Original Article

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Development of a Novel Pastille Formulation to Alleviate Dry Mouth Symptoms

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Abstract:

Objective: Dry mouth adversely affects oral function and quality of life, necessitating the development of effective salivary-stimulating systems. This study aimed to develop and characterize the properties of salivary stimulating pastilles (SSP) and to conduct a pilot study assessing patient satisfaction and clinical effectiveness in patients with dry mouth.

Material and Methods: SSPs were formulated using gelatin (15.0%) combined with gellan gum, xanthan gum, or pectin, with glycerin as a plasticizer. Nine formulations were prepared and characterized for physicochemical properties, rheological behavior, stability, and microbiological quality. Biocompatibility was assessed using human periodontal and gingival fibroblast cell lines. Salivary mucin levels were quantified using a FITC-based fluorescence method, followed by a pilot clinical evaluation in participants with low salivary flow.

Results: The optimized formulation containing gellan gum (0.3 % w/w) and xanthan gum (0.15 % w/w) demonstrated suitable pH (5.71-5.76), mechanical strength (<12,000 g), elastic-dominant viscoelastic properties (G′>G″), and acceptable disintegration time (200-235 s). Both formulations remained stable under refrigerated conditions and met microbiological standards. Cell viability exceeded 90.0% in the periodontal and gingival fibroblast assays. Clinical evaluation showed a significant increase in unstimulated salivary flow and elevated mucin levels (p-value<0.01).

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Conclusion: The results indicate that pastilles containing gellan gum (0.3 % w/w) and xanthan gum (0.15 % w/w) might serve as safe and promising saliva-stimulating systems with potential therapeutic application in the management of dry mouth.

Keywords: dry mouth, hydrocolloid, pastille, saliva, saliva stimulation

Introduction

Dry mouth is characterized by xerostomia, a subjective sensation of oral dryness, and/or decreased saliva (hyposalivation), defined as a reduction in salivary flow, both of which impair speech, swallowing, and taste[1–3]. Xerostomia is typically assessed through patient self-reported outcomes, whereas hyposalivation is clinically determined by the objective measurement of salivary flow rates[4]. Multiple etiological factors, including polypharmacy, systemic diseases, alcohol consumption, smoking, drug abuse, head-and-neck radiotherapy, aging, and psychological stress, contribute to the development of this condition[5,6]. Dry mouth is highly prevalent, affecting approximately 17–40% of homebound elderly individuals and 20–72% of nursing home residents[7].

Radiation-induced dry mouth results from direct damage to salivary glands, impairing their secretory function. Both major and minor glands are affected,[8] and irreversible damage may occur at radiation doses as low as 26 cGy. A substantial reduction in salivary flow, up to 93–95%, can occur within the first week of therapy [9]. This dysfunction increases the risk of dental caries, periodontitis, infections, delayed wound healing, dysphagia, and taste alterations, ultimately leading to a significant decline in quality of life[10].

The management of xerostomia and hyposalivation depends on the extent of salivary gland dysfunction and the underlying etiology. In patients with partially preserved gland function, saliva secretion can be stimulated through mechanical, chemical, or pharmacological approaches, whereas severe gland damage requires symptomatic management using water or artificial saliva[11]. Mechanical stimulation using products such as chewing gums, pastilles, lozenges, and candies enhances salivary flow primarily through gustatory stimulation[12]. A study by Bielfeldt et al.[13] shows that flavors stimulate the taste buds and increase salivary secretion.

Previous studies have demonstrated that mechanical saliva stimulants, such as lozenges and chewing gums, effectively enhance salivary secretion[13]. However, conventional formulations present several limitations: hard lozenges may cause mucosal irritation, burning sensations, and an unpleasant aftertaste, while chewing gums can interfere with dental prostheses and contribute to masticatory muscle fatigue[13,14]. Salivary-stimulating pastilles (SSP), designed as soft, non-sticky dosage forms, may therefore offer a prosthesis-friendly and patient-compliant alternative for individuals with xerostomia and hyposalivation. Despite these advantages, their clinical use remains limited due to the low availability and high costs associated with imported products. Therefore, this study aimed to develop an accessible and effective SSP formulation for patients with partially functioning salivary glands, with the goal of improving patient compliance and supporting long-term management.

Material and Methods

Materials

Gelatin, gellan gum, xanthan gum, pectin, glycerin, and sodium benzoate were purchased from Sigma-Aldrich (USA). All materials used were food-grade quality.

Table 1 Concentrations of gelling agents and thickening agents across 9 formulations

Formula	Gelling agent	Concentration (%w/w)	Thickening agent	Concentration (%w/w)	Glycerin (%w/w)
GG1	Gelatin (G)	15.0	Gellan gum (G)	0.1	10.0
GG2	Gelatin (G)	15.0	Gellan gum (G)	0.3	10.0
GG3	Gelatin (G)	15.0	Gellan gum (G)	0.5	10.0
GX1	Gelatin (G)	15.0	Xanthan gum (X)	0.1	10.0
GX2	Gelatin (G)	15.0	Xanthan gum (X)	0.15	10.0
GX3	Gelatin (G)	15.0	Xanthan gum (X)	0.2	10.0
GP1	Gelatin (G)	15.0	Pectin (P)	1.0	10.0
GP2	Gelatin (G)	15.0	Pectin (P)	1.5	10.0
GP3	Gelatin (G)	15.0	Pectin (P)	2.0	10.0

Preparation of the product

Hydrocolloids (gellan gum, xanthan gum, or pectin) were premixed with gelatin. Glycerin (10 g) was dissolved in distilled water and maintained at 40 °C under continuous magnetic stirring. The powder mixture was gradually added to the solution to ensure uniform dispersion, followed by the incorporation of sodium benzoate. The resulting mixture was cast into molds, allowed to gel at room temperature, and subsequently refrigerated at 0–4 °C for 3–4 hours. A total of nine formulations with varying hydrocolloid concentrations were prepared (Table 1), with the gelatin content held constant at 15.0% (w/w). Optimal formulations were selected based on predefined criteria (Table S1).

Physiochemical characterization of SSP

pH Measurement

The pH of all nine SSP formulations was measured using a calibrated Mettler Toledo SevenCompact S220 pH meter (Mettler Toledo, Zürich, Switzerland). Samples (5 g) were dissolved in 50 mL of distilled water prior to analysis. Ten samples per formulation were randomly selected, and results were expressed as mean±standard deviation (S.D.).

Hardness and springiness

The mechanical properties, including SSP hardness and springiness, were determined using a texture analyzer. Ten samples from each formulation were randomly selected and analyzed for testing, and the results were reported as mean±S.D.

Weight

The weight of SSP units was measured using a four-decimal analytical balance (Ohaus Adventure Analytical Balance, New Jersey, USA). Twenty samples per formulation were randomly selected, and the results were expressed as mean±S.D.

Appearance and dimensional analysis

The physical characteristics of SSP, including shape, size, and diameter, were recorded. Cross-sectional dimensions were measured using a vernier caliper. Twenty samples were randomly selected for each formulation, and the results were expressed as mean±S.D.

Stability of SSP

The following parameters were measured after the product was stored in a refrigerator at 0–4°C for 1 month.

Color assessment

Color changes before and after storage were evaluated by visual inspection. Ten samples per formulation were randomly selected for analysis.

Weight change

Weight measurements were performed using a four-decimal analytical balance. Ten samples per formulation were analyzed, and the results were expressed as mean±S.D. The percentage weight change was calculated using Equation (1).

$$Weight\ change\ (\%) = \frac{Wt-W0}{W0} \times 100 \quad (1)$$

Where W0 and Wt represent the weight of the product before and after 1 month of product placement, respectively.

Shape integrity

Shape integrity was evaluated using ten samples per formulation. Observed changes were classified as significant or non-significant, and the results were expressed as mean±S.D.

Visco-elasticity

Rheological properties were measured using a Discovery HR-2 hybrid parallel-plate rheometer (TA Instruments, USA) equipped with a 40mm parallel plate and Peltier-controlled steel plate (model 110974). Measurements were performed at 25, 30, and 37 °C.

Disintegration of SSP

The disintegration time of SSP was determined using a pharmacopeial tablet disintegration tester (ED 2SAPOx, Electro lab, Mumbai, India), following standard pharmacopeial procedures[15].

Cell culture studies

Cytotoxicity was evaluated using human periodontal and gingival fibroblast cell lines. Cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10.0% fetal bovine serum and antibiotics (100 U/mL penicillin and 100 U/ml streptomycin) (Gibco®, USA) at 37 °C in a humidified atmosphere containing 5.0% CO_2. The culture medium was replaced every 48 h. Upon reaching confluence, cells were detached using 0.05% trypsin-EDTA and resuspended to obtain a single-cell suspension.

Cells were seeded into 96-well plates at a density of 1×10^5 cells/mL and incubated for 24 h prior to treatment with the test samples at various concentrations, while the untreated cells served as the negative control. After 24 h exposure, cell viability was assessed using the MTT assay. Briefly, 80 µL of fresh medium and 20 µL of MTT solution were added to each well, followed by incubation for 4 h at 37 °C with 5.0% CO_2. The medium was then removed, and 100 µL of DMSO was added to dissolve the formazan crystals. Absorbance was measured at 570 nm using a SPECTROstar Nano Microplate Reader (BMG LABTECH, Germany). Cell proliferation (%) was calculated relative to the negative control.

Mucin analysis in saliva

A mucin-FITC stock solution was prepared by dissolving 20 mg of gastric porcine mucin in 9.80 mL of phosphate-buffered saline (PBS), followed by the addition of 125 µL of fluorescein isothiocyanate (FITC) solution (1 mg/mL in anhydrous dimethyl sulfoxide). The mixture was stirred for 24 h and subsequently dialyzed (MWCO 1000 Da) to remove unbound dye[16]. Serial dilutions were prepared from the stock solution and analyzed for fluorescence intensity using a Varioskan LUX Multimode Microplate Reader. Linear regression analysis demonstrated good linearity (R^2=0.987).

For in vivo assessment, saliva samples (1 mL) were collected from six volunteers before and after consumption of pastilles (GG2 and GX2). Each sample was mixed with 12.5 µL FITC solution and incubated at 37 °C for 24 h under constant stirring, followed by dialysis (MWCO 1000 Da) against 1 L filtered water to remove unbound FITC. Fluorescence intensity was measured using a SPECTROstar Nano Microplate Reader (BMG LABTECH, Germany). SSP efficacy was evaluated by comparing mucin levels before and after administration.

Microbiological study of SSP

The microbial quality of SSP was evaluated using the standard Association of Official Analytical Chemists (AOAC) 2012 methods. The total viable count (TVC) was 80 colony-forming units per gram (CFU/g). The presence of *Staphylococcus aureus* and *Escherichia coli* was assessed using Bacteriological Analytical Manual (BAM) methods (2016, 2020), and both were below the detection limit (<3 most probable number per gram, MPN/g). Yeast and mold counts were also below the detection limit (<3 CFU/g). Microbial limit testing was performed initially and repeated at one and three months to assess microbiological stability.

Clinical pilot study

This randomized crossover pilot study, with a minimum washout period of one day, was conducted to evaluate the feasibility of SSP and its potential to improve salivary parameters in healthy volunteers. A total of 25 participants aged 20–75 years with a Shortened Xerostomia Inventory questionnaire score of 7 or higher and an unstimulated salivary flow rate of less than 0.4 mg/min[17] were enrolled. Exclusion criteria included permanent salivary gland damage (e.g., prior salivary gland surgery), allergy to barium sulfate, neuropsychiatric disorders (e.g., depression or dementia), and inability to complete the study protocol. Ethical approval was obtained from the Ethics Committee of the Faculty of Dentistry, Prince of Songkla University (EC6507-026).

Participants were randomly assigned using simple randomization to receive either GG2 or GX2. Subjects were instructed to fast and refrain from tooth brushing for at least 1 hour prior to testing. Baseline unstimulated salivary flow rate and pH were measured, followed by administration of one SSP. Post-treatment measurements were recorded using the same parameters. After a washout period of at least one day, participants crossed over to the alternate formulation, and the protocol was repeated. Data were analyzed using paired t-tests at a 95% confidence level, and the results are presented as mean±S.D.

Results

pH

The pH of the formulations ranged from 5.16 to 5.76 (Table 2), falling within the acceptable physiological range of 5.0–7.0[18]. This range is suitable for oral formulations, as it minimizes the risk of mucosal irritation and enamel demineralization. These findings are consistent with previous reports indicating that saliva substitute formulations containing hydroxyethyl cellulose (0.5%–3.0%) exhibited pH values of 5.5–7.5 and were appropriate for oral use.

Hardness and springiness

All formulations exhibited fracture resistance values below 12,000 g, meeting the standard requirement for chewable tablets[19]. The highest hardness values were observed in GG3, GX3, and GP1 for gellan gum, xanthan gum, and pectin-based formulations, respectively. GP3 and GX1 exhibited the lowest percentage change (0.01 and 2.02, respectively).

Weight

The initial weight range of the formulations was evaluated. At 0 months, the pastilles had an average weight of 1.74 to 2.38 g. After 1 month of storage, all formulations exhibited weight loss of less than 5.0%, except for GG1 and GP2 (Table 2).

Appearance and dimensional analysis

All formulations were prepared in a cube shape according to the mold dimensions (≈1.5 cm×1.0 cm). At baseline, all samples appeared clear yellow. After one month of storage, no color changes were observed; however, shape deformation occurred in GG1 and GX1.

Stability studies

Two formulations were selected based on acceptable physicochemical properties, including pH, hardness, ease of production, reproducibility, disintegration time, and stability. These formulations were further evaluated for microbiological quality, viscoelastic properties, disintegration, and cytotoxicity.

GX2 exhibited predominantly elastic behavior across the tested frequency range, with the storage modulus (G′) consistently exceeding the loss modulus (G″) (Figure 1). The G′ values (10^4–10^5 Pa) were substantially higher than G″ (10^2–10^4 Pa), indicating a well-developed internal network with good mechanical strength.

GG2 also demonstrated G′>G″ across the frequency sweep, confirming elastic-dominant behavior. However, GG2 exhibited lower overall modulus values and a more pronounced increase at higher frequencies compared to GX2, suggesting reduced structural integrity and a greater viscous contribution under elevated shear conditions.

Table 2 Characterization of SSP

Formula	pH	Change after 1 month (Mean±S.D.) n=10			
		Volume (cm^3)	Weight (g)	Springiness (mm)	Hardness (g)
GG1	5.73	0.075±0.19	−0.13±0.17	0.04±0.06	−1011.86±1219.43
GG2	5.76	−0.10±0.06	−0.11±0.08	0.05±0.28	−1511.73±540.21
GG3	5.74	−0.09±0.13	−0.11±0.18	−0.70±0.17	−4382.37±1236.23
GX1	5.74	−0.09±0.14	−0.11±0.18	−0.16±0.13	76.90±538.97
GX2	5.71	−0.08±0.13	−0.04±0.09	−0.70±0.15	1898.90±1687.53
GX3	5.74	0.14±0.16	−0.05±0.11	0.34±0.07	1765.50±1402.05
GP1	5.21	−0.19±0.27	−0.09±0.17	−0.19±0.15	3314.33±1323.05
GP2	5.21	−0.11±0.17	−0.10±0.15	−0.87±0.33	1057.23±1280.97
GP3	5.16	−0.35±0.17	−0.09±0.13	−0.34±0.10	−42.87±1100.90

SSP=salivary-stimulating pastilles

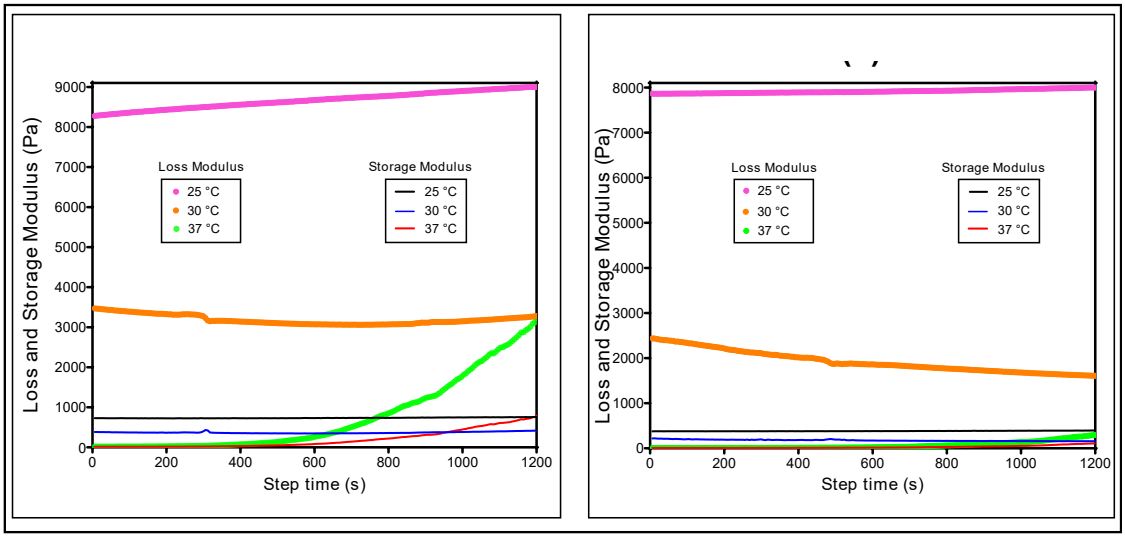

Figure 1 Viscoelastic behavior of (A) GX2 and (B) GG2 at varying temperatures (25, 30, and 37 °C)

Disintegration of SSP

The disintegration time of the formulated pastilles varied among formulations following production (Table 3). GG1, GG2, GX1, GX2, GX3, and GP1 exhibited comparable disintegration times ranging from 201.3±12.0 s to 235.7±7.1 s, with GX1 showing the shortest (201.3±12.0 s), and GG2 the longest within this group (235.7±7.1 s). In contrast, GP2 (291.0±6.2 s) and GP3 (342.0±8.7 s) demonstrated markedly prolonged disintegration times. After one month of storage, a slight increase in disintegration time was observed for GG2 and GX2, reaching 256.7±13.1 s and 221.7±11.1 s, respectively.

Cytotoxicity

The cytotoxic evaluation demonstrated that both formulations (GX2 and GG2) were non-cytotoxic and biocompatible toward human gingival fibroblasts and periodontal cells across the tested concentration range. No significant reduction in cell viability was observed, even at the highest concentration (10 mg/mL), compared with the control group (p-value>0.05), indicating the absence of dose-dependent cytotoxicity. Cell viability remained consistently above 90.0–95.0% in both cell lines (Figure 2).

Table 3 Disintegration time of saliva-stimulating pastilles immediately after production

Formulation	Average disintegration time (s)±S.D. n=10	
	0	1 month
GG1	206.7±9.3	-
GG2	235.7±7.1	256.7±13.1
GG3	623.0±8.5	-
GX1	201.3±12.0	-
GX2	206.3±5.0	221.7±11.1
GX3	211.0±11.4	-
GP1	212.0±13.1	-
GP2	291.0±6.2	-
GP3	342.0±8.7	-

S.D.=standard deviation

Mucin analysis in saliva

Administration of GX2 and GG2 resulted in increased salivary mucin levels in the majority of volunteers (Figure 3). In the GX2 group, mucin concentrations increased from approximately 2.0–6.5 μg/mL at baseline to 3.5–7.2 μg/mL post-administration, except for volunteer 5. Similarly, in the GG2 group, mucin levels increased from 1.8–3.2 μg/mL to 2.5–3.8 μg/mL in most participants, except for volunteers 4 and 5, who showed no observable increase.

Microbiological study

Both GG2 and GX2 complied with microbial limit specifications at baseline, 1 month, and 3 months. Total viable count and yeast and mold count remained <10 CFU/g, while *Escherichia coli* was <3 MPN/g and *Staphylococcus aureus* was < 10 CFU/g, these being within acceptable limits throughout the study period, confirming microbiological stability during storage.

Unstimulated salivary flow and pH

As shown in Figure 4, both GX2 and GG2 significantly increased unstimulated salivary flow rate following administration (p-value<0.01). Mean values of unstimulated salivary flow rate increased from 0.40 to 0.58 mL/min for GX2 and from 0.38 to 0.57 mL/min for GG2. A slight reduction in salivary pH was observed after administration; however, this change was statistically significant only in the GX2 group (p-value<0.05).

Discussion

In this study, gelatin-based pastille (SSP) systems were developed and evaluated for their effects on salivary mucin concentrations, unstimulated salivary flow rate, salivary pH, and overall efficacy in alleviating xerostomia. During preliminary formulation, a fixed gelatin concentration (15.0% w/w) combined with varying concentrations of gellan and xanthan gum significantly influenced the physico-mechanical properties of the pastilles. Among the nine

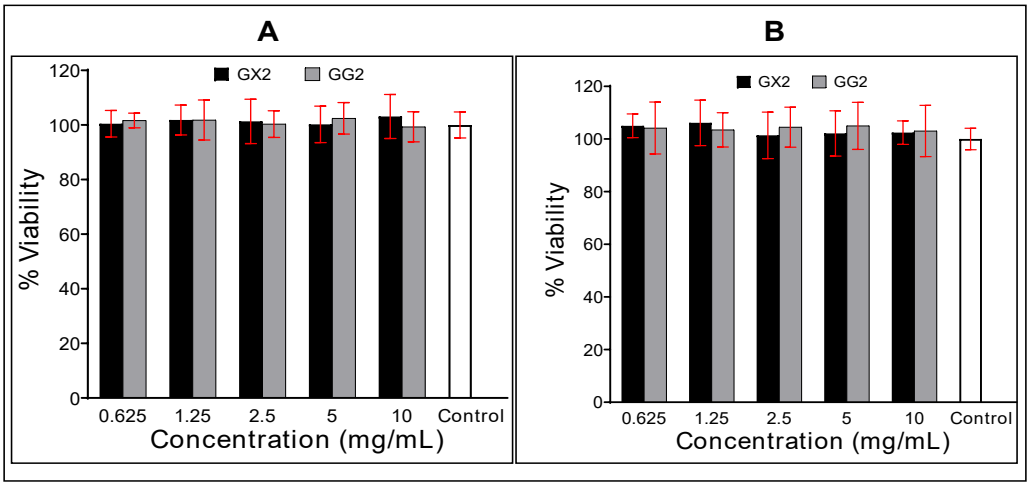

Figure 2 Cytotoxic evaluation of the selected formulations (GX2 and GG2), demonstrating no cytotoxic effects up to 10 mg/mL in (A) human gingival fibroblasts and (B) human periodontal cells. Data are presented as mean±S.D. (n=3)

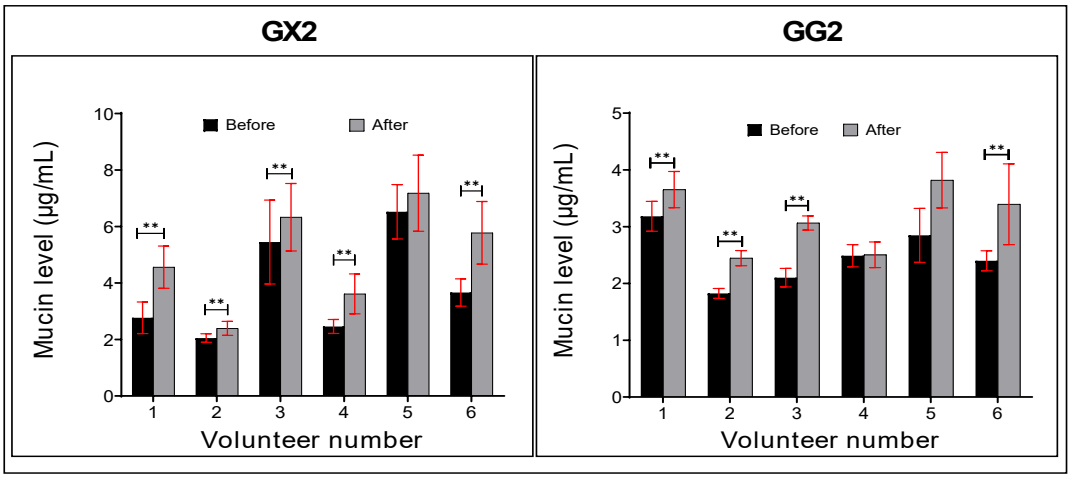

Figure 3 Salivary mucin levels (µg/mL) in saliva samples before and after administration of GX2 and GG2. Data are presented as mean±S.D. (n=3). Statistical significance is indicated as p-value<0.01 compared with baseline

formulations, those SSP containing gellan gum (0.3% w/w) and xanthan gum (0.15% w/w) exhibited optimal physical and mechanical characteristics suitable for oral application. These findings are consistent with previous reports demonstrating that gelatin-based systems combined with suitable thickening agents yield desirable mechanical properties[20]. Additionally, variations in polymer type and concentration have been shown to influence structural attributes, with xanthan gum producing (1.0% and 2.0% w/w) thinner matrices and carboxymethyl cellulose (4.0%

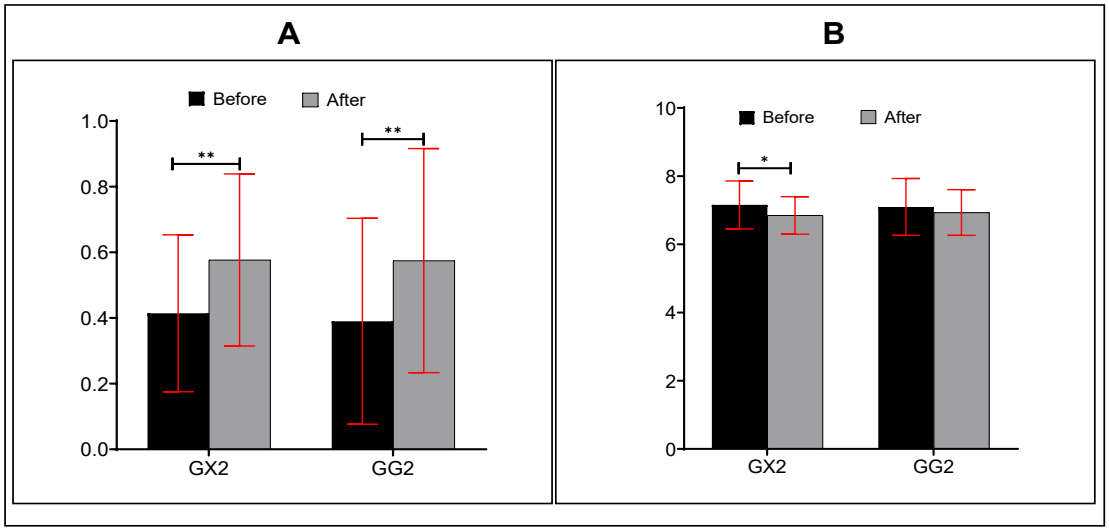

Figure 4 Effect of GX2 and GG2 on (A) unstimulated salivary flow rate and (B) salivary pH. Data are presented as mean±S.D. (n=25). Statistical significance is indicated as *p-value<0.05 and **p-value<0.01 compared with baseline

w/w) resulting in highly viscous systems[21]. Collectively, these results highlight the critical role of polymer composition in modulating the mechanical performance of pastille formulations.

Disintegration time is largely dependent on matrix composition and polymer concentration, which directly influence residence time in the oral cavity. Pastilles with higher gelatin content (20.0% w/w) have been shown to exhibit markedly prolonged disintegration (1020±120 s)[22], approximately four times greater than that observed in the present study using 12.5% w/w gelatin. In this study, disintegration times of 206–235 s were considered appropriate, as they provided extended oral residence compared with conventional mouthwash formulations (120–180 s) [23]. Clinically, an optimized disintegration profile may be beneficial for patients with xerostomia and oral mucositis, where softer dosage forms with controlled disintegration are better tolerated in painful erythematous and ulcerative conditions[24].

All nine formulations containing fixed gelatin (15.0% w/w) exhibited fracture resistance values below 12,000 g. Among the polymers evaluated, gellan gum and xanthan gum produced the highest hardness, whereas increasing pectin concentration (GP3) reduced fracture resistance, likely due to gel network formation via hydrogen bonding and ionic interactions[25]. In addition, formulation excipients such as glycerin play a key role in modulating the texture and mechanical strength of oral pastilles. For comparison, oral pastilles containing gelatin (20.0% w/w) and glycerol (5.0%) have been reported to exhibit favourable textural properties with hardness values ranging from 1019 to 1719 g[22]. In this study, GG2 demonstrated a shorter disintegration time (206.3±5.0 s) than GX2 (235.7±7.1 s); however, both increased after one month of storage (256.7±13.1 s and 221.7±11.1 s, respectively), likely due to a more rigid cation-mediated cross-linked network formed by gellan gum compared with the more flexible linear structure of xanthan gum[26]. Rheological analysis further revealed predominantly

elastic behavior for xanthan gum (G′>G″), whereas gellan gum exhibited a greater frequency-dependent increase in storage modulus (G′) but a comparatively lower overall modulus than GX2. The rheological behavior of oral pastilles, including storage modulus (G'), loss modulus (G"), and dynamic viscosity, is strongly influenced by formulation composition, particularly polymer concentration. In addition, solvent selection (glycerol or propylene glycol) modulates the balance between elastic and viscous responses, while incorporation of poly(acrylic acid) enhances intermolecular interactions, thereby improving the overall viscoelastic properties of the system[27].

The pH profile of all nine SSP formulations falls within the physiological range of 5.0–7.0[18], indicating their suitability for oral application and a low risk of mucosal irritation or enamel demineralization. These findings are consistent with previous studies reporting hydroxyethyl cellulose-based saliva substitutes (0.5% and 3.0%), with pH values of 5.5–7.5, which were deemed appropriate for oral use. Formulations within the pH range of 5.0–7.0 are considered optimal for maintaining mucosal hydration while ensuring compatibility with oral tissue[28]. From a clinical perspective, saliva substitutes should maintain a near-neutral pH, as increased acidity may promote enamel erosion, whereas alkalinity may disrupt the balance of oral microbiota[28].

Biocompatibility is a critical requirement for oral formulations to ensure safe application to oral tissues without inducing cytotoxicity or inflammatory responses[29]. In the present study, GX2 and GG2 demonstrated excellent biocompatibility toward human gingival fibroblasts and human periodontal ligament cells at concentrations up to 10 mg/mL. Both formulations maintained high cell viability (>90.0–95.0%), which is well above the commonly accepted biocompatibility threshold of 70.0%[20,29]. These findings are consistent with previous reports that gelatin, glycerin, citric acid, and erythritol-based pastilles are non-toxic and biocompatible with gingival fibroblasts at concentrations up to 100 µg/mL[19]. Similarly, propolis-based oral formulations (up to 10.0%) exhibited high cell viability (85.3%) in gingival fibroblasts. Collectively, these results confirm that such oral formulations can be safely applied to oral tissues without inducing significant cytotoxic effects[29].

Administration of GX2 and GG2 increased salivary mucin levels in most volunteers, likely attributable to mechanical stimulation associated with formulation disintegration in the oral cavity. Increased mucin secretion is clinically advantageous in xerostomia, where reduced mucin is associated with oral dryness, discomfort, and impaired swallowing function[30]. In the GX2 group, five volunteers showed statistically significant increases in mucin levels (p-value<0.01–0.001), rising from 2.0–6.5 µg/mL at baseline to 3.5–7.2 µg/mL post-administration. Similarly, four volunteers in the GG2 group exhibited significant increases (p-value < 0.01–0.001), from 1.8–3.2 µg/mL to 2.5–3.8 µg/mL. These findings are consistent with previous reports demonstrating that salivary substitute products significantly increase mucin levels (p-value < 0.01), improving lubrication, mucosal protection, and overall oral comfort[16].

In clinical practice, patients with hyposalivation often experience oral dryness, leading to thirst and increased fluid intake. Pastille administration has been shown to significantly stimulate unstimulated salivary flow, thereby alleviating symptoms of xerostomia[31]. In the present study, both GX2 and GG2 significantly increased unstimulated salivary flow after administration (***p-value<0.001), with mean values increasing from approximately 0.40 to 0.58 for GX2 and from 0.38 to 0.57 for GG2. GX2 induced a slight but significant reduction in salivary pH after administration (*p-value<0.05), whereas GG2 showed no significant change; however, all values remained within the physiological oral range. These findings are consistent with previous reports demonstrating that sucking or chewing pastilles (ipalat Hydro Med) significantly enhanced salivary flow compared with a tasteless control (Parafilm®), supporting their effectiveness in stimulating salivation.

This study has several limitations. Stability testing was conducted over a limited period of one month, which may not adequately represent long-term formulation stability. The clinical pilot study primarily assessed the acute salivary-stimulatory effects of SSP formulations and was not designed to evaluate long-term therapeutic outcomes or resolution of chronic xerostomia symptoms. In addition, the small sample size may limit statistical power and reduce the generalizability of the findings. The absence of a control group further restricts direct comparison of SSP efficacy. Future studies should address these limitations by including larger cohorts, incorporating appropriate control groups to strengthen clinical relevance, and conducting extended stability assessments under standard storage conditions.

Conclusion

This study successfully developed and characterized gelatin-based SSP formulations combined with gellan gum, xanthan gum, or pectin. After one month of refrigerated storage, all formulations demonstrated acceptable physicochemical stability, including physiological pH (5.16–5.76), adequate mechanical strength (<12,000 g), and overall formulation stability. Among them, GX2 and GG2 exhibited superior performance, characterized by microbiological compliance, elastic-dominant viscoelastic behavior, suitable disintegration times (200–235 s), and maintained structural integrity. Both formulations showed high biocompatibility (>90.0% cell viability) toward human gingival fibroblasts and periodontal ligament cells. Importantly, *in vivo* evaluation confirmed their functional efficacy, evidenced by increased unstimulated salivary flow and enhanced salivary mucin secretion.

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Conflict of interest

The authors declare that they have conflicts of interest.

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Ethical approval

Ethical approval for this clinical trial was obtained from the Ethics Committee of the Faculty of Dentistry, Prince of Songkla University (EC6507-026).

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Supplementary table 1 Selection criteria for SSP formulations

Formula	Hardness	Ease of production and reproducibility	pH stability	Disintegration	Overall stability
GG1	✓	✓	✓	✓	✗
GG2	✓	✓	✓	✓	✓
GG3	✓	✓	✓	✗	✗
GX1	✓	✓	✓	✓	✗
GX2	✓	✓	✓	✓	✓
GX3	✓	✓	✓	✓	✗
GP1	✓	✗	✗	✓	✗
GP2	✓	✓	✗	✓	✗
GP3	✓	✓	✗	✗	✗

Legend: ✓=Meets the criterion ✗=Does not meet the criterion

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