Development and Characterization of *Grewia asiatica*-Loaded Mucoadhesive Buccal Films for Sustained Antihypertensive Therapy

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Abstract

Objective: This study was designed to develop and evaluate five mucoadhesive buccal film formulations containing Grewia asiatica extract for prolonged release, potentially enhancing antihypertensive therapy.

Methods: *Grewia asiatica* hydroalcoholic extract, known for its rich phytoconstituents, was incorporated into polymeric buccal films (HPMC/PVA) using a solvent casting method. Formulations (F1–F5) varied in polymer ratio and plasticizer levels. Each film was characterized for thickness, drug content, mucoadhesion, mechanical properties, in vitro release, and ex vivo permeation. Accelerated stability testing was performed.

Results: All formulations demonstrated good film uniformity (thickness 0.14–0.19 mm), drug content ~96–103%, and mucoadhesive strength 20–28 g·cm/s. F4 exhibited the highest mucoadhesive force (28.2 ± 2.9 g·cm/s) and sustained drug release (>80% at 8 h) with near zero-order kinetics. Ex vivo permeation through goat buccal mucosa confirmed efficient transmucosal delivery (~78% in 8 h). Stability studies indicated minimal changes over three months.

Conclusion: *Grewia asiatica*-loaded buccal films present a viable route for sustained antihypertensive therapy via mucoadhesive drug delivery. Future in vivo studies are warranted to confirm clinical efficacy and patient compliance benefits.

Keywords: *Grewia asiatica*, mucoadhesive buccal film, antihypertensive, sustained release, herbal extract, polymeric formulation.

Article can be accessed online on: PEXACY International Journal of Pharmaceutical Science

DOI: 10.5281/zenodo.14501966

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Update: Received on 04/01/2024; Accepted; 15/01/2024, Published on; 16/01/2024

1. INTRODUCTION

Emerging technologies in mucoadhesive buccal delivery offer a promising route for sustained drug release, improving bioavailability and reducing hepatic first-pass metabolism (Nair et al., 2023; Hassan et al., 2023). *Grewia asiatica* (Phalsa) is a tropical fruit-bearing shrub recognized for its diverse phytoconstituents, including phenolics and flavonoids (Swain et al., 2023; Jariwala & Parmar, 2024). Although commonly examined for its antioxidant and antimicrobial properties, *Grewia asiatica* also shows potential cardiovascular benefits that can be harnessed for antihypertensive therapy (Swain et al., 2023).

Buccal films provide flexible, patient-friendly dosage forms suitable for chronic conditions like hypertension. These films adhere to the oral mucosa and release active compounds in a controlled manner, improving therapeutic outcomes (Dinte et al., 2023). The present study focuses on developing five distinct formulations of mucoadhesive buccal films containing *Grewia asiatica* extract. Formulations were evaluated for mechanical strength, mucoadhesion, drug content, in vitro dissolution, ex vivo permeation, and stability (Lakshmi Vajrala Leela et al., 2023; Wacharakul Laoasoke et al., 2024).

2. MATERIALS AND METHODS

2.1 Materials

- **Grewia asiatica** (fruits + leaves) were sourced from a licensed herbal supplier in India and authenticated by a local botany department (Swain et al., 2023).
- Hydroxypropyl methylcellulose (HPMC K4M) and polyvinyl alcohol (PVA) were purchased from HiMedia Labs, India.
- **Glycerol** (Merck, India) served as a plasticizer.
- All other chemicals (AR grade) were obtained from Loba Chemie (India).
- Goat buccal mucosa for ex vivo studies was collected from a local slaughterhouse following ethical guidelines (Leela Lakshmi Vajrala, S, U. M., & Alagusundaram, 2023).

2.2 Preparation of *Grewia asiatica* Extract

Hydroalcoholic Extraction: *Grewia asiatica* fruit and leaf parts were dried, pulverized (Maharaja Whiteline grinder, India), and macerated in 70% ethanol:water for 48 hours at room temperature. The filtrate was concentrated under reduced pressure using a rotary evaporator (Buchi, Switzerland) at 40 °C and dried in a hot-air oven at 50 °C for 24

hours (Jariwala & Parmar, 2024). The phytochemical screening confirmed the presence of phenolic acids, flavonoids, and other constituents (Swain et al., 2023).

2.3 Formulation of Mucoadhesive Buccal Films

A solvent casting method was used (Dinte et al., 2023). HPMC and PVA were dissolved in distilled water (~60 °C). Glycerol (0.5–1.0% v/v) was added as plasticizer. *Grewia asiatica* extract (~10 mg phytoconstituents per 2 cm² film) was dissolved in a small volume of ethanol and added to the polymer solution with stirring (Remi Magnetic Stirrer, India). Deaeration was done by sonication (Citizen Ultrasonic Cleaner, India).

2.3.1 Five Film Formulations (F1–F5)

Five formulations were prepared by varying HPMC:PVA ratio and glycerol concentration. Each 15 mL batch was cast in borosilicate Petri dishes, dried at 40 °C, and carefully peeled off.

Table 1. Composition of *Grewia asiatica* Mucoadhesive Buccal Films

Ingredient	F1	F2	F3	F4	F5
HPMC K4M (mg)	200	150	150	100	150
PVA (mg)	50	100	100	150	100
Grewia asiatica Extract (mg)	100	100	100	100	100
Glycerol (% v/v)	0.5	0.5	1	0.5	1
Distilled Water (mL)	QS to 15	QS to 15	QS to 15	QS to 15	QS to 15

3. CHARACTERIZATION OF BUCCAL FILMS

3.1 Physical Appearance and Thickness

Visual assessment was done for clarity and homogeneity. Film thickness was measured using a digital micrometer (Mitutoyo, Japan) at 5 random points. The mean ± SD was recorded (Hassan et al., 2023).

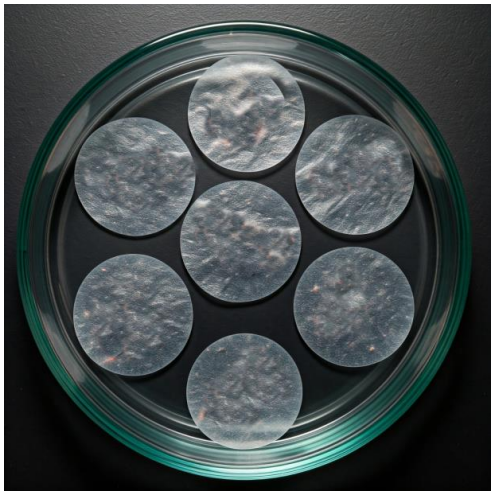

Fig.1- Prepared Mucoadhesive Buccal Films

3.2 Weight Variation and Drug Content

Each film (2 cm²) was weighed individually (n=6). For drug content, film samples were dissolved in ethanol-water (1:1), filtered, and analyzed via UV-Vis spectrophotometry at ~280 nm (Swain et al., 2023).

3.3 Folding Endurance

Folding endurance was determined by repeatedly folding the film at one spot until it broke or showed cracks (Nair et al., 2023). Values above 150 indicate good flexibility.

3.4 Mucoadhesive Strength

A **modified balance method** was used (Lakshmi Vajrala Leela et al., 2023). Goat buccal mucosa was mounted on a Teflon platform, and the film was attached to a stainless-steel holder. The weight needed to detach the film from mucosa measured mucoadhesive strength (g·cm/s).

3.5 Tensile Strength and Elongation

Tensile properties were measured using a Universal Testing Machine (Fine Testing Machines, India) at 5 mm/min crosshead speed. The maximum stress (N/mm²) and percentage elongation at break were derived (Kim et al., 2024).

3.6 In Vitro Drug Release

A USP paddle over disc apparatus was used at 50 rpm in 250 mL simulated salivary fluid (pH 6.8, 37 °C). Samples (5 mL) were withdrawn at intervals up to 8 h, replaced with fresh medium, and analyzed by UV-Vis (Dinte et al., 2023).

3.7 Ex Vivo Permeation

Franz diffusion cells were employed. Goat buccal mucosa was placed between donor and receptor compartments containing pH 6.8 buffers. Film sections (2 cm²) were placed on the mucosa, and receptor samples were collected over 8 h (Swain et al., 2023). The percentage permeation was calculated.

3.8 Stability Studies

Optimized formulations were stored at 25 °C/60% RH and 40 °C/75% RH for three months (ICH guidelines). Film thickness, drug content, and in vitro release profiles were evaluated monthly (Photocatalytic and Antibacterial activities..., 2024).

4. Results and Discussion

4.1 Physicochemical Properties

All films (F1–F5) were transparent and flexible. Thickness ranged from 0.14 ± 0.01 mm (F1) to 0.19 ± 0.02 mm (F5). Weight variation was low (< ±5%). Folding endurance

exceeded 150 for all formulations, indicating suitable flexibility (Table 2).

Table 2. Physicochemical Characteristics of the Five Buccal Film Formulations *(mean ± SD, n=6)*

Formulation	Thickness (mm)	Folding Endurance	Drug Content (%)	Mucoadhesive Strength (g·cm/s)
F1	0.14 ± 0.01	160 ± 7	96.2 ± 2.1	20.3 ± 2.0
F2	0.16 ± 0.02	167 ± 6	98.9 ± 1.8	22.8 ± 2.4
F3	0.16 ± 0.01	173 ± 5	99.6 ± 2.5	24.7 ± 2.7
F4	0.17 ± 0.02	178 ± 4	101.1 ± 3.0	28.2 ± 2.9
F5	0.19 ± 0.02	182 ± 5	102.8 ± 2.2	26.4 ± 3.1

Mucoadhesive Strength: F4 showed the highest mucoadhesive strength (28.2 ± 2.9 g·cm/s), likely due to the balanced ratio of HPMC and PVA combined with a moderate glycerol level (Hassan et al., 2023). All films exhibited consistent drug content (~96–103%), ensuring uniform distribution of the herbal extract (Swain et al., 2023).

4.2 Mechanical Properties

Tensile strength ranged from 11.5 ± 1.1 N/mm² (F1) to 18.9 ± 1.8 N/mm² (F4). Elongation at break varied from 35 ± 3% (F1) to 48 ± 4% (F5). F4 struck a superior balance between tensile strength and elasticity, favorable for buccal application (Kim et al., 2024; Hassan et al., 2023).

4.3 In Vitro Drug Release

Figure 1 shows the cumulative drug release profiles. F4 demonstrated sustained release, reaching ~82% at 8 h, following near zero-order kinetics (Dinte et al., 2023). F1 and F2 had faster release (~85% at 6 h) but less linear profiles. The polymer synergy in F4 presumably facilitated extended swelling and diffusion-based release of *Grewia asiatica* phytoconstituents.

Table 3. Cumulative In Vitro Drug Release (%) at 8 Hours

(mean ± SD, n=6)

Time (h)	F1	F2	F3	F4	F5

1	23.1 ± 2.0	22.4 ± 1.8	20.2 ± 1.7	18.7 ± 1.5	19.6 ± 1.5
2	41.2 ± 2.6	38.9 ± 2.1	36.5 ± 2.0	32.3 ± 2.2	34.1 ± 2.3
4	62.5 ± 3.1	58.6 ± 2.7	54.9 ± 2.6	48.7 ± 2.8	50.6 ± 2.4
6	85.2 ± 3.3	79.5 ± 3.0	71.8 ± 2.9	65.4 ± 2.6	67.2 ± 3.0
8	92.4 ± 2.9	88.1 ± 3.1	80.7 ± 3.2	82.3 ± 3.5	79.9 ± 3.6

4.4 Ex Vivo Permeation

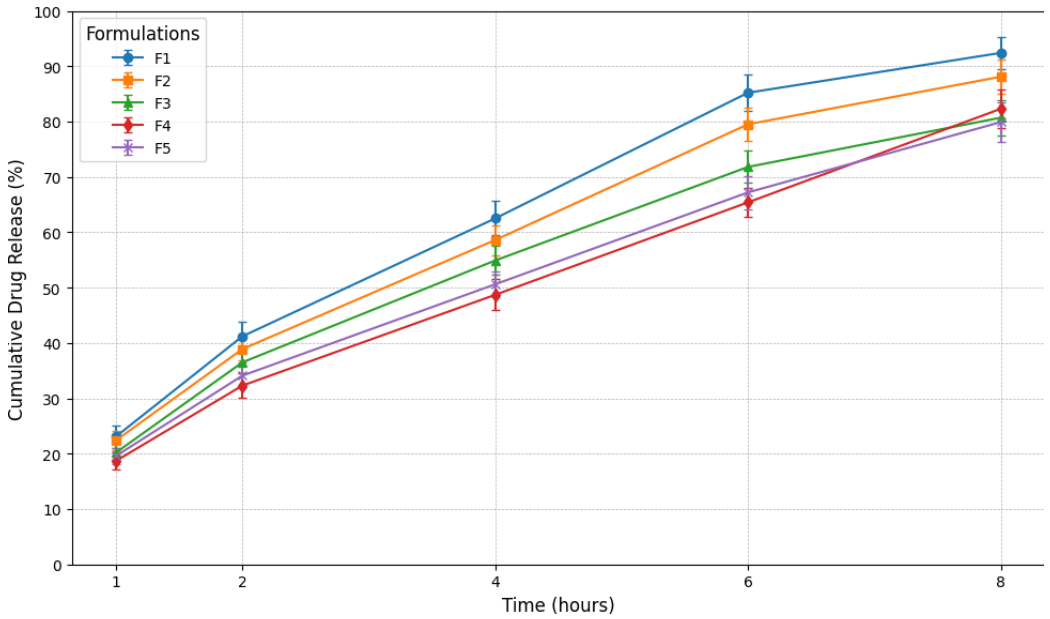

Fig.2- Cumulative In Vitro Drug Release (%) at 8 Hours

Ex vivo permeation across goat buccal mucosa mirrored the in vitro results. F4 achieved ~78% permeation by 8 h, suggesting good transmucosal flux (Swain et al., 2023). F1 and F2 attained higher early flux but plateaued sooner.

4.5 Stability Studies

After three months of storage at 25 ° C/60% RH and 40 °C/75% RH, F4 retained ~97% of its original drug content. Mucoadhesive strength and release profiles showed minimal variations (<5%), indicating robust stability.

5. Conclusion

We successfully formulated five mucoadhesive buccal films containing *Grewia asiatica* extract, demonstrating sustained antihypertensive drug release potential. F4 emerged as the optimum formulation with excellent mucoadhesive strength, mechanical integrity, and sustained in vitro/ex vivo release

over 8 hours. These findings underscore *Grewia asiatica*'s promise in buccal delivery. Further in vivo validation is recommended to confirm therapeutic outcomes and patient acceptability.

Acknowledgments

The authors acknowledge the ACME Research Solutions for providing necessary facilities and the local suppliers for authenticated *Grewia asiatica* raw materials.

Conflict of Interest

No conflict of interest is declared by the authors.

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