



Design and Development of Mebendazole-Loaded Mucoadhesive Buccal Tablets for Prolonged Drug Release and Enhanced Buccal Delivery

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Article Information

Received: 07-06-2026

Revised: 21-06-2026

Accepted: 13-07-2026

Published: 28-07-2026

Keywords

Mebendazole; Mucoadhesive buccal tablet; Carbopol 934; HPMC K4M; Buccal drug delivery

ABSTRACT:

The present study was aimed at the formulation and evaluation of mucoadhesive buccal tablets of mebendazole to provide prolonged drug residence at the buccal mucosa and potentially improve drug absorption. Mebendazole was selected as an anthelmintic drug, and the buccal route was explored as an alternative approach to conventional oral administration. Preformulation studies including organoleptic properties, melting point, solubility, loss on drying, calibration curve and drug–excipient compatibility studies were performed. The calibration curve of mebendazole was developed in the concentration range of 2–10 µg/mL at 291 nm. Mucoadhesive buccal tablets were prepared by the direct compression method using Carbopol 934, HPMC K4M and sodium carboxymethyl cellulose as mucoadhesive polymers. The prepared formulations were evaluated for pre-compression and post-compression parameters, including flow properties, weight variation, hardness, thickness, friability, drug content, surface pH, swelling behavior, mucoadhesive strength and in-vitro drug release. In-vitro drug permeation was also investigated using porcine buccal mucosa with a Franz diffusion cell. The formulations exhibited satisfactory physical characteristics and mucoadhesive properties. The study indicated that Carbopol 934-based formulations, particularly formulation F6, showed satisfactory swelling, mucoadhesion and drug-release characteristics. Overall, the findings suggest that mucoadhesive buccal tablets may serve as a promising approach for the buccal delivery of mebendazole.

1. INTRODUCTION:

Oral drug administration is the most widely accepted and convenient route for delivering therapeutic agents because of its simplicity, patient compliance, ease of administration and cost-effectiveness. However, conventional oral dosage forms may be associated with several physiological and biopharmaceutical limitations, including gastrointestinal degradation, variable absorption and hepatic first-pass metabolism. These limitations can reduce the systemic availability of certain drugs and may necessitate repeated administration. Consequently, alternative transmucosal delivery approaches have gained considerable attention for improving drug absorption and therapeutic performance. Among these approaches, the buccal route represents an attractive non-invasive pathway for systemic drug delivery.^{1,2}

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The buccal mucosa is particularly suitable for drug delivery because it is readily accessible, relatively immobile and well vascularized. Drug absorption through the buccal mucosa can provide direct access to systemic circulation while reducing exposure to the gastrointestinal environment and avoiding or minimizing hepatic first-pass metabolism. In addition, buccal administration provides the possibility of terminating therapy by removing the dosage form and can be advantageous for drugs for which conventional oral administration results in inadequate systemic exposure.[1,3]

Despite these advantages, conventional buccal dosage forms can be rapidly removed from the oral cavity because of salivary secretion, swallowing and continuous movement of the oral tissues. The short residence time of a formulation at the absorption site may consequently limit the extent and duration of drug absorption. Mucoadhesive drug delivery systems have therefore been developed to maintain intimate contact between the dosage form and the mucosal surface for an extended period. Mucoadhesion involves interactions between a formulation and the mucus layer and can increase residence time at the site of administration, thereby facilitating prolonged drug release and improving the opportunity for drug absorption.[2-4]

Mucoadhesive polymers are fundamental components of buccal drug delivery systems. Polymers such as Carbopol, hydroxypropyl methylcellulose (HPMC), sodium carboxymethyl cellulose (NaCMC), chitosan and other hydrophilic polymers have been investigated for their ability to hydrate, swell and establish interactions with mucin. The selection and concentration of polymer can substantially influence swelling behavior, mucoadhesive strength, drug diffusion and release kinetics. Carbopol-containing systems are particularly useful because their carboxylic functional groups can contribute to polymer–mucin interactions and prolonged adhesion, whereas cellulosic polymers such as HPMC can contribute to matrix formation and controlled drug release.[3,4]

Among the different buccal dosage forms, mucoadhesive buccal tablets offer several formulation advantages, including ease of manufacture, dose uniformity, mechanical integrity and the ability to incorporate polymers capable of controlling drug release. Direct compression is a particularly simple and economical manufacturing technique for tablet preparation. The resulting dosage form can be designed to hydrate gradually, adhere to the buccal mucosa and release the incorporated drug over an extended period. The performance of such systems is generally assessed using parameters such as weight variation, hardness, friability, drug content, surface pH, swelling index, mucoadhesive strength, in-vitro drug release and, where appropriate, ex-vivo/in-vitro permeation studies.[2-4] The present thesis similarly employed direct compression and evaluated pre-compression and post-compression characteristics, swelling, mucoadhesion, dissolution and buccal permeation.

Mebendazole is a broad-spectrum benzimidazole anthelmintic used in the management of intestinal helminthic infections. It acts primarily by interfering with microtubule formation and glucose utilization in susceptible parasites. Although conventional oral administration is convenient, mebendazole exhibits limited systemic absorption and undergoes substantial hepatic metabolism after absorption. Literature reports indicate that its low systemic availability is associated with poor aqueous solubility and extensive first-pass elimination.[5,6]

The pharmacokinetic limitations of mebendazole provide a rationale for investigating alternative delivery approaches that can improve drug transport across an accessible mucosal surface. Buccal administration is particularly interesting because drug absorption through the oral mucosa can reduce dependence on gastrointestinal dissolution and passage through the hepatic portal circulation. A mucoadhesive system may additionally prolong the residence of mebendazole at the buccal mucosa, thereby increasing the duration of contact between the drug and the absorption membrane. The thesis specifically identifies enhancement of mebendazole absorption and reduction of first-pass effects as important considerations for the proposed buccal system.[7]

Previous research has demonstrated the potential of Carbopol, HPMC and sodium CMC for developing mucoadhesive buccal formulations. The thesis literature survey reports that combinations of Carbopol and cellulosic polymers can provide satisfactory physical characteristics, swelling, bioadhesion and controlled drug release. The present formulation strategy therefore utilizes Carbopol 934, HPMC K4M and sodium CMC as mucoadhesive polymers, with different polymer combinations investigated to determine their influence on formulation performance.[8]

Accordingly, the present study was undertaken to develop and evaluate mucoadhesive buccal tablets of mebendazole using suitable mucoadhesive polymers. The study included preformulation characterization, drug–

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excipient compatibility assessment, formulation by direct compression, evaluation of physicochemical and mechanical properties, surface pH, swelling behavior, mucoadhesive strength and in-vitro drug release. Furthermore, buccal permeation was investigated using porcine buccal mucosa in a Franz diffusion cell to assess the potential of the developed system for enhanced mucosal drug transport.[9,10]The overall objective was to establish a mucoadhesive buccal platform capable of providing prolonged residence and sustained delivery of mebendazole and thereby offering a potentially useful alternative to conventional oral administration.

2. MATERIALS AND METHODS

2.1 Materials

Mebendazole was selected as the model anthelmintic drug. Carbopol, HPMC K4M and sodium carboxymethyl cellulose (NaCMC) were used as mucoadhesive polymers. Microcrystalline cellulose (MCC), magnesium stearate, talc, lactose and sodium saccharin were used as formulation excipients. All other chemicals and reagents used were of analytical grade. The selection of Carbopol and cellulosic polymers was consistent with established approaches for mucoadhesive buccal tablet development.[11-13]

2.2 Instruments

The major instruments used included a dissolution test apparatus, disintegration test apparatus, bioadhesion testing apparatus, UV–Visible spectrophotometer, Monsanto hardness tester, Roche friabilator, electronic balance, tablet punching machine and FTIR spectrophotometer. A Jasco V-530/FTIR-4100 instrument was used for FTIR analysis.

2.3 Preformulation Studies

2.3.1 Organoleptic evaluation

The drug sample was examined for its colour, physical state and odour/taste as preliminary identification characteristics.

2.3.2 Melting point

The melting point of mebendazole was determined by the capillary tube method. A sealed capillary tube was filled with the drug by repeated tapping and attached to a thermometer. The capillary was immersed in a Thiele's tube containing paraffin oil, and the temperature at which the drug started melting was recorded. The experiment was performed in triplicate and the mean value was considered.

2.3.3 Solubility study

The solubility of mebendazole was qualitatively assessed in selected solvents. Approximately 10 mg of mebendazole was placed in 10 mL of solvent and mixed using a vortex mixer for approximately 10 min. The presence of undissolved material was visually observed; when solid particles remained, additional solvent was added and the observation was continued. The thesis specifically reports the use of DMSO and formic acid for this study.

2.3.4 Preparation of calibration curve

A primary stock solution was prepared by dissolving 40 mg of mebendazole in 20 mL of formic acid. Working solutions in the concentration range of 2–10 µg/mL were prepared from the stock solution. The absorbance was measured using a UV–Visible spectrophotometer at 291 nm, and a calibration curve was constructed by plotting absorbance against concentration.

2.3.5 Loss on drying

Approximately 1 g of mebendazole was accurately weighed into a previously weighed porcelain dish. The sample was dried in an oven at 105°C for 1 h, cooled in a desiccator and reweighed. Percentage loss on drying was calculated using:

$$\%LOD = \frac{W_1 - W_2}{W_1} \times 100$$

where W1 is the initial weight of sample and W2 is the weight after drying.

2.4 Drug–Excipient Compatibility Study

Compatibility between mebendazole and the selected excipients was investigated by Fourier-transform infrared

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spectroscopy (FTIR). FTIR spectra of mebendazole, HPMC K4M, Carbopol and the physical mixture of drug and excipients were recorded over 400–4000 cm⁻¹ using the KBr pellet method. Approximately 50 mg of dry KBr was finely powdered, mixed with the sample and compressed into a disc using a hydraulic press. The spectra were examined for characteristic functional-group peaks and any substantial changes in peak position or appearance/disappearance of peaks indicative of possible drug–excipient interaction.

FTIR compatibility testing is commonly employed during development of mucoadhesive buccal tablets to investigate possible interactions between the drug and polymers/excipients.[11,12]

2.5 Formulation of Mucoadhesive Buccal Tablets

Mucoadhesive buccal tablets were prepared by the direct compression technique. Carbopol, HPMC K4M, sodium CMC, MCC, sodium saccharin, magnesium stearate and talc were passed through sieve no. 100. All ingredients except the lubricant were blended thoroughly in a glass mortar using a pestle for approximately 15 min. Magnesium stearate was subsequently incorporated and mixed for an additional 2–3 min. The final powder blend was compressed into 100 mg tablets using a rotary tablet compression machine equipped with 5-mm flat-faced punches.

The use of direct compression with Carbopol, HPMC and sodium CMC is consistent with previously reported mucoadhesive buccal tablet development approaches.[11,12]

Table 1. Composition of the experimental formulations

Ingredients	F1	F2	F3	F4	F5	F6
Drug*	4	4	4	4	4	6
Carbopol**	15	15	15	15	15	15
HPMC K4M	15	20	25	–	–	–
Sodium CMC	–	–	–	15	20	25
MCC	80	75	70	80	75	70
Magnesium stearate	4	4	4	4	4	4
Talc	4	4	4	4	4	4
Lactose	18	18	18	18	18	18
Sodium saccharin	10	10	10	10	10	10

Important thesis verification point: The uploaded formulation table actually labels the drug row as “Candesartan cilexetil” and the polymer as “Carbopol 943”, despite the thesis being a mebendazole study and other sections referring to Carbopol 934. Therefore, these two entries should be verified against the original laboratory formulation sheet before publication rather than silently corrected.

2.6 Evaluation of Powder Blend

2.6.1 Bulk density

A known quantity of powder blend was gently poured into a graduated measuring cylinder without tapping. The volume occupied by the powder was recorded and bulk density was calculated as:

$$\text{Bulk density} = \frac{\text{Weight of powder}}{\text{Bulk volume}}$$

The thesis reports bulk-density evaluation as one of the pre-compression parameters.

2.6.2 Tapped density

The powder was transferred into a graduated cylinder and mechanically tapped until a constant volume was obtained. Tapped density was calculated as:

$$\text{Tapped density} = \frac{\text{Weight of powder}}{\text{Tapped volume}}$$

2.6.3 Carr's compressibility index

Carr's index was calculated from bulk and tapped density:

$$\text{Carr's Index}(\%) = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

2.6.4 Hausner's ratio

Hausner's ratio was determined using:

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$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

2.6.5 Angle of repose

The angle of repose was determined by allowing the powder to flow through a funnel and form a conical heap. The angle was calculated from the height and radius of the powder cone. The thesis evaluated bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose as pre-compression characteristics.

2.7 Evaluation of Prepared Buccal Tablets

2.7.1 Weight variation

Individual tablets were weighed and compared with the average tablet weight to determine weight variation.

2.7.2 Tablet hardness

The crushing strength of the tablets was determined using a Monsanto hardness tester and expressed in kg/cm².

2.7.3 Friability

Friability was determined using a Roche friabilator. The test was used to assess the tendency of tablets to lose weight due to mechanical abrasion.

2.7.4 Tablet thickness

Tablet thickness was measured using a Vernier caliper. Ten tablets from each formulation were evaluated and the mean thickness was recorded.

2.7.5 Drug content uniformity

Six tablets were randomly selected from each formulation, finely powdered and dissolved in 100 mL phosphate buffer. The solution was thoroughly shaken and analyzed spectrophotometrically. The thesis reports UV analysis for drug-content determination at 277 nm.

Note: The thesis uses 291 nm for the calibration/dissolution assay but reports 277 nm for drug-content determination. This analytical wavelength discrepancy should be verified before publication.

2.8 Surface pH

The surface pH of the prepared buccal tablets was determined to assess the possibility of mucosal irritation. Tablets were placed in contact with 2 mL phosphate buffer, pH 6.6, and allowed to swell. Surface pH was measured at predetermined intervals using a digital pH meter by bringing the glass microelectrode close to the tablet surface and allowing approximately 1 min for equilibration before recording the reading. Measurements were performed in triplicate.

The surface-pH approach is commonly used in buccal tablet evaluation to determine whether the hydrated formulation remains within a physiologically acceptable range.³

2.9 In-Vitro Swelling Study

The swelling behavior of the prepared tablets was evaluated in phosphate buffer. A pre-weighed tablet was placed in a Petri dish containing 5 mL phosphate buffer, pH 6.8. At predetermined intervals, the tablet was removed, excess surface liquid was carefully removed using filter paper and the swollen tablet was weighed. The swelling index was calculated from the initial and swollen weights.

The swelling index was calculated as:

$$\text{Swelling Index}(\%) = \frac{W_t - W_0}{W_0} \times 100$$

where W₀ is the initial weight of the tablet and W_t is the weight of the swollen tablet at time t. This gravimetric approach is commonly used for mucoadhesive buccal systems.[13]

2.10 In-Vitro Mucoadhesive Strength

Mucoadhesive strength was evaluated using a modified two-arm balance apparatus and porcine buccal mucosa.

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Fresh porcine buccal mucosa was obtained and used within approximately 3 h. The mucosa was fixed to the apparatus and maintained in contact with phosphate buffer of pH 6.6. The tablet was brought into contact with the mucosal tissue under a predetermined preload and preload time, which were kept constant for all formulations.

Following the preload period, water was gradually added to the opposing pan at a constant rate until the tablet detached from the mucosal surface. The amount of water required for detachment was recorded as the mucoadhesive strength. The experiment was repeated using fresh mucosa under identical conditions.

This type of modified balance method is widely used for comparative evaluation of mucoadhesive strength of buccal tablets.

2.11 In-Vitro Drug Permeation Study

In-vitro drug permeation was investigated using a Franz diffusion cell with porcine buccal mucosa as the biological membrane. The diffusion area of the cell was reported as 6.16 cm², with an acceptor-compartment volume of 16 mL. The porcine buccal mucosa was clamped between the donor and receptor compartments. The receptor compartment contained phosphate buffer of pH 6.6, maintained at 37°C and continuously stirred at 600 rpm.

The tablet was placed in the donor compartment and wetted with 1 mL phosphate buffer. At predetermined intervals, aliquots were withdrawn from the receptor compartment and replaced with an equal volume of fresh buffer to maintain sink volume. The permeated drug was quantified using UV–Visible spectrophotometry at 205 nm, as reported in the thesis.

The use of porcine buccal mucosa for ex-vivo permeation and mucoadhesion assessment is consistent with published buccal drug-delivery studies.[11,12]

2.12 In-Vitro Drug Release Study

In-vitro dissolution testing was performed using a USP Type II paddle apparatus at 50 rpm and 37 ± 0.5°C. The dissolution medium was 900 mL phosphate buffer, pH 7.4. At predetermined time intervals, 5 mL samples were withdrawn and immediately replaced with an equivalent volume of fresh dissolution medium. The withdrawn samples were analyzed by UV spectroscopy at 291 nm, and cumulative percentage drug release was calculated using the calibration-curve equation.

The paddle method and evaluation of dissolution profiles are commonly employed for mucoadhesive buccal tablets.[11,12]

2.13 Drug Release Kinetic Analysis

The in-vitro drug-release data were fitted to different mathematical models to characterize the release behavior of mebendazole from the polymeric matrix. The models included:

- Zero-order model
- First-order model
- Higuchi model
- Korsmeyer–Peppas model

The model showing the highest correlation coefficient (R²) was considered indicative of the best fit. The Higuchi model describes drug release from matrix systems based primarily on diffusion, while the Korsmeyer–Peppas model can be used to investigate the mechanism of drug transport from polymeric systems.[14,15]

2.14 In-Vitro Retention Time Study

For determination of retention time, the adhesive tablet was pressed against excised porcine buccal mucosa for 30 s. The mucosa was secured on a glass slab and immersed in approximately 750 mL phosphate buffer, pH 6.6, maintained at 37°C. The paddle was positioned approximately 5 cm from the tablet and rotated at 25 rpm. The time required for complete erosion or detachment of the tablet from the mucosa was recorded as the retention time.

2.15 Moisture Absorption Study

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Moisture absorption was evaluated using 5% w/v agar. Agar was dissolved in hot water, transferred to Petri dishes and allowed to solidify. Six tablets from each formulation were dried overnight in a vacuum oven and weighed. One side of each tablet was laminated with an impermeable backing membrane. The tablets were placed on the solidified agar and incubated at 37°C for 1 h, after which they were reweighed. Percentage moisture absorption was calculated as:

$$\% \text{Moisture absorption} = \frac{W_f - W_i}{W_i} \times 100$$

where W_i is the initial tablet weight and W_f is the final weight after moisture exposure.

2.16 Stability Study

Stability studies were performed on the promising formulations F4 and F6. Sufficient numbers of tablets were packed in amber-coloured screw-capped bottles and stored in a stability chamber at 25°C and 60% relative humidity for 2 months (60 days). The formulations were evaluated during the stability period for relevant physical and performance characteristics.

3. RESULTS AND DISCUSSION

3.1 Preformulation Studies

3.1.1 Organoleptic properties and preliminary characterization

Mebendazole was obtained as a white to slightly yellow solid powder. The drug was reported to be practically insoluble in water and soluble in selected organic solvents. The melting point was reported as approximately 288.5°C, which was consistent with the expected thermal behavior of mebendazole and supported the identity and purity of the selected drug.

The preformulation assessment was important for establishing the suitability of mebendazole for incorporation into a mucoadhesive buccal dosage form.

3.1.2 UV calibration curve of mebendazole

The calibration curve of mebendazole was prepared in the concentration range of 2–10 µg/mL. The absorbance values increased progressively with increasing drug concentration, indicating a concentration-dependent response. The recorded absorbance values were 0.1177, 0.2244, 0.3303, 0.4488 and 0.5893 for 2, 4, 6, 8 and 10 µg/mL, respectively.

The linear increase in absorbance demonstrated the suitability of the developed spectrophotometric method for quantitative estimation of mebendazole during formulation evaluation.

3.1.3 Drug–excipient compatibility study

FTIR spectroscopy was used to investigate the compatibility of mebendazole with the selected polymers. FTIR spectra of mebendazole and physical mixtures containing HPMC K4M and Carbopol were recorded in the range of 400–4000 cm⁻¹. The characteristic functional groups of the drug were retained in the physical mixture, with the reported peaks including 3610.46, 1687.10, 1202.87, 1190.93, 1079.74, 764.44 and 722.96 cm⁻¹.

The retention of the characteristic spectral features suggested that there **was** no major chemical interaction between mebendazole and the investigated excipients under the conditions of the compatibility study. Therefore, Carbopol and HPMC K4M were considered suitable for further formulation development.

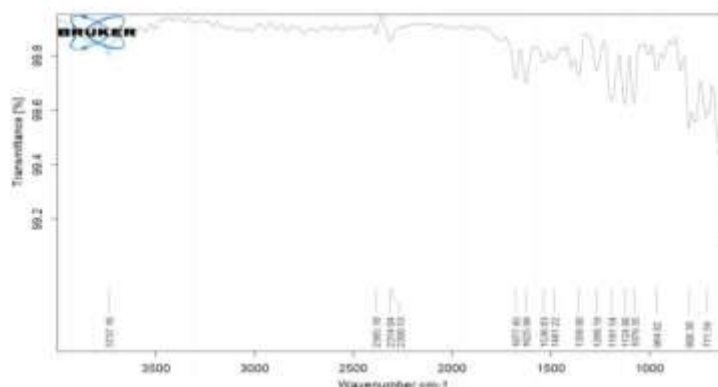


Figure: FTIR spectra of mebendazole

3.2 Evaluation of Powder Blends

The powder blends were evaluated for bulk density, tapped density, Carr's compressibility index, Hausner's ratio and angle of repose.

Table 1. Pre-compression parameters of mebendazole buccal tablet formulations

Formulation	Bulk density (g/cm ³)	Tapped density (g/cm ³)	Carr's index (%)	Hausner's ratio	Angle of repose (°)
F1	0.576	0.63	16.84	1.2	29.56
F2	0.53	0.626	15.49	1.18	28.19
F3	0.528	0.63	14.63	1.17	27.89
F4	0.523	0.632	17.24	1.2	27.21
F5	0.561	0.623	16.37	1.19	27.97
F6	0.496	0.56	14.23	1.18	27.61

The bulk density ranged from 0.496 to 0.576 g/cm³, while tapped density ranged from 0.560 to 0.632 g/cm³. Carr's index ranged from 14.23 to 17.24%, and Hausner's ratio ranged from 1.17 to 1.20. The angle of repose was between 27.21° and 29.56°.

The relatively low Carr's index and Hausner's ratio values, together with the angle of repose values, indicated acceptable flow characteristics of the powder blends. Thus, the prepared blends were considered suitable for direct compression.

3.3 Evaluation of Buccal Tablets

3.3.1 Weight variation, hardness, thickness, friability and drug content

The prepared tablets showed satisfactory physical characteristics.

Table 2. Post-compression parameters

Formulation	Weight (mg)	Hardness (kg/cm ²)	Thickness (mm)	Friability (%)	Drug content (%)
F1	149.21	4.25	2.12	0.39	98.51
F2	148.1	4.3	2.15	0.56	95
F3	152.5	4.3	2.18	0.4	97.85
F4	150.1	4.3	2.12	0.43	98.79
F5	148.5	4.2	2.32	0.42	97.01
F6	149.3	4.25	2.19	0.5	99.15

The average tablet hardness ranged from 4.20 to 4.30 kg/cm², indicating adequate mechanical strength.

Tablet friability ranged from 0.39 to 0.56%, which was below the 1% limit reported in the thesis. This indicated adequate resistance of the tablets to abrasion during handling and storage.

Tablet weights ranged from 148.10 to 152.50 mg, with no formulation exceeding the stated weight-variation limit.

Drug content ranged from 95.00 to 99.15%, with the highest value observed for F6 (99.15%) and the lowest for F2 (95.00%). The relatively narrow variation in drug content indicated reasonably uniform distribution of mebendazole within the prepared tablets.

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The post-compression findings indicated that the direct-compression process produced tablets with satisfactory mechanical integrity and drug-content uniformity.

3.4 Surface pH

The surface pH of the formulations ranged from **5.22 to 6.42**. Formulation F1 showed the lowest surface pH (5.22), whereas F6 showed the highest value (6.42).

The reported surface-pH values were within the salivary pH range of approximately 5–7 stated in the thesis. This finding is important for buccal delivery because a formulation with a surface pH close to physiological salivary conditions is less likely to cause local irritation. The results therefore suggested acceptable mucosal compatibility of the developed formulations.

3.5 In-Vitro Mucoadhesive Strength

Mucoadhesive strength increased progressively from F1 to F3 and was highest for F6 among the investigated formulations.

Table 3. Mucoadhesive strength

Formulation	Mucoadhesive strength (g)	Mucoadhesive force (N)
F1	30.2	2.9
F2	32.14	3.19
F3	34.18	3.17
F4	29.14	3.52
F5	32.17	2.94
F6	36.14	2.8

F1 exhibited a mucoadhesive strength of **30.20 g**, whereas F6 exhibited the highest reported value of **36.14 g**.

The increase in mucoadhesive strength can be associated with the presence and concentration of Carbopol, which provides functional groups capable of interacting with mucin. The higher mucoadhesive performance observed with the Carbopol/NaCMC system suggests that polymer type and polymer combination strongly influenced adhesion.

The thesis also notes that excessive mucoadhesion should be avoided because very strong adhesion may potentially damage the buccal mucosa.

3.6 In-Vitro Drug Release Study

The cumulative drug release after 8 h increased progressively from F1 to F6.

Table 4. Cumulative drug release after 8 h

Formulation	Cumulative drug release at 8 h (%)
F1	82.1
F2	85.13
F3	88.14
F4	93.16
F5	94.17
F6	98.13

The cumulative drug release values after 8 h were 82.10, 85.13, 88.14, 93.16, 94.17 and 98.13% for F1–F6, respectively.

The progressive increase in drug release from F1 to F6 was associated in the thesis with differences in the concentration and nature of the secondary polymer. Increased polymer hydration and swelling can facilitate penetration of dissolution medium into the matrix and promote drug diffusion. The thesis specifically attributes the increased release to greater hydration and swelling associated with increased concentrations of HPMC K4M and sodium CMC. Among all formulations, F6 showed the highest drug release (98.13% at 8 h), indicating efficient drug liberation from the formulation while maintaining the intended mucoadhesive characteristics.

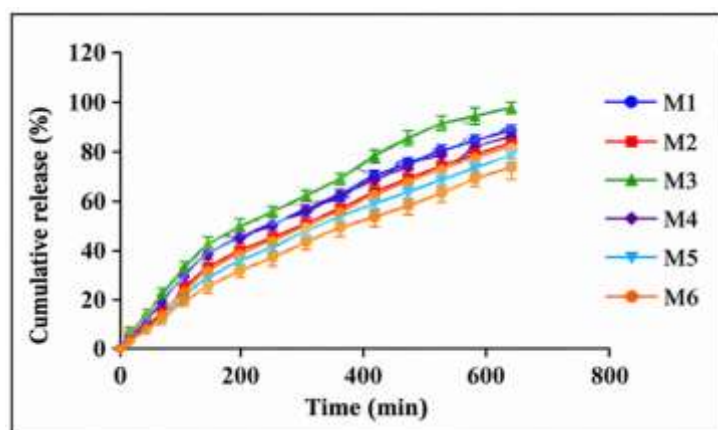


Figure 2: In vitro drug release graph

3.7 In-Vitro Swelling Study

The swelling behavior of the formulations was evaluated at 1, 2, 4 and 8 h.

Table 5. Percentage hydration/swelling of formulations

Formulation	1 h (%)	2 h (%)	4 h (%)	8 h (%)
F1	30.11	38.12	28.12	70.12
F2	35.15	48.15	35.16	78.13
F3	38.12	55.18	45.12	85.14
F4	45.12	62.17	60.13	88.12
F5	50.13	66.13	71.12	87.18
F6	48.23	58.12	80.13	90.12

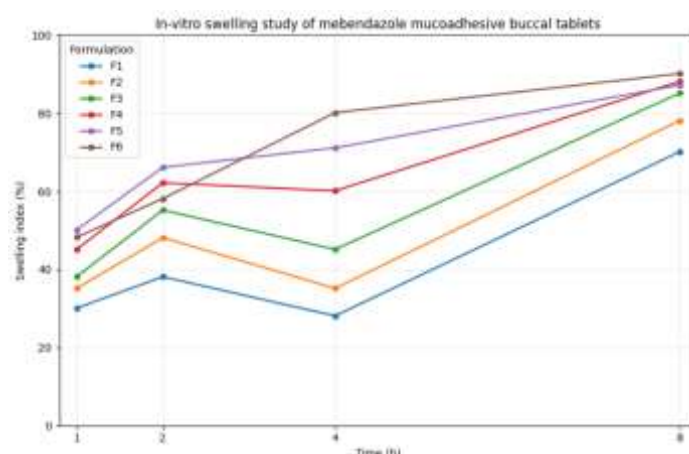


Figure 3: In-vitro swelling study of mebendazole mucoadhesive buccal tablets

The percentage hydration increased considerably during the study period, with F6 showing the highest reported 8-h hydration value of 90.12%. F1 showed the lowest 8-h value of 70.12%.

The increased swelling can be attributed to hydration of the hydrophilic polymers. Polymer swelling is particularly important in mucoadhesive systems because hydration facilitates polymer chain mobility and intimate contact with the mucus layer. The high swelling observed for F6 may therefore have contributed to its favorable mucoadhesive and drug-release behavior.

The results also demonstrate that polymer concentration and polymer type influenced the extent of hydration.

3.8 Moisture Absorption Study

Moisture absorption increased markedly across the formulations. The reported values were 12.24, 12.43, 53.80, 57.43 and 89.95% for F1–F5, respectively, with the F6 value not visible in the retrieved table segment.

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The thesis interpreted the increase in moisture absorption as being related to the increased concentration of hydrophilic polymers. The higher moisture uptake observed with Carbopol-containing formulations indicates the strong water-absorbing capacity of the polymeric matrix.

However, excessive moisture uptake may adversely affect tablet integrity. Therefore, moisture absorption must be balanced against swelling and mucoadhesion when selecting the optimum formulation.

3.9 In-Vitro Retention Time

The retention time of the formulations varied considerably.

Table 6. Mucoadhesion, moisture absorption and retention time

Formulation	Mucoadhesive strength (g)	Moisture absorption (%)	Retention time
F1	3.29*	12.24	7 h 12 min
F2	4.97*	12.43	8 h 24 min
F3	6.50*	53.8	8 h 27 min
F4	2.53*	57.43	3 h 41 min
F5	2.03*	89.95	2 h 11 min
F6	11.70*	8.54*	8 h 51 min

*Values reproduced as reported in the thesis. There is a discrepancy between this table and the separate mucoadhesive-strength table; therefore, the original raw data should be checked before publication.

F6 showed the highest reported retention time of 8 h 51 min, followed by F3 (8 h 27 min) and F2 (8 h 24 min). F4 and F5 demonstrated substantially shorter retention times.

The reduction in retention time at higher polymer concentrations in some formulations may be associated with excessive hydration and loss of tablet integrity. Thus, an optimum level of hydration appears necessary: insufficient hydration may reduce polymer–mucin interaction, whereas excessive hydration may weaken the matrix and accelerate erosion or detachment.

3.10 Release Kinetic Analysis

The drug-release data were fitted to different mathematical models, including zero-order, first-order, Higuchi and Korsmeyer–Peppas models. The thesis states in the Results section that the release data were best described by first-order kinetics.

However, the conclusion section of the thesis states that the in-vitro release obeyed zero-order kinetics with a non-Fickian mechanism.

Therefore, this point cannot be presented as a confirmed result without checking the actual R^2 values from the kinetic plots. For a manuscript, the correct model should be selected based on the highest R^2 value and the Korsmeyer–Peppas exponent (n) where applicable.

3.11 Selection of Optimized Formulation

Based on the overall evaluation, F6 was selected as the optimized/promising formulation. The formulation demonstrated:

- Highest drug content: **99.15%**
- Highest reported mucoadhesive strength: **36.14 g**
- Highest 8-h swelling/hydration: **90.12%**
- Highest 8-h drug release: **98.13%**
- Highest reported retention time: **8 h 51 min**

These findings indicate that F6 provided a favorable balance between mechanical properties, drug-content uniformity, swelling, mucoadhesion, retention and drug release.

The superior performance of F6 may be related to the presence of Carbopol together with sodium CMC, which provides a combination of strong mucoadhesive interaction and favorable hydration behavior. The thesis similarly concludes that Carbopol and sodium CMC provided satisfactory mucoadhesive characteristics and identifies F6

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as the promising formulation.

3.12 DISCUSSION:

The results demonstrate that incorporation of Carbopol and secondary hydrophilic polymers such as HPMC K4M and sodium CMC significantly influenced the functional characteristics of the mebendazole buccal tablets. Changes in polymer composition affected powder flow, tablet characteristics, swelling, moisture uptake, mucoadhesive strength, retention time and drug release.

The prepared powder blends exhibited suitable flow properties for direct compression, while all tablet formulations showed acceptable hardness, friability, weight variation and drug content. The surface pH values were within the reported salivary range, suggesting a low likelihood of significant mucosal irritation. The swelling study demonstrated progressive hydration of the polymeric matrix, which is important for development of intimate contact with the buccal mucosa.

Among the formulations, F6 demonstrated the most favorable overall performance, particularly with respect to drug content, swelling, mucoadhesive strength, drug release and retention time. The 98.13% drug release at 8 h together with 8 h 51 min retention time indicates that the formulation could maintain prolonged contact with the mucosal surface while allowing efficient drug release.

Thus, the results support the potential of Carbopol-based mucoadhesive buccal tablets of mebendazole as a promising formulation approach. Nevertheless, the discrepancies in the thesis concerning the formulation composition, mucoadhesive-strength values and release-kinetic model should be resolved by checking the original experimental records before submission of the manuscript.

4. CONCLUSION:

The present study was undertaken to develop and evaluate mucoadhesive buccal tablets of mebendazole using Carbopol 934 as the primary mucoadhesive polymer in combination with secondary polymers such as HPMC K4M and sodium carboxymethyl cellulose. The tablets were successfully prepared by the direct compression method. The prepared formulations exhibited acceptable physical characteristics with respect to weight variation, hardness, thickness, friability and drug content. The surface pH of the developed buccal tablets was within the reported salivary pH range, indicating a low potential for mucosal irritation. The formulations exhibited satisfactory swelling behavior up to 8 h, which is important for maintaining intimate contact between the tablet and buccal mucosa. Increasing polymer concentration influenced the swelling characteristics of the formulations. The developed formulations demonstrated satisfactory mucoadhesive strength, with F6 showing the highest reported mucoadhesive strength of 36.14 g. The cumulative drug release at 8 h was 82.10%, 85.13%, 88.14%, 93.16%, 94.17% and 98.13% for F1–F6, respectively, with F6 showing the highest drug release. The release data were fitted to zero-order, first-order, Higuchi and Korsmeyer–Peppas models. According to the Results section of the thesis, the drug-release data followed first-order kinetics. Therefore, this should be reported as first-order kinetics unless the original kinetic plots/R² values establish otherwise. F6 was identified as the most promising formulation, exhibiting satisfactory drug content, swelling, mucoadhesive properties, prolonged retention and drug-release characteristics. The findings suggest that mucoadhesive buccal delivery of mebendazole may provide a promising alternative approach for prolonged buccal residence and potentially reduce the impact of hepatic first-pass metabolism. However, the proposed improvement in bioavailability requires confirmation through appropriate pharmacokinetic and in-vivo studies.

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