Development and Evaluation of Buprenorphine Buccal Film for Controlled Release

Dr Nansri Saha [1*], Bavugi Arathi [2], Dr A Saritha [3]

[1] Professor, Department of Pharmaceutics, SSJ College of Pharmacy, Vattinagulapally, Gandipet, Rangareddy District, Telangana, India

[2] Student, Department of Pharmaceutics, SSJ College of Pharmacy, Vattinagulapally, Gandipet, Rangareddy District, Telangana, India

[3] Professor and HOD, Department of Pharmaceutics, SSJ College of Pharmacy, Vattinagulapally, Gandipet, Rangareddy District, Telangana, India

* Corresponding Author: **Dr Nansri Saha**

Article Info

ISSN (online): 3049-0421
Volume: 03
Issue: 01
Received: 14-11-2025
Accepted: 16-12-2025
Published: 18-01-2026
Page No: 01-08

Abstract

The present study focuses on the development and evaluation of a controlled-release buprenorphine buccal film to enhance bioavailability, ensure sustained therapeutic effect, and improve patient compliance. Buccal films were prepared using various hydrophilic and mucoadhesive polymers via the solvent casting method, incorporating suitable plasticizers to achieve flexibility and uniformity. Formulations were evaluated for physical characteristics, including thickness, weight uniformity, surface pH, and drug content, all of which met pharmacopeial standards. *In vitro* drug release studies demonstrated sustained release over 8 hours, with the optimized formulation (F6) achieving approximately 97.85% cumulative release, following diffusion-controlled kinetics with a contribution from matrix erosion. Kinetic modeling indicated compatibility with Higuchi and first-order release models, confirming controlled release behavior. Stability studies under various temperature and humidity conditions (25°C/60% RH, 30°C/75% RH, 40°C/75% RH) revealed no significant changes in physical properties or drug release over 90 days, highlighting the formulation's robustness. Overall, the developed buprenorphine buccal film demonstrates a safe, stable, and patient-friendly platform for sustained drug delivery, offering potential advantages over conventional oral dosage forms in pain management and opioid therapy.

DOI: https://doi.org/10.54660/IJPGRR.2026.3.1.01-08

Keywords: Buprenorphine, FTIR Studies, Solvent evaporation method, Polymers, *In vitro* drug release studies

1. Introduction

Buccal drug delivery has emerged as a promising route for systemic drug administration due to its unique anatomical and physiological advantages, including a rich blood supply, reduced enzymatic degradation, and avoidance of extensive first-pass hepatic metabolism. Buccal films, in particular, offer a versatile and patient-friendly platform, providing flexibility, ease of administration, and the potential for controlled and sustained release of medications [1]. Buprenorphine, a potent semi-synthetic opioid analgesic, is widely used in the management of moderate to severe pain and opioid dependence. However, its conventional oral administration is associated with significant limitations, including poor oral bioavailability (approximately 10–15%) due to substantial first-pass metabolism and variable therapeutic response [2]. Alternative delivery systems such as transdermal patches and sublingual tablets have been explored, however, these dosage forms may present drawbacks, including delayed onset of action, dose dumping, irritation, and reduced patient acceptability [3]. To overcome these challenges, buccal delivery of buprenorphine offers a compelling strategy. The buccal mucosa allows for rapid absorption and sustained plasma levels, ensuring prolonged therapeutic action while minimizing systemic side effects and metabolic loss. The formulation of buccal films using suitable bioadhesive polymers further enhances the residence time at the site of absorption, improving drug permeability and therapeutic performance [4].

Therefore, the present study focuses on the development and evaluation of a controlled release buprenorphine buccal film aimed at improving bioavailability, prolonging therapeutic effect, and enhancing patient convenience. The formulated films were evaluated for physicochemical properties, drug content uniformity, surface pH, mucoadhesion strength, *In vitro* drug release, permeation studies, and stability analysis to determine their suitability as an effective controlled drug delivery system [5].

Materials

Buprenorphine were procured from Hetero Labs, HYD. Sodium alginate and Carbopol 934 were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

Methodology

FTIR Analysis [6]

Purpose: detect chemical bonding changes, new peaks, shifts, disappearance of characteristic functional group peaks.
Sample: neat powder or KBr pellet / ATR crystal.
Typical settings: 4000–400 cm^{-1}, resolution 4 cm^{-1}, 32–64 scans.
Interpretation: compare API, polymer, and mixture spectra. Look for peak shifts > 5–10 cm^{-1}, new peaks, or intensity changes in characteristic bands (e.g., C=O, N–H, O–H).

Formulation design [7]

Preparation of buccal films:

Table 1: Formulation Design of Buprenorphine Buccal films

F. Code	Buprenorphine (mg)	Sodium alginate (mg)	Carbopol 934 (mg)	Propylene glycol (ml)	Methanol (ml)	Aspartame (mg)	DMSO (mg)
F1	20	100	-	2	5	2	1
F2	20	200	-	2	5	2	1
F3	20	300		2	5	2	1
F4	20	400		2	5	2	1
F5	20	-	100	2	5	2	1
F6	20	-	200	2	5	2	1
F7	20	-	300	2	5	2	1
F8	20	-	400	2	5	2	1

Solvent casting technique

Dissolve film-forming polymer(s) in the appropriate solvent. Stir continuously (magnetic stirrer/hotplate) until a clear, homogenous solution forms. Add the plasticizer to improve the flexibility and prevent brittleness of the film Stir the mixture until uniformly dispersed. Add the *Buprenorphine* to the polymer-plasticizer mixture. Mix gently to avoid foaming and ensure uniform distribution of the extract. Add sweetener (aspartame). Allow the solution to stand to remove entrapped air bubbles. Pour the final homogenous solution into a clean petri dish. Spread uniformly using a casting knife or film applicator to maintain consistent thickness. Allow the film to dry at controlled temperature (usually 40–50°C) in a hot air oven or at room temperature in a dust-free environment. Drying time may vary (typically 24–48 hours). Once dried, carefully peel off the film and cut it into uniform strips of desired size (e.g., 2 cm x 2 cm). Store in moisture-proof, airtight packaging (e.g., aluminum pouches) to protect from humidity and light [8].

Evaluation of buccal patch formulation: [9]

Appearance & Physical Inspection

- **Long-term (general):** 25 ± 2 °C / 60% RH ± 5% RH — minimum 12 months; typical timepoints: 0, 3, 6, 9, 12 months (and thereafter 18, 24 months as required).
- **Accelerated:** 40 ± 2 °C / 75% RH ± 5% RH — test at 0, 3, 6 months (6 months minimum). If significant change occurs at accelerated between 3–6 months, follow ICH guidance on using long-term data for shelf-life decisions.
- **Intermediate (if required):** 30 ± 2 °C / 65% RH ± 5% RH — include when accelerated conditions cause significant change and long-term is 25 °C.
- **Alternative long-term (for hot/humid climates):** 30 ± 2 °C / 65% RH ± 5% RH (if chosen, intermediate not required).

Visual check for color, clarity, homogeneity, cracks, air bubbles, edges.

Procedure: Inspect patches (n = 3–6) under good light and record observations. Photograph representative patches.
Pass/fail: Smooth, uniform appearance; no cracks or large bubbles.

Dimensions, Thickness & Weight Uniformity [10]

Ensures dose uniformity & reproducible adhesion/contact area.

Dimensions: Measure length × width of each patch with a Vernier caliper

Thickness: Use digital micrometer at three points (center + two opposite points).

Weight variation [11]

Weigh individually (analytical balance, 0.1 mg) n = 6; calculate mean and % RSD.

Acceptance: % RSD for weight typically <5%.

Folding Endurance [12]

Flexibility and mechanical robustness.

Procedure: Fold a patch repeatedly at same place until it breaks or cracks. Count folds. Test n=3.

Interpretation: >200 folds indicates good flexibility (adjust to polymer expectations).

Tensile Strength & % Elongation (Mechanical Properties) [13]

Measures strength and elasticity—important for handling and

retention.

Apparatus: Universal Testing Machine (UTM) / Texture Analyser.

Procedure:
Cut rectangular strip (e.g., 25 mm × 10 mm).
Fix ends in grips with initial gauge length (e.g., 10 mm).
Pull at constant speed (e.g., 5 mm/min) until break.
Record maximum force at break (N) and extension at break (mm).

Calculations:
Tensile strength (MPa) = Force at break (N) / Cross-sectional area (m^2).
% Elongation = (Increase in length at break / original gauge length) × 100.

Surface pH [14]
Prevents Mucosal Irritation.
Procedure: Soak patch in 5 mL distilled water for 1 h at 37 °C. Measure pH of the medium with calibrated pH meter.
Acceptance: pH 6.5–7.5 (approx. neutral). Deviations should be justified.

Moisture Content & Moisture Uptake/Loss
Stability, Tack and Microbial Risk.
Moisture content (loss on drying): Dry known weight at 60 °C to constant weight; calculate % moisture.

Moisture uptake: Store patches in desiccator over saturated KCl (75% RH) for 72 h; weigh periodically.

Calculation: % Moisture uptake = [(Wt_final − Wt_initial)/Wt_initial] × 100.

Swelling Index [15]
Hydration influences mucoadhesion and drug release.

Weigh dry patch (W_0).
Immerse patch in simulated saliva (pH 6.8) at 37 °C.
At fixed times (15, 30, 60, 120 min), remove, blot surface, weigh (W_t).

Calculation: Swelling (%) = $[(W_t - W_0)/W_0] \times 100$.

***In vitro* Drug Content Uniformity / Assay** [16]
Confirms dose per patch.
Procedure:
Cut whole patch or defined area; dissolve in suitable solvent (sonicate if needed).

Filter and analyze by validated UV method.
Calculation: Drug content (mg/patch) and %Label claim.

Acceptance: 95–105% of label claim (or per pharmacopeial criteria).

Moisture absorption studies [17]
Dry samples in a hot air oven at 40–60 °C (temperature depends on sample thermal stability) or in a vacuum desiccator with silica gel until constant weight (two consecutive weighing 24 h apart differing <0.5% or as defined). Record this initial dry weight as W_0.
Alternatively, pre-equilibrate to a known low RH (e.g., LiCl, ~11% RH) if oven drying is unsuitable. Place each sample in a labelled weighing dish. Record initial dry weight W_0 (mg) to 3 significant figures.
Use at least three replicates (n = 3) per RH condition.

$$\text{Perentage moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Moisture loss studies [18]
The buccal films were weighed accurately and kept in desiccators containing anhydrous calcium chloride. After 3 days, the films were taken out and weighed. The moisture content (%) was determined by calculating moisture loss (%) using the formula:

$$\text{Percentage moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

***In-vitro* Drug release studies** [19]
Mount excised synthetic membrane on Franz cell, clamp donor side. Place film in donor compartment (drug-loaded side facing membrane). If film adheres poorly, use small amount of isotonic buffer to wet. Fill receptor compartment with pre-warmed receptor medium (degassed), ensuring no air bubbles near membrane. Typical receptor volume: 5–10 mL (Franz diffusion cell apparatus) Maintain temperature at 37 ± 0.5 °C and stirring for 600 rpm. Start experiment (t = 0). Withdraw samples (e.g., 1.0 mL) at predetermined timepoints (e.g., 5, 15, 30, 60, 120, 240, 480 min; extend as needed) and immediately replace with equal volume of fresh pre-warmed medium to maintain constant volume. Keep removed samples protected from light if needed. Filter samples (0.45 µm), dilute if necessary, and assay by validated UV method.

Drug release kinetics [20]
Use the cumulative release data (as fraction of drug released, M_t/M_∞ or % release) and fit to models below. For each model, transform as indicated, perform linear regression, and compute R^2 (and if possible Akaike information criterion or residuals) to choose best fit.

Zero-order (constant release rate)
Equation: $M_t = M_0 + k_0 \cdot t$ or in fractional form: $M_t/M_\infty = k_0 \cdot t$
Linear fit: cumulative % release vs time (t).
Slope = k_0 (units: %/h or mg/h).

First-order (concentration dependent)
Equation: $\ln(1 - M_t/M_\infty) = -k_1 \cdot t$
Linear fit: ln(remaining fraction) vs time.
Slope = $-k_1$ (units: 1/h).

Higuchi model (diffusion-controlled from planar matrix)
Equation: Mt/M∞ = k_H · t^{1/2}
Linear fit: cumulative % release vs √t.
Slope = k_H (units: % / h^{1/2}).

Korsmeyer–Peppas (empirical, for early-time release or when mechanism unknown)
Equation: Mt/M∞ = kKP·t^{n} (use when Mt/M∞ ≤ ~0.6)
Linear fit: log(Mt/M∞) vs log(t).
Slope = n (release exponent), intercept = log kKP.

Interpretation of n for thin films/films (slab geometry):
$n \leq 0.5 \rightarrow$ Fickian diffusion
$0.5 < n < 1.0 \rightarrow$ anomalous (non-Fickian) transport (diffusion + erosion)
$n = 1.0 \rightarrow$ Case II transport (polymer relaxation/erosion)
$n > 1 \rightarrow$ Super case II transport

Stability studies [21]
Determine the effect of time, temperature, humidity and light on the quality of the drug substance or drug product and establish shelf life / storage conditions. Use the appropriate condition set for the intended label/storage climate (choose one long-term set plus accelerated; include intermediate if needed).

Results and Discussion
Compatibility studies of drug and polymers:
All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between Buprenorphine and polymer. It also confirmed that the stability of drug during encapsulation process.

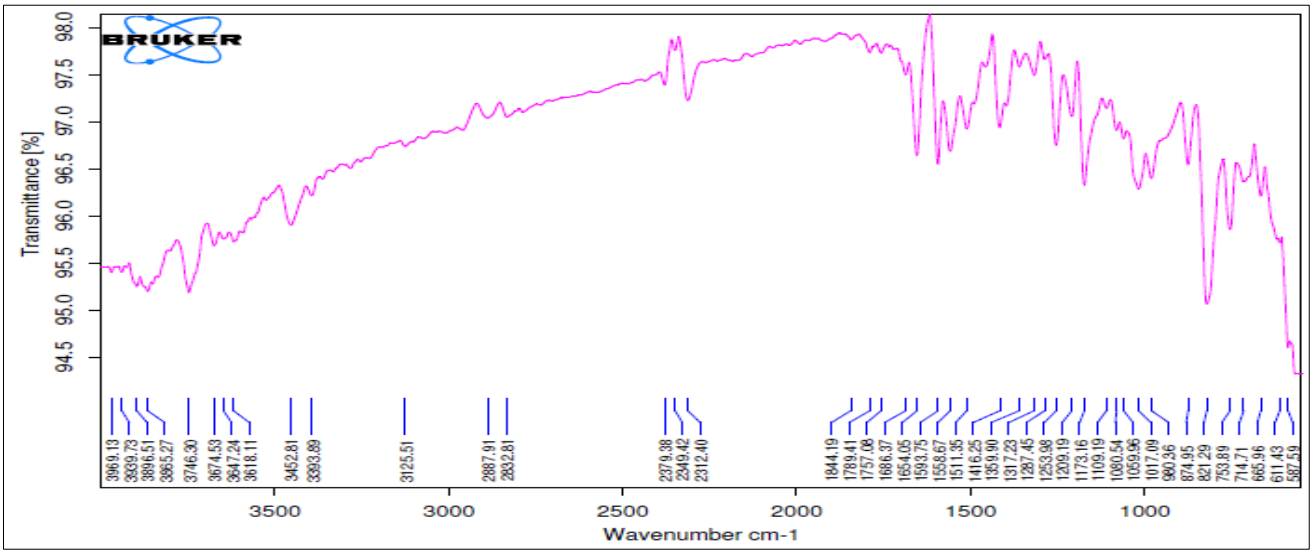

Fig 1: FT-IR Sample for Buprenorphine

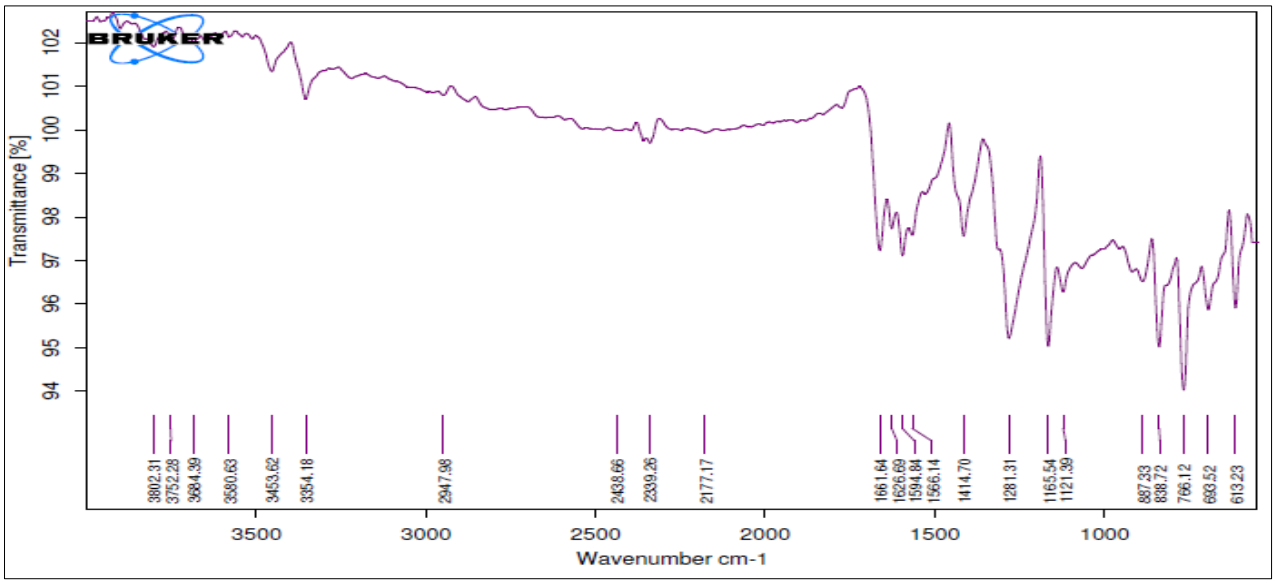

Fig 2: FT-IR Sample for physical mixture of drug and excipients

Physical appearance and surface texture of buccal films:
These parameters were checked simply with visual inspection of films and by feel or touch. The observation reveals that the films are having smooth surface and they are elegant in appearance.

Thickness (mm)
Thickness values ranged between 0.37 mm (F3) and 0.56 mm (F1).
The slight variation is expected due to differences in polymer concentrations and casting conditions.
All films showed uniform thickness within acceptable limits, indicating good reproducibility of the solvent casting method.

Weight Variation (mg)
Weight varied from 31.25 mg (F8) to 45.25 mg (F6).
Increase in polymer concentration (e.g., HPMC, PVP) led to higher film weight.
The variations remained within reasonable range, confirming uniform film casting and drug loading.

Drug Content Uniformity (%)
Drug content ranged from 79.38% (F1) to 86.93% (F6). Most formulations showed values close to 80–85%, ensuring good drug distribution across the films. F6 exhibited the highest drug content, suggesting better incorporation of drug in that polymer ratio.

Folding Endurance
Values ranged from 46 (F4) to 55 (F5 & F8).
All films tolerated more than 40 folds, indicating good mechanical strength and flexibility.
Higher folding endurance in F5 and F8 may be due to optimum polymer–plasticizer ratio.

% Moisture Loss
Ranged from 8.15% (F3) to 8.72% (F7). Values remained fairly consistent, indicating good stability under dry conditions. Slight increase in some formulations may be attributed to polymer hygroscopicity.

% Moisture Absorption
Ranged between 9.16% (F8) and 9.82% (F3). Moisture absorption was within a narrow range, reflecting low hygroscopicity and stability during storage. F8 showed the least absorption, making it less prone to microbial contamination or storage instability.

Swelling Index (%)
Values varied from 13.20% (F5) to 14.55% (F4). Swelling index depends on the hydrophilic polymer content, which regulates mucoadhesion and drug release. F4 showed maximum swelling, suggesting higher hydration and possibly better mucoadhesive strength.

Table 2: Physicochemical evaluation data of Buprenorphine Buccal Films

F. code	F1	F2	F3	F4	F5	F6	F7	F8
Thickness (mm)	0.56	0.49	0.37	0.46	0.52	0.51	0.43	048
Weight variation (mg)	38.96	41.23	35.68	40.55	43.57	45.25	39.86	31.25
Drug content Uniformity	79.38	80.12	81.25	83.68	84.50	86.93	81.24	79.86
Folding endurance	49	53	52	46	55	49	53	55
% Moisture loss	8.25	8.39	8.15	8.46	8.55	8.62	8.72	8.55
%Moisture absorption	9.65	9.55	9.82	9.35	9.41	9.28	9.22	9.16
Swelling index (%)	13.69	14.52	13.99	14.55	13.20	13.58	13.69	13.25

Drug release studies

Table 3: *In vitro* release data of film F_1 to F_8

Time (hrs.)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
0	0	0	0	0	0	0	0	0
1	24.58	25.69	22.69	19.68	25.94	28.98	25.91	24.69
2	35.69	35.60	34.25	35.60	36.82	38.42	37.46	38.21
3	42.20	40.22	42.38	43.17	44.58	45.98	46.93	45.82
4	55.36	53.16	55.19	54.59	55.25	56.47	55.81	56.25
5	63.49	63.98	65.37	66.37	68.19	69.25	65.72	66.58
6	75.82	72.54	70.25	72.25	75.36	76.82	78.81	79.25
7	85.63	83.26	83.36	84.69	85.15	86.15	85.25	88.85
8	92.52	93.26	94.50	95.20	96.39	97.85	94.57	95.20

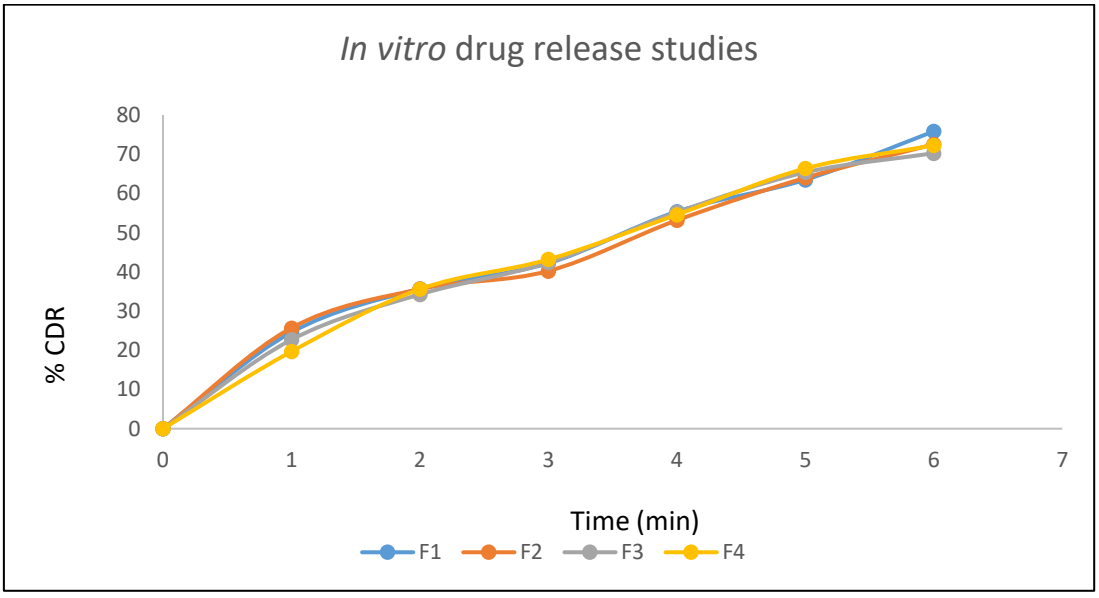

Fig 3: *In vitro* drug release of (F1- F4) formulation

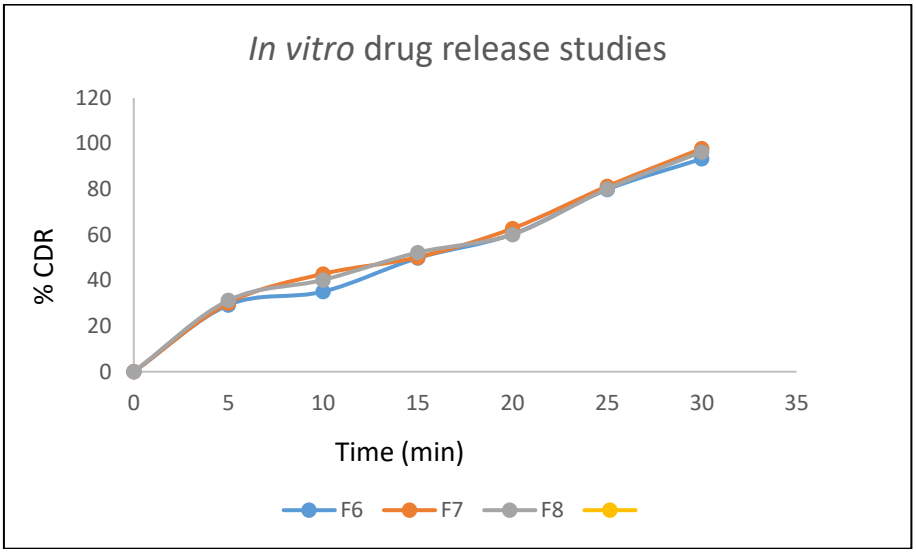

Fig 4: *In vitro* drug release of (F5- F8) formulation

All formulations achieved controlled release with >90% drug release within 8 hrs, suitable for sustained drug delivery.
Among them, F6 provided the most rapid and complete release (97.85%), while F3 was the slowest (94.50%).
Depending on the therapeutic need (faster vs. prolonged release), F6 (fastest) or F3 (slowest) may be considered optimal.

Drug release kinetics:
All the formulation of prepared Buprenorphine buccal films was subjected to *In vitro* release studies these studies were carried out using Franz diffusion cell apparatus.

Zero order kinetics

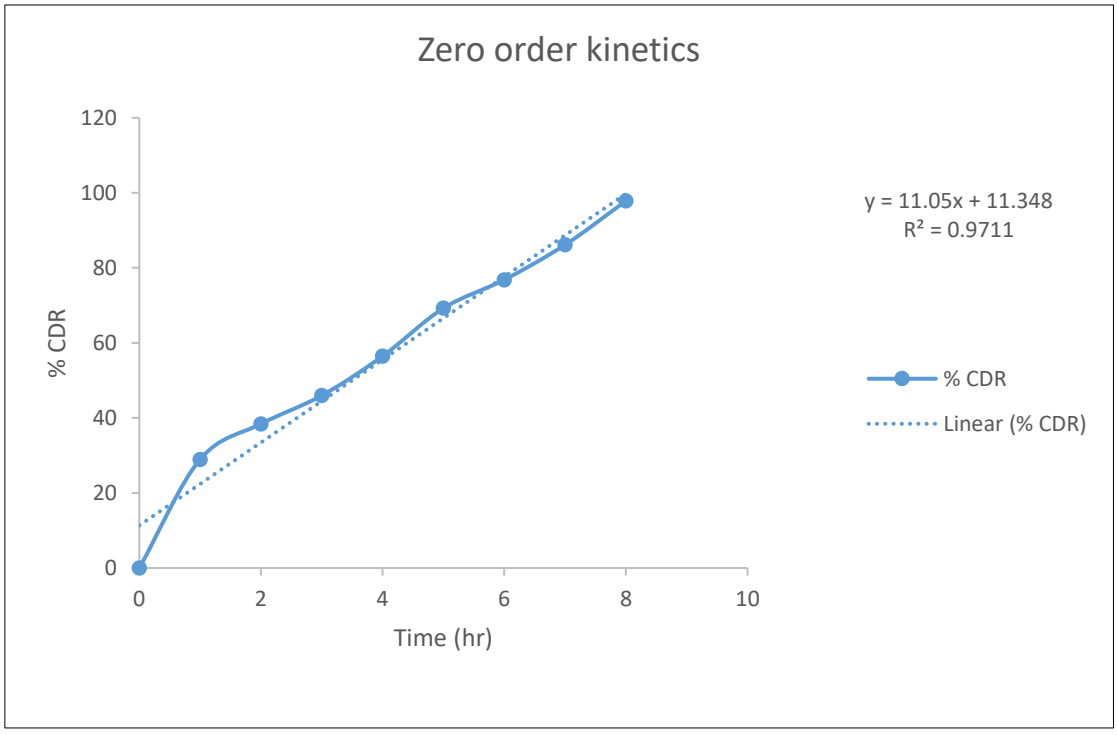

Fig 5: Zero order kinetics of Optimized formulation

First order kinetics

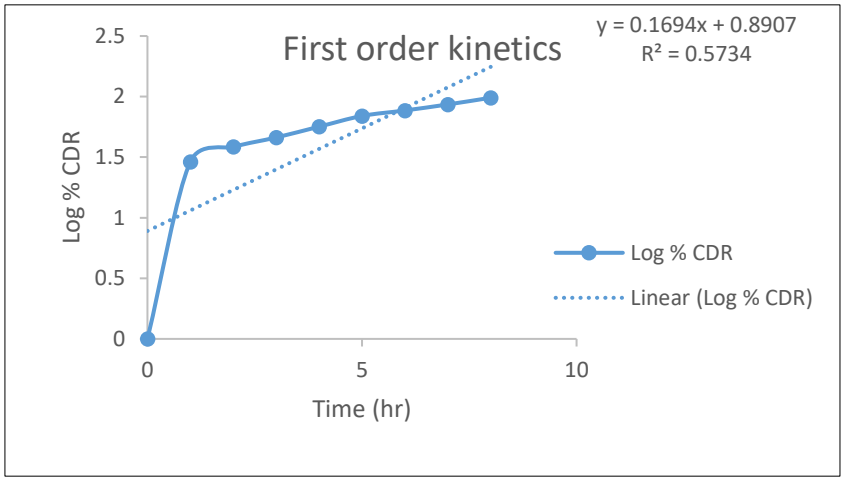

Fig 6: First order kinetics of Optimized formulation

Higuchi model

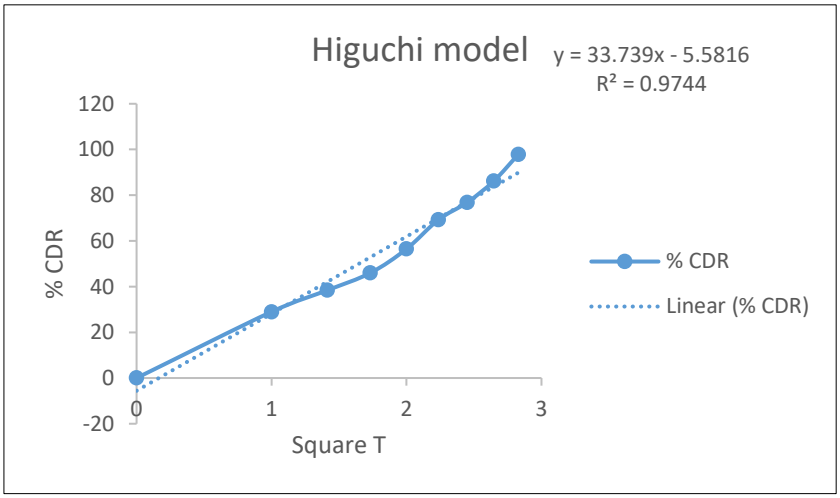

Fig 7: Higuchi model of Optimized formulation

Korsmeyer Peppas

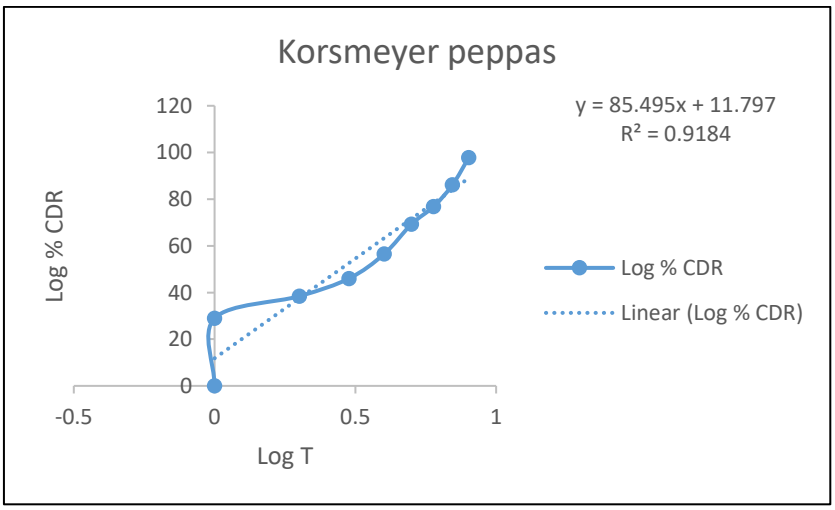

Fig 8: Korsmeyer peppas of Optimized formulation

The values of *In vitro* release were attempted to fit into various mathematical models. Plots of zero order, first order, Higuchi matrix, Peppas were respectively.

Regression values are higher with Zero order release kinetics. Therefore, all the Buprenorphine buccal films Zero order release kinetics.

Formulation F6 exhibits sustained-release behavior, with drug release controlled primarily by diffusion, but also influenced by matrix erosion in later stages. It is suitable for achieving controlled therapeutic levels over 8 hrs.

Stability studies:

Optimized formulations F6 was selected for accelerated stability studies as per ICH guidelines. The films were observed for color, appearance and flexibility for a period of three months. % cumulative drug release of the formulation was found to be decreasing. This decrease may be attributed to the harsh environment (40^0C) maintained during the studies.

Table 4: Stability studies of optimized formulations

S.NO	Time in days	Physical changes	Mean % drug release		
			Buprenorphine		
			25^0C/60%	30^0C/75%	40^0C/75%
1	01	No Change	98.62	98.62	98.62
2	30	No Change	97.28	97.36	97.67
3.	60	No Change	96.21	96.01	96.50
4.	90	No Change	95.62	95.02	95.52

The formulation maintains physical integrity and >95% drug release under all tested conditions for 90 days. This indicates good chemical and physical stability, making it suitable for commercial development and patient use.

Conclusion

The optimized buprenorphine buccal film is a promising alternative to conventional oral formulations, capable of providing controlled drug delivery, improved bioavailability, and enhanced patient adherence. This formulation can potentially reduce dosing frequency and improve therapeutic efficacy in pain management and opioid dependence therapy

References

1. Poliwoda S, Noor N, Jenkins JS, Stark CW, Steib M, Patel K, *et al*. Buprenorphine and its formulations: a comprehensive review. Health Psychol Res. 2022;10(3):37517.
2. Cassidy JP, Landzert NM, Quadros E. Controlled buccal delivery of buprenorphine. J Control Release. 1993;25(1-2):21-9.
3. Shipp L, Liu F, Kerai-Varsani L, Okwuosa TC, Hider R. Buccal films: A review of therapeutic opportunities, formulations & relevant evaluation approaches. J Control Release. 2022;352:113-25.
4. Dodou K. Research and developments in buccal and sublingual drug delivery systems. Pharm J. 2012;288(7700):446-8.
5. Bahraminejad S, Almoazen H. Sublingual and buccal delivery: A historical and scientific prescriptive. Pharmaceutics. 2025;17(8):1073.
6. Diaz del Consuelo I, Falson F, Guy RH, Jacques Y. Ex vivo evaluation of bioadhesive films for buccal delivery of fentanyl. J Control Release. 2007;122(2):135-40.
7. Nicolazzo JA, Reed BL, Finnin BC. Buccal penetration enhancers--how do they really work? J Control Release. 2005;105(1-2):1-15.
8. Patel VF, Liu F, Brown MB. Advances in oral transmucosal drug delivery. J Control Release. 2011;153(2):106-16.
9. Shojaei AH. Buccal mucosa as a route for systemic drug delivery: a review. J Pharm Pharm Sci. 1998;1(1):15-30.
10. Smart JD. The basics and underlying mechanisms of mucoadhesion. Adv Drug Deliv Rev. 2005;57(11):1556-68.
11. Zhang H, Zhang J, Streisand JB. Oral mucosal drug delivery: clinical pharmacokinetics and therapeutic applications. Clin Pharmacokinet. 2002;41(9):661-80.
12. Ahad A, Al-Saleh AA, Al-Mohizea AM, Al-Jenoobi FI, Raish M, Yassin AEB, *et al*. Formulation and characterization of novel soft mucoadhesive buccal films: a potential platform for drug delivery. Saudi Pharm J. 2017;25(8):1140-6.
13. Madhav NV, Shakya AK, Shakya P, Singh K. Orotransmucosal drug delivery systems: a review. J Control Release. 2009;140(1):2-11.
14. Singh J, Deep P. Buccal drug delivery: an alternative route for systemic drug delivery. Int J Pharm Sci Rev Res. 2012;16(2):78-83.
15. Rao NGR, Shravani B, Reddy MSR. Buccal drug delivery: a promising route for enhancing bioavailability. Int J Pharm Pharm Sci. 2013;5(3):39-47.
16. Fiza F, *et al*. Buccal drug delivery system: a promising route of drug delivery. World J Pharm Pharm Sci. 2017;6(7):1452-67.
17. Sharma S, Yogananda R, *et al*. Buccal adhesive drug delivery system: a review. Int J Res Ayurveda Pharm. 2014;5(2):246-51.
18. Sharma K, *et al*. Formulation and evaluation of mucoadhesive buccal patch of timolol maleate. Int J Pharm Sci Res. 2020;11(6):2782-90.
19. Jasti BR, Lo X, Upadrasha S. Design and development of mucoadhesive drug delivery systems: an overview. Pharm Technol. 2003;27(2):36-52.
20. Kumar SK, Nagabhushanam MV, Rao KRSS, Bhikshapathi DV. Preparation and in-vivo evaluation of oral dissolving films containing sumatriptan succinate. Der Pharmacia Lett. 2013;5(3):27-38.
21. Low AQJ, Parmentier J, Khong YM, Chai CCE, Tun TY, Berania JE, *et al*. Effect of type and ratio of solubilizing polymer on characteristics of hot-melt extruded orodispersible films. Int J Pharm. 2013;455(1-2):138-47.

How to Cite This Article

Saha N, Arathi B, Saritha A. Development and evaluation of buprenorphine buccal film for controlled release. Int J Pharma Growth Res Rev. 2026;3(1):1–9. doi:10.54660/IJPGRR.2026.3.1.01-08.

Creative Commons (CC) License