- und Säurezusatz (C). Die restlichen Bonbons hatten zusätzliche Eigenschaften wie Apfelgeschmack (A), Säure (S), Apfelgeschmack mit Säure (SA) sowie Apfelgeschmack mit Säure und Pektin (P). Das Pektin dient dazu, die Oberfläche des Bonbons anzurauen. Alle Probanden mussten alle Bonbons in willkürlicher Reihenfolge testen. Die unstimulierte Speichelfliessrate (UWSF) wurde an jedem Versuchstag vor dem Lutschen des Bonbons und die stimulierte Speichelfliessrate (SWSF) danach gemessen. Um die Speichelfliessratendifferenz (SFRdiff) zu quantifizieren, wurde die UWSF-Rate von der SWSF-Rate subtrahiert. Zusätzlich erfolgte die Messung des pH-Werts sowohl vor als auch nach dem Lutschen des Bonbons. Die Auswertung der Speichelfliessrate erfolgte objektiv (Volumen) als auch subjektiv (anhand einer visuellen Analogskala = VAS).

Resultate

Von den 39 zu Beginn rekrutierten Probanden erfüllten 4 die Aufnahmekriterien nicht und 2 lehnten die Teilnahme an der Studie ab, sodass 33 Teilnehmer untersucht werden konnten. Jeder Proband hat alle 5 Bonbons an unterschiedlichen Tagen getestet. Die durchschnittliche UWSF betrug 0.65 ±0.26 ml/min (p=0.794). Die Probanden hatten die stärkste Zunahme der Speichelfliessrate (SFRdiff) mit Bonbon P mit 2.41 ±0.69 ml/min (p<0.001). Dicht gefolgt vom Bonbon SA mit 2.17 ±0.73 ml/min (p<0.001). Das Kontrollbonbon C bewirkte die niedrigste SFRdiff mit 1.57 ±0.46 ml/min (p<0.001). Der pH-Wert der UWSF betrug im Durchschnitt 7.05 ±0.28 (p=0.983). Die Bonbons mit Säurezusatz (S, SA und P) zeigten pH-Werte unterhalb von 5.5. Die Auswertung der Visuellen Analogskalen ergab, dass die Probanden mit den Bonbons SA und P das stärkste Gefühl von mehr Speichel hatten und das Bonbon SA am ehesten Patienten mit Mundtrockenheit empfehlen würden.

Diskussion

Die Ergebnisse dieser Studie zeigen, dass Bonbons mit Zusatz von Geschmack, Säure und rauer Oberfläche die Speichelproduktion signifikant anregen. Ebenfalls konnte gezeigt werden, dass eine raue Oberfläche zwar zu mehr Speichel führt, von den Probanden jedoch nicht als angenehm empfunden wurde. Der Zusatz von Säure führt einerseits zu einer erhöhten Stimulation von Speichel, anderseits kann die Säure bei bezahnten Probanden mit Mundtrockenheit negative Auswirkungen wie Erosionen an der Restdentition oder Irritationen der Mundschleimhaut verursachen. Weitere Studien mit mehr Teilnehmern sowie mit Patienten, die unter Mundtrockenheit leiden, sollten folgen. Ebenfalls sollte in zukünftigen Studien der pH-Wert der Bonbons möglichst basisch gehalten werden.

Résumé

Introduction

La sécheresse buccale est un symptôme complexe qui peut être perçu à la fois subjectivement et objectivement. Sa prévalence augmente avec l'âge et dépend largement de la fonction résiduelle des glandes salivaires. Cette étude clinique en crossover visait à comparer l'effet stimulant de la salive de différentes caractéristiques de bonbons.

Matériels et méthodes

Dans cette étude en crossover randomisée et en double aveugle, 33 adultes en bonne santé ont testé différents bonbons à sucer pour évaluer leurs effets sur la salivation. L'étude a été approuvée par la Commission d'éthique du Nord-Ouest et du Centre de la Suisse et menée conformément à la 1964 Déclaration d'Helsinki. Les bonbons, fournis par Ricola AG, incluaient des caractéristiques variées. Le groupe de contrôle était sans goût ni ajout d'acide (C). Les bonbons restants avaient des caractéristiques supplémentaires telles que le goût de pomme (A), l'acidité (S), l'acidité et le goût de pomme (SA) et l'acidité avec le goût de pomme et la pectine (P). Les participants les ont testés dans un ordre aléatoire. La salivation a été mesurée avant et après la prise des bonbons, ainsi que le pH, à la fois de manière objective (mesure du volume) et subjective (à l'aide d'une échelle analogique visuelle, VAS).

Résultats

Sur les 39 participants initialement recrutés, 4 ne répondaient pas aux critères d'inclusion et 2 ont refusé de participer à l'étude, laissant ainsi 33 participants pour les enquêtes. Chaque participant a testé les 5 bonbons différents à des jours différents. Le taux de UWSF moyen était de 0.65 ± 0.26 ml/min (p=0.794). Les participants ont montré la plus grande augmentation du taux de salivation (SFRdiff) avec le bonbon P, avec 2.41 ± 0.69 ml/min (p<0.001), suivi de près par le bonbon SA avec 2.17 ± 0.73 ml/min (p<0.001). Le bonbon témoin C a entraîné la plus faible augmentation du taux de salivation, avec 1.57 ± 0.46 ml/min (p<0.001). La valeur pH de UWSF était en moyenne de 7.05 ± 0.28 (p=0.983), tandis que les bonbons contenant de l'acidité (S, SA et P) avaient des valeurs de pH inférieures à 5.5. L'évaluation des échelles analogiques visuelles a montré que les participants ressentaient une plus grande sensation de salivation avec les bonbons SA et P, et qu'ils recommanderaient probablement le bonbon SA aux patients souffrant de sécheresse buccale.

Discussion

Les résultats de cette étude montrent que les bonbons contenant des saveurs, de l'acidité et une surface rugueuse stimulent significativement la production de salive. De plus, il a été démontré qu'une surface rugueuse, bien qu'augmentant la salivation, n'était pas perçue comme agréable par les participants. L'ajout d'acidité entraîne une stimulation plus forte de la salivation, mais chez les participants souffrant de sécheresse buccale, l'acidité pourrait avoir des effets négatifs tels que des érosions sur la dentition restante ou des irritations de la muqueuse buccale. Des études supplémentaires avec un plus grand nombre de participants, y compris des personnes souffrant de xérostomie, sont nécessaires. De plus, les futures études devraient s'efforcer de maintenir un pH des bonbons aussi basique que possible.

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