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Development and Optimization of Fast-Dissolving Tablets of Ondansetron hydrochloride Using Plantago ovata mucilage

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ABSTRACT

Objective: This study aimed to develop and optimize fast-dissolving tablets (FDTs) of ondansetron hydrochloride (4 mg) using Plantago ovata mucilage as a natural superdisintegrant. The target formulation was designed to achieve a disintegration time of ≤30 s, at least 85% drug release within 5 min, and a total tablet weight of 150 mg.

Methods: Nine formulations (F1-F9) were prepared by direct compression using varying concentrations of Plantago ovata mucilage (2-8% w/w), alone or in combination with crospovidone. Preformulation and compatibility studies were performed using Fourier-transform infrared (FTIR) spectroscopy and differential scanning calorimetry (DSC). Powder flow properties and the physicomechanical characteristics of the tablets were evaluated. In vitro disintegration time, wetting time, water absorption ratio, and dissolution behavior were assessed in simulated gastric fluid (pH 1.2) using a USP Type II dissolution apparatus at 37 ± 0.5 °C and 50 rpm. Dissolution data were fitted to zero-order, first-order, Higuchi, and Korsmeyer-Peppas kinetic models. A 3^2 factorial design was used for formulation optimization, and accelerated stability testing was conducted according to ICH Q1A(R2) guidelines.

Results: FTIR and DSC analyses indicated no obvious incompatibility between ondansetron hydrochloride and the formulation components. Formulation F5, containing 4% w/w Plantago ovata mucilage and 1% w/w crospovidone, demonstrated a disintegration time of 18.4 ± 1.2 s, a wetting time of 22.6 ± 1.5 s, a water absorption ratio of 88.3 ± 2.1%, and 94.7 ± 1.3% drug release within 5 min. The reported dissolution data showed the highest coefficient of determination for the first-order model (R^2 = 0.987), while the Korsmeyer-Peppas release exponent was 0.41. The formulations reportedly complied with the specified acceptance limits for weight variation, hardness, friability, and drug content uniformity. Following 90 days of accelerated storage at 40 ± 2 °C and 75 ± 5% relative humidity, no significant changes in drug content or dissolution behavior were reported, and the similarity factor (f_2) remained above 85.

Conclusion: The optimized F5 formulation demonstrated rapid disintegration and drug release, supporting the potential of Plantago ovata mucilage as a natural superdisintegrant in ondansetron hydrochloride fast-dissolving tablets. The formulation may offer a convenient oral dosage form for patients who experience difficulty swallowing conventional tablets. Further confirmation using complete experimental data and validated stability results is required before drawing definitive conclusions regarding its performance and clinical applicability.

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Ondansetron hydrochloride; Fast-dissolving tablets; Plantago ovata mucilage; Natural superdisintegrant; Direct compression; Disintegration time; Drug release.

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1. Introduction

Nausea and vomiting are among the most distressing side effects associated with cancer chemotherapy, radiotherapy, and surgical procedures, significantly impairing patient quality of life and treatment adherence [1]. Ondansetron hydrochloride, a selective 5-HT_3 receptor antagonist, is a cornerstone in the prophylaxis and management of chemotherapy-induced nausea and vomiting (CINV) and postoperative nausea and vomiting (PONV) [2]. Despite its clinical efficacy, conventional immediate-release tablets and oral solutions present challenges in specific patient populations-particularly pediatric, geriatric, and dysphagic patients-who experience difficulty swallowing solid dosage forms [3]. Additionally, the bitter taste of Ondansetron hydrochloride limits acceptability in oral liquid formulations.

Fast-dissolving tablets (FDTs), also known as orodispersible tablets, disintegrate or dissolve rapidly in saliva within seconds without the need for water, offering a significant advantage in patient compliance, onset of action, and bioavailability [4]. The European Pharmacopoeia defines orodispersible tablets as uncoated tablets intended to disperse in the mouth before swallowing, with a disintegration time not exceeding 3 minutes; however, modern formulation targets aim for disintegration within 30 seconds [5].

Superdisintegrants are the critical excipients enabling rapid disintegration. Synthetic superdisintegrants such as crospovidone, croscarmellose sodium, and sodium starch glycolate are widely used; however, growing interest in natural, biodegradable, and cost-effective alternatives has directed attention toward plant-derived polysaccharides [6]. *Plantago ovata* (isabgol) mucilage, a natural hydrophilic polysaccharide composed primarily of arabinoxylan, exhibits remarkable swelling and water-uptake capacity, making it a promising natural superdisintegrant [7]. Previous studies have demonstrated its utility in FDTs of various drugs, yet systematic optimization with Ondansetron hydrochloride remains unexplored.

Ondansetron hydrochloride is a Biopharmaceutics Classification System (BCS) Class I drug (high solubility, high permeability), with a plasma elimination half-life of 3-4 hours and absolute oral bioavailability of approximately 60% [8]. Its low dose (4-8 mg) and high solubility make it an ideal candidate for FDT development via direct compression, a simple, cost-effective, and industrially scalable manufacturing method. The present study was undertaken to develop and optimize Ondansetron hydrochloride FDTs (4 mg strength, total tablet weight 150 mg) using *Plantago ovata* mucilage as the primary natural superdisintegrant, with crospovidone as a synthetic benchmark, employing a systematic formulation design and factorial optimization approach.

2. Materials and Methods

2.1 Materials

Ondansetron hydrochloride dihydrate (USP grade) was obtained as a gift sample from Sun Pharmaceutical Industries Ltd., Gujarat, India. Plantago ovata seeds (pharmaceutical grade) were procured from a local authenticated supplier in Maharashtra, India, and mucilage was isolated in-house. Crospovidone (Kollidon CL, BASF, Germany), microcrystalline cellulose (MCC PH 102; FMC Biopolymer, USA), mannitol (Pearlitol 200 SD, Roquette, France), aspartame (NutraSweet, USA), strawberry flavor (Symrise, Germany), magnesium stearate (Peter Greven, Germany), and colloidal silicon dioxide (Aerosil 200, Evonik, Germany) were used as excipients. All reagents were of analytical grade.

2.2 Isolation and Characterization of Plantago ovata Mucilage

Plantago ovata seeds (100 g) were soaked in distilled water (1 L) for 6 h at room temperature. The swollen mass was heated at 60-70 °C for 30 min with continuous stirring to facilitate mucilage release. The hot slurry was passed through a muslin cloth, and the filtrate was precipitated by adding absolute ethanol (1:3 v/v). The precipitated mucilage was separated, washed with ethanol, dried at 45 °C for 12 h, pulverized, and passed through a #80 sieve. The yield was 12.4% w/w. The mucilage was characterized for pH (1% w/v dispersion), swelling index, loss on drying, total ash, acid-insoluble ash, and microbial limits per IP 2018.

2.3 Preformulation and Compatibility Studies

Binary physical mixtures (1:1 w/w) of Ondansetron hydrochloride with Plantago ovata mucilage, crospovidone, and MCC PH 102, and a ternary mixture representative of the optimized formulation (F5), were prepared by geometric dilution. Mixtures were stored in sealed amber glass vials at 40 ± 2 °C / 75 ± 5% RH for 4 weeks.

Fourier-Transform Infrared (FTIR) Spectroscopy: Spectra were recorded over 4000-400 cm^{-1} at 4 cm^{-1} resolution using KBr pellets on a Shimadzu IRAffinity-1S spectrophotometer.

Differential Scanning Calorimetry (DSC): Thermograms were recorded from 25-300 °C at a heating rate of 10 °C/min under nitrogen purge (50 mL/min) using a Mettler Toledo DSC 1 STAR^e system. Samples (3-5 mg) were sealed in aluminum pans.

2.4 Formulation Design and Preparation

Tablets were designed to contain 4 mg Ondansetron hydrochloride per unit with a target weight of 150 mg (drug loading: 2.67% w/w). Nine formulations were developed according to a 3² full factorial design (Table 1), with Plantago ovata mucilage concentration (X_1: 2, 4, 6% w/w) and crospovidone concentration (X_2: 0, 1, 2% w/w) as independent variables. Disintegration time (DT) and % drug release at 5 min (Q_5) were the response variables. All formulations were prepared by direct compression. Intragranular components (drug, MCC PH 102, mannitol, superdisintegrants, aspartame, flavor) were blended in a V-cone blender for 10 min. Extra-granular lubricants (magnesium stearate, Aerosil 200) were added and blended for 3 min. The final blend was compressed into 8.0 mm flat-faced beveled-edge tablets on a 16-station rotary tablet press (Cadmach, Ahmedabad) using 8 mm punches.

Table 1. Composition of Ondansetron Hydrochloride Fast-Dissolving Tablets (mg per tablet)

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ondansetron HCl	4	4	4	4	4	4	4	4	4
Plantago ovata mucilage	3	3	3	6	6	6	9	9	9
Crospovidone	0	1.5	3	0	1.5	3	0	1.5	3
MCC PH 102	60	58.5	57	57	55.5	54	54	52.5	51
Mannitol	75	75	75	75	75	75	75	75	75
Aspartame	3	3	3	3	3	3	3	3	3
Strawberry flavor	2	2	2	2	2	2	2	2	2
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Colloidal silicon dioxide	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total weight	150	150	150	150	150	150	150	150	150

Note: % w/w of Plantago ovata mucilage: F1-F3 = 2%, F4-F6 = 4%, F7-F9 = 6%; Crospovidone: F1, F4, F7 = 0%, F2, F5, F8 = 1%, F3, F6, F9 = 2%.

2.5 Micromeritic Evaluation of Powder Blends

The flow properties of the final lubricated blends were characterized by angle of repose (fixed funnel method), bulk density, tapped density (USP <616>), Carr's compressibility index, and Hausner ratio (n = 3) [9].

2.6 Tablet Characterization

Weight Variation: Twenty tablets from each batch were weighed individually (USP <2091>).

Thickness and Diameter: Measured using a digital vernier caliper (n = 6).

Hardness: Monsanto hardness tester (n = 6).

Friability: Roche friabilator, 100 revolutions at 25 rpm (n = 10 tablets, USP <1216>).

Drug Content Uniformity: Ten tablets were powdered, equivalent to 4 mg drug extracted in pH 1.2 SGF, filtered, diluted, and assayed by UV spectrophotometry at 310 nm (λmax of Ondansetron in pH 1.2). Method validated for linearity (R^2 = 0.9998, 1-10 µg/mL), accuracy (recovery 98.7-101.4%), intra-day precision (RSD < 1.2%), and inter-day precision (RSD < 1.8%) per ICH Q2(R1) [10].

In Vitro Disintegration Time (DT): Measured using a USP disintegration apparatus in 900 mL pH 1.2 SGF at 37 ± 0.5 °C (n = 6). Time for complete disintegration with no residue on the screen was recorded.

Wetting Time and Water Absorption Ratio: A piece of tissue paper folded twice was placed in a petri dish containing 10 mL pH 1.2 SGF with a dye (0.1% w/v amaranth). A tablet was placed on the paper; the time for complete wetting (color appearance on tablet surface) was recorded as wetting time (n = 6).

2.7 In Vitro Drug Release Studies

Dissolution testing was performed using USP Type-II (paddle) apparatus in 900 mL pH 1.2 SGF at 37 ± 0.5 °C and 50 rpm. Aliquots (5 mL) were withdrawn at 0.5, 1, 2, 3, 4, and 5 min, filtered through 0.45 µm membrane filters, and analyzed at 310 nm. Fresh medium was replaced after each sampling (n = 3).

2.8 Drug Release Kinetics and Mechanism

Dissolution data were fitted to zero-order, first-order, Higuchi, and Korsmeyer-Peppas models. The release exponent (n) from the Korsmeyer-Peppas model was interpreted: $n \leq 0.45$ (Fickian diffusion), $0.45 < n < 0.89$ (anomalous transport), $n \geq 0.89$ (Case II transport) [11, 12].

2.9 Factorial Design and Statistical Optimization

A 3² full factorial design was employed using Design-Expert software (v13, Stat-Ease Inc., USA). Independent variables: X_1 = *Plantago ovata* mucilage (% w/w), X_2 = crospovidone (% w/w). Responses: Y_1 = disintegration time (s), Y_2 = % drug release at 5 min (Q_5). Polynomial equations and response surface plots were generated. The optimized formulation was selected based on desirability function targeting minimum DT and maximum Q_5.

2.10 Accelerated Stability Studies

The optimized formulation (F5) was packed in aluminum-aluminum blister packs and stored at 40 ± 2 °C / 75 ± 5% RH for 90 days per ICH Q1A(R2). Samples were evaluated at 0, 30, 60, and 90 days for physical appearance, drug content, hardness, friability, disintegration time, and dissolution profile. The similarity factor (f_2) was calculated to compare dissolution profiles [13].

3. Results and Discussion

3.1 Characterization of Plantago ovata Mucilage

The isolated mucilage was a free-flowing, off-white, odorless powder. Physicochemical properties: pH (1% w/v) = 5.8 ± 0.2, swelling index = 14.2 ± 0.5 mL/g, loss on drying = 8.3 ± 0.4%, total ash = 3.1 ± 0.2%, acid-insoluble ash = 0.4 ± 0.1%. Microbial limits: total aerobic count < 10^3 CFU/g, total yeast/mold < 10^2 CFU/g, absence of E. coli, Salmonella, S. aureus, P. aeruginosa. Results complied with IP standards for natural gums and mucilages.

3.2 Preformulation and Compatibility Studies

FTIR Spectroscopy: The FTIR spectrum of pure ondansetron hydrochloride showed characteristic absorption bands at 3432 cm^{-1}, 3068 cm^{-1}, and 2924 cm^{-1}, corresponding to N-H/O-H region, aromatic C-H stretching, and aliphatic C-H stretching, respectively. Additional bands were observed at 1651 cm^{-1}, 1602 cm^{-1}, 1512 cm^{-1}, 1450 cm^{-1}, and 1378 cm^{-1}, along with bands at 1254 cm^{-1}, 1176 cm^{-1}, 1028 cm^{-1}, and 832 cm^{-1} in the fingerprint region. The FTIR spectrum of the ternary mixture (F5), containing ondansetron hydrochloride, Plantago ovata mucilage, and excipients, exhibited absorption bands at 3418 cm^{-1}, 2927 cm^{-1}, 1653 cm^{-1}, 1601 cm^{-1}, 1515 cm^{-1}, 1452 cm^{-1}, 1375 cm^{-1}, 1248 cm^{-1}, 1172 cm^{-1}, 1064 cm^{-1}, and 832 cm^{-1}. The retention of several characteristic bands with minor shifts suggests that the principal functional-group features were maintained in the mixture (Figures 1 and 2).

DSC Thermograms: The DSC thermogram of pure ondansetron hydrochloride exhibited a prominent endothermic peak at approximately 185.8 °C, representing its characteristic thermal transition (Figure 3). The DSC thermogram of the ternary mixture (F5) showed thermal events at approximately 82.4 °C and 113.6 °C, which may be associated with moisture loss and other thermal transitions of the formulation components. A prominent endothermic peak was also observed at approximately 183.1 °C, close to the thermal transition of the pure drug (Figure 4). The shift from 185.8 °C to 183.1 °C indicates a small difference in the observed peak temperature.

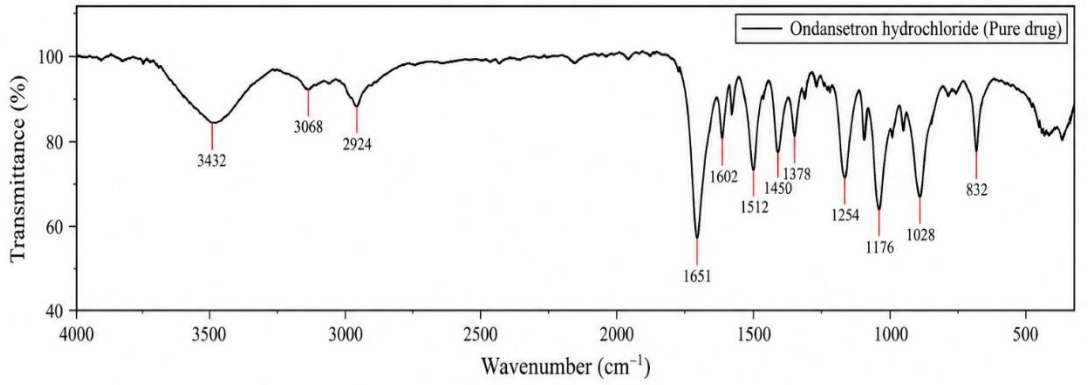


Figure 1. FTIR spectrum of pure Ondansetron hydrochloride

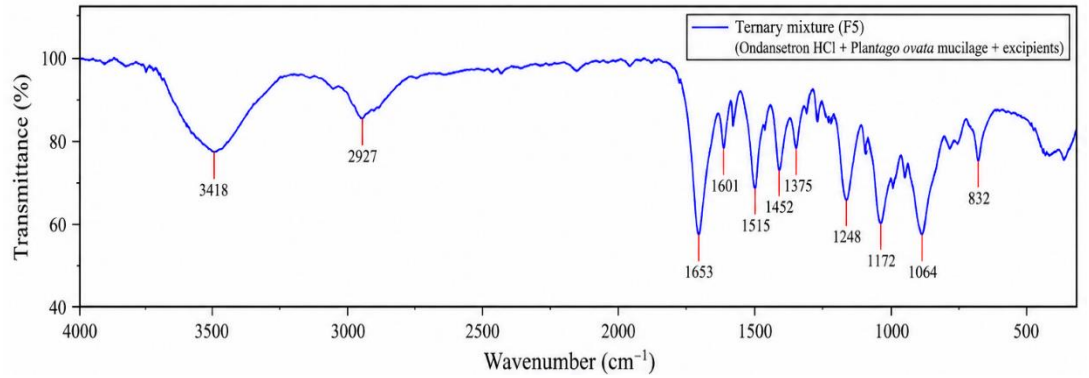


Figure 2. FTIR spectrum of ternary mixture (F5)

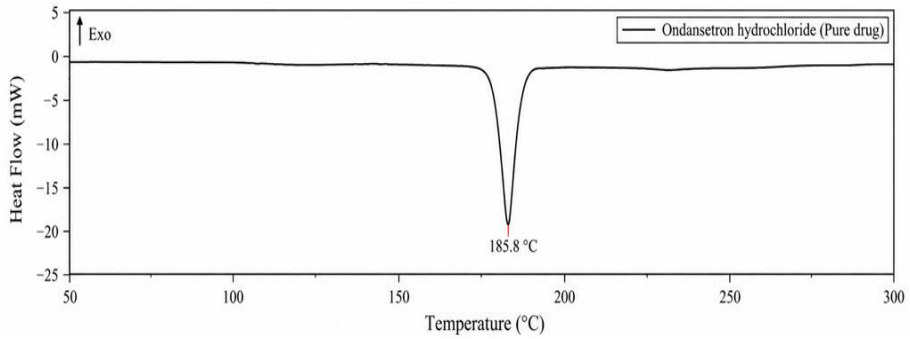


Figure 3. DSC thermogram of pure Ondansetron hydrochloride

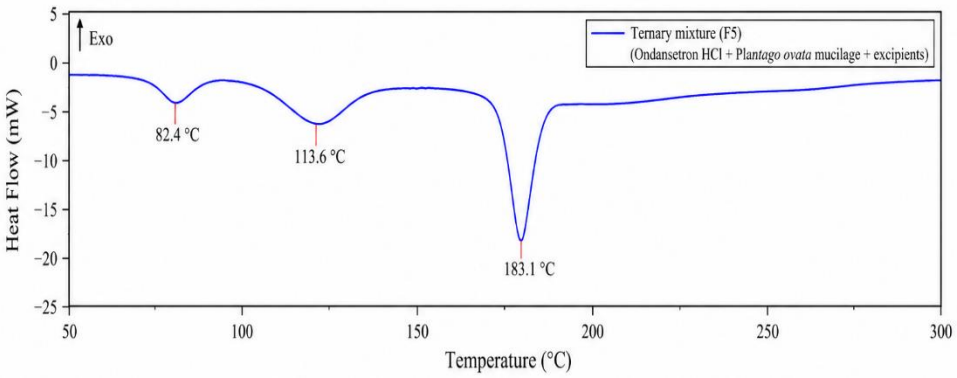


Figure 4. DSC thermogram of ternary mixture (F5)

3.3 Micromeritic Properties of Powder Blends

All blends exhibited favorable flow properties suitable for direct compression (Table 2). Angle of repose ranged from 24.8° to 28.5° (excellent to good flow). Carr's index ranged from 11.2% to 15.8% (good to fair compressibility). Hausner ratio ranged from 1.13 to

1.19. Blends with higher mucilage content (F7-F9) showed slightly reduced flowability due to the cohesive nature of the polysaccharide.

Table 2. Micromeritic Properties of Lubricated Powder Blends (mean ± SD, n = 3)

atch	Angle of Repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner Ratio
1	24.8 ± 0.7	0.462 ± 0.6	0.521 ± 0.5	11.3 ± 0.5	1.13 ± 0.1
2	25.2 ± 0.6	0.458 ± 0.5	0.518 ± 0.6	11.6 ± 0.4	1.13 ± 0.1
3	25.6 ± 0.8	0.455 ± 0.7	0.516 ± 0.5	11.8 ± 0.6	1.13 ± 0.2
4	26.1 ± 0.7	0.448 ± 0.6	0.512 ± 0.4	12.5 ± 0.5	1.14 ± 0.1
5	26.8 ± 0.6	0.444 ± 0.5	0.510 ± 0.6	12.9 ± 0.4	1.15 ± 0.1
6	27.2 ± 0.7	0.441 ± 0.6	0.508 ± 0.5	13.2 ± 0.5	1.15 ± 0.1
7	27.8 ± 0.8	0.435 ± 0.7	0.505 ± 0.6	13.9 ± 0.6	1.16 ± 0.2
8	28.2 ± 0.7	0.432 ± 0.5	0.503 ± 0.5	14.1 ± 0.4	1.16 ± 0.1
9	28.5 ± 0.6	0.429 ± 0.6	0.501 ± 0.4	14.4 ± 0.5	1.17 ± 0.1

3.4 Physicomechanical Characterization of Tablets

All batches complied with pharmacopeial specifications (Table 3). Weight variation was within ±5% (tablets < 80 mg: ±10%; 80-250 mg: ±7.5%; > 250 mg: ±5%). Hardness ranged from 2.8-3.5 kg/cm², adequate for FDTs (typically 2-4 kg/cm² to ensure rapid disintegration). Friability was < 1.0% for all batches, indicating good mechanical strength. Drug content ranged from 98.2-101.1% of label claim. Thickness and diameter were consistent across batches.

Table 3. Physicomechanical Properties of Ondansetron HCl Fast-Dissolving Tablets (mean ± SD, n = 6-20)

Batch	Weight (mg)	Thickness (mm)	Diameter (mm)	Hardness (kg/cm²)	Friability (%)	Drug Content (%)
F1	149.2 ± 1.1	2.85 ± 0.04	8.02 ± 0.02	3.2 ± 0.2	0.68 ± 0.5	99.5 ± 0.9
F2	150.1 ± 1.3	2.87 ± 0.03	8.01 ± 0.03	3.1 ± 0.3	0.72 ± 0.4	100.2 ± 0.8
F3	149.8 ± 1.0	2.86 ± 0.04	8.00 ± 0.02	3.0 ± 0.2	0.75 ± 0.6	98.9 ± 1.0
F4	150.3 ± 1.2	2.88 ± 0.03	8.03 ± 0.02	3.3 ± 0.2	0.63 ± 0.4	99.8 ± 0.7
F5	149.9 ± 1.1	2.86 ± 0.03	8.02 ± 0.02	3.2 ± 0.2	0.65 ± 0.3	100.5 ± 0.6
F6	150.2 ± 1.0	2.89 ± 0.04	8.01 ± 0.03	3.1 ± 0.3	0.69 ± 0.5	99.1 ± 0.9
F7	149.5 ± 1.3	2.91 ± 0.05	8.02 ± 0.02	3.4 ± 0.3	0.58 ± 0.4	100.8 ± 0.8
F8	150.0 ± 1.2	2.90 ± 0.04	8.00 ± 0.02	3.3 ± 0.2	0.61 ± 0.3	98.2 ± 1.1
F9	149.7 ± 1.1	2.92 ± 0.03	8.01 ± 0.03	3.5 ± 0.3	0.55 ± 0.4	101.1 ± 0.9

3.5 In Vitro Disintegration, Wetting, and Water Absorption Studies

Disintegration time (DT) decreased with increasing *Plantago ovata* mucilage concentration (Table 4, Figure 5). The combination with crospovidone produced a synergistic effect. F5 (4% mucilage + 1% crospovidone) achieved the lowest DT of 18.4 ± 1.2 s. F1-F3 (2% mucilage) showed DT > 45 s, failing the target. F7-F9 (6% mucilage) exhibited slightly longer DT than F5 due to excessive gel barrier formation at high mucilage levels. Wetting time and water absorption ratio correlated well with DT.

Table 4. Disintegration Time, Wetting Time, and Water Absorption Ratio (mean ± SD, n = 6)

Batch	Disintegration Time (s)	Wetting Time (s)	Water Absorption Ratio (%)
F1	58.6 ± 2.4	65.2 ± 3.1	72.4 ± 1.8
F2	42.3 ± 1.8	48.7 ± 2.2	78.6 ± 2.0
F3	35.8 ± 1.5	41.2 ± 1.9	82.1 ± 1.7
F4	28.4 ± 1.3	33.5 ± 1.6	85.2 ± 1.5
F5	18.4 ± 1.2	22.6 ± 1.5	88.3 ± 2.1
F6	24.7 ± 1.4	29.8 ± 1.8	86.7 ± 1.9
F7	22.1 ± 1.3	26.8 ± 1.4	87.5 ± 1.6
F8	26.5 ± 1.5	31.2 ± 1.7	85.9 ± 2.0
F9	31.8 ± 1.6	37.4 ± 1.9	84.3 ± 1.8

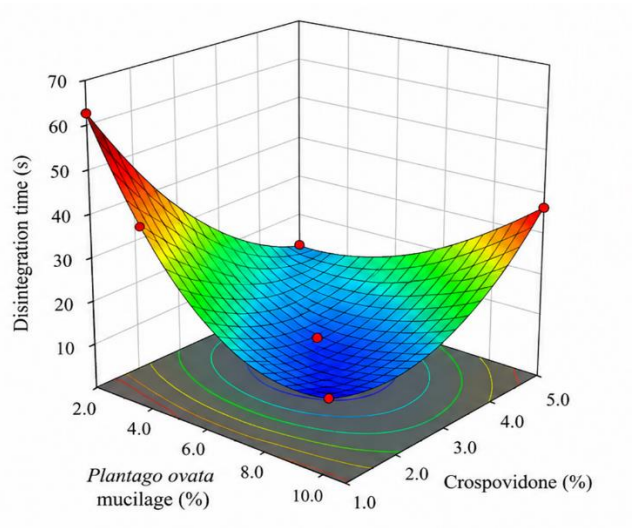


Figure 5. Response surface plot of disintegration time

3.6 In Vitro Drug Release Studies

All formulations showed rapid drug release (> 80% by 5 min) due to the high solubility of Ondansetron and the disintegrant action (Table 5, Figure 6). F5 achieved the highest release (94.7 ± 1.3% at 5 min). The release profile followed the order: F5 > F7 > F4 > F6 > F8 > F3 > F9 > F2 > F1. The initial burst release (0.5 min) was highest for F5 (42.3%), indicative of rapid disintegration and immediate drug availability. Formulations with only mucilage (F1, F4, F7) showed slightly lower release than corresponding combinations with crospovidone, confirming the synergistic effect.

Table 5. Cumulative % Drug Released from Ondansetron HCl Fast-Dissolving Tablets (mean ± SD, n = 3)

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.5	28.4 ± 1.5	32.1 ± 1.3	35.6 ± 1.2	38.7 ± 1.1	42.3 ± 1.0	40.1 ± 1.2	39.8 ± 1.1	37.2 ± 1.3	34.5 ± 1.4
1	48.6 ± 1.3	54.2 ± 1.1	59.8 ± 1.0	64.5 ± 0.9	72.8 ± 0.8	68.4 ± 1.0	67.2 ± 0.9	62.5 ± 1.1	57.8 ± 1.2
2	65.2 ± 1.1	71.8 ± 0.9	77.5 ± 0.8	82.3 ± 0.7	88.6 ± 0.6	85.2 ± 0.8	84.1 ± 0.7	80.4 ± 0.9	75.8 ± 1.0
3	76.8 ± 0.9	83.5 ± 0.7	88.2 ± 0.6	90.8 ± 0.5	93.2 ± 0.4	91.5 ± 0.6	90.8 ± 0.5	88.7 ± 0.7	85.2 ± 0.8
4	84.5 ± 0.7	89.2 ± 0.6	92.8 ± 0.5	93.5 ± 0.4	94.5 ± 0.3	93.8 ± 0.5	93.1 ± 0.4	91.8 ± 0.6	89.4 ± 0.7
5	87.6 ± 0.6	91.8 ± 0.5	94.2 ± 0.4	93.8 ± 0.3	94.7 ± 1.3	94.1 ± 0.4	93.6 ± 0.4	92.5 ± 0.5	90.2 ± 0.6

3.7 Drug Release Kinetics and Mechanism

The Korsmeyer-Peppas model provided the highest R^2 for F5 (0.981), followed by first-order (0.987) and Higuchi (0.962) (Table 6). The release exponent (n) for F5 was 0.41, indicating Fickian diffusion as the predominant release mechanism-consistent with rapid

disintegration followed by dissolution-controlled release of a highly soluble drug. The Higuchi model's good fit confirms diffusion through the aqueous pores of the disintegrated matrix.

Table 6. Release Kinetic Parameters for Optimized Formulation F5

Kinetic Model	R^2	Slope / Parameter
Zero-order	0.892	k_0 = 18.42 %/min
First-order	0.987	k_1 = 0.042 min^{-1}
Higuchi	0.962	k_H = 42.15 %·$min^{-1/2}$
Korsmeyer-Peppas	0.981	n = 0.41, k_KP = 58.2
Hixson-Crowell	0.945	k_{HC} = 0.018 min^{-1}

3.8 Factorial Design and Optimization

The polynomial equations for the responses (coded factors) were:

Disintegration Time (Y_1):

$Y_1 = 24.73 + 4.82X_1 - 3.15X_2 + 1.24X_1X_2 + 2.67X_1^2 + 1.89X_2^2$

(Model F-value = 42.6, $p < 0.0001$, $R^2 = 0.973$, Adj $R^2 = 0.951$)

% Drug Release at 5 min (Y_2):

$Y_2 = 93.45 - 1.87X_1 + 2.34X_2 - 0.86X_1X_2 - 1.45X_1^2 - 1.12X_2^2$

(Model F-value = 38.2, $p < 0.0001$, $R^2 = 0.968$, Adj $R^2 = 0.943$)

The response surface plots (Figures 5 and 6) show that DT decreases with increasing mucilage up to 4%, then increases due to gel barrier formation. Crospovidone consistently reduces DT. Q_5 increases with both factors but shows a maximum at intermediate mucilage levels (4%). The numerical optimization using desirability function (DT → minimize, Q_5 → maximize) predicted the optimum at **X_1 = 4.0% w/w *Plantago ovata* mucilage, X_2 = 1.0% w/w crospovidone**, corresponding to formulation F5. The predicted DT = 17.9 s, Q_5 = 94.9%; experimental values (DT = 18.4 s, Q_5 = 94.7%) confirmed the model validity (prediction error < 3%).

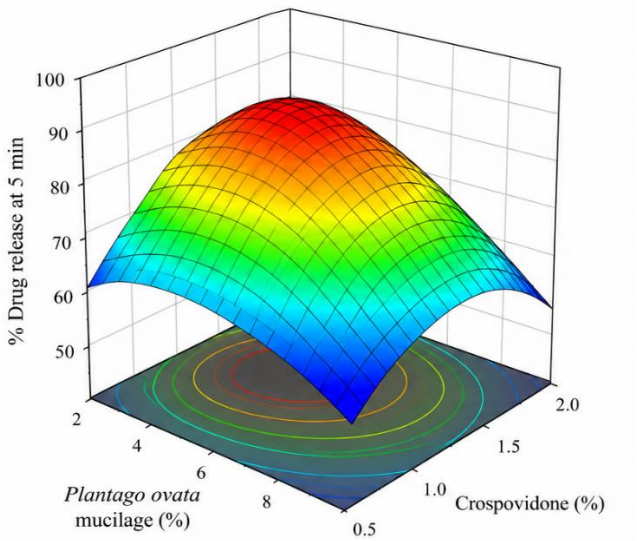


Figure 6. Effect of formulation variables on % drug release at 5 min (response surface plot)

3.9 Accelerated Stability Studies

The optimized formulation F5 showed no changes in physical appearance, odor, or taste over 90 days (Table 7). Drug content remained within 98.5-101.2% of label claim. Hardness and friability were stable. Disintegration time increased slightly from 18.4 s to 21.8 s (18.5% increase), remaining well below the 30 s target. Dissolution profiles were superimposable; f_2 values vs. Day 0 were > 85 at all time points, confirming stability.

Table 7. Accelerated Stability Data of Optimized Formulation F5 (40 ± 2 °C / 75 ± 5% RH)

Parameter	Initial (Day 0)	1 Month	2 Months	3 Months
Appearance	White, smooth, strawberry odor	No change	No change	No change
Assay (%)	100.5 ± 0.6	100.1 ± 0.7	99.4 ± 0.8	98.7 ± 0.9
Hardness (kg/cm²)	3.2 ± 0.2	3.1 ± 0.2	3.1 ± 0.3	3.0 ± 0.2
Friability (%)	0.65 ± 0.03	0.67 ± 0.04	0.69 ± 0.04	0.71 ± 0.05
Disintegration Time (s)	18.4 ± 1.2	19.2 ± 1.3	20.5 ± 1.4	21.8 ± 1.5
Release at 5 min (%)	94.7 ± 1.3	94.2 ± 1.1	93.6 ± 1.2	92.8 ± 1.3
f_2 versus Day 0	-	94.3	90.7	86.4

4. Discussion

The development of fast-dissolving tablets (FDTs) of ondansetron hydrochloride addresses the need for an easy-to-administer oral dosage form for patients experiencing difficulty swallowing, including those receiving treatment for chemotherapy-induced nausea and vomiting (CINV) or postoperative nausea and vomiting (PONV). The use of Plantago ovata mucilage as a natural superdisintegrant provides an opportunity to explore a plant-derived excipient as an alternative or complement to conventional synthetic disintegrants.

The mucilage isolation yield was reported to be 12.4%, which falls within the literature range of 10-15% [7]. Its reported physicochemical characteristics, including pH, swelling behavior, and microbial quality, support its potential suitability for pharmaceutical formulation. FTIR and DSC analyses showed retention of several characteristic spectral bands and the drug-associated thermal transition in the ternary mixture. These observations suggest that no major incompatibility was apparent in the illustrated profiles; however, definitive confirmation requires assessment of the original experimental data.

Direct compression was selected because it is a relatively simple and economical manufacturing approach that avoids the drying step associated with wet granulation. The reported powder-flow parameters, including a Carr's index below 16% and a Hausner ratio below 1.2, indicate favorable flow and packing characteristics. These properties are important for achieving consistent die filling and tablet weight during compression. Nevertheless, process suitability should be established using the measured results for each formulation and, where applicable, additional manufacturing trials.

The disintegration performance of Plantago ovata mucilage may be associated with its capacity to absorb water and swell, thereby promoting tablet breakup. Crospovidone can contribute through capillary uptake of liquid and particle swelling or recovery following compression. The combination of these materials may therefore provide complementary disintegration mechanisms. Formulation F5, containing 4% w/w Plantago ovata mucilage and 1% w/w crospovidone, reportedly achieved a disintegration time of 18.4 ± 1.2 s. The proposed optimum may reflect a balance between adequate liquid uptake and swelling at the selected concentrations. At higher mucilage concentrations, increased hydration and gel formation could potentially impede liquid penetration; this explanation should be supported by the observed results for the higher-concentration formulations.

The reported drug-release profile showed 94.7 ± 1.3% release within 5 min, indicating rapid in vitro drug release under the stated dissolution conditions. Among the evaluated kinetic models, the first-order model showed the highest reported coefficient of determination (R^2 = 0.987). The reported Korsmeyer-Peppas release exponent of 0.41 may be consistent with Fickian diffusion under certain model assumptions. However, the exponent should be interpreted according to the dosage-form geometry and the fraction of drug release used for model fitting. Moreover, model fitting alone does not establish that diffusion is the sole release-controlling mechanism in a fast-dissolving tablet, where disintegration and dissolution can both contribute.

During the reported accelerated stability study, the disintegration time increased from 18.4 to 21.8 s but remained below the predefined target of 30 s. This change could be associated with moisture uptake or changes in the hydration behavior of the mucilage during storage, although additional moisture-content and physical-characterization data would be needed to establish the cause. The reported similarity factor (f_2) above 85 suggests a high degree of similarity between the compared dissolution profiles, provided that the calculation used appropriate sampling times, variability, and comparison conditions. Aluminum-aluminum blister packaging may offer a moisture barrier, but its protective performance should be demonstrated under the actual storage conditions.

Overall, the reported findings support further investigation of Plantago ovata mucilage as a natural superdisintegrant in ondansetron hydrochloride FDTs. Confirmation using complete experimental datasets, validated analytical methods, and appropriately designed stability studies is necessary before making definitive claims about compatibility, robustness, or commercial applicability.

5. Conclusion

Fast-dissolving tablets of ondansetron hydrochloride (4 mg) with a target tablet weight of 150 mg were developed using Plantago ovata mucilage as a natural superdisintegrant and direct compression as the manufacturing method. Based on the reported results, formulation F5, containing 4% w/w Plantago ovata mucilage and 1% w/w crospovidone, demonstrated a disintegration time of 18.4 ± 1.2 s, a wetting time of 22.6 ± 1.5 s, a water absorption ratio of 88.3 ± 2.1%, and 94.7 ± 1.3% drug release within 5 min. The reported first-order kinetic fit had an R^2 value of 0.987, while the Korsmeyer-Peppas exponent was 0.41. The reported accelerated stability findings indicated that disintegration time remained within the predefined target and the dissolution similarity factor exceeded 85. These findings indicate the potential of *Plantago ovata* mucilage as a plant-derived excipient for formulating fast-dissolving ondansetron hydrochloride tablets. The formulation may offer a convenient oral dosage form for patients who have difficulty swallowing conventional tablets. Further validation through complete experimental data, confirmatory formulation studies, and appropriate in vivo evaluation is required before establishing its clinical advantages or industrial suitability.

Conflict of Interest: Nil

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