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Influence of Hydroxypropyl Methylcellulose E6–Carbopol 934P Composition on Drug Release and Buccal Mucoadhesion Time of Ondansetron Hydrochloride Tablets

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ABSTRACT

Background: Ondansetron hydrochloride is a selective antagonist of serotonin receptor used to manage nausea and vomiting, but oral administration is limited by first-pass metabolism and may be unreliable during active vomiting. Buccal delivery may overcome these limitations. This study aimed to develop and evaluate ondansetron hydrochloride mucoadhesive buccal tablets with various concentrations of hydroxypropyl methylcellulose E6 (HPMC E6) and Carbopol 934P.

Methods: Seven ondansetron hydrochloride mucoadhesive buccal tablet formulations (F1–F7) were prepared by direct compression using various concentrations of HPMC E6 and Carbopol 934P. Powder flow and compressibility were evaluated using the fixed-funnel, bulk-density, and tapped-density methods. Tablet weight, hardness, friability, and thickness were assessed using standard procedures, and drug content was quantified by ultra-high-performance liquid chromatography. Drug release, swelling, and in vivo mucoadhesion duration on the human buccal mucosa were also determined.

Results: All powder blends exhibited micromeritic properties compatible with direct compression. The tablets had mean weights of 148.0–152.3 mg, hardness values of 13.32–15.80 kgf, and friability values below 1%. Drug content ranged from 88.63 ± 0.36% to 94.77 ± 0.18%; six formulations met the prespecified 90%–110% assay range, whereas F4 was below the lower limit. Drug release at 2 h ranged from 36.2 ± 3.7% to 96.4 ± 2.8%, while mucoadhesion duration ranged from 80 ± 3.0 to 264 ± 4.0 min. Swelling varied among the formulations, with negative values in several formulations indicating that matrix erosion or material loss exceeded water uptake. F2 demonstrated a balanced profile, with 92.7 ± 0.6% drug release at 2 h, a mucoadhesion duration of 198 ± 2.0 min, and positive mean swelling indices at both measurement times.

Conclusion: HPMC E6 and Carbopol 934P show the potential to enhance the mucoadhesion and drug-release properties of ondansetron hydrochloride buccal tablets. It offers a promising candidate for further evaluation, but additional studies are needed on the release kinetics, permeability, stability, safety, and bioavailability studies are required.

Keywords: Ondansetron • Buccal tablets • Mucoadhesion • Hydroxypropyl methylcellulose E6 • Carbopol



1. Introduction

Nausea and vomiting may occur during chemotherapy, postoperative recovery, infections, and pregnancy and can adversely affect quality of life and treatment adherence.⁽¹⁾ Uncontrolled emesis can cause dehydration, electrolyte imbalance and discontinuation of treatment, particularly in cancer patients.⁽²⁾ Antiemetic medications are thus important in clinical practice and they operate by regulating the central and peripheral pathways in the emetic reflex.⁽³⁾

Ondansetron hydrochloride is a selective antagonist of serotonin (5-hydroxytryptamine type 3, 5-HT₃) receptor, with a high efficacy and a good safety profile that have led to its use popularity.⁽⁴⁾ It suppresses serotonin-induced activation of vagal afferents and central emetic circuits, thereby preventing nausea and vomiting.⁽⁴⁾ Ondansetron is effective but has a limited oral bioavailability because of high hepatic first-pass metabolism, resulting in an oral bioavailability of approximately 60%.⁽⁵⁾ In addition, oral administration may be unreliable in patients with active vomiting as absorption will not be consistent. These limitations have forced the need to develop alternative drug delivery methods. The use of buccal delivery has become a popular topic with growing interest as an alternative route because of its non-invasiveness and effectiveness. The buccal mucosa is highly vascular and permits direct absorption of drugs into the bloodstream bypassing first-pass metabolism and gastrointestinal breakdown.⁽⁶⁾ Recent advances have identified buccal delivery as an attractive platform to deliver both small molecules and biologics, offering rapid onset of action, and enhanced therapeutic efficacy.^(7,8) Mucoadhesive buccal systems also help to improve the delivery of drugs by prolonging the residence time of the dosage form at the absorption site.

Carbopol and hydroxypropyl methylcellulose (HPMC) are polymers that help to enhance adhesion, swelling and controlled drug release.^(9,10) Although ondansetron is commonly used clinically, its traditional dosage preparations are limited by first-pass metabolism and inconsistent gastrointestinal absorption. Buccal delivery systems offer a promising approach to overcome these limitations by increasing bioavailability and providing a uniform therapeutic effect.⁽¹¹⁾ Recent developments in mucoadhesive drug delivery systems emphasize the importance of optimizing the polymer to achieve the desired outcome of controlled drug release and effective adhesion.⁽¹²⁾ Nevertheless, few studies have scientifically compared the combined action of HPMC and Carbopol concentrations on the activity of ondansetron buccal tablets. Therefore, this study aimed to develop and evaluate ondansetron hydrochloride mucoadhesive buccal tablets through varying concentrations of polymers to optimize their physicochemical properties, mucoadhesive performance, and drug-release.

2. Methods

2.1. Chemicals and reagents

Ondansetron hydrochloride was procured from Anugraha Chemicals (Hyderabad, India), HPMC E6 from DuPont (Wilmington, DE, USA), and Carbopol 934P from Gloria Interchem Pvt. Ltd. (Morbi, Gujarat, India). Mannitol was supplied by Roquette Pharma (Lestrem, France). Talc and magnesium stearate were obtained from Merck KGaA (Darmstadt, Germany). All remaining chemicals and reagents used in the study were of analytical grade.

2.2. Preparation of mucoadhesive buccal tablets

Mucoadhesive buccal tablets of ondansetron hydrochloride were prepared using the direct compression method. All ingredients were accurately weighed using an analytical balance and passed



through a No. 60 mesh sieve to ensure uniform particle size. The drug, polymers (HPMC E6 and Carbopol 934P), and diluent (mannitol) were mixed thoroughly using a mortar and pestle to obtain a uniform powder blend. Magnesium stearate and talc were added as the lubricant and glidant, respectively, and mixed gently to minimize over-lubrication. The final blends were compressed using a single punch tablet compression machine (Expert-1-1014T, Cadmach Machinery Co. Pvt. Ltd., Ahmedabad, India) equipped with 6 mm flat-faced punches and operated at a constant compression force. Seven formulations (F1–F7) were prepared by varying the polymer concentrations while keeping the other excipients constant (Table 1).

Table 1: Quantitative composition of ondansetron mucoadhesive buccal tablets

Ingredients	% w/w of the target tablet weight (150 mg)						
	F1	F2	F3	F4	F5	F6	F7
Ondansetron	3	3	3	3	3	3	3
HPMC E6	10	10	15	15	20	25	30
Carbopol 934P	3	5	3	5	5	5	5
Mannitol	81	79	76	74	69	64	59
Talc	2	2	2	2	2	2	2
Magnesium stearate	1	1	1	1	1	1	1

HPMC, hydroxypropyl methylcellulose.

2.3. Precompression evaluation of powder blends

Before compression, the powder blend for each formulation (F1–F7) was evaluated for micromeritic properties to characterize flowability and compressibility.

2.3.1. Angle of repose

The angle of repose was determined by the fixed-funnel method.⁽¹³⁾ Each powder blend was passed through a funnel to form a conical heap, and the angle was calculated as follows:

$$\tan \theta = h/r, \text{ where } h \text{ is the height and } r \text{ is the radius of the powder heap}$$

All measurements were performed in triplicate.

2.3.2. Bulk and tapped density estimation

Bulk density was determined by transferring an accurately weighed quantity of 10 g of powder blend into a 50 mL graduated cylinder and recording its volume. Tapped density was determined by mechanical tapping of the cylinder with a tapped-density tester (Electrolab, India) until a constant volume was obtained. All measurements were performed in triplicate.

2.3.3. Carr's index and Hausner ratio

Carr's index and Hausner ratio were determined using the following equations:⁽¹³⁾

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

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

2.4. Postcompression evaluation of prepared mucoadhesive buccal tablets

Quality control tests were conducted on the prepared mucoadhesive buccal tablets of seven formulations (F1–F7) to ensure compliance with pharmacopeial specifications.⁽¹⁴⁾

2.4.1. Weight variation

Weight variation was assessed by individual weighing of 20 randomly selected tablets from each formulation using an analytical balance. Then, the mean tablet weight and percentage deviation of each tablet from the mean were calculated. For tablets with a mean weight of 130–324 mg, the acceptance criterion was a deviation of no more than 7.5%, with no more than two tablets exceeding this limit.⁽¹⁴⁾

2.4.2. Hardness

Hardness of the prepared mucoadhesive buccal tablets was determined using a hardness tester (TBH 425TD, Erweka GmbH, Heusenstamm, Germany). Each formulation (F1–F7) was chosen to obtain ten



tablets, and the force needed to break them was measured. Mean hardness of each formulation was calculated.⁽¹³⁾

2.4.3. Friability

Friability was evaluated using an EF-2 friabilator (Electrolab, India). A tablet sample was rotated at 25 rpm for 4 min, and percentage weight loss was calculated. A weight loss of no more than 1%, with no cracking, breaking, or capping, was considered acceptable.⁽¹⁴⁾

2.4.4. Thickness

A digital caliper (Mitutoyo Corp., Kawasaki, Japan; Model: 500-196-30) was used to measure the thickness of the prepared mucoadhesive buccal tablets. Ten tablets of each formulation (F1-F7) were picked and the thickness of each tablet was noted. The tablet thickness should have a range of $\pm 5\%$ of the average thickness that is acceptable, which will ensure that the tablets will be similar in size and compress similarly during the process of manufacturing.⁽¹³⁾

2.5. Ondansetron assay

The ondansetron content of the developed tablets was measured using an ultra-high-performance liquid chromatography (UHPLC) method based on the US Pharmacopeia,⁽¹⁴⁾ with modifications for the sample size.

2.5.1. Mobile phase preparation

Monobasic potassium phosphate (2.7 g) was dissolved in 1000 mL distilled water, and the pH was adjusted to 5.4 with 1 N sodium hydroxide. The resulting buffer solution was filtered using a 0.45- μ m membrane filter. The mobile phase was prepared by mixing acetonitrile and the buffer solution at a 20:80, v/v ratio and was filtered through a 0.45- μ m membrane prior to use.

2.5.2. UHPLC conditions

Chromatographic separation was performed using a 4.6 mm $\times$ 25 cm L10 column with 5- μ m packing material. The mobile phase pumped at 1.5 mL/min. and 10 μ L of each sample was injected. Detection was performed at 310 nm using an ultraviolet detector. Prior to analysis, all solutions were passed through a 0.45- μ m membrane filter.

2.5.3. Preparation of standard solution

Ondansetron hydrochloride reference standard (5 mg, equivalent to 4 mg ondansetron base) was accurately weighed into a 100-mL flask. The standard was dissolved in phosphate buffer (pH 6.8), and diluted to volume to obtain a nominal ondansetron concentration of 0.04 mg/mL. Before injection, the solution was filtered using a 0.45- μ m membrane filter.

2.5.4. Preparation of calibration curve

A calibration curve was prepared using a series of standard ondansetron solutions at different concentrations. The peak area corresponding to each concentration was recorded, and the calibration equation ($y = a + b \times x$) was obtained from linear regression analysis, where y represents the peak area and x represents the drug concentration. The linearity of the method was confirmed by the correlation coefficient (r^2).⁽¹⁴⁾

2.5.5. Preparation of sample solution

One tablet from each formulation (equivalent to 5 mg ondansetron hydrochloride, approximately 4 mg ondansetron base) was placed in a 100-mL flask. Approximately 70 mL of phosphate buffer (pH 6.8) was added, and the mixture was then sonicated for 20 min. The resulting solution was diluted to volume with the same buffer, yielding a nominal ondansetron concentration of 0.04 mg/mL, and filtered through a 0.45- μ m membrane before analysis.



2.5.6. Calculation of percentage assay

The percentage assay was calculated as follows:

$$\% \text{ Assay} = \frac{\text{AUC of sample}}{\text{AUC of standard}} \times \frac{\text{Concentration of standard}}{\text{Concentration of sample}} \times 100$$

According to the US Pharmacopeia, the pre-specified acceptance range was 90–110% of the labeled amount of ondansetron.⁽¹⁴⁾

2.6. In vitro dissolution ondansetron study

Because the US Pharmacopeia does not provide a monograph for this buccal dosage form, a standardized dissolution method was used to compare drug-release behavior among formulations.⁽¹⁵⁾

Dissolution testing was conducted using USP Apparatus II (TDT-08L, Electrolab, India) with 500 mL of phosphate buffer (pH 6.8) kept at 37 ± 0.5 °C and operated at 50 rpm. Aliquots of 5 ml were collected at 30 and 120 min, filtered, and analyzed using a spectrophotometer (TP-6000, Chongqing TOP Oil Purifier Co., Ltd., Chongqing, China) at 310 nm. After each withdrawal, the removed volume was replenished with an equal volume of fresh dissolution medium.

2.7. Swelling index

The swelling of the prepared buccal tablets was assessed by measuring the swelling index.⁽¹⁶⁾ The correct amount of each tablet was weighed (W_0) and put in a Petri dish with phosphate buffer solution (pH 6.8). The tablets were left to swell at room temperature and were removed from the medium at specific time intervals (1 and 2 h). The excess surface moisture was dried by placing a filter paper on the tablets. The swollen tablets were reweighed (W_t) to calculate the swelling index using the following formula:

$$\text{Swelling index} = \frac{W_t - W_0}{W_0} \times 100, \text{ where } W_0 \text{ is initial weight, and } W_t \text{ is weight at time (t).}$$

The experiment was performed in triplicate, and the results were expressed as mean $\pm$ standard deviation (SD).

2.8. In vivo mucoadhesive residence time

In vivo mucoadhesive residence time was evaluated on the human buccal mucosa.⁽¹⁵⁾ Tablets were placed against the inner cheek and held with gentle fingertip pressure for several seconds to establish adhesion. The time to detachment was measured with a stopwatch under normal physiological conditions. Each formulation was tested in triplicate and the results expressed as the mean $\pm$ SD. A residence time of at least 60 min was considered acceptable.⁽¹⁷⁾

2.9. Data analysis

Data were summarized as the mean $\pm$ SD. Statistical analyses were conducted using GraphPad Prism software, version 8 (GraphPad, San Diego, CA, USA). One-way analysis of variance (ANOVA), followed by Tukey's post hoc test, was used to test the statistical significance of various formulations. A p -value < 0.05 was considered statistically significant.

3. Results

3.1. Micromeritic properties of the powder blend

Table 2 shows the micromeritic properties of the powder blends. The angle of repose was between 25.90° and 30.40° , with F1 and F2 exhibiting lower values, indicating comparatively better flowability, and F7 showing the highest value. Bulk density was between 0.39 and 0.47 g/cm³. The Hausner ratio was between 1.14 and 1.23, with F2 exhibiting the lowest value and F7 a comparatively higher value. Carr's index ranged from 12.28% to 18.70%; F1 and F2 had lower values, whereas F6 and F7 had comparatively higher values, consistent with less favorable flow properties.



3.2. Physicochemical evaluation of prepared mucoadhesive buccal tablets

The mean tablet weight ranged from 148.0 ± 1.3 mg (F3) to 152.3 ± 1.5 mg (F5). Tablet hardness ranged from 13.32 ± 0.50 kgf (F5) to 15.80 ± 1.23 kgf (F6). Significant differences in hardness were observed among the formulations ($p < 0.001$). All formulations showed low friability values, indicating resistance to abrasion. F5 ($0.04 \pm 0.01\%$) had the lowest friability, and F6 ($0.23 \pm 0.09\%$) had the highest with mean values below 1% for all formulations. The mean tablet

thickness ranged from 3.01 ± 0.02 mm (F3) to 3.18 ± 0.01 mm (F5). Statistical analysis demonstrated significant differences among formulations ($p < 0.001$). Assay values ranged from $88.63 \pm 0.36\%$ (F4) to $94.77 \pm 0.18\%$ (F1). One-way ANOVA revealed significant differences among the formulations ($p < 0.001$). F4 was below the stated lower assay limit of 90%; therefore, not all formulations met the specified assay criterion. Drug release at 2 h ranged from $36.2 \pm 3.7\%$ (F7) to $96.4 \pm 2.8\%$ (F3) (Table 3). Formulations showed a difference in the drug release after 2 hours ($p < 0.001$).

Table 2: Micrometric properties of the powder blend*

Formulation code	Angle of repose (°)	Bulk density (g/cm ³)	Tapped density (g/cm ³)	Hausner ratio	Carr's index (%)
F1	26.80 ± 0.10	0.47 ± 0.01	0.54 ± 0.02	1.15 ± 0.01	13.04 ± 0.13
F2	25.90 ± 0.10	0.46 ± 0.01	0.52 ± 0.01	1.14 ± 0.01	12.28 ± 0.13
F3	27.07 ± 0.15	0.45 ± 0.01	0.53 ± 0.02	1.17 ± 0.01	14.53 ± 0.13
F4	26.50 ± 0.20	0.40 ± 0.02	0.51 ± 0.02	1.16 ± 0.01	13.79 ± 0.14
F5	27.83 ± 0.29	0.42 ± 0.01	0.50 ± 0.01	1.18 ± 0.01	15.25 ± 0.15
F6	29.10 ± 0.36	0.40 ± 0.02	0.48 ± 0.02	1.21 ± 0.01	17.35 ± 0.14
F7	30.40 ± 0.26	0.39 ± 0.02	0.48 ± 0.03	1.23 ± 0.01	18.70 ± 0.15

*All values are expressed as mean $\pm$ SD ($n = 3$).

Table 3: Physicochemical evaluation of prepared ondansetron mucoadhesive buccal tablets

Formulation code	Weight variation* (mg)	Hardness** (kgf)	Friability*** (%)	Thickness** (mm)	Assay** (%)	Drug release at 2 h**** (%)
F1	150.8 ± 2.6^{bc}	15.63 ± 0.69^a	0.12 ± 0.04^a	3.07 ± 0.05^a	94.77 ± 0.18^a	90.9 ± 1.2^b
F2	149.3 ± 2.2^{ab}	14.95 ± 0.42^{ab}	0.08 ± 0.03^c	3.04 ± 0.02^a	91.47 ± 0.03^c	92.7 ± 0.6^b
F3	148.0 ± 1.3^b	15.42 ± 0.85^a	0.11 ± 0.05^b	3.01 ± 0.02^a	90.31 ± 0.67^d	96.4 ± 2.8^a
F4	149.3 ± 1.5^b	15.30 ± 0.40^a	0.11 ± 0.06^b	3.03 ± 0.01^a	88.63 ± 0.36^b	88.9 ± 1.2^b
F5	152.3 ± 1.5^c	13.32 ± 0.50^c	0.04 ± 0.01^c	3.18 ± 0.01^b	94.03 ± 0.40^a	76.9 ± 4.0^c
F6	152.2 ± 1.0^c	15.80 ± 1.23^a	0.23 ± 0.09^d	3.13 ± 0.02^b	90.73 ± 0.11^d	57.5 ± 3.9^d
F7	152.0 ± 1.3^c	14.87 ± 0.42^b	0.11 ± 0.07^b	3.13 ± 0.01^b	92.73 ± 0.14^c	36.2 ± 3.7^e

*mean $\pm$ % deviation, $n = 20$; ** mean $\pm$ SD, $n = 10$; *** equivalent to 6.5 g tablet. **** mean $\pm$ SD, $n = 3$. Different superscript letters within the same column indicate statistically significant differences among formulations according to Tukey's post hoc test following one-way ANOVA ($p < 0.05$).

3.3. Swelling index of mucoadhesive buccal tablets

Table 4 shows that the swelling index of the prepared mucoadhesive buccal tablets at 1 and 2 h varied among formulations (F1–F7). At 1 h, the swelling index ranged from $-7.43 \pm 3.08\%$ (F1) to $9.41 \pm 5.12\%$ (F6). F6 and F7 had relatively higher swelling indices ($9.41 \pm 5.12\%$ and $5.52 \pm 2.44\%$, respectively), indicating greater initial net water uptake, whereas F1 had a negative value, indicating net weight loss under the test conditions. F2 showed a swelling index of $3.81 \pm 6.12\%$.

At 2 h, the swelling index ranged from $-11.95 \pm 9.88\%$ (F1) to $2.63 \pm 1.80\%$ (F6), with F2 decreasing to $1.91 \pm 1.50\%$. Most formulations showed a decrease in swelling index between 1 and 2 h. At 2 h, F6 retained the highest positive swelling index ($2.63 \pm 1.80\%$), whereas F1, F3, F4, F5, and F7 had negative values, suggesting that matrix erosion or material loss exceeded water uptake under the test conditions (Table 4).



Table 4: Swelling index of prepared ondansetron mucoadhesive buccal tablets*

Formulation code	Swelling index after 1 h (%)	Swelling index after 2 h (%)
F1	-7.43 ± 3.08	-11.95 ± 9.88
F2	3.81 ± 6.12	1.91 ± 1.50
F3	-2.92 ± 1.95	-17.70 ± 5.14
F4	1.56 ± 2.10	-2.69 ± 4.35
F5	-3.25 ± 2.82	-9.79 ± 2.64
F6	9.41 ± 5.12	2.63 ± 1.80
F7	5.52 ± 2.44	-9.23 ± 3.65

* All values are expressed as mean ± SD (n = 3).

3.4. Mucoadhesion time of prepared mucoadhesive buccal tablets

The longest mucoadhesion time was observed for F1 (264 ± 4.0 min), followed by F3 (228 ± 3.0 min) and F2 (198 ± 2.0 min). Intermediate adhesion time was observed for F4 (168 ± 1.0 min) and F7 (138 ± 4.0 min), while the shortest time was observed for F6 (112 ± 2.0 min) and F5 (80 ± 3.0 min) (Table 5).

Table 5: Mucoadhesion time of prepared ondansetron mucoadhesive buccal tablets*

Formulation code	Mucoadhesion time (min)
F1	264.0 ± 4.0
F2	198.0 ± 2.0
F3	228.0 ± 3.0
F4	168.0 ± 1.0
F5	80.0 ± 3.0
F6	112.0 ± 2.0
F7	138.0 ± 4.0

* All values are expressed as mean ± SD (n = 3).

4. Discussion

This study developed and evaluated mucoadhesive buccal tablets of ondansetron hydrochloride using HPMC E6 and Carbopol 934P as the rate-controlling and mucoadhesive polymers, respectively. Differences in polymer composition were associated with variations in powder flow, tablet mechanical properties, swelling behavior, mucoadhesion duration, and drug release. The micromeritic characteristics of all powder blends were compatible with direct compression, with angle of repose, Carr's index, and Hausner ratio collectively indicating acceptable flow properties. The formulations with lower polymer

concentrations had better flow properties, which may reflect reduced interparticle cohesion and fewer polymer-polymer interactions.⁽¹³⁾ At higher polymer concentrations, increased cohesion may have contributed to poorer flow. Particle size, morphology, and surface interactions are possible contributing factors; however, these mechanisms were not directly evaluated in this study.^(18,19)

The formulations showed relatively similar mean weights and thicknesses and low mean friability values. However, F4 had an assay value of 88.63%, below the specified lower limit of 90%, indicating that not all formulations met the assay criterion. The hardness values observed may partly reflect the deformation and bonding behavior of the polymer-containing blends during compression; hardness measurements alone, however, do not establish the underlying compaction mechanism.⁽¹⁸⁾ The low friability values indicated resistance to abrasion under the test conditions. Potential explanations for differences in assay values include blend heterogeneity, incomplete drug extraction during analysis, or drug-polymer interactions.⁽²⁰⁾ These possibilities require investigation, particularly for F4, and cannot be distinguished using the reported assay results alone.

Drug release generally decreased with increasing polymer concentration, although no statistical correlation or release mechanism was established from the reported results. Lower polymer content formulations (F1–F3) released a greater proportion of the drug (90.9–96.4% at 2 h), possibly because a less substantial hydrated polymer barrier facilitated medium penetration and drug diffusion. Conversely, the higher polymer-loaded formulations (F5–F7) exhibited lower drug release at 2 h (36.2–76.9%), potentially reflecting greater resistance to diffusion through the hydrated matrix. These interpretations are consistent with hydrophilic matrix systems, in which diffusion, polymer relaxation, and erosion can



contribute to drug release.^(21–23) However, gel-layer thickness and viscosity were not measured, and the dominant release mechanism cannot be inferred from the 2-h release values alone.

Swelling behavior varied among formulations. F6 and F7 showed comparatively higher positive swelling indices at 1 h, consistent with initial net water uptake by the hydrophilic polymer matrices. Ionization of Carbopol carboxyl groups can promote polymer expansion, depending on the medium pH, whereas HPMC hydration can contribute to gel formation.⁽²⁴⁾ At 2 h, F1, F3, F4, F5, and F7 had negative swelling indices, suggesting that matrix erosion or material loss exceeded water uptake. Hydration-related loss of matrix cohesion is one possible explanation for this behavior.^(25–27) However, the swelling index represents net weight change and does not independently quantify water uptake and erosion; negative values therefore do not establish excessive hydration as the cause.

Mucoadhesion duration varied among formulations and did not consistently increase with the measured swelling index. F1 (264 min), F3 (228 min), and F2 (198 min) showed the longest mucoadhesion durations. Mucoadhesion can involve initial wetting, swelling of polymer chains, interpenetration with mucin, and formation of hydrogen bonds.⁽²⁸⁾ Carbopol may contribute to these interactions through its carboxyl groups.⁽²⁹⁾ Although F5–F7 had shorter mucoadhesion durations, attributing this finding to excessive swelling or an overhydrated gel layer would require additional evidence. Excessive hydration can weaken interfacial adhesion or matrix cohesion in some mucoadhesive systems,^(30–32) but this mechanism was not demonstrated here. Notably, F1 combined the longest mucoadhesion duration with negative swelling indices, indicating that the separate swelling and mucoadhesion tests do not support a simple causal relationship.

The findings suggest that hydration, matrix integrity, mucoadhesion, and drug release must be considered jointly when selecting a formulation. However, the reported measurements do not establish correlations or causal relationships among these properties. Formulation selection should therefore be guided by predefined targets for mucoadhesion duration and drug release, alongside acceptable tablet quality. Based on the combined results, F2 appears to be a promising formulation for further evaluation. The formulation had a mucoadhesion duration of 198 min, drug release of 92.7% at 2 h, and positive mean swelling indices at both measurement times. These findings do not, however, demonstrate complete release, controlled-release kinetics, or the absence of erosion. F3 also exhibited a favorable profile, with greater drug release at 2 h and a longer mucoadhesion duration than F2, although its swelling index was negative at 2 h. The preference for F2 over F3 should therefore be justified using explicit selection criteria rather than an unqualified claim of optimal performance. Overall, the study identifies formulation-dependent differences that can guide further optimization of ondansetron hydrochloride buccal tablets. Additional evaluation is needed to establish release mechanisms, buccal permeability, and clinical performance.

5. Conclusion

HPMC E6 and Carbopol 934P offer potential for tailoring the mucoadhesion and drug-release properties of ondansetron hydrochloride buccal tablets prepared by direct compression. F2 represents a promising candidate for further evaluation, although additional studies are needed to establish release mechanisms, buccal permeability, and clinical performance.



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Ethical approval

The research proposal of human study was reviewed and approved by the UST Ethics Committee of the Faculty of Pharmacy, USTY, Sana'a, Yemen (UST-UREC-1448-00115). The research was carried out in compliance with the principles of the ethical considerations described in the Declaration of Helsinki. All participants were informed and gave their informed consent before taking part in the study.

Conflict of interest

The authors declare no conflicts of interest.

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