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Development and Pharmaceutical Characterization of an Oral Gel Containing Articaine and Aqueous Propolis Extract

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A B S T R A C T

Objective: Diseases and inflammatory conditions of the oral mucosa are often accompanied by pain, irritation, and disruption of tissue integrity. The development of topical oral dosage forms is challenging because the formulation is continuously exposed to saliva and mechanical clearance. A viscous dosage form capable of prolonging contact with the oral mucosa is therefore a relevant pharmaceutical objective. To develop the composition and extemporaneous technology of an oral gel containing articaine (in the form of Artifrine) and aqueous propolis extract, and to experimentally characterize its physicochemical, rheological, analytical, mucoadhesive, and microbiological quality attributes.

Methods: The formulation contained Artifrine solution for injection (40 mg/mL articaine hydrochloride and 0.006 mg/mL epinephrine hydrochloride; ALC "Pharmaceutical Firm Darnytsia", Ukraine), providing 0.2 g articaine hydrochloride per 100 g gel; aqueous propolis extract; sodium carboxymethylcellulose (Na-CMC); glycerol; propylene glycol; menthol; sodium saccharin; triclosan; and purified water. Na-CMC concentrations of 1.8–2.2% were evaluated, and 2.0% was selected. The gel was prepared using a seven-stage compounding process. Physicochemical, rheological, HPLC-UV, ex vivo mucoadhesive, microbiological, and preliminary stability assessments were performed.

Results: The optimized formulation contained Artifrine (5.0 mL), aqueous propolis extract (5.0 mL), Na-CMC (2.0 g), glycerol (8.0 g), propylene glycol (6.0 g), menthol (0.1 g), sodium saccharin (0.1 g), triclosan (0.2 g), and purified water to 100 g. The measured pH was 6.15 ± 0.08 and viscosity was 4850 ± 210 mPa·s at 20 rpm and 20 °C. Articaine content was 99.4 ± 1.2% of the target by HPLC-UV. Ex vivo detachment force was 0.42 ± 0.03 N. Microbiological testing after method-suitability neutralization met the stated limits. Preliminary three-month storage data at 25 °C/60% RH showed articaine and epinephrine contents of 98.1 ± 1.1% and 96.8 ± 1.4%, respectively.

Conclusions: An oral gel prototype containing articaine (as Artifrine) and aqueous propolis extract in a 2.0% Na-CMC matrix, together with a seven-stage extemporaneous manufacturing process, was developed and characterized. The results provide a basis for further pharmaceutical development. Long-term stability, drug-release, in vivo pharmacokinetic, and clinical studies remain necessary.

Keywords: Articaine, Artifrine, Dental gel, Oral mucosa, Propolis

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Introduction

Diseases of the oral mucosa are common clinical conditions that can be accompanied by pain, inflammation, irritation, and impairment of normal tissue function. Factors contributing to their development include infectious, inflammatory, traumatic, and other local or systemic causes. Management of such conditions may require a combined application of analgesic, anti-inflammatory, antimicrobial, and reparative (supportive) approaches [1,2,3].

Topical dosage forms are particularly attractive for treating lesions of the oral mucosa because they allow targeted drug delivery directly to the affected site. However, the formulation of topical oral products is complicated by continuous salivary secretion, mechanical movements of the tongue or cheek, swallowing, and rapid removal of the product from the mucosal surface. Accordingly, an appropriate pharmaceutical base (vehicle) must provide suitable viscosity and sufficient residence time at the application site [11,12,13,21].

Conventional topical oral preparations containing local anesthetics may be rapidly cleared from the mucosal surface and may not combine local anesthesia with the additional biological properties attributed to propolis. The present formulation was designed to investigate the combination of articaine and standardized aqueous propolis extract in a viscous Na-CMC vehicle.

Articaine is an amide-type local anesthetic widely used in dentistry. Its pharmacological properties make it suitable for local pain management associated with dental procedures and oral diseases. Articaine-containing preparations may also contain epinephrine (adrenaline), which is used to prolong the local anesthetic effect via vasoconstriction. In the present formulation, the commercial medicinal product Artifrine (solution for injection; 1 mL contains 40 mg articaine hydrochloride and 0.006 mg epinephrine hydrochloride; ALC “Pharmaceutical Firm Darnytsia”, Ukraine) was used as the source of articaine [2,3,4,5]. Because epinephrine is susceptible to oxidative degradation, pH control and protection from light were considered during formulation, packaging, and preliminary storage assessment.

Propolis is a natural bee product containing a complex mixture of phenolic compounds, flavonoids, terpenoids, and other constituents. Biological properties described in the literature include antimicrobial, antifungal, anti-inflammatory, antioxidant, and immunomodulatory effects. The chemical composition and biological activity of propolis may vary according to geographical and botanical origin. To support batch-to-batch consistency, the extract used in this study was characterized by density, dry residue, and total polyphenol content; further development should also consider specific marker compounds [6,7,8,9,10].

Sodium carboxymethylcellulose (Na-CMC) is a hydrophilic polymer widely used in pharmaceutical formulations to increase viscosity and induce gelling. Its rheological properties make it suitable for semisolid topical dosage forms. Na-CMC was selected as the gelling agent alongside glycerol, propylene glycol, menthol, sodium saccharin, and triclosan [11,12,14–19]. Triclosan was included at 0.2% as an auxiliary antimicrobial/preservative component; its suitability and local tolerability require further assessment before clinical use.

The combination of a local anesthetic with a natural product possessing reported antimicrobial and anti-inflammatory potential provides a rationale for designing a multifunctional oral gel. This study focused on the formulation, compounding technology, and experimental physicochemical, rheological, analytical, mucoadhesive, and microbiological characterization of a gel containing Artifrine and aqueous propolis extract [1,6,9,21].

The aim of the study was to develop the composition and technology of an oral gel containing articaine (in the form of Artifrine) and aqueous propolis extract, and to experimentally characterize its physicochemical, rheological, analytical, mucoadhesive, and microbiological quality attributes.

Materials and Methods

Materials

The formulation was developed using:

Finished medicinal product "Artifrine" (solution for injection in ampoules; 1 mL of solution contains 40.0 mg articaine hydrochloride and 0.006 mg epinephrine hydrochloride; ALC "Pharmaceutical Firm "Darnytsia", Ukraine; Batch No. 10223). The incorporation of 5.0 mL of solution provides 0.2 g of articaine hydrochloride and 0.03 mg of epinephrine hydrochloride per 100.0 g of finished gel (0.2% w/w articaine) [2,4,5].

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Aqueous propolis extract 1:10 (batch EP-2024-03, prepared by aqueous maceration at 60 °C for 4 hours of raw propolis collected in May-July 2023 from apiaries in the Lviv region, Ukraine; botanical origin predominantly Populus nigra L.; density d = 1.02 g/mL, dry residue 4.2% w/v, total polyphenol content calculated as gallic acid equivalents - 2.68 ± 0.12 mg/mL determined by Folin-Ciocalteu assay; stored at 4–8 °C protected from light)) [6,7,9,10].

Na-CMC (degree of substitution 0.7, viscosity 1500–3000 mPa·s for 2% solution at 25 °C, average molecular weight ~250 kDa, Sigma-Aldrich, St. Louis, MO, USA) [11,12,14].

Pharmacopeial-grade excipients: glycerol 85% (Ph. Eur.), propylene glycol (Ph. Eur.), L-menthol (Ph. Eur.), sodium saccharin (Ph. Eur.), triclosan (USP grade, purity ≥97.0%), and purified water (Ph. Eur./SPhU) [15,16,17,18,19].

The proposed formulation was designed as an aqueous viscous oral gel intended for local application onto the oral mucosa.

Method of Oral Gel Compounding

The preparation was manufactured following a seven-stage technological scheme:

Stage 1. Preparation of the gelling matrix

Na-CMC (2.0 g) was wetted with 4.0 g of glycerol in a porcelain mortar. Purified water (65.0 mL at 20 ± 2 °C) was added in a single portion under continuous low-speed stirring (150 rpm using an overhead mechanical stirrer, IKA Eurostar 20). The mixture was allowed to hydrate and swell for 60 min at room temperature (20 ± 2 °C).

Stage 2. Preparation of the auxiliary phase

Triclosan (0.2 g) and L-menthol (0.1 g) were dissolved in propylene glycol (6.0 g) combined with the remaining glycerol (4.0 g) by magnetic stirring at 300 rpm for 15 min at room temperature (20 ± 2 °C).

Stage 3. Incorporation into the gel base:

The prepared auxiliary phase was gradually added to the swollen Na-CMC hydrogel matrix under controlled planetary stirring at 200 rpm for 10 min until complete integration was achieved.

Stage 4. Incorporation of active ingredients

Aqueous propolis extract (5.0 mL) and Artifrine injection solution (5.0 mL) were mixed together and added dropwise to the gel matrix under gentle stirring (100 rpm) for 10 min to prevent air entrapment.

Stage 5. Preparation of sweetener solution

Saccharin (0.1 g) was dissolved in 5.0 mL of purified water heated to 80–90 °C, then cooled to 20 ± 2 °C.

Stage 6. Final homogenization and weight adjustment

The cooled sweetener solution was added to the mixture. Purified water was added to bring the total batch weight to exactly 100.0 g. Final homogenization was carried out using a vacuum mixer/homogenizer at 300 rpm for 5 min to remove entrapped air bubbles.

Stage 7. Packaging

The finished gel was transferred into collapsible aluminum tubes coated with internal protective varnish (30 g capacity), crimped, sealed, labeled, and stored at 2–8 °C protected from light.

Organoleptic Evaluation

The obtained gel was evaluated visually and organoleptically for appearance, color, odor, taste, and consistency. Comparative selection of Na-CMC concentration was conducted across five formulations (1.8%, 1.9%, 2.0%, 2.1%, and 2.2% w/w), considering measured viscosity, spreadability, and extrusion behavior [13,21].

Determination of pH

The pH value was determined potentiometrically according to Ph. Eur./SPhU 2.2.3 at 20 ± 1 °C in a 10% (w/v) aqueous dispersion of the gel using a calibrated digital pH meter (Mettler Toledo SevenCompact S210) equipped with a glass combination electrode (InLab Expert Pro-ISM). Measurements were performed in sextuplicate across three independently prepared batches (n = 6). The target pH range was 5.5–6.8.

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Determination of Dynamic Viscosity and Rheological Characterization

Dynamic viscosity and rheological flow curves were measured using a rotational viscometer (Brookfield DV-II+ Pro) equipped with an LV-3 (63) spindle. Measurements were performed at 20 ± 0.5 °C after thermal equilibration for 30 min. Viscosity values were recorded at rotational speeds from 0.5 to 100 rpm (corresponding to shear rates from 0.1 to 21.5 s^{-1}) to establish the pseudoplastic (shear-thinning) flow profile. Samples were loaded gently into a temperature-controlled cup without air entrapment. The target specification interval was 2000–10000 mPa·s at 20 rpm.

Analytical Identification and Quantification of Articaine

Articaine hydrochloride was identified and quantified in the presence of propolis phenolics using an HPLC method (Shimadzu Prominence LC-20AD). Separation was performed on a C18 column (250 × 4.6 mm, 5 µm) at 30 °C using phosphate buffer (pH 3.0) and acetonitrile (70:30, v/v) as the mobile phase, at a flow rate of 1.0 mL/min and UV detection at 272 nm. The reported validation parameters were linearity (R^2 = 0.9998 over 10–100 µg/mL), precision (RSD < 1.5%), recovery (98.5–101.2%), and selectivity in the presence of propolis phenolics and excipients. Articaine hydrochloride reference standard (Sigma-Aldrich, purity ≥99.0%) was used.

Microbiological Quality Assessment and Method Suitability

Microbiological quality was evaluated using principles of pharmacopeial microbiological control of non-sterile pharmaceutical products, including microbial enumeration tests (Ph. Eur. 2.6.12 / SPhU 2.6.12) and tests for specified microorganisms (Ph. Eur. 2.6.13 / SPhU 2.6.13). Acceptance criteria were applied according to Ph. Eur. 5.1.4 / SPhU 5.1.4 for cutaneous and oral topical preparations.

Test microorganisms included: Staphylococcus aureus ATCC 6538, Pseudomonas aeruginosa ATCC 9027, Bacillus subtilis ATCC 6633, Candida albicans ATCC 10231, and Aspergillus brasiliensis ATCC 16404.

Method-suitability testing was performed to account for the intrinsic antimicrobial activity of triclosan and propolis extract. Neutralization was achieved by adding 3.0% polysorbate 80, 0.3% lecithin, and 0.5% sodium thiosulfate to the initial dilution medium (Tryptic Soy Broth/Letheen Broth). Microbial recovery in the presence of formulation components exceeded 85% relative to control suspensions.

Proposed microbiological purity criteria were: TAMC ≤ 10^2 CFU/g; TYMC ≤ 10^1 CFU/g; absence of *S. aureus* in 1 g; absence of *P. aeruginosa* in 1 g.

Assessment of Ex Vivo Mucoadhesive Properties

Ex vivo mucoadhesive strength was evaluated using a texture analyzer (TA.XTplus, Stable Micro Systems) equipped with a mucoadhesion rig. Freshly isolated porcine buccal mucosa obtained from a local abattoir was mounted on the lower platform and hydrated with simulated saliva (pH 6.8, 37 ± 0.5 °C). Gel samples (1.0 g) were applied to the probe, brought into contact with the mucosa with an applied force of 0.5 N for 60 s, and detached at 0.5 mm/s. Peak detachment force and total work of adhesion were recorded in sextuplicate (n = 6).

Preliminary Stability Studies

Preliminary stability assessment was initiated with reference to ICH Q1A(R2). Gel samples packed in sealed aluminum tubes were stored at 25 ± 2 °C/60 ± 5% RH and 40 ± 2 °C/75 ± 5% RH for three months. At 0, 1, 2, and 3 months, samples were assessed for appearance, pH, viscosity, articaine and epinephrine content (HPLC), degradation products, and microbiological purity. The results reported in this study include the 25 °C/60% RH condition.

Statistical Analysis

Experiments were conducted using three independently manufactured gel batches (n = 3), with individual laboratory tests performed in triplicate or sextuplicate as specified. Data are presented as mean ± standard deviation (SD). Comparisons among polymer concentration groups were performed using one-way analysis of variance (ANOVA), followed by Tukey's post-hoc test in GraphPad Prism 9.0. Differences were considered statistically significant at $P < 0.05$.

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Results

Optimization of Na-CMC Concentration

Five Na-CMC concentrations (1.8%, 1.9%, 2.0%, 2.1%, and 2.2% w/w) were systematically evaluated. Apparent dynamic viscosity, organoleptic consistency, and extrudability from tubes were recorded (n = 6; Table 1).

Table 1. Rheological and physical evaluation of Na-CMC gel formulations (n=6, Mean ± SD)

Na-CMC Conc. (% w/w)	Dynamic Viscosity at 20 rpm (mPa·s)	Visual & Technological Consistency	Extrudability & Entrapped Air
1.8	1240 ± 85	Fluid, low consistency	High flowability, unstable layer
1.9	2650 ± 120	Moderately viscous	Acceptable, low structural recovery
2.0	4850 ± 210	Optimal viscous hydrogel	Excellent extrudability, minimal air
2.1	8200 ± 340	Highly viscous, dense	Difficult extrusion, structural rigidity
2.2	11450 ± 490	Rigid paste-like gel	Excessive air entrapment, high yield

As shown in Table 1, 1.8% and 1.9% Na-CMC concentrations provided lower viscosity, whereas concentrations of 2.1% and 2.2% resulted in dense gels with reduced spreadability and increased air entrapment during compounding. The 2.0% Na-CMC formulation demonstrated a viscosity of 4850 ± 210 mPa·s at 20 rpm and the most suitable balance of consistency and extrudability. ANOVA indicated significant differences in viscosity among the tested concentrations ($P < 0.001$).

Composition of the Proposed Oral Gel

The final formulation contained Artifrine, aqueous propolis extract, and Na-CMC as the main components, together with glycerol, propylene glycol, menthol, sodium saccharin, and triclosan. The composition is outlined in Table 2.

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Table 2. Composition of the optimized oral gel (100 g batch)

Component	Quantity per 100 g	Function / Active ingredient content
Artifrine (solution for injection)	5.0 mL	Equivalent to 0.2 g articaine HCl and 0.03 mg epinephrine HCl
Aqueous propolis extract	5.0 mL	Extract 1:10, polyphenols 2.68 ± 0.12 mg/mL
Sodium carboxymethylcellulose	2.0 g	Gelling matrix agent
Glycerol 85%	8.0 g	Humectant / plasticizer
Propylene glycol	6.0 g	Co-solvent / penetration enhancer
Menthol	0.1 g	Flavoring / cooling agent
Sodium saccharin	0.1 g	Sweetening agent
Triclosan	0.2 g	Auxiliary preservative / antimicrobial agent
Purified water	to 100.0 g	Solvent vehicle

Manufacturing Process Flow Scheme

The preparation was manufactured using seven consecutive technological stages as detailed in Table 3.

Table 3. Seven-stage technological flow scheme for oral gel compounding

Stage	Technological operation & Process parameters
1	Wetting of 2.0 g Na-CMC with 4.0 g glycerol; hydration in 65.0 mL water at 150 rpm for 60 min
2	Dissolution of 0.2 g triclosan and 0.1 g menthol in 6.0 g PG + 4.0 g glycerol at 300 rpm (15 min)
3	Incorporation of auxiliary phase into hydrated Na-CMC matrix under planetary stirring at 200 rpm (10 min)
4	Addition of aqueous propolis extract (5.0 mL) and Artifrine (5.0 mL) under slow stirring at 100 rpm (10 min)
5	Dissolution of 0.1 g sodium saccharin in 5.0 mL hot water (80–90 °C), cooling to 20 °C
6	Addition of sweetener solution, bringing mass to 100.0 g with water; vacuum degassing (300 rpm, 5 min)

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7	Filling into light-protected aluminum tubes (30 g), crimping, sealing, and storage at 2–8 °C

Measured Pharmaceutical Quality Parameters

Experimental evaluation of the physicochemical and structural-mechanical parameters of the prepared gel batches yielded the results summarized in Table 4.

Table 4. Measured physical-chemical and quality parameters of the oral gel (n=6, Mean ± SD)

Quality parameter	Specification Target	Measured Experimental Result	Method / Status
Appearance	Homogeneous gel	Homogeneous, glossy gel	Visual inspection
Color	Light yellow–brown	Uniform light yellow-brown	Visual inspection
Odor	Characteristic propolis	Characteristic pleasant propolis	Organoleptic
Taste	Slightly sweet, cooling	Slightly sweet, mild cooling	Organoleptic
Consistency	Homogeneous viscous	Viscous, plastic hydrogel	Organoleptic / Texture
pH	5.5–6.8	6.15 ± 0.08	Potentiometric (10% aq.)
Dynamic viscosity	2000–10000 mPa·s	4850 ± 210 mPa·s	Rotational (20 rpm, 20 °C)
Rheological flow	Pseudoplastic	Shear-thinning (n = 0.42)	Viscosimetry (0.5–100 rpm)
Articaine Assay	95.0–105.0%	99.4 ± 1.2% (1.988 mg/g)	Validated HPLC-UV (272 nm)
Mucoadhesiveness	Report value	0.42 ± 0.03 N (Work: 0.85 ± 0.06 mJ)	Ex vivo texture analyzer
Stability (3-month)	Complies	Articaine: 98.1 ± 1.1%, Epinephrine: 96.8 ± 1.4%	Accelerated (25 °C/60% RH)

Rheological Profiling

Rheological characterization across shear rates demonstrated pronounced non-Newtonian pseudoplastic (shear-thinning) behavior. Dynamic viscosity decreased from 45,200 ± 1,800 mPa·s at 0.5 rpm (0.1 s^{-1}) to 1,420 ± 80 mPa·s at 100 rpm (21.5 s^{-1}). This flow behavior ensures easy extrusion from container tubes and smooth application onto mucosal tissue, followed by rapid viscosity recovery at rest to prevent runoff.

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Microbiological Purity and Method Suitability Results

Experimental microbiological analysis of three finished gel batches following valid neutralization of preservatives demonstrated full compliance with pharmacopeial requirements for non-sterile oral preparations (Ph. Eur. 5.1.4 / SPhU 5.1.4), as presented in Table 5.

Table 5. Microbiological quality test results for oral gel batches (n=3)

Microbiological Parameter	Pharmacopeial Limit	Experimental Result	Status
Total Aerobic Microbial Count (TAMC)	≤ 10^2 CFU/g (100 CFU/g)	< 10 CFU/g	Complies
Total Yeasts & Moulds Count (TYMC)	≤ 10^1 CFU/g (10 CFU/g)	< 10 CFU/g	Complies
Staphylococcus aureus	Absence in 1 g	Absent in 1 g	Complies
Pseudomonas aeruginosa	Absence in 1 g	Absent in 1 g	Complies
Escherichia coli	Absence in 1 g	Absent in 1 g	Complies

Discussion

Disruption of oral mucosal integrity, inflammation, and pain are common clinical problems associated with dental disorders, including caries, periodontitis, stomatitis, and postsurgical trauma. Topical gel formulations combining local pain relief, mucosal contact, and antimicrobial support may be useful in managing such conditions [2,3,6,7,8,9,10]. The formulation investigated here combines articaine hydrochloride with standardized aqueous propolis extract in an Na-CMC hydrogel matrix.

Continuous salivary flow and tongue movement lead to rapid clearance of topical dosage forms from the oral cavity. To overcome this limitation, a viscous hydrophilic matrix of Na-CMC (2.0% w/w) was selected. Systematic evaluation across 1.8–2.2% Na-CMC showed that 2.0% Na-CMC provides ideal pseudoplastic flow profile (4850 ± 210 mPa·s at 20 rpm), high structural viscosity at low shear rates, and excellent extrudability.

Artifrine injection solution was incorporated to provide 0.2% articaine hydrochloride and 0.03 mg epinephrine hydrochloride per 100 g of gel. Since epinephrine is susceptible to oxidative degradation, the formulation pH, co-solvent system, and light-protected packaging were considered during development. Preliminary three-month storage at 25 °C/60% RH showed retention of articaine and epinephrine contents of 98.1 ± 1.1% and 96.8 ± 1.4%, respectively [2,3,4,5].

The aqueous propolis extract (1:10; total polyphenols 2.68 ± 0.12 mg/mL) contributed a chemically characterized natural component with biological activities reported in the literature [6,7,8,9,10]. Standardization by total polyphenol content and controlled extraction parameters is important because propolis composition varies with botanical and geographical origin.

Glycerol and propylene glycol served as humectant and co-solvent components; L-menthol provided a cooling sensation; and sodium saccharin provided sweetness [15,16]. Triclosan (0.2%) was included as an auxiliary antimicrobial/preservative component. Its safety and mucosal tolerability in this formulation have not been established clinically and require further evaluation.

The measured gel pH was 6.15 ± 0.08 (n = 6), within the proposed target range of 5.5–6.8. This finding supports compliance with the formulation target but does not, by itself, establish mucosal safety or physiological compatibility.

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Rheological investigation revealed shear-thinning pseudoplastic behavior, characterized by a substantial drop in dynamic viscosity under applied shear rate. This parameter is critical for easy dispensing from tubes and rapid retention after application onto target lesions.

HPLC-UV analysis at 272 nm provided chromatographic separation of articaine (reported retention time 4.8 min) from propolis phenolic peaks (reported retention times 1.2–3.2 min), supporting the selectivity of the assay. The measured articaine content was 99.4 ± 1.2% of the target amount.

Microbiological evaluation met the stated pharmacopeial criteria for non-sterile oral preparations. Neutralizing agents (polysorbate 80, lecithin, and sodium thiosulfate) were used during method-suitability testing to reduce interference from the antimicrobial activity of propolis and triclosan.

Ex vivo testing on porcine buccal mucosa demonstrated a peak detachment force of 0.42 ± 0.03 N and work of adhesion of 0.85 ± 0.06 mJ. These measurements provide preliminary evidence of mucoadhesive behavior under the test conditions.

During the preliminary three-month assessment at 25 °C/60% RH, no phase separation was reported; pH changed from 6.15 to 6.10, while articaine and epinephrine contents were 98.1 ± 1.1% and 96.8 ± 1.4%, respectively. Longer-term and formal stability studies are still required.

Study limitations. The study reports initial physicochemical, rheological, analytical, ex vivo mucoadhesive, and microbiological characterization. Long-term stability studies, in vivo pharmacokinetic evaluations, drug-release studies, and prospective clinical trials remain to be conducted.

Conclusion

An oral hydrogel prototype containing articaine (as Artifrine injection solution, equivalent to 0.2% w/w articaine hydrochloride) and aqueous propolis extract in a 2.0% Na-CMC matrix was developed, together with a seven-stage compounding technology. The proposed composition per 100 g contains Artifrine solution (5.0 mL), aqueous propolis extract 1:10 (5.0 mL; total polyphenols 2.68 ± 0.12 mg/mL), Na-CMC (2.0 g), glycerol (8.0 g), propylene glycol (6.0 g), L-menthol (0.1 g), sodium saccharin (0.1 g), triclosan (0.2 g), and purified water to 100.0 g. The measured pH was 6.15 ± 0.08 and dynamic viscosity was 4850 ± 210 mPa·s at 20 rpm and 20 °C, with shear-thinning pseudoplastic flow (flow index n = 0.42). The reported HPLC-UV method at 272 nm quantified articaine at 99.4 ± 1.2% of the target amount without reported interference from propolis phenolics. Microbiological testing following method-suitability neutralization met the stated limits: TAMC < 10 CFU/g, TYMC < 10 CFU/g, and absence of S. aureus and P. aeruginosa in 1 g. Ex vivo testing demonstrated a detachment force of 0.42 ± 0.03 N. Preliminary three-month storage data at 25 °C/60% RH showed articaine and epinephrine contents of 98.1 ± 1.1% and 96.8 ± 1.4%, respectively. These findings support further development but do not establish clinical efficacy or long-term stability.

Declaration

Ethical Approval and Institutional Statement

This study involved in vitro pharmaceutical formulation, physicochemical and microbiological testing, and ex vivo testing of post-mortem porcine buccal mucosal tissue obtained from a commercial abattoir. No human participants or live animals were involved. The authors state that formal institutional ethical approval was not required under the applicable institutional and national requirements.

Conflict of Interest

The authors declare no conflicts of interest regarding the research, authorship, or publication of this article.

Author Contributions

Ihor Hrynovets (IH): Conceptualization, methodology, formal analysis, investigation, supervision, project administration, writing – original draft, writing – review & editing.

Yana Ostapchuk (YO): Methodology, validation, laboratory investigation, data curation, writing – review & editing.

Roman Lysiuk (RL): Conceptualization, resources, literature analysis, writing – original draft, writing – review & editing.

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Data Availability Statement

All relevant experimental data generated and analyzed during this study are included within this published article.

AI Declaration

None.

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