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Comparison of sesame oil wafers and lozenges as saliva substitutes for dry mouth in head and neck cancer patients: A crossover randomized control trial

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Abstract: **Background**: Dry mouth is a condition associated with significant morbidity. It not only causes discomfort but also increases risk of many health and oral health problems. **Objectives**: This study compared the efficacy and patient satisfaction of a novel sesame oil wafer, called "Freeze-Dried Sesame Oil Emulsion Salivary Substitute (FD-SOESS)," with ACT® lozenges in managing dry mouth in patients who had undergone treatment for head and neck cancer. **Methods**: A randomized, single-blind, crossover trial was conducted in 35 patients. Subjective dry mouth (Shortening Xerostomia Inventory), objective dry mouth (Clinical Oral Dryness Score, CODS), dysphagia (Eating Assessment Tool-10, EAT-10) and oral mucositis (WHO Oral Toxicity Scale) were assessed before and after 2 weeks of use. Satisfaction was rated using a visual analog scale (VAS 0-10). Outcomes were compared using paired t-tests and Wilcoxon signed-rank tests at a significance level of 0.05. **Results**: Both products showed significant improvements in objective dry mouth. While the lozenges group showed a borderline significant improvement in subjective dry mouth (P=0.037). Notably, the FD-SOESS group demonstrated significant improvement in dysphagia scores (P=0.003). Satisfaction levels were moderate to high in both groups, with slightly higher levels in the FD-SOESS group. **Conclusion**: To conclude, FD-SOESS significantly improved objective dry mouth and dysphagia but not subjective dry mouth. It received a relatively high level of satisfaction. Therefore, this newly developed product has the potential to be an alternative product for dry mouth patients.

Keywords: Artificial saliva; Dysphagia; Lozenges; Sesame oil; Xerostomia

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INTRODUCTION

Dry mouth has been used to describe hyposalivation and xerostomia that can occur separately or together (Liu *et al*., 2012, Johansson *et al*., 2012). Xerostomia is defined as the subjective experience of dry mouth and is diagnosed through self-report, whereas hyposalivation is defined as a low salivary flow that can be determined objectively (Alaraudanjoki *et al*., 2016). Dry mouth can be caused by numerous factors such as aging, medications, various systemic diseases (i.e., diabetes, hypertension, cardiovascular disorders, neurological disorders and psychological disorders) (Flink *et al*., 2008, Lee *et al*., 2015) and particularly radiation therapy (Han *et al*., 2015).

According to the Global Cancer Statistics Report (2022), there were 1.22 million deaths and 2.60 million new cases of head and neck cancer worldwide (Bray *et al*., 2024). Dry mouth is a common side effect in head and neck cancer patients, caused by radiation damage to salivary glands, which reduces saliva production (Han *et al*., 2015). A cumulative radiation dosage of 30 Gy or more is known to be the salivary gland threshold and can result in severe and irreversible dry mouth (Jasmer *et al*., 2020). The high prevalence of hyposalivation is linked to both higher radiation doses and a shorter interval between radiotherapy treatments (Schulz *et al*., 2021). The prevalence of dry mouth in radiotherapy for treating head and neck cancer patients is usually high. A recent study by Abo el Fadel *et al.* in 2024 reported a dry mouth prevalence of 85% among head and neck cancer patients undergoing radiotherapy (Abo el Fadel *et al*., 2024).

Dry mouth can affect both oral and general health. It can lead to dental caries, periodontal diseases, oral mucositis, halitosis, masticatory problems, dysphagia and eventually malnutrition (Millsop *et al*., 2017). If the salivary glands are partly damaged, dry mouth can be relieved by an endogenous approach that tries to increase the salivary gland function through mechanical and pharmaceutical stimulation, acupuncture, electro-stimulators and gene therapy (Sreebny, 2000). However, if the salivary glands are permanently damaged, the exogenous approach is used. This includes frequent water drinking, using moisturizing preparations and saliva substitutes *(Łysik et al*., 2019). Salivary substitutes help reduce chronic dry mouth by creating a protective film that reduces the risk of mechanical trauma (Hu *et al*., 2021). Dry mouth products

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come in several forms, including oral spray, gel, toothpaste, mouthwash, lozenges, pastilles, tablets, etc (Sardellitti *et al*., 2024). In Thailand and many other developing countries, saliva substitutes are rare and expensive due to importation costs from abroad.

The present study is an extension of our previous study. In our earlier study, we reported the development and characterization of our novel product for dry mouth called "sesame oil wafer" or "Freeze-dried Sesame Oil Emulsion Salivary Substitute (FD-SOESS)," which combines the benefit of sesame oil and the freeze-drying process. Our previous study found that FD-SOESS can stimulate and substitute saliva. Sesame oil could provide moisturizing and antioxidant properties and elevated salivary mucus concentrations in vitro (Amanat *et al*., 2024). In this study, we aimed to compare the efficacy in the management of dry mouth (subjective dry mouth, objective dry mouth, oral mucositis and dysphagia) and satisfaction (for taste, smell, ease of use, lubrication and moisturizing) and the side effects of FD-SOESS with the control (ACT® lozenges) among patients who had undergone treatment for head and neck cancer. We hypothesized the comparable relief of dry mouth and its related symptoms between FD-SOESS and ACT® lozenges.

MATERIALS AND METHODS

Study design

This study was a randomized, single-blind, two-sequence, crossover trial in which the examiners were blinded to treatment allocation. Blinding was achieved by coded labels. The trial was conducted on an equivalence framework to compare FD-SOESS and ACT® lozenges. The study treatment was FD-SOESS, or sesame oil wafer, which contains sesame oil (Huay Saew Royal Project Development Center, Chiang Mai, Thailand), sodium caseinate (Sigma-Aldrich, St. Louis, MO, USA), xanthan gum (Sigma-Aldrich, St. Louis, MO, USA) and stevia (Sigma–Aldrich, St. Louis, MO, USA). The control treatment was ACT® lozenges (Chattem, Inc., Chattanooga, TN, USA) containing isomalt, xylitol, sucralose, glycerin and flavors (Fig. 1).

Study population

The study was conducted at the Dental Clinic, Hat Yai Hospital, Songkhla, Thailand. The inclusion criteria consisted of adults aged 20 years and above with stable post head and neck cancer treatment with moderate to severe dry mouth. The exclusion criteria included no or mild xerostomia (subjective dryness score ≤ 7), allergy to sesame oil, xanthan gum and/or sodium caseinate, taking other dry mouth treatments, not tolerating a dental examination and dementia patients. The study was performed according to the Declaration of Helsinki and ICH-GCP. The required sample size was calculated based on paired t-test statistics, assuming a medium effect size of 0.5, 80% power and a 95% confidence level. The calculations were performed using G Power 3.1.9.7 software (Faul *et al*., 2009). The minimum required sample size was 34 participants. However, considering a potential dropout rate of 30%, the total recruited sample size was increased to 50 participants.

Study procedures

The random sequence was generated by the main investigator utilizing Random Allocation Software (https://mahmoodsaghaei.tripod.com/Softwares/randalloc.html). The randomization was done prior to data collection and allocation information was securely stored in sealed envelopes. According to the crossover design, the participants were randomly allocated the sequence of the use of products, either intervention (FD-SOESS) or control (ACT® lozenges), using a block randomization method with a block size of 10 for 5 blocks. A 2-week or 14 days washout period was given between intervention (FD-SOESS) or control (ACT® lozenges). Eligibility criteria were reassessed before starting round 2 to ensure similar baseline conditions and no potential carryover effect.

A trained research assistant gave the initial intervention and control products to the participants at the dental clinic. Participants in both groups were instructed to use the product four times daily before meals and at bedtime. They were advised to suck and gently move the product in the oral cavity to aid dissolution and ingredient distribution. Those with severe dry mouths were permitted to take a sip of water with the product to enhance its effectiveness. The participants were asked not to use any other saliva substitutes during the study period and were consequently checked for the convenience of care or product received at the follow-up. All the participants were sent text reminders on the third day after receiving the product as well as a weekly follow-up call to remind and facilitate them to come for follow-up, as well as ensure adherence to our study protocol. Moreover, participants were instructed to bring back the used FD-SOESS or lozenge packages during follow-up visits.

Data collection

The questionnaire for collecting characteristics of the participants comprised socio-demographic details, co-morbidities, medication history, radiotherapy treatment, type and site of cancer, as well as the participant's history of substance use (including smoking, alcohol, marijuana and kratom) and oral health care practices were collected. The primary outcomes included subjective dry mouth, objective dry mouth and patient satisfaction levels, while the secondary outcomes included mucositis and dysphagia. The following are the measurements of these outcomes.

Subjective dry mouth

A shorter version of the xerostomia inventory was used (Thomson *et al*., 2011). The questionnaire consists of 5 questions and the total score ranges from 5 to 15.

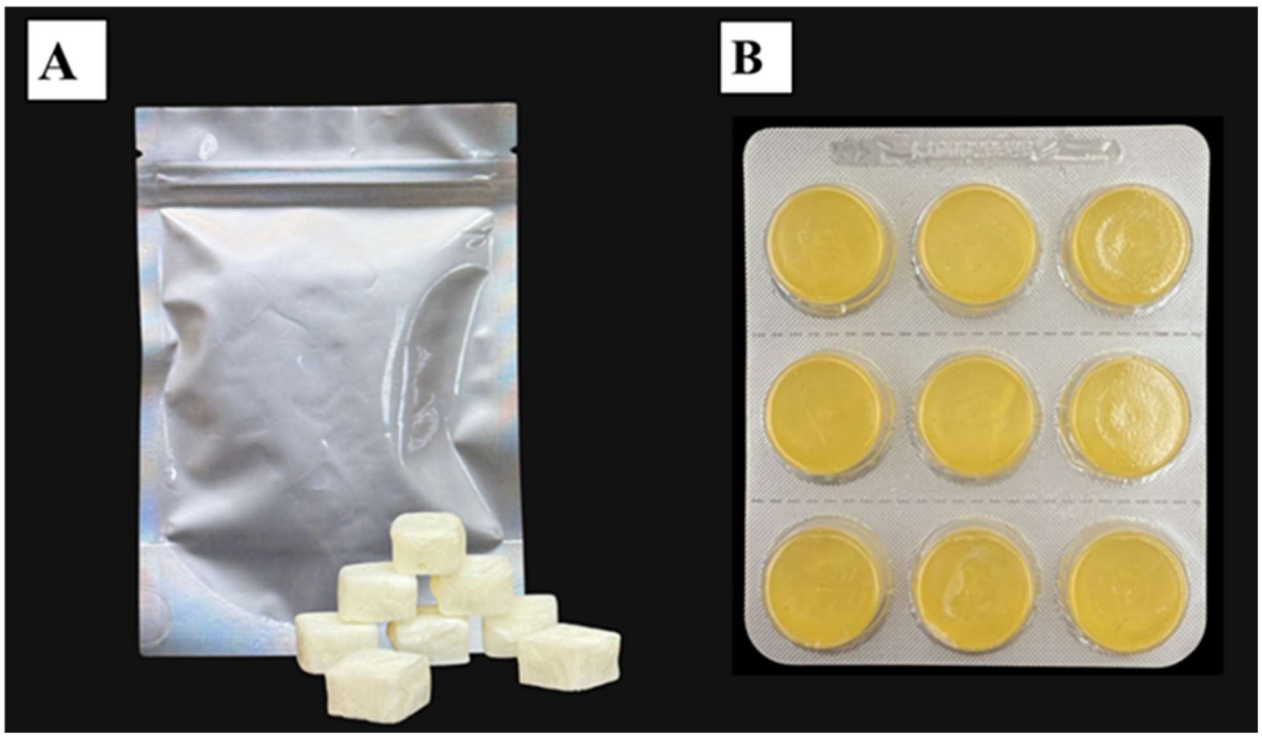

Fig. 1: Products and packages: (A) FD-SOESS and (B) ACT® lozenges.

Objective dry mouth

A clinical oral dryness score (CODS) was used (Osailan *et al*., 2012). This examination is carried out using a dental mirror and clinical observation. Only 8 items for CODS were used by removing the 2 items (altered/smooth gingival architecture and active or recently restored cervical caries) because they would not be changed within the observed duration (2 weeks) and 31.4% of our participants were edentulous. Therefore, the possible score for objective dry mouth in our study ranged from 0 to 8.

Patient satisfaction

Product satisfaction level was collected regarding overall satisfaction level, product characteristics (taste, smell, texture and ease of use) and symptom improvement (improvement in dry mouth, chewing, swallowing, speech and burning sensation) using a visual analog scale (VAS) of 0-10.

Oral mucositis

The WHO Oral Toxicity Scale was used for oral mucositis measurement (WHO, 1979). It is graded on a five-point scale: 1) no oral mucositis, 2) erythema and soreness, 3) ulcers and able to eat solids, 4) ulcers, requires liquid diet and 5) ulcers, alimentation not possible.

Dysphagia

The Eating Assessment Tool-10 (EAT-10) was used to document the initial dysphagia symptom in patients with swallowing disorders (Belafsky *et al*., 2008). It is a validated 10-item tool with a 0 to 4 score for each item. The total score ranges from 0 to 40.

In addition, we also recorded the side effects, average dissolving time (time since intake until all product was dissolved) and the average retention time (time from the product dissolving until the need to drink water or to relieve dry mouth symptoms) for both the FD-SOESS and lozenges.

Quality control

To validate the developed questionnaires, including the satisfaction level, the index of concordance (IOC) was assessed by three experts. The overall IOC score for all three experts was 0.86 and relevancy to the objectives was 0.90, which is well above the acceptable threshold of 0.80 (Fouzul Kareema and Bt Zubairi, 2021). Three examiners collected clinical data and were blinded to the product used by the participants. Before the clinical data collection on objective dry mouth (CODS) and oral mucositis (WHO Oral Toxicity Scale), they were trained and standardized against an experienced examiner on 10 participants. The participants were re-examined to evaluate intra-examiner reliability. The kappa coefficients of inter-examiner reliability for CODS and oral mucositis were 0.891 (0.811-0.942) and 0.852 (0.793-0.924), respectively, while the intra-examiner reliability (kappa coefficient) for CODS was 0.861 (0.834-0.903) and for oral mucositis 0.883 (0.852-0.921). Those values indicate a near-perfect agreement (Chaturvedi and Shweta, 2015).

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 29.0.2.0 (IBM Corp.,

Armonk, NY, USA) and tested at the significance level of 0.05. Descriptive statistics, including frequency, percentage, mean (standard deviation) and median (interquartile range, IQR), were used to summarize the variables of the study participants. To compare the outcome between the FD-SOESS and control groups as well as before and after the intervention, a paired t-test and Wilcoxon signed rank test were employed. Analyses were conducted under both Intention-to-Treat (ITT) and Per-Protocol (PP) frameworks. ITT was conducted using a multiple imputation approach (n=5) to measure the missing data values (Austin *et al*., 2021).

RESULTS

The data was collected from March 2024 to August 2024. The consort diagram (Fig. 2) shows that 50 participants were assessed for eligibility, and 48 individuals were included in the study. In the first round, 24 participants were allocated to the intervention group, and 24 participants were allocated to the control group. The intervention group lost 7 participants, and the control group lost 4. In the second round, the remaining participants crossed over: 17 from intervention to control and 20 from control to intervention. Each group then lost 2 more participants. In the second round, 18 participants in the intervention group and 15 in the control group completed the study. Ultimately, a total number of 35 participants completed the treatment in both rounds (groups) and were included in the final analysis for the intervention (first round 17, second round 18) as well as the control group (first round 20, second round 15). The loss of follow-up rates was 27% for the two groups.

Demographic characteristics

The baseline characteristics of the study participants are summarized in table 1. The average age of the participants was 56.49 years. Most of them were aged 40 years and above (85.7%), male (82.9%) and Buddhist (80.0%). A substantial percentage had no occupation (37.1%) and completed elementary school (37.1%). More than half of them had a normal BMI and 28.6% were underweight. Almost 46% of them were in cancer stage 4 before the cancer treatment. Most participants had cancers in the nasopharynx (40%) or pharynx (25.7%), with 91.4% receiving a radiation dose of 69.96 Gy. Over 80% underwent radiotherapy and/or chemotherapy for more than 6 weeks (table 1). One-third had no systemic diseases, while two-thirds were on medications, with about half using drugs that could cause dry mouth. Over 60% had a history of regular alcohol and tobacco use for more than 10 years and around 10% used kratom and/or marijuana.

Oral health status

As shown in table 2, 68.3% of the participants were dentate, while 31.4% were edentulous. All participants cleaned their mouths (brushing and/or rinsing) at least 2 times a day. More than half of them used fluoride toothpaste and about 31.4% did not use toothpaste. In the last year, 54.3% had dental visits more than 2 times and about 31% of them visited for routine check-ups or follow-ups, while 11.4% came for ulcerative mucositis treatment. Only 54.3% of participants could eat a normal diet, whereas 37.1% could eat a semi-solid diet and 8.6% could eat only a liquid diet.

Comparison of outcome variables

The result in fig. 3 followed a Per-Protocol (PP) approach. It compares the outcomes between the intervention (FD-SOESS) and control (lozenges) groups before and after treatment. At baseline (before the treatment), there was no significant difference between the intervention and control groups concerning all outcomes. After treatment, only the objective dry mouth score was significantly different ($P=0.017$), where the FD-SOESS group had a lower objective dry mouth score than the lozenges.

The objective dry mouth scores significantly decreased in both the intervention and control groups ($P<0.001$), with FD-SOESS showing a greater reduction than lozenges. However, the subjective dry mouth scores exhibited a statistically significant improvement ($P=0.037$) in the lozenges group, but not in the FD-SOESS group. Oppositely, the FD-SOESS group exhibited a significant improvement in the dysphagia scores ($P=0.003$), but the significance was not found in the lozenges group. Only 4 participants (11.4%) and 6 participants (17.1%) were found to have some levels of mucositis at baseline in the intervention and control groups, respectively. No significant change in mucositis was found in either group. Additionally, Intention-to-Treat (ITT) was analysed for primary outcomes to assess the loss of follow-up bias. The results of ITT and PP are shown in supplementary table 1 and supplementary table 2. Both ITT and PP analyses were consistent in directions and magnitudes.

Comparison of satisfaction scores (VAS)

The results regarding the satisfaction levels of the products are presented in table 3. Both products had moderate to high levels of satisfaction. No significant difference in the satisfaction levels of any aspect was found between the FD-SOESS and lozenges groups. Concerning overall satisfaction and all items related to the improvement in symptoms, slightly higher satisfaction scores were noticed in the FD-SOESS group as compared to the lozenges group.

The result showed that 85.8% of the participants reported that FD-SOESS met or exceeded their expectations compared to 65.7% of those in the lozenges group. Most participants (44.1%) liked the lubrication property of FD-SOESS, while 41.2% of them favored the taste of lozenges. The most common negative remarks regarding FD-SOESS were poor texture (sticky) (17.6%) and excessive salivation (14.7%). While the negative comments were that the lozenges were too sweet (38.2%) and too hard and sticky (14.7%).

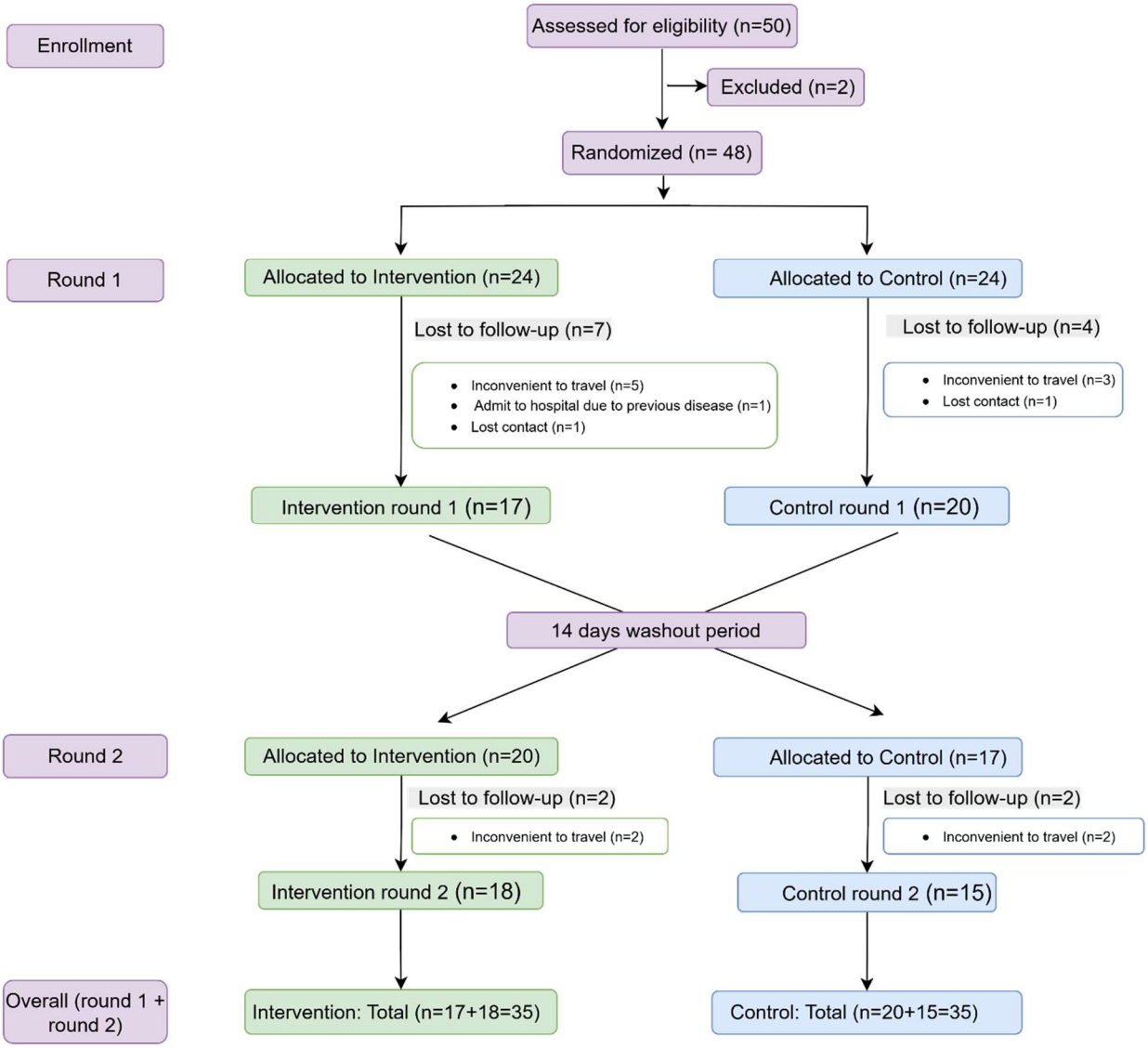

Fig. 2: Consort flow of the trial.

The average dissolving time was 1.80 ± 1.00 minutes for FD-SOESS (range 1.00-6.00 minutes) and 3.60 ± 1.64 minutes for lozenges (range 2.30-8.00 minutes). The average retention time for FD-SOESS was significantly longer at 24.53 ± 7.26 minutes (range 10.00-45.00 minutes) compared to lozenges, which was 18.2 ± 7.39 minutes (range 9.43-35.00 minutes) ($p<0.001$). Approximately 97% of participants reported no negative effects. Only 2 participants reported side effects. One in the FD-SOESS group experienced a burning sensation and one in the lozenges group reported impaired taste.

DISCUSSION

The participants in this study were post head and neck cancer treated patients and were predominantly men and older individuals. Numerous studies have reported that there was a substantial age- and sex-related association with cancer incidence (Rettig and D'Souza, 2015). Most participants in the current study were regular smokers and drinkers, with about 60% reporting a history of more than 10 years of smoking and alcohol intake. These findings confirmed that alcohol and tobacco use are related to head and neck cancer (Barsouk *et al*., 2023). Oral cleansing at least twice a day was reported in all participants in our study. However, only 57% of the participants regularly used fluoridated toothpaste. This behavior might increase the risk of caries in addition to dry mouth in the dentate participants (Millsop *et al*., 2017). Almost 45% of participants changed their diet to be either a semi-solid or liquid diet. The reason was that dry mouth patients usually had dysphagia, which made it difficult for the patients to consume regular solid foods (Müller *et al., 2023)*. This result was supported by the fact that before the intervention, our participants had a mean objective dry mouth score of 6.71 and 6.83 and a mean EAT-10 score of 16.17 and 16.43 for the FD-SOESS and lozenges groups, respectively.

Table 1: Baseline characteristics of participants (n=35).

Variable	n	%
Age (mean = 56.49 ± 12.22 min-max 24-77)		
21-40	5	14.3
41-60	17	48.6
>60	13	37.1
Sex		
Male	29	82.9
Female	6	17.1
Religion		
Buddhist	28	80.0
Muslim	6	17.1
Christian	1	2.9
Occupation		
No Occupation	13	37.1
Business/Employee/Officer	10	28.6
Farmer	7	20.0
Others	5	14.3
Level of Education		
Elementary school	13	37.1
Secondary school	5	14.3
Vocational/Diploma	9	25.7
Bachelor's degree and higher	8	22.9
BMI		
Underweight	10	28.6
Normal	19	54.3
Overweight/Obese	6	17.1
Cancer staging prior to cancer therapy		
Stage 1	1	2.9
Stage 2	7	20.0
Stage 3	7	20.0
Stage 4	16	45.7
Cannot identify	4	11.4
Duration of radiotherapy (weeks)		
< 6	7	20.0
6 and above	28	80.0
Duration of chemotherapy (weeks)		
Nil	3	8.5
< 6	2	5.8
6 and above	30	85.7
Location of cancer		
Nasopharynx	14	40.0
Pharynx	9	25.7
Oral cavity	8	22.9
Larynx	2	5.7
Salivary glands	1	2.9
Thyroid	1	2.9
Current medication		
No	10	28.6
Yes	25	71.4
History of regular cigarette smoking[1]		
No	8	22.9
<10 years	6	17.1
10 years and above	21	60.0

Table 1 is continue…

Variable	n	%
History of regular alcohol drinking[2]		
No	8	22.9
<10 years	4	11.4
10 years and above	23	65.7

Note: [1] At least 1 cigarette per day, [2] At least 1 glass per day

Table 2: Oral health status and oral health care of participants (n=35).

Variable	n	%
Dentate Yes	24	68.6
No (Edentulous)	11	31.4
Mouth cleansing		
Less than 2 times/day	0	0
2 times/day	20	67.1
More than 2 times/day	15	32.9
Use of toothpaste		
Fluoridated toothpaste	20	57.1
Non-Fluoridated toothpaste	4	11.5
Don't use toothpaste	11	31.4
Dental visit in last one year		
No	6	17.1
1-2 times	10	28.6
More than 2 times	19	54.3
Reason for dental visit (n=29)		
Regular checkup	11	31.4
Treatment of ulcer/mucositis	4	11.4
Other dental treatments	9	25.7
Follow-up	5	14.3
Diet preference		
Normal diet	19	54.3
Semi-solid diet	13	37.1
Liquid diet	3	8.6

Table 3: Comparison of satisfaction score (VAS) between the intervention (FD-SOESS) and control (lozenges) (n=35).

Variables	FD-SOESS		Lozenges		*P*-value
	Mean ± SD	Min-Max	Mean ± SD	Min-Max	
Characteristics					
Taste	6.62 ± 2.54	0-10	6.56 ± 2.50	2-10	0.924
Texture	7.44 ± 1.89	3-10	7.03 ± 2.05	3-10	0.412
Smell	7.44 ± 2.48	0-10	7.53 ± 1.95	1-10	0.871
Ease of Use	7.91 ± 1.91	4-10	8.41 ± 1.72	5-10	0.262
Symptom improvement					
Improve oral dryness (Moisturizing and lubrication)	6.82 ± 1.99	1-10	6.94 ± 2.07	3-10	0.812
Improve chewing	5.97 ± 2.32	1-10	5.56 ± 2.09	2-10	0.444
Improve swallowing	6.41 ± 1.94	2-10	6.09 ± 1.88	3-10	0.488
Improve speech	6.35 ± 1.99	1-10	6.35 ± 2.23	0-10	1.000
Improved sensation	6.18 ± 1.95	0-10	5.97 ± 1.98	2-10	0.667
Improved burning sensation	5.59 ± 1.74	0-9	5.03 ± 1.85	0-9	0.204
Overall satisfaction	7.47 ± 1.83	3-10	7.35 ± 1.98	4-10	0.800

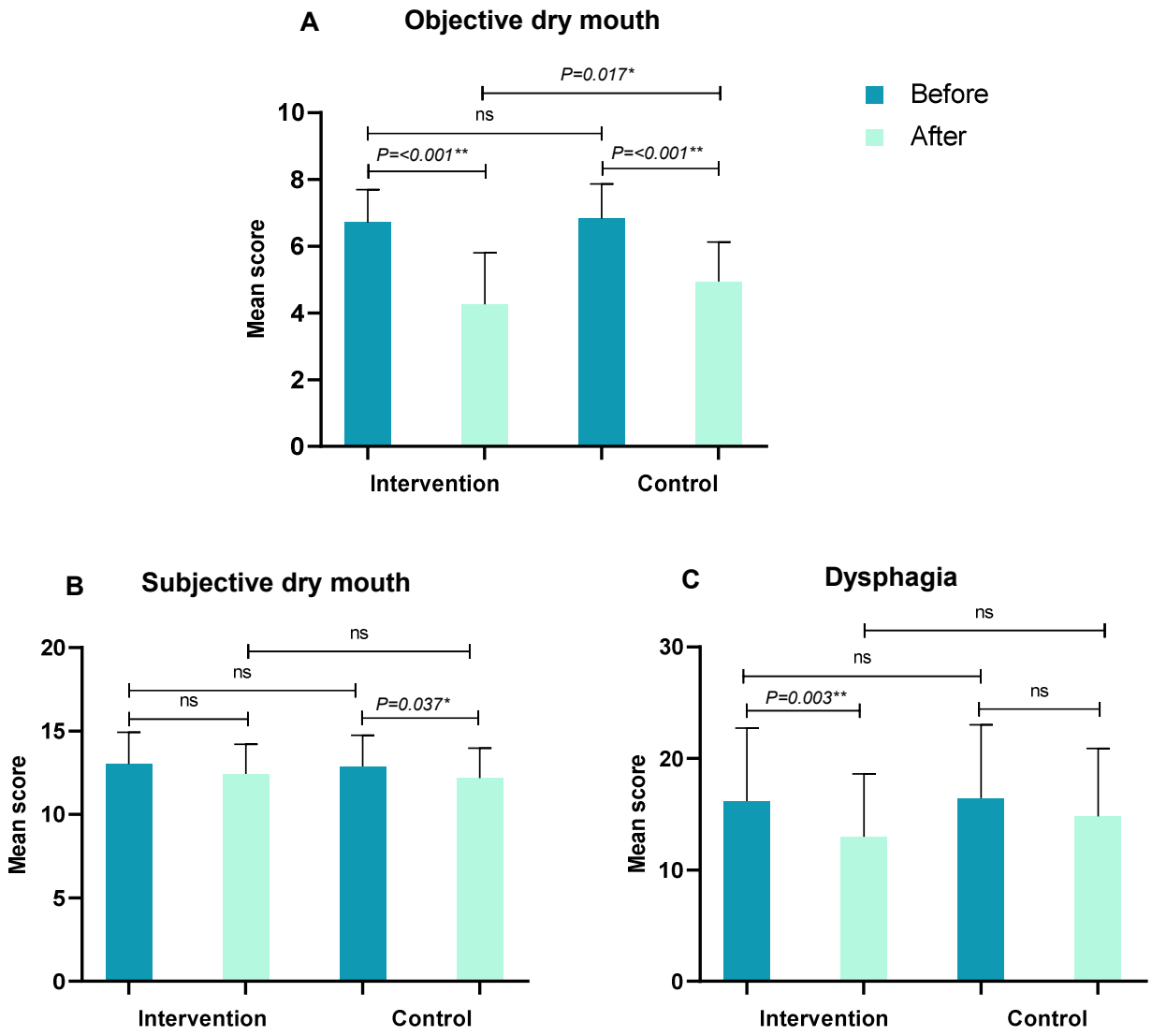

Fig. 3: Comparing dry mouth and dysphagia scores (Mean ± SD) before and after using the products between intervention (FD-SOESS) and control (Lozenges) groups: (A) Objective dry mouth, (B) Subjective dry mouth, (C) Dysphagia. (n=35)

A previous study also reported that 66.7% of the participants had functional swallowing problems due to high dysphagia levels (De Carvalho *et al*., 2021). The dry mouth levels of participants in both groups were severe, exhibited by the mean score of 13 for subjective dry mouth and 7 for objective dry mouth. Mucositis was found in a few individuals (11% in the intervention and 17% in the control groups). The main reason for the low prevalence might be that all our participants in this study had completed their radiotherapy for at least one month and were not in the active stage of post-radiotherapy symptoms, including oral mucositis (Trotti *et al*., 2003, Bentzen *et al*., 2001).

At baseline, there were no significant differences between the intervention (FD-SOESS) and control (lozenges) groups in dry mouth, dysphagia, or mucositis, minimizing the effect of confounding factors. After product use, both groups showed significant improvements in both objective and subjective dry mouth scores. The evidence suggests that both products can relieve dry mouth symptoms through the mechanical stimulation of saliva as well as having ingredients that can provide moisture. FD-SOESS showed better improvement in dry mouth, especially objective dry mouth, than lozenges. FD-SOESS could improve dry mouth symptoms because it contains sesame oil, which might provide more moisture (Wei *et al*., 2022). This finding is similar to other studies, which showed that herbal products were observed to exhibit greater dry mouth recovery than plain artificial saliva (Ameri *et al*., 2016, Heydarirad *et al*., 2017).

Although the subjective dry mouth improved in both groups, the statistical significance was found only in the

lozenges group. The lack of significance in the FD-SOESS group can be explained by the fact that FD-SOESS was processed by removing the water, resulting in a dry texture. Patients with severe dry mouth may consider FD-SOESS uncomfortable and some may dislike the taste or smell of sesame oil, leading to unpleasant experiences. The lozenges group showed similar results to a previous crossover randomized trial, where lozenges containing malic acid significantly reduced subjective dry mouth scores ($p<0.05$), while the citric acid mouthwash did not (Da Mata *et al*., 2020).

Only the FD-SOESS group had a significant improvement in EAT-10 scores. The result indicated that FD-SOESS could help in the alleviation of dysphagia problems of post head and neck cancer treated patients because of the salivary stimulant and lubrication properties of FD-SOESS. This result corresponds to the prior study on the effect of gel types of saliva substitutes (oral moisturizing jelly (OMJ) and GC® gel) on dysphagia of post-radiotherapy head and neck cancer patients, which found that they significantly reduced EAT-10 scores ($P < 0.001$) (Nuchit *et al*., 2020).

The results indicated that FD-SOESS dissolved faster than lozenges but had a longer retention time than lozenges. While the slow dissolution of the lozenges may cause discomfort for use, especially when used before mealtime or bedtime, as complained by some participants. The longer retention time of FD-SOESS could be explained by the fact that FD-SOESS contains sesame oil in addition to lubricating polysaccharides, so it could provide more moisturizing and create a protective layer to prolong the effect (Austin *et al*., 2024). FD-SOESS could prolong drinking or sipping water from every 5-10 minutes to about 25 minutes, which is helpful for the most severe dry mouth patients.

FD-SOESS and commercial lozenges showed moderate to high satisfaction levels in terms of product characteristics and symptom improvement, with no significant differences between them. However, slightly higher satisfaction, particularly regarding ease of use, was observed with the commercial lozenges compared to FD-SOESS. This distinction is not unexpected, as FD-SOESS was still in development and lacked proper packaging, unlike the commercially available lozenges (fig. 1). A previous study also found that dry mouth patients tend to prefer formulations that are easier to use and consume (Mhatre *et al*., 2024, Matear and Barbaro, 2005). Interestingly, the participants reported a slightly higher satisfaction level in the symptom improvement for FD-SOESS than for lozenges. These corresponded with the results of improving the objective dry mouth score. In addition, the results of the open-ended questions indicated that most participants liked the lubrication property of FD-SOESS and the taste of lozenges. Overall, more participants in the FD-SOESS group than in the lozenges group reported that the product met or exceeded their expectations.

The side effects were minimal. Only 3% of the 35 participants (1 participant in each group) reported negative effects. The symptoms included burning mouth sensation in the FD-SOESS group and impaired taste sensation in the lozenges group. This result was similar to the pilot study that compared lozenges (interferon-α 150 IU) and placebo (maltose) in relieving dry mouth symptoms in patients with Sjögren's syndrome, which reported no adverse effect in either group (Khurshudian, 2003). To investigate the side effects of the products among the dropouts, follow-up calls were made to check if there were any. It was found that almost all participants reported no side effects. This indicates that the side effects were low no matter whether they stayed in the study or not.

The strengths of our study include the use of a crossover randomized controlled trial design and randomization, which helped minimize confounding bias. Multiple outcome measurements, including subjective dry mouth, objective dry mouth, mucositis and dysphagia, as well as satisfaction levels, helped to increase the validity and reliability of the study.

This study had some limitations. First, total loss to follow-up was 13 out of 48 (27%) in both groups. This amount of missing data was considerably high. This loss is likely because this study was a crossover RCT design requiring longer engagement of the participants (4 times of follow-up). The loss to follow-up in the crossover trial may introduce attrition bias (Mills *et al*., 2009), Therefore, in order to reduce this bias, we performed both ITT and PP analysis. It showed comparable results, indicating the effects of assigning participants to treatment and receiving the treatment were similar and the loss to follow-up did not substantially affect the interpretation (Smith *et al*., 2021). Additionally, the reason for the lost to follow-up of almost all the participants was the inconvenience of travel, rather than treatment-related side effects. It is likely that the missing was at random (Little and Rubin, 2019).

The second limitation was the possibility of information bias due to the lack of blinding the participants, especially for the subjective outcomes (Wood, 2006), such as subjective dry mouth, EAT-10 and product satisfaction. The participants might judge the outcomes based on the products' features and their preferences, instead of the real effect. The bias would favor ACT® lozenges, especially on the satisfaction of the product, as it was a commercial and well-packaged product as compared to FD-SOESS, in which their packaging had not been properly designed (fig. 1). However, this single-blind approach would not affect clinical measurements (objective dry mouth) because the examiners were blinded.

Third, our results used 8-item CODS, which may not be comparable with other studies that used 10-item CODS. However, this 8-item CODS would increase the validity of the study because it omitted 2 items that could not be measured in the edentulous subjects, who accounted for 31.4% of the total sample. Furthermore, they cannot change over the follow-up duration (2 weeks).

Other limitations included that the duration of the product use might be too short to observe long-term results. A small number of patients with mucositis could affect the power of statistical testing for this outcome. However, mucositis was not the primary outcome in this study.

Future studies should explore the effects of FD-SOESS on dry mouth in longer durations and diverse patient groups, such as the elderly and those with diabetes or on medications that induce dry mouth, as well as assess its impact on mucositis with a larger sample size. This study indicated that sesame oil wafers or FD-SOESS effectively improved both objective dry mouth and dysphagia in head and neck cancer patients. Our product or other similar products containing sesame oil can be used for relieving clinical symptoms of dry mouth as well as dysphagia in dry mouth patients.

CONCLUSION

In conclusion, FD-SOESS, or sesame oil wafer, shows efficacy in improving dry mouth, especially in objective or clinical dry mouth symptoms and dysphagia, which proved to be superior to commercial lozenges. However, FD-SOESS did not show a significant improvement in subjective dry mouth as compared to commercial lozenges. The satisfaction levels of FD-SOESS were relatively high and close to those of commercial lozenges. Therefore, the newly developed product, FD-SOESS, has the potential to be an alternative product for dry mouth patients.

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Authors' contribution
Muhammad Abbas Amanat: Methodology, data curation, formal analysis, writing – original draft and writing – review and editing; Teerapol Srichana: Conceptualization and final approval of the published version; Chutha Takahashi Yupanqui: Conceptualization and final approval of the published version; Angkana Thearmontree: Conceptualization, funding acquisition, methodology, project administration, supervision, writing – review and editing and final approval of the published version.

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Data availability statement
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical approval
The study protocol was approved by the Research Ethics Committee of the Faculty of Dentistry, Prince of Songkla University (EC6604-027) and the Research Ethics Committee of Hat Yai Hospital (HYH EC 073-66-02). All participants provided written informed consent before entering the study. The clinical trial was registered with the Thai Clinical Trials Registry (TCTR20240326002).

Conflict of interest
The authors have no conflicts of interest.

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