RESEARCH PAPER

Formulation and Optimization of Dexrabeprazole Mucoadhesive Buccal Tablets for Enhanced Bioavailability

Manisha R. Kale[1]*, Sanjay B. Bhawar[2]

[1]Research Scholar, Bhagwant University, Ajmer, India

[2]Professor, Pravara Rural College of Pharmacy, Loni, Maharashtra, India

Corresponding author

Manisha R. Kale[1]

Address: Research Scholar, Bhagwant University, Ajmer, India

Objectives: The present study aimed to design and optimize dexrabeprazole buccal tablets to enhance drug bioavailability, improve mucoadhesion, and achieve sustained release, using a 3^2 factorial design. **Methods:** Formulations (F1–F9) were prepared with varying concentrations of Carbopol 934P and xanthan gum. The tablets were evaluated for post-compression parameters, mucoadhesive strength, swelling index, surface pH, drug content, and in-vitro release. Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared Spectroscopy (FTIR) confirmed drug–excipient compatibility. Optimization was performed using ANOVA-based factorial design, with validation through predicted versus experimental values. Stability studies were conducted under accelerated conditions (40 ± 2 °C / 75 ± 5% RH). **Results:** All batches showed acceptable weight variation (199.6–200.5 mg), hardness (4.8–5.1 kg/cm²), friability (<0.5%), and drug content (97.8–99.3%). Surface pH remained within the buccal physiological range (6.65–6.74). Mucoadhesive strength ranged from 5.6 g (F1) to 8.9 g (F5), while swelling index varied from 42.6% to 64.3%. In-vitro release at 8 h ranged between 86.5% (F6) and 95.4% (F1). Batch F3 (20 mg Carbopol 934P and 60 mg xanthan gum) was optimized, exhibiting 6.4 g mucoadhesive strength, 53.5% swelling index, and 90.8% cumulative release at 8 h, closely matching predicted values with <3% error. Stability data confirmed no significant changes in physical or functional properties over 3 months. **Conclusion:** The optimized buccal tablet formulation of dexrabeprazole demonstrated desirable mechanical strength, controlled release, and excellent stability, with potential clinical benefits in improving therapeutic efficacy and patient compliance. Future in-vivo studies are warranted to establish translational relevance.

Keywords: Dexrabeprazole; Buccal tablet; Factorial design; Mucoadhesion; Sustained release; Stability.

How to cite this article: Kale MR, Bhawar SB. Formulation and optimization of dexrabeprazole mucoadhesive buccal tablets for enhanced bioavailability. Int J Drug Deliv Technol. 2026;16(8s): 190-206; DOI: 10.25258/ijddt.16.8s.20

INTRODUCTION

Peptic ulcer disease, gastroesophageal reflux, and related acid-mediated gastrointestinal disorders represent a significant global health concern, affecting millions worldwide with a rising prevalence in both developed and developing nations [1]. According to recent epidemiological surveys, nearly 10–20% of the global population experiences recurrent acid-related conditions, with an increasing incidence linked to stress, dietary habits, and polypharmacy [2]. Conventional proton pump inhibitors (PPIs) remain the mainstay of therapy; however, their oral administration is limited by low bioavailability due to extensive hepatic first-pass metabolism and degradation in the acidic gastric environment [3]. This not only results in inconsistent therapeutic outcomes but also necessitates higher dosing, contributing to increased treatment costs and greater risk of adverse effects. The cumulative healthcare burden of acid-related diseases is substantial, with billions of dollars spent annually on medications, diagnostic interventions, and hospitalizations [4]. Despite the availability of advanced PPIs, clinical management still faces challenges such as variable absorption, poor patient compliance, and recurrence of symptoms, highlighting the urgency for innovative formulations that ensure reliable drug delivery and enhanced therapeutic efficacy [5].

Dexrabeprazole, the S-isomer of rabeprazole, is a potent PPI with superior acid suppression activity, rapid onset, and longer duration of action compared to its racemic

counterpart [6]. Its pharmacological action involves irreversible inhibition of the H+/K+ ATPase enzyme in gastric parietal cells, thereby effectively reducing gastric acid secretion and promoting mucosal healing [7]. Dexrabeprazole possesses favorable chemical stability under neutral conditions but undergoes significant degradation in acidic environments, limiting its oral bioavailability [8]. Additionally, extensive first-pass hepatic metabolism further compromises systemic exposure, resulting in suboptimal therapeutic efficacy. Previous studies have demonstrated its clinical benefits in treating gastroesophageal reflux disease and peptic ulcers; however, conventional oral dosage forms often fail to achieve consistent plasma concentrations [9]. The compound's physicochemical properties, including moderate solubility and lipophilicity, underscore the need for novel delivery approaches that can circumvent its limitations [10]. Its established safety profile and proven therapeutic potential make dexrabeprazole an ideal candidate for reformulation strategies aimed at enhancing stability, absorption, and patient compliance through alternative drug delivery systems [11].

Mucoadhesive buccal tablets present a promising platform for overcoming the limitations of conventional dexrabeprazole delivery [12]. The buccal mucosa offers a highly vascularized surface that enables direct systemic absorption while bypassing gastrointestinal degradation and hepatic first-pass metabolism [13]. Incorporation of bioadhesive polymers prolongs the residence time at the site of administration, ensuring sustained drug release and improved therapeutic effectiveness. Compared to oral tablets and capsules, buccal systems enhance patient convenience, minimize dosing frequency, and provide better pharmacokinetic predictability [14]. Advances in polymer science and formulation technologies have further enabled the design of controlled-release buccal tablets with improved mucoadhesion, swelling behavior, and drug permeation. Recent research trends have shown increasing interest in such non-invasive drug delivery platforms, particularly for molecules with poor oral bioavailability and high first-pass metabolism [15]. The scientific rationale behind selecting this system for dexrabeprazole lies in its ability to protect the drug from acidic degradation, achieve higher bioavailability, and ensure consistent plasma drug levels, thereby improving clinical outcomes and reducing the economic burden of long-term therapy [16].

The present study aims to formulate and optimize dexrabeprazole mucoadhesive buccal tablets to enhance bioavailability and overcome the drawbacks of conventional oral administration. The specific objectives include designing buccal tablets using suitable polymers, evaluating their physicochemical and mucoadhesive properties, and optimizing formulation parameters to achieve maximum drug release and adhesion. The scope of the study also involves in-vitro and ex-vivo characterization to assess performance, with an expectation of developing a patient-friendly, effective, and innovative dosage form capable of improving therapeutic efficiency in acid-related disorders.

MATERIALS AND METHODS

MATERIALS

Dexrabeprazole (API, pharmaceutical grade, MW: 359.4 g/mol) was obtained from Sciquaint Innovations Pvt. Ltd. (Pune, India). Carbopol 934P (analytical grade, viscosity ~30,000–40,000 cP) was procured from Neeta Chemicals (Pune, India). Hydroxypropyl methylcellulose K4M (USP grade, viscosity 4000 mPa·s) was purchased from Research Lab Fine Chem Industries (Mumbai, India). Xanthan gum (analytical grade, food/pharma grade polysaccharide) was obtained from Sciquaint Chemicals (Pune, India). Microcrystalline cellulose (analytical grade, particle size ~50 µm), PVP K30 (analytical grade, MW ~40,000 g/mol), sodium saccharin (analytical grade, ≥98% purity), peppermint flavor (pharma grade), talc (pharmaceutical grade, hydrous magnesium silicate), magnesium stearate (USP grade, ≥98% purity), and mannitol (pharmaceutical grade, excipient grade) were all procured from Sciquaint Chemicals (Pune, India). All other chemicals and reagents used in the study were of analytical grade and procured from standard suppliers.

METHODS

Calibration curve determination

The calibration curve of dexrabeprazole was prepared using a UV–Vis spectrophotometer (Systronics, Model 2203, Ahmedabad, India) with 1 cm quartz cuvettes in phosphate buffer pH 6.8. A stock solution of 100 µg/mL was obtained by dissolving 10 mg drug in buffer and diluting to 100 mL, from which working standards of 10–60 µg/mL were prepared. Absorbance was recorded at λmax 284 nm against buffer blank at 25 ± 2 °C in triplicate (n=3). Mean absorbance was plotted versus concentration to generate the calibration curve, and linear regression provided slope, intercept, and correlation coefficient (R^2) [17,18].

Solubility study

The solubility of dexrabeprazole was determined by the solvent saturation method, wherein an excess quantity of

drug was added to 10 mL of different solvents such as distilled water, phosphate buffer pH 6.8, 0.1 N HCl, and ethanol in separate glass vials. The vials were sealed and maintained in a thermostatically controlled orbital shaker (Remi Instruments, Mumbai, India) at 25 ± 2 °C and 100 rpm for 24 h to reach equilibrium. After equilibration, the samples were centrifuged at 5000 rpm for 10 min, and the supernatant was filtered through a 0.45 µm membrane filter. The filtrates were suitably diluted with the respective solvents, and the concentration of drug in each medium was determined using a UV–Visible spectrophotometer (Systronics, Model 2203, Ahmedabad, India). All experiments were performed in triplicate (n=3), and solubility was calculated from the corresponding calibration curve [19,20].

Differential scanning colorimetry

Differential scanning calorimetry (DSC) was performed to study the thermal behavior and possible interactions of dexrabeprazole with excipients. Accurately weighed samples (2–5 mg) of pure drug, excipients, and physical mixtures were sealed in aluminum pans and analyzed using a DSC instrument (PerkinElmer DSC 4000, Mumbai, India) under a nitrogen purge at a flow rate of 50 mL/min. The samples were scanned over a temperature range of 30–300 °C at a constant heating rate of 10 °C/min, with an empty sealed aluminum pan used as reference. Each measurement was carried out in triplicate (n=3) to ensure reproducibility. The obtained thermograms were evaluated for characteristic endothermic and exothermic transitions to assess drug crystallinity and potential interactions with formulation components [21,22].

Fourier transform infrared spectroscopy

Fourier transform infrared (FTIR) spectroscopy was carried out to evaluate the functional groups of dexrabeprazole and to detect possible interactions with excipients. Samples of pure drug, polymers, and their physical mixtures were finely ground, blended with dry potassium bromide (KBr), and compressed into thin transparent pellets using a hydraulic press at 10 tons pressure for 2 min. The prepared pellets were analyzed using an FTIR spectrophotometer (Shimadzu IR Affinity-1S, Kyoto, Japan) over a scanning range of 4000–400 cm^{-1} with a resolution of 4 cm^{-1}. Each spectrum was recorded in triplicate (n=3) under identical conditions. The obtained spectra were compared to identify characteristic absorption peaks and to assess any shifts, disappearance, or appearance of new bands that may indicate drug–excipient interactions [23,24].

Experimental design

A 3^2 full factorial design was employed to optimize Dexrabeprazole mucoadhesive buccal tablets by evaluating the influence of two formulation factors: HPMC K4M concentration (X_1: 20, 40, and 60 mg per tablet) and Carbopol 934P concentration (X_2: 20, 40, and 60 mg per tablet), each studied at three levels. The design generated a total of nine experimental batches (F1-F9). The dependent variables investigated were Y_1: cumulative drug release at 8 h (%), Y_2: mucoadhesive strength (N), and Y_3: swelling index (%). Experimental data were analyzed using Design Expert® software (Stat-Ease Inc., USA) and fitted to a second-order polynomial model to determine the linear, quadratic, and interaction effects of the formulation factors. The general regression equation was expressed as:

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_{12} X_1 X_2 + \beta_{11} X_1^2 + \beta_{22} X_2^2$$

where *Y* is the response, β_0 the intercept, β_1 and β_2 the linear coefficients, β_{12} the interaction coefficient, and β_{11} and β_{22} the quadratic coefficients. Model adequacy was confirmed by ANOVA ($p < 0.05$), lack-of-fit, R^2 values, adequate precision, and residual analysis to ensure reliability [25,26].

Table 1: 3^2 Factorial Design showing independent factors and levels

Independent Variables				
Label	Factors	Level (mg)		
		Low (-)	Medium	High (+)
A	Carbopol 934P	20	40	60
B	Xanthan gum	20	40	60
Dependant Variables				
Y_1	Cumulative drug release at 8 h (%)			
Y_2	mucoadhesive strength (g)			
Y_3	Swelling index (%)			

Table 2: Formulation Composition of Dexrabeprazole Mucoadhesive Buccal

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Dexrabeprazole (mg)	10	10	10	10	10	10	10	10	10
Carbopol 934P (A) (mg)	20	20	20	40	40	40	60	60	60

Xanthan gum (B) (mg)	20	40	60	20	40	60	20	40	60
Microcrystalline cellulose (mg)	30	30	30	30	30	30	30	30	30
PVP K30 (mg)	3	3	3	3	3	3	3	3	3
Sodium saccharin (mg)	2	2	2	2	2	2	2	2	2
Peppermint flavor (mg)	1	1	1	1	1	1	1	1	1
Talc (mg)	2	2	2	2	2	2	2	2	2
Magnesium stearate (mg)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Mannitol (q.s to 200 mg)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total weight (mg)	200	200	200	200	200	200	200	200	200

Precompression study

Micromeritic studies were carried out to evaluate the flow and packing properties of dexrabeprazole buccal tablet blends before compression. About 10 g of accurately weighed powder was transferred into a 50 mL graduated cylinder to determine the initial bulk volume. The cylinder was then tapped using a tapped densitometer (Electrolab ETD-1020, Mumbai, India) for 500 taps at a constant rate until a constant volume was observed, and the final volume was recorded as tapped volume. Flow behavior was further assessed by the fixed funnel method, where the powder blend was allowed to pass freely through a funnel with a 10 mm orifice placed at a fixed height of 10 cm to form a conical heap, and the height and radius of the heap were measured to determine flow characteristics. Each test was performed in triplicate (n=3) to ensure reproducibility [27,28].

Formulation of Dexrabeprazole Mucoadhesive Buccal Tablets

Dexrabeprazole mucoadhesive buccal tablets were prepared by the direct compression method using the compositions outlined in Table 2. The required quantities of dexrabeprazole and excipients were accurately weighed and sieved through a #60 mesh. The drug was first blended with mannitol and microcrystalline cellulose to ensure uniform distribution, followed by the addition of Carbopol 934P and xanthan gum as mucoadhesive polymers. The blend was homogenized with PVP K30, sodium saccharin, and peppermint flavor for 10 minutes. Finally, talc and magnesium stearate were incorporated as glidant and lubricant, respectively, and mixed for 2 minutes to avoid excessive lubrication. The resulting blend was compressed into tablets of 200 mg each using a rotary tablet press (Rimek Minipress, Ahmedabad, India) fitted with flat-faced punches, maintaining hardness between 4–6 kg/cm². Each batch was prepared in triplicate (n=3) [29-31].

Evaluation of Dexrabeprazole Mucoadhesive Buccal Tablets

Weight Variation Test

Weight variation was evaluated as per IP/USP specifications using twenty tablets selected randomly (n=20). Each tablet was individually weighed on an analytical balance (Citizen CX-220, Mumbai, India; readability 0.1 mg), and the average tablet weight was calculated. The individual weights were compared with the mean, and percentage deviation was determined. The results were assessed against pharmacopeial acceptance limits, where for tablets weighing 200 mg, not more than two units may deviate by more than ±7.5% and none should deviate by more than ±15% [32].

Thickness and Diameter

Thickness and diameter of the tablets were determined to ensure uniformity of size and shape. Ten tablets from each batch (n=10) were randomly selected and measured individually using a digital Vernier caliper (Mitutoyo, Model CD-6, Japan; least count 0.01 mm). The mean values with standard deviation were calculated and compared with acceptable pharmacopeial limits to confirm dimensional consistency of the compressed tablets [33].

Friability Test

Friability of the prepared tablets was evaluated using a Roche friabilator (Electrolab EF-2, Mumbai, India). A sample of ten tablets (n=10) was accurately weighed, placed in the friabilator drum, and subjected to 100 revolutions at 25 rpm for 4 minutes. The tablets were then dedusted and reweighed, and the percentage weight loss was calculated. According to pharmacopeial standards, a weight loss of not more than 1% was considered

acceptable, indicating adequate mechanical strength of the tablets [34].

Hardness Test

The hardness of the prepared buccal tablets was evaluated to determine mechanical strength and resistance to handling stress. Six tablets from each batch (n=6) were randomly selected and tested individually using a Monsanto hardness tester (Campbell Electronics, Mumbai, India). The force required to break each tablet diametrically was recorded in kg/cm², and the mean hardness with standard deviation was calculated to ensure compliance with acceptable limits (4–6 kg/cm²) for buccal tablets [35].

Drug Content Uniformity

Drug content uniformity was determined by randomly selecting ten tablets from each batch (n=10). Each tablet was accurately weighed, powdered, and an amount equivalent to 10 mg of dexrabeprazole was transferred to a 100 mL volumetric flask. The drug was dissolved in phosphate buffer pH 6.8 with sonication for 10 minutes and the volume was made up to the mark with the same medium. The resulting solution was filtered through a 0.45 µm membrane filter, and suitable dilutions were prepared. The absorbance of each sample was measured using a UV–Visible spectrophotometer (Systronics, Model 2203, Ahmedabad, India) at the predetermined wavelength, and the drug content was calculated from the calibration curve. The results were expressed as mean ± standard deviation, and compliance was verified against pharmacopeial limits (85–115% of the labeled claim) [36].

Surface pH

Surface pH of the buccal tablets was determined to evaluate their potential for causing mucosal irritation. Tablets from each batch (n=3) were allowed to swell for 2 hours in 5 mL of phosphate buffer pH 6.8 at room temperature. The surface pH was then measured by gently placing a calibrated digital pH meter electrode (Eutech Instruments, pH Tutor, Mumbai, India) in close contact with the surface of the swollen tablet until a stable reading was obtained. Measurements were carried out in triplicate, and the mean values were recorded to ensure the surface pH remained within the neutral range suitable for buccal application [37].

Swelling Index (%)

The swelling behavior of buccal tablets was evaluated to assess hydration capacity and polymeric expansion. Pre-weighed tablets (W_1) from each batch (n=3) were placed separately in Petri dishes containing 10 mL of phosphate buffer pH 6.8 and kept at room temperature. At predetermined time intervals (1, 2, 4, 6, and 8 h), tablets were carefully removed, excess surface water was blotted with filter paper, and the swollen tablets were reweighed (W_2). The swelling index was calculated as the percentage increase in weight relative to the initial weight. The test was performed in triplicate, and mean values were recorded to determine swelling capacity of the formulations [38].

Ex-vivo Mucoadhesive Strength

Ex-vivo mucoadhesive strength of the buccal tablets was evaluated using freshly excised goat buccal mucosa obtained from a local slaughterhouse and used within 2 hours of excision. The mucosal tissue was washed with phosphate buffer pH 6.8 and mounted on a glass slide using cyanoacrylate adhesive. The tablet was attached to the lower side of a pan connected to a modified physical balance, and the mucosa-bearing slide was placed beneath it in such a way that the tablet could directly contact the mucosal surface. A preload force of 50 g was applied for 2 minutes to establish adhesion, after which weights were gradually added to the opposite pan until detachment of the tablet from the mucosal surface occurred. The total weight required for detachment was recorded as the mucoadhesive strength, expressed in grams. The experiment was performed in triplicate (n=3) for each batch to ensure reproducibility [39].

In-vitro Drug Release Study

In-vitro release of dexrabeprazole from buccal tablets was evaluated using a USP Apparatus II paddle dissolution tester (Electrolab TDT-08L, Mumbai, India) with 900 mL phosphate buffer pH 6.8 as medium maintained at 37 ± 0.5 °C and 50 rpm. Individual tablets (n=3) were placed in the vessels, and 5 mL aliquots were withdrawn at predetermined intervals (e.g., 0.5, 1, 2, 4, 6, and 8 h), immediately replacing with equal volumes of fresh medium pre-equilibrated at test temperature to maintain sink conditions and constant volume. Samples were filtered through 0.45 µm membrane filters, suitably diluted with dissolution medium, and analyzed by UV–Visible spectrophotometry (Systronics 2203, Ahmedabad, India) at the predetermined wavelength using the calibration curve to compute cumulative drug release. Care was taken to prevent foaming and air entrapment; vessels were covered to minimize evaporation and light exposure throughout the test [40].

Stability Study

Stability assessment of the optimized dexrabeprazole buccal tablet and one representative formulation was

conducted per ICH Q1A(R2) under accelerated conditions. Tablets (alu–alu blister packed; 10 units per pull point) were stored in a calibrated stability chamber (Thermo Lab, Mumbai, India) maintained at 40 ± 2 °C/75 ± 5% RH for 3 months, with samples withdrawn at 0, 1, 2, and 3 months. At each interval, tablets were examined for appearance, weight variation, thickness/diameter, hardness, friability, surface pH, drug content, swelling index, mucoadhesive strength, and in-vitro drug release to detect any changes in performance attributes. Instruments and procedures matched those described in the respective evaluation methods; all tests were performed in triplicate (n = 3). Long-term storage (25 ± 2 °C/60 ± 5% RH) may be initiated in parallel where required by journal policy, using identical packaging, sampling, and test panels [41].

Statistical Analysis

All results were expressed as mean ± SD (n as specified) and analyzed at a 5% significance level. Factorial design data were fitted to a second-order polynomial model and evaluated by ANOVA for significance, factor effects, interactions, and lack-of-fit, with R^2 values confirming model adequacy. Numerical desirability optimization was applied to identify the best formulation, and a checkpoint batch was used to validate predictions by comparing experimental and predicted responses through % relative error [42].

RESULTS AND DISCUSSION

RESULTS

Calibration curve of Dexrabeprazole in phosphate buffer pH 6.8

The calibration curve of Dexrabeprazole in phosphate buffer (pH 6.8) at 278 nm showed a strong linear relationship between absorbance and concentration in the tested range (Figure 1). The regression equation obtained was y = 0.0184x + 0.0015 with a correlation coefficient (R^2 = 0.9997), indicating excellent linearity and reliability of the method for quantitative estimation. The close alignment of experimental points with the regression line confirms that Beer–Lambert's law was obeyed within the selected concentration range, validating the suitability of the method for further analytical and formulation studies.

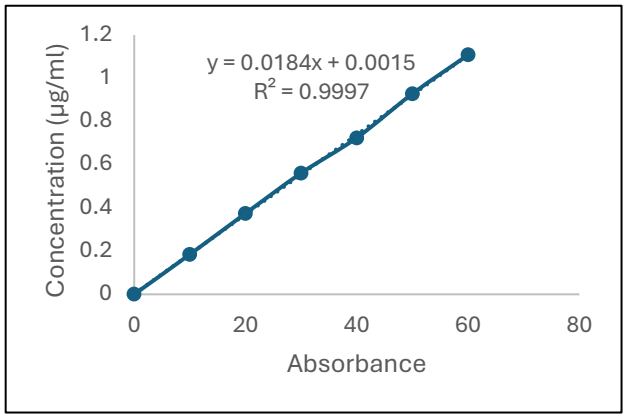

Figure 1: Calibration curve of Dexrabeprazole in phosphate buffer (pH 6.8) at 278 nm

Solubility study

The solubility study of Dexrabeprazole in various solvents revealed significant variations depending on the medium (Table 3). The drug exhibited poor solubility in distilled water (10.2 mg/mL), classifying it as soluble, whereas a marked enhancement in solubility was observed in phosphate buffer (112.5 mg/mL) and simulated saliva fluid (111.3 mg/mL), where it was categorized as freely soluble. Similarly, in acidic conditions (0.1 N HCl), the solubility was highest at 113.2 mg/mL, confirming its favorable dissolution in gastric-like media. Among organic solvents, methanol (45.8 mg/mL) and ethanol (30.6 mg/mL) demonstrated good solubility, placing the drug in the freely soluble category. These findings indicate that Dexrabeprazole shows medium-dependent solubility, with maximum solubility in phosphate buffer and acidic conditions, supporting its potential for oral formulations requiring efficient dissolution.

Table 3: Solubility of Dexrabeprazole in Different Solvents (mean ± SD, n = 3)

Sr. No.	Solvent	Solubility (mg/mL) (mean ± SD)	Inference
1	Distilled water	10.2 ± 0.3	Soluble
2	Phosphate buffer (pH 6.8)	112.5 ± 2.1	Freely soluble
3	Simulated saliva fluid (pH 6.8)	111.3 ± 1.9	Freely soluble
4	Ethanol	30.6 ± 0.8	Freely soluble

5	Methanol	45.8 ± 1.2	Freely soluble
6	0.1 N HCl	113.2 ± 2.4	Freely soluble

Differential scanning colorimetry

The DSC thermogram of pure Dexrabeprazole exhibited a sharp endothermic peak at 141.41 °C, corresponding to its melting point, which confirmed its crystalline nature (Figure 2A). In contrast, the physical mixture of Dexrabeprazole with excipients showed a slightly shifted endothermic peak at 143.01 °C, along with an additional peak at 216.62 °C (Figure 2B). The minor shift in melting point indicates the presence of excipients but without significant interaction, as no major changes or disappearance of the drug's characteristic peak were observed. This suggests that Dexrabeprazole retains its crystalline identity in the physical mixture and is largely compatible with the selected excipients.

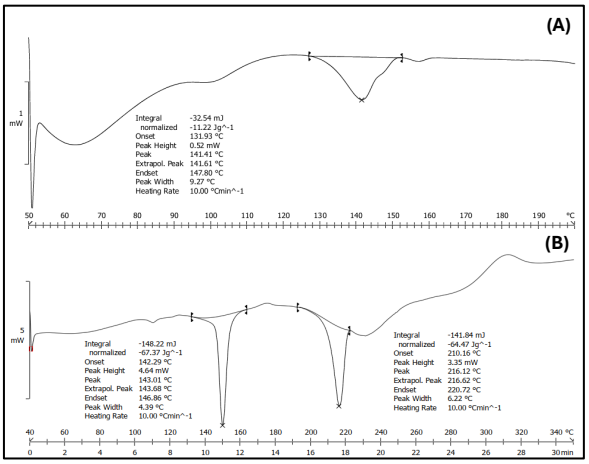

Figure 2: DSC spectra of (A) Pure Dexrabeprazole and (B) Physical mixture

FTIR analysis

The FTIR spectra of pure Dexrabeprazole (Figure 3A) and its physical mixture with excipients (Figure 3B) were analyzed to assess potential drug–excipient interactions. Pure Dexrabeprazole displayed characteristic absorption bands at 2488.69 cm^{-1} (O–H stretching), 1587.13 cm^{-1} (C=C aromatic stretching), 1278.71 cm^{-1} (C–N stretching), 978.01 cm^{-1} and 739.56 cm^{-1} (aromatic C–H bending), confirming the presence of functional groups associated with its structure. In the physical mixture, the major characteristic peaks of Dexrabeprazole were retained, with slight shifts observed at 1564.95 cm^{-1}, 1358.63 cm^{-1}, and 1244.83 cm^{-1}, along with peaks at 849.49 cm^{-1} and 647.00 cm^{-1}, suggesting the presence of excipients. Importantly, no significant disappearance of characteristic peaks was noted, indicating that no strong chemical interactions occurred between the drug and excipients. These results confirm the compatibility of Dexrabeprazole with the selected excipients.

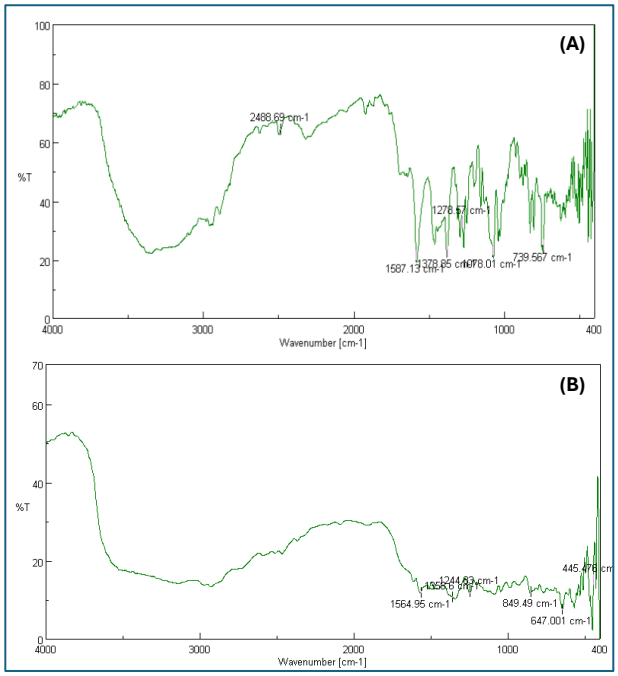

Figure 3: FTIR spectra of (A) pure drug (B) Physical mixture

Results of precompression study

The pre-compression parameters of Dexrabeprazole buccal tablet blends (F1–F9) were evaluated to assess flow and packing properties (Table 4). The bulk density of the formulations ranged from 0.45 to 0.48 g/cm³, while the tapped density varied between 0.51 and 0.55 g/cm³, indicating uniform packing characteristics across all batches. The Carr's Index values (11.3–12.9%) and corresponding Hausner's ratios (1.13–1.15) suggest that all blends exhibited good flowability and compressibility. Additionally, the angle of repose values, ranging from 27.8° to 29.5°, further confirmed excellent flow properties, as they fall within the acceptable range (<30°). These results indicate that all formulations demonstrated suitable pre-compression characteristics, ensuring their suitability for direct compression into tablets without processing difficulties.

Table 4: Pre-compression Parameters of Dexrabeprazole Buccal Tablet Blends (F1–F9)

Batch	Bulk Density (g/cm³)	Tapped Density (g/cm³)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (°)
F1	0.46 ± 0.01	0.52 ± 0.01	11.5 ± 0.5	1.13 ± 0.01	28.4 ± 0.6
F2	0.47 ± 0.01	0.54 ± 0.01	12.9 ± 0.7	1.15 ± 0.01	29.1 ± 0.5
F3	0.45 ± 0.01	0.51 ± 0.01	11.8 ± 0.6	1.13 ± 0.01	27.8 ± 0.7
F4	0.48 ± 0.01	0.55 ± 0.01	12.7 ± 0.6	1.15 ± 0.01	29.5 ± 0.6
F5	0.47 ± 0.01	0.53 ± 0.01	11.3 ± 0.5	1.13 ± 0.01	28.2 ± 0.5
F6	0.46 ± 0.01	0.52 ± 0.01	11.5 ± 0.5	1.13 ± 0.01	27.9 ± 0.6
F7	0.48 ± 0.01	0.55 ± 0.01	12.7 ± 0.6	1.15 ± 0.01	29.4 ± 0.7
F8	0.47 ± 0.01	0.53 ± 0.01	11.3 ± 0.5	1.13 ± 0.01	28.3 ± 0.6
F9	0.46 ± 0.01	0.52 ± 0.01	11.5 ± 0.5	1.13 ± 0.01	28.0 ± 0.7

The post-compression evaluation of Dexrabeprazole buccal tablets (F1–F9) demonstrated that all formulations complied with pharmacopeial specifications, confirming uniformity and mechanical stability (Table 5). The weight variation among batches was consistent, ranging from 199.6 to 200.5 mg, indicating excellent uniformity of tablet mass. Tablet thickness (3.19–3.23 mm) and diameter (8.05–8.08 mm) remained uniform across formulations, reflecting precise die filling during compression. The friability values (0.38–0.42%) for all batches were well below the acceptable limit of 1%, suggesting that the tablets possessed adequate mechanical strength and resistance to abrasion. These findings indicate that the prepared buccal tablets exhibited desirable physical characteristics with uniform geometry and high durability, making them suitable for subsequent evaluation.

Table 5: Post-compression Parameters of Dexrabeprazole Buccal Tablets (F1–F9)

Batch	Weight Variation (mg)	Thickness (mm)	Diameter (mm)	Friability (%)
F1	200.4 ± 2.1	3.21 ± 0.04	8.05 ± 0.03	0.41 ± 0.02
F2	199.6 ± 1.9	3.19 ± 0.05	8.07 ± 0.04	0.38 ± 0.01
F3	200.2 ± 2.3	3.22 ± 0.06	8.06 ± 0.03	0.42 ± 0.02
F4	199.8 ± 1.8	3.20 ± 0.05	8.08 ± 0.04	0.40 ± 0.01
F5	200.5 ± 2.0	3.23 ± 0.04	8.07 ± 0.03	0.39 ± 0.01
F6	199.9 ± 2.2	3.21 ± 0.05	8.06 ± 0.04	0.41 ± 0.02
F7	200.1 ± 2.1	3.22 ± 0.06	8.07 ± 0.03	0.40 ± 0.01
F8	200.3 ± 1.9	3.20 ± 0.05	8.08 ± 0.04	0.42 ± 0.02
F9	199.7 ± 2.0	3.21 ± 0.04	8.06 ± 0.03	0.39 ± 0.01

The hardness, drug content uniformity, and surface pH evaluation of Dexrabeprazole buccal tablets (F1–F9) confirmed their mechanical integrity, content accuracy, and physiological compatibility (Table 6). The hardness values (4.8–5.1 kg/cm²) indicated sufficient mechanical strength to withstand handling while remaining within the optimal range for buccal administration. The drug content uniformity (97.8–99.3%) across all formulations confirmed accurate and reproducible dosing, ensuring each tablet delivered the intended amount of Dexrabeprazole without significant variation. The surface pH values (6.65–6.74) were close to the physiological pH of the buccal cavity (6.5–7.0), indicating that the tablets are unlikely to cause irritation or discomfort upon administration. These results collectively suggest that all formulations exhibited consistent quality, with uniform strength, accurate drug content, and buccal-friendly surface pH, meeting the requirements for further performance evaluations.

Table 6: Hardness, Drug Content Uniformity, and Surface pH of Dexrabeprazole Buccal Tablets (F1–F9)

Batch	Hardness (kg/cm²)	Drug Content (%)	Surface pH
F1	4.8 ± 0.2	98.2 ± 1.1	6.65 ± 0.04
F2	5.0 ± 0.3	99.1 ± 0.9	6.72 ± 0.05

F3	4.9 ± 0.2	97.8 ± 1.3	6.68 ± 0.06
F4	5.1 ± 0.3	98.7 ± 1.2	6.70 ± 0.04
F5	4.8 ± 0.2	99.3 ± 1.0	6.74 ± 0.05
F6	5.0 ± 0.3	98.5 ± 1.1	6.71 ± 0.06
F7	4.9 ± 0.2	97.9 ± 1.4	6.67 ± 0.05
F8	5.0 ± 0.3	98.6 ± 1.2	6.73 ± 0.04
F9	4.8 ± 0.2	99.0 ± 1.1	6.69 ± 0.05

The ex-vivo mucoadhesive strength and swelling index of Dexrabeprazole buccal tablets (F1–F9) are shown in Table 7. Results revealed that increasing concentrations of Carbopol 934P and Xanthan gum improved both mucoadhesion and swelling. Mucoadhesive strength ranged from 5.6 ± 0.2 g (F1) to 8.9 ± 0.4 g (F5), while swelling index increased from 42.6 ± 1.5% (F1) to 64.3 ± 1.9% (F9). Formulations F5 and F8 showed the best balance of adhesion and swelling, indicating that a combination of Carbopol and Xanthan gum enhances buccal retention and hydration properties.

Table 7: Ex-vivo Mucoadhesive Strength and Swelling Index of Dexrabeprazole Buccal Tablets (F1–F9)

Batch	Carbopol 934P (mg)	Xanthan gum (mg)	Mucoadhesive Strength (g)	Swelling Index (%)
F1	20	20	5.6 ± 0.2	42.6 ± 1.5
F2	20	40	6.8 ± 0.3	49.8 ± 1.7
F3	20	60	6.4 ± 0.3	53.5 ± 1.6
F4	40	20	7 ± 0.3	50.2 ± 1.5
F5	40	40	8.9 ± 0.4	58.4 ± 1.8
F6	40	60	7.5 ± 0.3	61.2 ± 1.7
F7	60	20	7.2 ± 0.4	55.1 ± 1.6
F8	60	40	8.7 ± 0.3	62.7 ± 1.8
F9	60	60	8 ± 0.4	64.3 ± 1.9

The in-vitro cumulative drug release data for Dexrabeprazole buccal tablets (F1–F9) are summarized in Table 8. All formulations exhibited a controlled release profile with rapid initial drug release followed by sustained release up to 8 h. At 0.5 h, release ranged from 9.2 ± 0.6% (F9) to 18.2 ± 1.1% (F1), indicating a formulation-dependent burst effect. By 2 h, drug release extended to 30.8 ± 1.1% (F9) and 50.4 ± 1.6% (F1). At 6 h, formulations achieved 73.6–88.3% release, and by 8 h, almost complete release was observed with values ranging from 86.5 ± 1.4% (F6) to 95.4 ± 1.5% (F1). Among all, F1 showed the highest release (95.4%), while F6 and F8 displayed more sustained profiles, indicating the role of polymer composition in modulating drug release.

Table 8: In-vitro Cumulative Drug Release (%) of Dexrabeprazole Buccal Tablets at Predetermined Intervals (mean ± SD, n=3)

Time (h)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
0.5	18.2 ± 1.1	16.5 ± 1.0	14.3 ± 0.9	15.4 ± 1.0	13.2 ± 0.8	11.6 ± 0.7	13.1 ± 0.8	11.4 ± 0.7	9.2 ± 0.6
1.0	28.7 ± 1.3	26.1 ± 1.2	23.5 ± 1.1	24.6 ± 1.1	22.0 ± 1.0	19.2 ± 0.9	21.1 ± 1.0	18.6 ± 0.9	16.4 ± 0.8
2.0	50.4 ± 1.6	47.2 ± 1.5	43.6 ± 1.4	45.1 ± 1.5	41.0 ± 1.3	37.8 ± 1.2	39.6 ± 1.3	36.4 ± 1.2	30.8 ± 1.1

4.0	72.1 ± 1.7	68.3 ± 1.6	63.9 ± 1.6	66.0 ± 1.6	61.5 ± 1.5	58.0 ± 1.4	59.4 ± 1.5	56.1 ± 1.4	54.7 ± 1.4
6.0	88.3 ± 1.8	84.2 ± 1.7	79.5 ± 1.6	82.0 ± 1.7	77.1 ± 1.6	73.6 ± 1.5	75.2 ± 1.6	71.5 ± 1.5	72.1 ± 1.5
8.0	95.42± 1.5	92.4 ± 1.6	90.8 ± 1.5	90.3 ± 1.6	91.6 ± 1.5	86.5 ± 1.4	89 ± 1.5	87.2 ± 1.4	88.6 ± 1.4

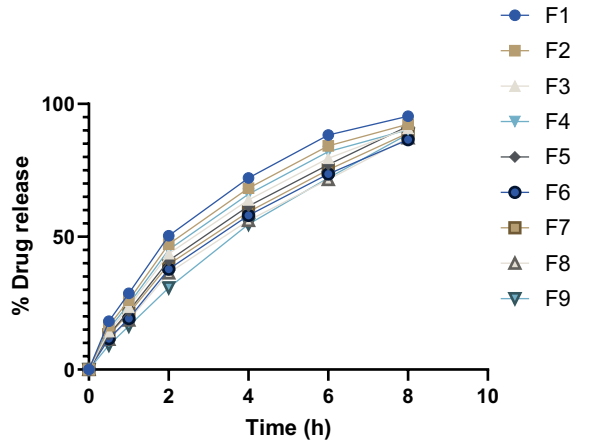

Figure 4: Cumulative drug release profile of batch F1-F9

Optimization

Mucoadhesive Strength

The quadratic model was found to be significant for mucoadhesive strength, with a sequential p-value of 0.0182 and a lack of fit p-value of 0.9184, confirming good model adequacy (Table 9). The adjusted R^2 value of 0.7410 and predicted R^2 of 0.7411 indicate strong agreement between predicted and experimental data, ensuring the robustness of the model. The ANOVA results (Table 10) demonstrated that the model was highly significant ($F = 19.01$, $p = 0.0176$). Among the factors, Carbopol 934P (Factor A) was the most influential ($F = 46.81$, $p = 0.0063$), while xanthan gum (Factor B) exhibited moderate significance ($F = 7.93$, $p = 0.0669$). Quadratic terms also played an important role, particularly B^2 ($F = 30.25$, $p = 0.0118$), followed by A^2 ($F = 10.08$, $p = 0.0502$), indicating curvature effects in the design space. The interaction term AB was not significant ($p = 1.0$).

The polynomial equation for mucoadhesive strength can be expressed as:

$$\mathbf{Y = 2.68 + 0.74A + 0.30B – 0.12AB – 0.48A^2 – 0.72B^2}$$

Contour and response surface plots (Figures 5) revealed that increasing Carbopol concentration markedly enhanced mucoadhesive strength, whereas xanthan gum exhibited a less pronounced effect. A clear downward curvature was observed at higher levels of both polymers, confirming the significance of quadratic terms. The 3D surface plots showed a dome-shaped response, where optimal mucoadhesive strength was attained at intermediate concentrations of Carbopol and xanthan gum. These visual trends complement the statistical findings, highlighting Carbopol 934P as the dominant contributor while quadratic effects shaped the response profile.

Swelling Index

The quadratic model provided the best fit for swelling index, with a sequential p-value of 0.0086 and an insignificant lack of fit ($p = 0.9942$), validating model adequacy (Table 9). The adjusted R^2 (0.9741) and predicted R^2 (0.9741) were highly consistent, indicating excellent predictive ability. ANOVA results (Table 10) confirmed overall model significance ($F = 276.40$, $p = 0.0003$). Both Carbopol 934P (Factor A) and xanthan gum (Factor B) were highly significant contributors, with extremely high F-values of 754.33 ($p = 0.0001$) and 556.76 ($p = 0.0002$), respectively. Quadratic terms A^2 ($F = 25.82$, $p = 0.0147$) and B^2 ($F = 42.59$, $p = 0.0073$) were also significant, indicating curvature in the response. The AB interaction term, however, was not statistically significant ($p = 0.2123$).

The polynomial equation for swelling index is given as:

$$\mathbf{Y = 21.86 + 5.23A + 4.72B – 0.21AB – 1.21A^2 – 1.56B^2}$$

Contour and response surface plots (Figures 5) showed a pronounced synergistic increase in swelling index with rising concentrations of both Carbopol and xanthan gum. The plots illustrated a steep slope in the response surface, confirming strong main effects. However, curvature was evident at higher polymer concentrations, consistent with significant quadratic terms, indicating that beyond a certain threshold, the swelling index plateaued or declined. The contour plots further highlighted elliptical regions, signifying strong quadratic contributions. Collectively, the visual trends and statistical analysis establish Carbopol 934P and xanthan gum as dominant swelling enhancers with well-defined nonlinear effects.

Cumulative Drug Release at 8 h

The quadratic model was found suitable for describing cumulative drug release at 8 h, with a sequential p-value of 0.0745 and a non-significant lack of fit (p = 0.8768), suggesting acceptable model adequacy (Table 9). The adjusted R^2 value of 0.5829 confirmed moderate predictive ability. ANOVA analysis (Table 10) indicated that the model was significant (F = 12.39, p = 0.0323). Factor A (Carbopol 934P) exhibited the highest significance (F = 31.38, p = 0.0112), followed by Factor B (Xanthan gum) with F = 12.55 (p = 0.0383). Quadratic terms A^2 (F = 7.35, p = 0.0731) and B^2 (F = 6.59, p = 0.0826) were moderately significant, while the interaction AB was non-significant (p = 0.137).

The polynomial equation for drug release at 8 h is:

$$Y = 62.10 - 3.92A - 2.76B - 0.71AB - 1.54A^2 - 1.43B^2$$

Contour and surface plots (Figures 5) depicted that increasing Carbopol concentration significantly reduced drug release, reflecting its strong matrix-forming ability. Xanthan gum also decreased release, but to a lesser extent. The curvature observed in 3D plots confirmed the contribution of quadratic terms, showing diminishing returns at higher polymer concentrations. The surface maps illustrated concave trends, where drug release decreased progressively with rising polymer content. The contour maps displayed clear zones of reduced release at higher levels of Carbopol, reinforcing its dominant role. Overall, the visual and statistical data demonstrate that both polymers restrict drug release, with Carbopol exerting a stronger effect.

Table 9: Model fit summary of mucoadhesive strength, Swelling index and drug release at 8 hr

Response	Source	Sequential p-value	Adjusted R^2	Predicted R^2	
Mucoadhesive strength	Quadratic	0.0182	0.9184	0.7411	Suggested
Swelling index	Quadratic	0.0086	0.9942	0.9741	Suggested
Cumulative drug release at 8hr	Quadratic	0.0745	0.8768	0.5829	Suggested

Table 10: ANOVA for quadratic model of mucoadhesive strength, Swelling index and drug release at 8 hr

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Mucoadhesive sttrength						
Model	8.80	5	1.76	19.02	0.0177	significant
A-Carbopol 934P	4.34	1	4.34	46.82	0.0064	
B-Xanthan gum	0.7350	1	0.7350	7.94	0.0669	
AB	0.0000	1	0.0000	0.0000	1.0000	
A^2	0.9339	1	0.9339	10.09	0.0503	
B^2	2.80	1	2.80	30.25	0.0118	
Residual	0.2778	3	0.0926			
Cor Total	9.08	8				
Swelling index						
Model	400.14	5	80.03	276.40	0.0003	significant
A-Carbopol 934P	218.41	1	218.41	754.33	0.0001	
B-Xanthan gum	161.20	1	161.20	556.76	0.0002	
AB	0.7225	1	0.7225	2.50	0.2123	
A^2	7.48	1	7.48	25.82	0.0147	
B^2	12.33	1	12.33	42.60	0.0073	
Residual	0.8686	3	0.2895			

Cor Total	401.01	8				
Cumulative drug release at 8hr						
Model	60.85	5	12.17	12.39	0.0323	significant
A-Carbopol 934P	30.83	1	30.83	31.38	0.0112	
B-Xanthan gum	12.33	1	12.33	12.55	0.0383	
AB	4.00	1	4.00	4.07	0.1369	
A^2	7.22	1	7.22	7.35	0.0731	
B^2	6.48	1	6.48	6.60	0.0826	
Residual	2.95	3	0.9822			
Cor Total	63.80	8				

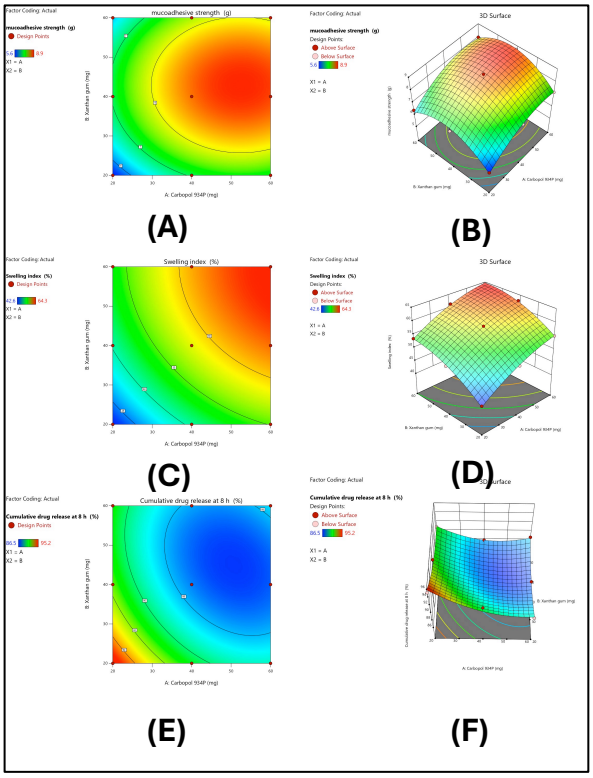

Figure 5: Contour and 3D surface plots illustrate the effects of Carbopol 934P (A) and Xanthan gum (B) on mucoadhesive strength, swelling index, and cumulative drug release at 8 h. Plots (A–B) show a marked increase in mucoadhesive strength with higher Carbopol concentrations, (C–D) demonstrate strong synergistic enhancement of swelling index by both polymers with curvature at higher levels, while (E–F) depict a pronounced reduction in drug release as polymer concentrations increase, confirming dominant effects of Carbopol and quadratic contributions.

Validation of statistical model

The comparison of experimental and predicted values for batch F3 showed very low relative errors (<3%), indicating close agreement between observed and model-generated data. Mucoadhesive strength, swelling index, and cumulative drug release values matched well with predictions, confirming the accuracy and reliability of the statistical model used for optimization.

Table 11: Comparison of Experimental and Predicted Values with % Relative Error for Optimized Batch.

Batch	**Response**	Experimental value	Predicted value	% Relative error
F3	Mucoadhesive strength	6.4	6.22	2.81
	Swelling index	53.5	53.414	0.16
	Cumulative drug release at 8hr	90.8	90.967	0.18

Stability study

The stability study of optimized batch F3 under accelerated conditions (40 ± 2 °C / 75 ± 5% RH) for three months showed no significant changes in appearance, physical parameters, drug content, swelling index, mucoadhesive strength, or drug release profile. All values remained consistent, confirming good stability of the formulation.

Table 12: Stability Study Results of Optimized Batch (F3) under Accelerated Conditions (40 ± 2 °C / 75 ± 5% RH)

Parameter	**0 Month**	**1 Month**	**2 Months**	**3 Months**

Appearance	No change	No change	No change	No change
Weight variation (mg)	200.2	200.1	199.9	200.0
Thickness (mm)	3.22	3.21	3.21	3.20
Diameter (mm)	8.06	8.06	8.07	8.06
Hardness (kg/cm²)	4.9	4.9	5.0	5.0
Friability (%)	0.42	0.41	0.41	0.42
Surface pH	6.68	6.69	6.70	6.70
Drug content (%)	97.8	98.0	98.1	97.9
Swelling index (%)	53.5	53.2	53.3	53.4
Mucoadhesive strength (g)	6.4	6.3	6.4	6.3
Cumulative drug release at 8 h (%)	90.8	90.6	90.7	90.5

DISCUSSION

The present study focused on the formulation and evaluation of Dexrabeprazole buccal tablets to enhance solubility, stability, and controlled release through a mucoadhesive platform. The solubility study (Table 3) revealed that Dexrabeprazole is poorly soluble in water (10.2 ± 0.3 mg/mL) but exhibited high solubility in phosphate buffer (112.5 ± 2.1 mg/mL), simulated saliva (111.3 ± 1.9 mg/mL), methanol (45.8 ± 1.2 mg/mL), ethanol (30.6 ± 0.8 mg/mL), and 0.1N HCl (113.2 ± 2.4 mg/mL), classifying the drug as freely soluble in most solvents [43]. This property highlighted its suitability for buccal delivery to achieve improved dissolution and absorption. The solid-state characterization provided further insights into drug–excipient compatibility. DSC thermograms (Figure 2) showed a sharp endothermic peak at 141.41 °C for pure Dexrabeprazole, whereas the physical mixture exhibited slightly shifted peaks at 143.01 °C and an additional signal at 216.62 °C, indicating possible minor interactions without affecting the crystalline integrity. Similarly, FTIR spectra (Figure 3) confirmed the presence of characteristic peaks of Dexrabeprazole in both pure form and physical mixtures, with no significant shifts, thereby validating compatibility with the selected excipients [44].

Evaluation of post-compression parameters (Table 5) demonstrated that all formulations (F1–F9) complied with pharmacopoeial limits, showing uniform weight variation (~200 mg), thickness (~3.2 mm), diameter (~8.0 mm), and friability (<0.5%). Further analysis of hardness, drug content, and surface pH (Table 6) revealed consistent hardness (4.8–5.1 kg/cm²), drug content ranging from 97.8–99.3%, and surface pH between 6.65–6.74, confirming suitability for buccal mucosa without causing irritation [45]. Mucoadhesive properties and swelling behavior were strongly influenced by polymer concentration. As shown in Table 7, higher levels of Carbopol 934P and xanthan gum enhanced mucoadhesive strength (5.6–8.9 g) and swelling index (42.6–64.3%). Notably, formulation F5 and F8 exhibited the highest mucoadhesion and swelling, highlighting the synergistic role of both polymers [46]. The in-vitro drug release profiles (Table 8, Figure 4) demonstrated sustained release up to 8 hours, with cumulative release ranging from 86.5% to 95.4%. Formulation F3 achieved an optimum release of 90.8% at 8 hours, balancing swelling and drug release, thus selected as the optimized batch [47].

The statistical model was validated by comparing predicted and experimental values for F3 (Table 11). The negligible % relative error (0.16–2.81%) confirmed the reliability of the polynomial model in predicting formulation performance [48]. Furthermore, stability studies conducted under accelerated conditions (Table 12) showed no notable changes in physical, mechanical, or release parameters over three months, confirming the robustness and stability of the optimized batch. Collectively, these findings confirm that Dexrabeprazole buccal tablets developed using Carbopol 934P and xanthan gum achieved desirable mechanical strength, bioadhesion, controlled swelling, and sustained drug release [49]. The combination of solubility enhancement, compatibility, robust post-compression quality, and validated stability positions this formulation as a promising strategy for effective buccal delivery of Dexrabeprazole [50].

CONCLUSION

The present study successfully formulated and optimized Dexrabeprazole buccal tablets using Carbopol 934P and xanthan gum as mucoadhesive polymers, achieving desirable hardness, bioadhesion, swelling behavior, and sustained drug release up to 8 hours. The optimized batch

(F3) demonstrated excellent drug content uniformity, surface pH suitable for buccal application, and strong correlation between experimental and predicted responses, while stability studies confirmed robustness under accelerated conditions. These results highlight the formulation's potential to overcome solubility and stability limitations of Dexrabeprazole, ensuring prolonged therapeutic action and improved patient compliance. Clinically, such a buccal delivery system could enhance bioavailability by bypassing hepatic first-pass metabolism, thereby offering more effective treatment for acid-related disorders. Future studies, particularly in vivo pharmacokinetic and pharmacodynamic evaluations, are warranted to confirm its therapeutic applicability and translational potential.

Abbreviations

ANOVA: Analysis of Variance; FTIR: Fourier-Transform Infrared Spectroscopy; UV: Ultraviolet Spectroscopy; DSC: Differential Scanning Calorimetry; HPMC: Hydroxypropyl Methylcellulose; RH: Relative Humidity; SD: Standard Deviation; min: Minutes; hr: Hours; rpm: Revolutions per Minute; cm^2: Square Centimeter; mg: Milligram; mm: Millimeter; g: Gram; %: Percentage.

References

1. Xie X, Ren K, Zhou Z, Dang C, Zhang H. The global, regional and national burden of peptic ulcer disease from 1990 to 2019: a population-based study. BMC Gastroenterol. 2022;22(1):58. doi: 10.1186/s12876-022-02130-2
2. Hooi JKY, Lai WY, Ng WK, Suen MMY, Underwood FE, Tanyingoh D, et al. Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. Gastroenterology. 2017;153(2):420-429. doi: 10.1053/j.gastro.2017.04.022
3. Lanas Á, Chan FKL. Peptic ulcer disease. Lancet. 2017;390(10094):613-624. doi: 10.1016/S0140-6736(16)32404-7
4. Kaunitz JD. Peptic Ulcer Disease: A Review. JAMA. 2024;332(21):1832-1842. doi: 10.1001/jama.2024.19094
5. Shanika LGT, Reynolds A, Pattison S, Braund R. Proton pump inhibitor use: systematic review of global trends and practices. Eur J Clin Pharmacol. 2023;79(9):1159-1172. doi: 10.1007/s00228-023-03534-z
6. Ahmed A, Clarke JO. Proton Pump Inhibitors (PPI). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557385/
7. Shin JM, Sachs G. Pharmacokinetics and pharmacodynamics of the proton pump inhibitors. J Clin Pharmacol. 2008;48(12):1409-1417. doi: 10.1177/0091270008324153
8. Lee TJ, Kim D, Kim JC, Ro S, Na DH. Formulation development and pharmacokinetic evaluation of enteric-coated dexrabeprazole tablets. J Pharm Investig. 2023;53(3):323-331. doi: 10.1007/s40005-022-00597-4
9. Demiray G, Özdüven P, Durucu E, Bilgiç M, Aydonat H, Güney B, et al. Bioequivalence Study of Dexrabeprazole Gastro Resistant Tablets in Healthy Male Subjects Under Fasting and Fed Conditions. Int J Bioanal Methods Bioequival Stud. 2023;6(1):93-99. doi: 10.25141/2469-4490-2023-1.0093
10. Salado-Mejía M, Martínez-Pérez Y, Carmona-Aparicio L, García-Jiménez S, Coballase-Urrutia E, Pineda-Ramírez N, et al. Efficacy and safety comparative study of dexrabeprazole vs. esomeprazole for the treatment of gastroesophageal reflux disease. Gac Med Mex. 2023;159(1):21-29. doi: 10.24875/GMM.22000441
11. Pant A, Sharma G, Saini S, Kaur G, Jain A, Thakur A, et al. Design, characterization and in vivo performance of solid lipid nanoparticles (SLNs)-loaded mucoadhesive buccal tablets for efficient delivery of Lornoxicam in experimental inflammation. Drug Deliv Transl Res. 2024;14(3):730-756. doi: 10.1007/s13346-023-01427-3
12. Çelik B. Risperidone mucoadhesive buccal tablets: formulation design, optimization and evaluation. Drug Des Devel Ther. 2017;11:3355-3365. doi: 10.2147/DDDT.S150774
13. Jin H, Ngo HV, Park C, Lee BJ. Mucoadhesive buccal tablet of leuprolide and its fatty acid conjugate: Design, in vitro evaluation and formulation strategies. Int J Pharm. 2023;639:122963. doi: 10.1016/j.ijpharm.2023.122963

14. Koirala S, Nepal P, Ghimire G, Basnet R, Rawat I, Dahal A, et al. Formulation and evaluation of mucoadhesive buccal tablets of aceclofenac. Heliyon. 2021;7(3):e06439. doi: 10.1016/j.heliyon.2021.e06439
15. Hassan AS, Hosny KM, Murshid SSA, Alhadlaq HA, Alharbi WS, Naguib IA, et al. Mucoadhesive buccal tablets containing silymarin Eudragit-loaded nanoparticles: formulation, characterisation and ex vivo permeation. Drug Deliv. 2019;26(1):643-650. doi: 10.1080/10717544.2019.1631406
16. Obaidat RM, Al-Jbour N, Al-Sou'd KA, Al-Remawi M, Badwan AA, Al-Omari MM. Formulation and In Vitro Evaluation of Xanthan Gum or Carbopol 934-Based Mucoadhesive Patches, Loaded with Nicotine. AAPS PharmSciTech. 2011;12(1):21-27. doi: 10.1208/s12249-010-9544-x
17. Jadav M, Pooja D, Adams DJ, Kulhari H. Advances in Xanthan Gum-Based Systems for the Delivery of Therapeutic Agents. Pharmaceutics. 2023;15(2):402. doi: 10.3390/pharmaceutics15020402
18. Guo A, Tang L, Yang B, Xie N, Cui Y, Sun W, et al. A xanthan gum and carbomer-codispersed divalent manganese ion-loaded tannic acid nanoparticle adjuvanted inactivated pseudorabies virus vaccine induces balanced humoral and cellular immune responses. Int J Biol Macromol. 2024;269(Pt 2):132172. doi: 10.1016/j.ijbiomac.2024.132172
19. Cattani VB, Fiel LA, Jäger A, Jäger E, Colomé LM, Uchoa F, et al. Bioadhesive hydrogels for cosmetic applications. Int J Cosmet Sci. 2015;37(5):511-518. doi: 10.1111/ics.12227
20. Alhamhoom Y, Honmane SM, Hani U, Osmani RAM, Kandasamy G, Vasudevan R, et al. Study of Formulation and Process Variables for Optimization of Piroxicam Nanosuspension Using 3^2 Factorial Design to Improve Solubility and In Vitro Bioavailability. Polymers (Basel). 2023;15(3):483. doi: 10.3390/polym15030483
21. El-Sebaiy MT, Alyami MH, Alyami HS, Kamal MA, Eissa N, Balata G, et al. 2^4 Factorial Design Formulation Optimization and In vitro Characterization of Desloratadine Nanosuspension Prepared Using Antisolvent Precipitation. Curr Drug Deliv. 2024;21(8):1135-1150. doi: 10.2174/0115672018312715240604054857
22. Preethi Sudha M, Rani RHS, Rohini Reddy G, Chandra Sekhar KB. Formulation and optimization of temozolomide nanoparticles by 3 factor 2 level factorial design. Saudi Pharm J. 2013;21(4):421-427. doi: 10.1016/j.jsps.2013.05.001
23. Sharma K, Somavarapu S, Colombani A, Govind N, Taylor KMG. Assessment of Fractional Factorial Design for the Selection and Screening of Appropriate Components of a Self-nanoemulsifying Drug Delivery System Formulation. Chem Pharm Bull (Tokyo). 2019;67(12):1320-1329. doi: 10.1248/cpb.c19-00572
24. Abbas N, Riaz A, Rasul A, Alam MT, Hanif M, Akhlaq M, et al. Formulation Optimization and In-vitro Evaluation of Oral Floating Captopril Matrix Tablets using Factorial Design. Trop J Pharm Res. 2015;14(11):2059-2068. doi: 10.4314/tjpr.v14i11.16
25. González-González O, Ballesteros MP, Torrado JJ, Serrano DR. Drug Stability: ICH versus Accelerated Predictive Stability Studies. Pharmaceutics. 2022;14(11):2324. doi: 10.3390/pharmaceutics14112324
26. González-González O, Ballesteros MP, Torrado JJ, Serrano DR. Enhanced Stability and Compatibility of Montelukast and Levocetirizine in a Fixed-Dose Combination Monolayer Tablet. Molecules. 2023;28(23):7925. doi: 10.3390/molecules28237925
27. Hornick T, Mao C, Koynov A, Khinast J, Jiang C, Leavesley I, et al. In silico formulation optimization and particle engineering of pharmaceutical products using a generative artificial intelligence structure synthesis method. Nat Commun. 2024;15:9622. doi: 10.1038/s41467-024-54011-9
28. Kim S, Day CM, Song Y, Holmes A, Garg S. Innovative Topical Patches for Non-Melanoma Skin Cancer: Current Challenges and Key Formulation Considerations. Pharmaceutics. 2023;15(11):2577. doi: 10.3390/pharmaceutics15112577
29. Alagusundaram M, Jain NK, Begum MY, Parameswari SA, Nelson VK, Bayan MF, et al.

Development and Characterization of Gel-Based Buccoadhesive Bilayer Formulation of Nifedipine. Gels. 2023;9(9):688. doi: 10.3390/gels9090688

30. Salari N, Darvishi N, Shohaimi S, Bartina Y, Ahmadipanah M, Shiri Y, et al. The Global Prevalence of Peptic Ulcer in the World: a Systematic Review and Meta-analysis. Curr Med Imaging. 2022;18(2):145-159. doi: 10.2174/1573405617666210927111012
31. Ratibad B, India MP, Singh S. Effect of formulation parameters on enalapril maleate mucoadhesive buccal tablet using quality by design (QbD) approach. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2024;40:e20240003.
32. Koirala S, Nepal P, Ghimire G, Basnet R, Rawat I, Dahal A, Pandey J, Parajuli-Baral K. Formulation and evaluation of mucoadhesive buccal tablets of aceclofenac. Heliyon. 2021 Mar 1;7(3).
33. Patel P, Jain P, Patel H, Tiwari A, Rathi S, Singh S. FORMULATION, OPTIMIZATION AND EVALUATION OF MUCOADHESIVE BUCCAL TABLETS OF ONDANSETRON FOR ENHANCED BIOAVAILABILITY AND SUSTAINED DRUG RELEASE. Biochemical & Cellular Archives. 2025 Apr 1;25(1).
34. Razzaq S, Syed MA, Irfan M, Khan I, Sarfraz RM, Shakir R, Ali S, Iqbal Z, Niaz Y, Mujtaba SH, Raza SA. Optimization of metronidazole SR buccal tablet for gingivitis using genetic algorithm. Pak. J. Pharm. Sci. 2021 Nov 1;34(6):2149-58.
35. Hanif S, Sarfraz RM, Syed MA, Mahmood A, Minhas MU, Irfan M. Development and optimization of tibezonium iodide and lignocaine hydrochloride containing novel mucoadhesive buccal tablets: A pharmacokinetic investigation among healthy humans. Drug Development and Industrial Pharmacy. 2021 Aug 3;47(8):1209-22.
36. Zewail MB, Asaad GF, Swellam SM, Abd-Allah SM, Hosny SK, Sallah SK, Eissa JE, Mohamed SS, El-Dakroury WA. Design, characterization and in vivo performance of solid lipid nanoparticles (SLNs)-loaded mucoadhesive buccal tablets for efficient delivery of Lornoxicam in experimental inflammation. International Journal of Pharmaceutics. 2022 Aug 25;624:122006.
37. Suruse PB, Gawali MB, Kalkotwar RS, Bhabad RB, Bagdane SB, Barde LG. Design, development and optimization of buccal tablet containing extract of Terminalia chebula Retz. for the treatment of asthma. Ind J Pharm Edu Res. 2023 Oct 1;57:993-1001.
38. Winarti LI, Laily AZ, Sari LO, Irawan ED, Nurrahmanto D, Rosyidi VA, Barikah KZ, Ameliana LI. Formula optimization and in vitro release kinetic studies of diltiazem hydrochloride mucoadhesive bilayer buccal film. International Journal of Applied Pharmaceutics. 2021 Feb 10;13:7-12.
39. Ambarish S, Shirsand S, Anandkumar Y, Shirsand S. To study the effect of HPMC and Carbopol in mucoadhesive buccal tablets of Meclizine hydrochloride using Central Composite Design: In-vitro Characterization. German Journal of Pharmaceuticals and Biomaterials. 2024 Apr 6;3(1):3-18.
40. Leela LV, Umashankar MS, Alagusundaram M. Formulation, Optimization and In-Vivo Pharmacokinetic Evaluation of Carvedilol Mucoadhesive Buccal Films by Using Natural Polymers. Tropical Journal of Natural Product Research. 2023 Nov 20;7(10):4927-36.
41. Hanif S, Sarfraz RM, Syed MA, Ali DS, Iqbal Z, Shakir R, Iqbal J. Formulation and evaluation of chitosan-based polymeric biodegradable mucoadhesive buccal delivery for locally acting drugs: In vitro, ex vivo and in vivo volunteers characterization.
42. Tikait AV, Wankhade VP, Mhaske Y, Atram SC, Bobade NN, SD P. Formulation and Evaluation Immediate Release Mucoadhesive Buccal Tablet of Midodrine HCL. Asian Journal of Pharmaceutical Research and Development. 2024 Aug 15;12(4):28-36.
43. Javed QU, Syed MA, Arshad R, Rahdar A, Irfan M, Raza SA, Shahnaz G, Hanif S, Díez-Pascual AM. Evaluation and optimization of prolonged release mucoadhesive tablets of dexamethasone for wound healing: In vitro–in vivo profiling in healthy volunteers. Pharmaceutics. 2022 Apr 7;14(4):807.
44. Kurćubić I, Vajić UJ, Cvijić S, Crevar-Sakač M, Bogavac-Stanojević N, Miloradović Z,

Mihajlović-Stanojević N, Ivanov M, Karanović D, Jovović Đ, Djuriš J. Mucoadhesive buccal tablets with propranolol hydrochloride: Formulation development and in vivo performances in experimental essential hypertension. International Journal of Pharmaceutics. 2021 Dec 15;610:121266.

45. Chaudhari PD, Deore AB, Jagtap MJ, Gupta DS. Formulation development and evaluation of mucoadhesive buccal tablets of acebutolol hydrochloride. Asian Journal of Pharmaceutical Research and Development. 2022 Aug 13;10(4):34-46.
46. Nagaveni P, Sirisha S, Rao CA. Formulation and evaluation of mucoadhesive buccal tablets of anti-diabetic drug using 23 factorial design. Asian Journal of Pharmacy and Technology. 2021;11(4):261-6.
47. Samanthula KS, Bairi AG, Mahendra Kumar CB. Muco-adhesive buccal tablets of candesartan cilexetil for oral delivery: preparation, in-vitro and ex-vivo evaluation. J. Drug Deliv. Ther. 2021 Jan 2;11:35-42.
48. Mohammed MF, Sadeq ZA, Salih OS. Formulation and evaluation of mucoadhesive buccal tablet of Anastrozole. Journal of Advanced Pharmacy Education & Research. 2022;12(2):39-44.
49. Nigusse B, Gebre-Mariam T, Belete A. Design, development and optimization of sustained release floating, bioadhesive and swellable matrix tablet of ranitidine hydrochloride. PloS one. 2021 Jun 25;16(6):e0253391.
50. Nasr M, Ramzy M, Abdel-moneum R, Abdel-Rashid RS. Optimization of nano-structured lipid carriers for enhanced salbutamol delivery via buccal mucoadhesive film. Journal of Drug Delivery Science and Technology. 2025 Feb 1;104:106468.