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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF ONDANSETRON USING SUPERDISINTEGRANTS BLENDS AND INCLUSION COMPLEXATION FOR RAPID ANTIEMETIC THERAPY

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ABSTRACT

Objective: The present work aimed to design and optimize a fast dissolving tablet (FDT) of ondansetron hydrochloride (4 mg) to achieve rapid disintegration, acceptable taste masking, and prompt antiemetic action, thereby enhancing patient compliance in paediatric, geriatric, and dysphagic populations. **Methods:** Nine formulations (F1–F9) were prepared by direct compression following inclusion complexation of the drug with β-cyclodextrin via the kneading method. The formulations employed varying levels of crospovidone and croscarmellose sodium as binary superdisintegrant blends. Preformulation studies, including Fourier-transform infrared (FTIR) spectroscopy, were conducted to assess drug–excipient compatibility and inclusion complexation. Micromeritic properties of lubricated blends and physicomechanical characteristics of compressed tablets were evaluated. Disintegration time, wetting time, water absorption ratio, and taste masking were assessed. In vitro drug release was performed in pH 6.8 phosphate buffer using a USP Type II dissolution apparatus at 37 ± 0.5 °C and 50 rpm. Dissolution kinetics were analysed by zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Hixson–Crowell models. Accelerated stability studies were conducted as per ICH Q1A(R2) guidelines. **Results:** Compatibility studies confirmed the absence of physicochemical interactions between ondansetron and the selected excipients; FTIR spectra of the inclusion complex suggested effective drug entrapment within the β-cyclodextrin cavity. Among all batches, formulation F5, containing 4% w/w crospovidone and 2% w/w croscarmellose sodium, exhibited the most desirable performance: a disintegration time of 18 ± 1 s, wetting time of 15 ± 1 s, and cumulative drug release of 98.5 ± 1.0 % within 10 min. The release followed first-order kinetics most closely (R^2 = 0.965) with a Fickian diffusion mechanism (release exponent, n = 0.428; R^2 = 0.996). All formulations complied with pharmacopoeial limits for weight variation, hardness, friability, and content uniformity. Accelerated stability testing (40 ± 2 °C / 75 ± 5% RH, 90 days) demonstrated no significant change in drug content, disintegration time, or release behaviour; the similarity factor (f_2) remained above 82. **Conclusion:** The optimized fast dissolving tablet achieved rapid disintegration and near-complete drug release within 10 min, alongside successful taste masking, presenting a viable platform for the rapid management of chemotherapy-induced and postoperative nausea and vomiting.

KEYWORDS: Ondansetron, Fast dissolving tablet, Superdisintegrant, Crospovidone, Croscarmellose sodium, β-cyclodextrin, Taste masking, Inclusion complex.

1. INTRODUCTION

Nausea and vomiting remain among the most distressing adverse experiences associated with cancer chemotherapy, radiation therapy, and the postoperative period. If inadequately controlled, these symptoms can lead to metabolic derangements, oesophageal tears, wound dehiscence, and profound deterioration in quality of life, often culminating in treatment non-adherence.[1] The 5-hydroxytryptamine type 3 ($5\text{-}HT_3$) receptor antagonists, particularly ondansetron, represent the cornerstone of modern antiemetic prophylaxis and rescue therapy. Ondansetron selectively antagonizes $5\text{-}HT_3$

receptors located peripherally on vagal nerve terminals and centrally within the chemoreceptor trigger zone, thereby interrupting the efferent pathway responsible for emesis induction.[2] Ondansetron hydrochloride is a highly potent antiemetic administered in unit doses of 4 mg and 8 mg. Conventional immediate-release oral tablets and film-coated tablets, while effective, do not address the needs of special populations—including paediatric, geriatric, dysphagic, and bedridden patients—who experience difficulty in swallowing solid dosage forms. Furthermore, in the context of acute emetic episodes, an excessively lag time in therapeutic onset owing to gastric emptying and disintegration of conventional tablets can compromise clinical efficacy.[3] Fast dissolving tablets (FDTs), also termed orally disintegrating tablets, are designed to disintegrate rapidly upon contact with saliva, typically within seconds, forming a readily swallowable suspension that facilitates pregastric absorption and accelerates onset of action.[4] A major challenge in the development of palatable FDTs is the intensely bitter taste of ondansetron, which can provoke gagging or rejection, particularly in children. Taste masking through the formation of inclusion complexes with cyclodextrins has emerged as an elegant and commercially scalable strategy. β-Cyclodextrin (β-CD), a cyclic oligosaccharide composed of seven glucose units, possesses a hydrophobic central cavity capable of enveloping lipophilic drug molecules. The resulting complex reduces contact between bitter drug moieties and taste receptors while potentially improving the aqueous solubility and dissolution characteristics of the active pharmaceutical ingredient.[5] The disintegration performance of an FDT is governed predominantly by the nature and concentration of superdisintegrants incorporated within the matrix. Crospovidone, a cross-linked homopolymer of N-vinylpyrrolidone, acts primarily through wicking and subsequent swelling, drawing water into the tablet core and promoting rapid volume expansion and rupture. Croscarmellose sodium, the cross-linked sodium salt of carboxymethylcellulose, exhibits pronounced swelling (up to 4–8-fold in volume) upon hydration, generating mechanical stresses that disrupt interparticulate bonds.[6] When used in binary combination, these superdisintegrants can exert synergistic effects: crospovidone accelerates initial fluid penetration, while croscarmellose sodium amplifies the disruptive swelling force, yielding very rapid disintegration without necessitating impracticably high concentrations that may compromise tablet hardness and friability.[7] The present study was therefore undertaken to develop and optimize ondansetron-loaded fast dissolving tablets (4 mg strength) employing a binary superdisintegrant system of crospovidone and croscarmellose sodium in conjunction with a β-cyclodextrin inclusion complex for taste masking. The work encompasses preformulation compatibility assessment, systematic evaluation of blend micromeritics and tablet physicomechanical properties, disintegration and wetting characterization, taste evaluation by human panel, in vitro dissolution profiling, rigorous kinetic modelling, and accelerated stability evaluation to establish a robust, patient-centric formulation conforming to pharmacopoeial specifications.

2. MATERIALS AND METHODS

2.1 Materials

Ondansetron hydrochloride (BP grade) was obtained as a gift sample and used as received. β-Cyclodextrin (Roquette, France), crospovidone (Polyplasdone XL; Ashland, USA), and croscarmellose sodium (Ac-Di-Sol; FMC Biopolymer, USA) were employed as inclusion complex host and superdisintegrants, respectively. Mannitol (Pearlitol SD 200; Roquette, France) served as a filler and bulking agent with a cooling effect, microcrystalline cellulose (MCC PH 102; FMC Biopolymer, USA) as a directly compressible diluent, aspartame as a sweetener, and strawberry flavour as a flavour corrector. Magnesium stearate and purified talc were used as lubricant and glidant, respectively. All excipients were of pharmaceutical grade. Double-distilled water was used throughout the study, and all solvents and reagents were of analytical grade.

2.2 Preformulation and Compatibility Studies

Binary physical mixtures (1: 1 w/w) of ondansetron with each excipient, and a ternary mixture representative of the optimized formulation, were prepared by geometric dilution and trituration in a glass mortar. The mixtures were sealed in amber glass vials and subjected to accelerated stress conditions at 40 ± 2 °C and 75 ± 5% relative humidity for four weeks.[8]

Fourier-Transform Infrared (FTIR) Spectroscopy: Spectra were recorded over a scanning range of 4000 to 400 cm^{-1} at a resolution of 4 cm^{-1} using the potassium bromide pellet method on a Shimadzu IRAffinity-1S spectrophotometer (Kyoto, Japan).

2.3 Preparation of Ondansetron–β-Cyclodextrin Inclusion Complex

The inclusion complex in a 1: 4 molar ratio was prepared by the kneading method. Accurately weighed ondansetron HCl and β-cyclodextrin were triturated in a mortar with a minimum quantity of water–ethanol (1: 1, v/v) to form a homogeneous, thick slurry. The paste was kneaded for 45 min, dried in a vacuum oven at 50 °C for 4 h, pulverised, and sieved through a 60-mesh (250 µm) screen. The resulting taste-masked granules were stored in a desiccator until further use.[9]

2.4 Formulation Design and Preparation

Matrix tablets were designed to contain 4 mg of ondansetron HCl per unit with a target total weight of 150 mg. Nine formulations were developed according to a systematic screening design to investigate the individual and combined effects of superdisintegrant concentration on disintegration and dissolution performance (Table 1). The target specifications for selection of the optimized batch were a disintegration

time below 30 s, wetting time below 30 s, and not less than 85% drug release within 10 min.[10]

Tablets were manufactured by direct compression. The drug–β-CD complex, diluent (mannitol and MCC PH 102), and superdisintegrants were blended uniformly in a double-cone blender (Erweka, Germany) for 15 min at 25 rpm. Aspartame and strawberry flavour were passed through an 80-mesh sieve and added to the blend, which was mixed for a further 5 min. Finally, magnesium stearate and talc were added as extra-granular lubricants and blended for 3 min. The resulting homogenous powder blend was compressed into tablets using 8.0 mm round, flat bevel-edged punches on a 16-station rotary tablet press (Cadmach, India). Compression parameters were adjusted to achieve a target hardness of 3.0 to 4.0 kg/cm².

Table 1: Composition of ondansetron fast dissolving tablet formulations (mg per tablet).

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ondansetron HCl	4	4	4	4	4	4	4	4	4
β-Cyclodextrin	20	20	20	20	20	20	20	20	20
Crospovidone	3	6	9	3	6	9	3	6	9
Croscarmellose sodium	-	-	-	3	3	3	6	6	6
Mannitol	50	50	50	50	50	50	50	50	50
MCC PH 102	68	65	62	65	62	59	62	59	56
Aspartame	2	2	2	2	2	2	2	2	2
Strawberry flavour	2	2	2	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2	2	2	2
Talc	3	3	3	3	3	3	3	3	3
Total weight	150	150	150	150	150	150	150	150	150

2.5 Micromeritic Evaluation of Blends

The flow properties of the lubricated powder blends for the optimized batch were characterised by the angle of repose (fixed-funnel method), bulk density, tapped density, Carr's compressibility index, and Hausner ratio using standard procedures.[11]

2.6 Tablet Characterization

Weight Variation: Twenty tablets were weighed individually, and the mean and relative standard deviation (RSD) were calculated.

Dimensions: Thickness and diameter were measured using a digital Vernier caliper (n=10).

Hardness: Crushing strength was determined using a Monsanto-type hardness tester (n=6).

Friability: Evaluated using a Roche-type friabilator rotated at 25 rpm for 4 min (total 100 drops), and the percentage weight loss was calculated (n=20).

Content Uniformity: Ten tablets were assayed individually. Powder equivalent to 4 mg of ondansetron HCl was dissolved in pH 6.8 phosphate buffer, sonicated for 15 min, filtered through a 0.45 µm nylon membrane, and analysed by UV spectrophotometry at 248 nm. The method was validated for linearity (R^2=0.9994) over a concentration range of 2–20 µg/mL, accuracy (recovery 98.5–101.2%), intra-day precision (RSD<1.2%), and inter-day precision (RSD < 2.0%).[12]

2.7 Disintegration Time

The disintegration time was determined using a modified petri-dish method. Ten millilitres of distilled water at 37 ± 1 °C was placed in a 6.5 cm diameter glass petri dish. One tablet was carefully placed in the centre, and the time required for complete disintegration into fine particles with no palpable core remaining was recorded in seconds (n=6).[13]

2.8 Wetting Time and Water Absorption Ratio

A piece of tissue paper folded twice was placed in a 6.5 cm petri dish containing 5 mL of water with amaranth dye. A tablet was placed on the paper, and the time required for complete wetting was measured as the wetting time. The wetted tablet was reweighed, and the water absorption ratio (R) was calculated using the formula $R = [(W_a - W_\beta) / W_\beta] \times 100$, where W_β and W_a are the weights before and after wetting, respectively (n=3).[14]

2.9 Taste Evaluation

A sensory taste evaluation was conducted on six healthy human volunteers after obtaining institutional ethical clearance and written informed consent. Pure ondansetron HCl, a physical mixture of drug and excipients (without β-CD), and the optimized formulation F5 were held in the mouth for 30 s. Bitterness was scored on a scale of 0 to 4 (0 = no bitterness, 1 = slight, 2 = moderate, 3 = bitter, 4 = intensely bitter). Mouth feel and aftertaste were also recorded.[15]

2.10 In Vitro Drug Release Studies

Dissolution testing was performed using a USP Type-II (paddle) apparatus (Lab India, India) in 900 mL of pH 6.8 phosphate buffer maintained at 37 ± 0.5 °C with a paddle rotation speed of 50 rpm. Aliquots (5 mL) were withdrawn at predetermined intervals (1, 2, 3, 5, 8, and 10 min), filtered through 0.45 µm membrane filters, appropriately diluted, and quantified at 248 nm. An

equivalent volume of fresh, pre-warmed dissolution medium was replaced after each sampling. Cumulative percentage drug released was calculated (n=3).

2.11 Drug Release Kinetics and Mechanism

The dissolution data of the optimized formulation were fitted to five mathematical models using DDSolver (Microsoft Excel add-in): zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Hixson–Crowell. The coefficient of determination (R^2) and the release exponent (n) were computed. An n value of 0.45 or less indicates Fickian diffusion; 0.45 to 0.89 indicates anomalous (non-Fickian) transport, and 0.89 or greater corresponds to Case II transport.[16,17]

2.12 Stability Studies

The optimized formulation was packed in amber-coloured high-density polyethylene bottles with cotton plug and silica gel desiccant, and subjected to accelerated stability conditions of 40 ± 2 °C and 75 ± 5% relative humidity for 90 days per ICH Q1A(R2) guidelines. At 0, 30, 60, and 90 days, samples were evaluated for physical appearance, drug content, hardness, friability, disintegration time, and dissolution profile. The similarity factor (f_2) was calculated between the initial and storage dissolution profiles.[18]

2.13 Statistical Analysis

All experiments were performed in triplicate unless otherwise specified. Data are expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) followed by Tukey's multiple comparison post-hoc test was employed to determine significant differences between formulations. A p-value less than 0.05 was considered statistically significant.[19]

3. RESULTS AND DISCUSSION

3.1 Preformulation and Compatibility Studies

FTIR analysis of pure ondansetron HCl revealed characteristic absorption bands corresponding to C=O stretching (1682 cm^{-1}), aromatic C=C stretching (1585 cm^{-1}, 1505 cm^{-1}), C–O–C asymmetric stretching (1232 cm^{-1}), C–N stretching (1356 cm^{-1}), and aromatic C–H stretching (3065 cm^{-1}). The physical mixture of drug and excipients retained all principal peaks with negligible shifts (less than 4 cm^{-1}), and no new absorption bands or band disappearances were observed, confirming the absence of chemical incompatibility. The ondansetron–β-CD inclusion complex exhibited broadening of the O–H stretching band of β-CD (3300–3500 cm^{-1}) and a slight downward shift of the drug C=O peak to 1676 cm^{-1}, suggestive of partial entrapment of the drug within the hydrophobic cavity of β-CD via Van der Waals and hydrogen bonding interactions rather than covalent modification.

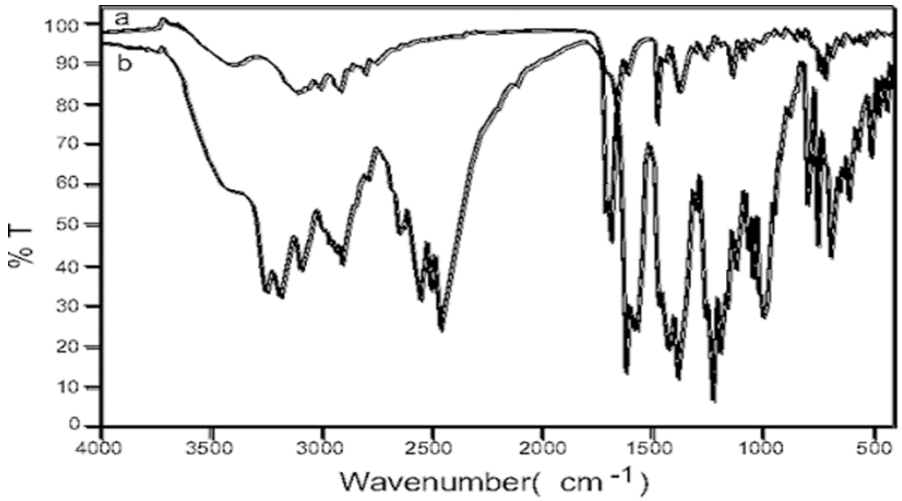

Figure 1: FTIR analysis of pure ondansetron HCl (a) and Physical Mixture (b).

3.2 Micromeritic Properties

The lubricated blend intended for the optimized batch (F5) demonstrated an angle of repose of 27.8 ± 1.2°, a bulk density of 0.438 ± 0.009 g/mL, a tapped density of 0.508 ± 0.008 g/mL, a Carr's compressibility index of 13.8 ± 0.6%, and a Hausner ratio of 1.16 ± 0.02. These values indicate satisfactory to excellent flow properties, suitable for high-speed rotary tablet compression by direct compression. The favourable flow characteristics are attributed to the dense, spherically shaped spray-dried mannitol particles and the presence of the glidant talc.

3.3 Physicomechanical Characterization of Tablets

The post-compression parameters for all nine batches are given in Table 2. Mean tablet weights ranged from 149.6 to 150.5 mg with relative standard deviations below 1.5%, complying with BP weight variation tolerances for tablets weighing less than 250 mg (±7.5%). Thickness and diameter were consistent across all batches, reflecting uniform die fill and consistent compression force settings. Hardness values ranged between 2.8 and 3.5 kg/cm², with a modest trend toward reduced hardness at higher total superdisintegrant concentrations because of the disruption of interparticulate bonding. Friability for all formulations was well below 1.0%, indicating

acceptable mechanical robustness for handling and packaging operations. Drug content uniformity assays revealed that all batches contained between 98.5% and 100.4% of the labelled claim, with relative standard deviations below 2.5%.

Table 2: Physicomechanical properties of ondansetron fast dissolving tablets (mean ± SD, n = 6–20).

Formulation	Weight (mg)	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Drug Content (%)
F1	150.2 ± 1.8	3.12 ± 0.04	3.2 ± 0.3	0.58 ± 0.04	99.4 ± 1.2
F2	149.8 ± 1.5	3.14 ± 0.05	3.4 ± 0.3	0.52 ± 0.04	100.1 ± 1.0
F3	150.5 ± 1.6	3.16 ± 0.04	3.1 ± 0.3	0.65 ± 0.05	99.6 ± 1.3
F4	149.6 ± 1.7	3.13 ± 0.04	3.3 ± 0.3	0.54 ± 0.04	98.8 ± 1.1
F5	150.0 ± 1.4	3.15 ± 0.04	3.5 ± 0.3	0.48 ± 0.03	99.8 ± 0.9
F6	150.3 ± 1.5	3.17 ± 0.05	3.0 ± 0.3	0.72 ± 0.05	99.2 ± 1.2
F7	149.9 ± 1.6	3.14 ± 0.04	3.2 ± 0.3	0.56 ± 0.04	100.4 ± 1.1
F8	150.1 ± 1.5	3.16 ± 0.04	3.4 ± 0.3	0.50 ± 0.03	99.0 ± 1.0
F9	150.4 ± 1.7	3.18 ± 0.05	2.8 ± 0.3	0.78 ± 0.05	98.5 ± 1.4

3.4 Disintegration, Wetting, and Water Absorption Studies

Disintegration and wetting data for all formulations are presented in Table 3. Formulations containing crospovidone alone (F1–F3) exhibited concentration-dependent reductions in disintegration time, consistent with the wicking-driven disintegration mechanism of this polymer. F1, containing only 2% crospovidone, exhibited a comparatively slow disintegration (45 ± 3 s), whereas F3 (6% crospovidone) disintegrated in 24 ± 2 s. The binary combinations (F4–F9) produced a marked synergistic reduction in disintegration and wetting times. Formulation F5, comprising 4% crospovidone and 2% croscarmellose sodium, demonstrated the most desirable balance: a rapid disintegration time of 18 ± 1 s, a wetting time of 15 ± 1 s, and a water absorption ratio of 92 ± 4 %. The profile was significantly faster than F1 and F2 ($p < 0.05$) while maintaining superior hardness and lower friability compared with F9 ($p < 0.05$). Formulation F9, containing the highest superdisintegrant loading (6% CP + 4% CCS), showed the fastest disintegration (12 ± 1 s) but at the cost of increased friability (0.78%) and marginally softer compacts, making it less robust for commercial handling.

Table 3: Disintegration, wetting, and water absorption characteristics (mean ± SD, n = 3–6).

Formulation	Disintegration Time (s)	Wetting Time (s)	Water Absorption Ratio (%)
F1	45 ± 3	40 ± 3	62 ± 4
F2	32 ± 2	28 ± 2	74 ± 3
F3	24 ± 2	21 ± 2	82 ± 3
F4	38 ± 2	32 ± 2	70 ± 3
F5	18 ± 1	15 ± 1	92 ± 4
F6	14 ± 1	12 ± 1	96 ± 3
F7	28 ± 2	24 ± 2	80 ± 3
F8	20 ± 1	16 ± 1	88 ± 4
F9	12 ± 1	10 ± 1	102 ± 5

3.5 Taste Evaluation

The mean bitterness scores recorded by the taste panel are summarised in Table 4. Pure ondansetron HCl was perceived as intensely bitter (score 3.8 ± 0.4). The physical mixture lacking β-CD remained unpalatable (score 3.2 ± 0.3), demonstrating that flavourants and sweeteners alone were insufficient to mask the drug's aversive taste. In contrast, the optimised batch F5, incorporating the drug as a β-CD inclusion complex, received a mean score of 0.8 ± 0.3, indicating barely detectable bitterness and an acceptable mouth feel. Volunteers reported a pleasant cooling sensation attributable to mannitol, with no gritty aftertaste.

Table 4: Taste evaluation scores for ondansetron and optimised formulation (mean ± SD, n = 6).

Sample	Bitterness Score (0–4)	Interpretation
Pure ondansetron HCl	3.8 ± 0.4	Intensely bitter
Physical mixture (no β-CD)	3.2 ± 0.3	Bitter
Optimised formulation F5	0.8 ± 0.3	Slight / acceptable

3.6 In Vitro Drug Release Studies

The dissolution profiles for all formulations are presented in Table 5 and Figure 2. Formulations prepared with lower superdisintegrant levels (F1, F4) exhibited comparatively slower initial release, with less than 30% drug released at 1 min. The binary superdisintegrant matrices demonstrated progressively accelerated release as a function of total disintegrant concentration. F5

achieved approximately 35.2 ± 1.1 % release at 1 min, 68.5 ± 1.4 % at 3 min, and near-complete release of 98.5 ± 1.0 % by 10 min. The rapid dissolution is mechanistically attributed to the instantaneous wicking of saliva/dissolution medium by crospovidone, creating channels that are subsequently expanded by the swelling force of croscarmellose sodium, leading to rapid dispersion of the β-CD complex and consequent drug dissolution. F9, despite marginally faster release (99.6% at 10 min), offered no practical advantage over F5 while exhibiting higher friability.

Table 5: Cumulative % drug released from ondansetron fast dissolving tablets (mean ± SD, n = 3).

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	18.5 ± 1.1	24.2 ± 1.2	30.5 ± 1.3	28.4 ± 1.2	35.2 ± 1.1	38.5 ± 1.4	32.8 ± 1.2	36.5 ± 1.3	40.2 ± 1.5
2	30.2 ± 1.4	38.5 ± 1.3	45.2 ± 1.5	42.5 ± 1.4	52.8 ± 1.5	56.2 ± 1.6	48.5 ± 1.5	54.2 ± 1.4	58.5 ± 1.6
3	42.5 ± 1.5	52.4 ± 1.5	58.6 ± 1.6	55.2 ± 1.5	68.5 ± 1.4	72.4 ± 1.5	62.4 ± 1.6	70.5 ± 1.5	74.2 ± 1.7
5	58.4 ± 1.6	68.8 ± 1.6	72.5 ± 1.5	70.2 ± 1.6	85.4 ± 1.3	88.2 ± 1.4	78.5 ± 1.5	84.2 ± 1.4	88.5 ± 1.5
8	74.2 ± 1.4	82.5 ± 1.4	86.4 ± 1.4	84.5 ± 1.3	94.6 ± 1.2	96.2 ± 1.1	90.2 ± 1.4	93.5 ± 1.2	96.8 ± 1.1
10	85.5 ± 1.2	92.4 ± 1.2	94.8 ± 1.1	92.8 ± 1.2	98.5 ± 1.0	99.2 ± 0.9	96.5 ± 1.1	98.2 ± 1.0	99.6 ± 0.8

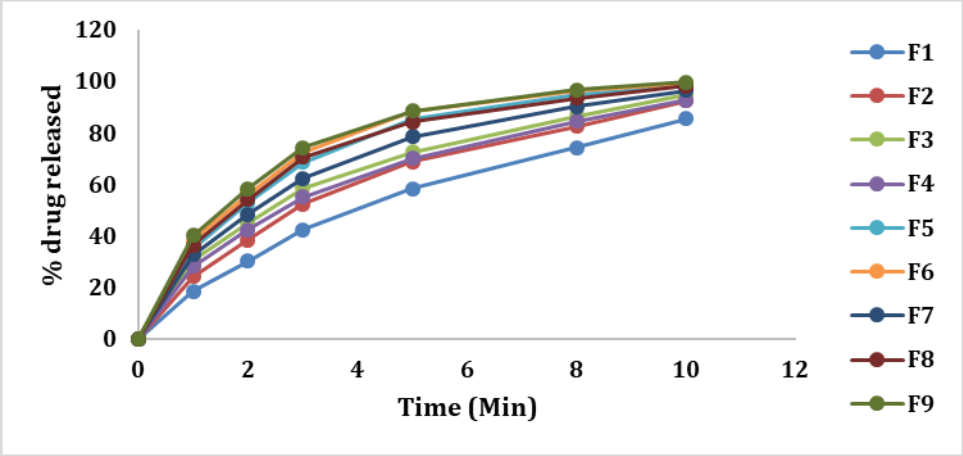

Figure 2. Cumulative % drug released from ondansetron fast dissolving tablets.

3.7 Drug Release Kinetics and Mechanism

The dissolution data for the optimized formulation F5 were fitted to established mathematical models to elucidate the release mechanism (Table 6). The Korsmeyer–Peppas model provided the highest coefficient of determination (R^2 = 0.996), followed closely by the first-order model (R^2 = 0.965). The zero-order, Higuchi, and Hixson–Crowell models exhibited comparatively weaker correlations, indicating that drug release is not governed purely by constant-rate surface erosion or Fickian planar diffusion alone. The release exponent (n) calculated from the Korsmeyer–Peppas equation was 0.428. Since this value is marginally below 0.45, the dominant release mechanism is classified as Fickian diffusion, indicating that drug dissolution and transport through the disintegrating matrix are primarily diffusion-controlled. This is mechanistically consistent with the rapid hydration and structural collapse of the binary superdisintegrant network, which promptly exposes drug-loaded β-CD particles to the dissolution medium without the formation of a persistent viscous gel barrier.

Table 6. Kinetic modelling parameters for optimized formulation F5.

Model	Equation Form	R^2	Rate Constant (k)
Zero-order	$Q_t = Q_0 + k_0 t$	0.924	9.850
First-order	$\log Q_t = \log Q_0 + k_1 t / 2.303$	0.965	0.285
Higuchi	$Q_t = k^H t^{0.5}$	0.878	38.520
Korsmeyer–Peppas	$M_t / M_\infty = k^{KP} t^n$	0.996	0.368 (n = 0.428)
Hixson–Crowell	$(100 - Q_t)^{1/3} = (100 - Q_0)^{1/3} - k^{Hc} t$	0.942	0.042

3.8 Accelerated Stability Studies

The optimized batch F5 demonstrated excellent physicochemical stability under accelerated stress conditions over a 90-day period (Table 7). No changes in physical appearance, odour, or colour were observed at any time point. The mean drug content remained within the acceptance criteria (98.5–99.8%), and tablet hardness and friability did not deviate substantially from baseline values, indicating that the compressed matrix remained mechanically intact. Importantly, the disintegration time increased only marginally (from 18 s to 21 s), and the dissolution profile remained essentially unchanged, with the similarity factor (f_2) between the initial and 90-day profiles exceeding 82. These results indicate that the ondansetron fast dissolving tablets are chemically stable and that the superdisintegrant functionality is retained under elevated temperature and humidity conditions.

Table 7: Accelerated stability data of optimised formulation F5 at 40 ± 2 °C / 75 ± 5% RH.

Parameter	Initial (Day 0)	1 Month	2 Months	3 Months
Appearance	White, smooth	No change	No change	No change
Assay (%)	99.8 ± 0.9	99.2 ± 1.0	98.5 ± 1.1	97.8 ± 1.2
Hardness (kg/cm²)	3.5 ± 0.3	3.4 ± 0.3	3.4 ± 0.4	3.3 ± 0.3
Friability (%)	0.48 ± 0.03	0.50 ± 0.04	0.52 ± 0.03	0.55 ± 0.04
Disintegration time (s)	18 ± 1	19 ± 1	20 ± 1	21 ± 1
Release at 10 min (%)	98.5 ± 1.0	97.2 ± 1.2	96.4 ± 1.1	95.2 ± 1.3
f_2 versus Day 0	-	89.4	85.2	82.8

4. DISCUSSION

The therapeutic rationale for developing an FDT of ondansetron stems from the clinical need for rapid antiemetic action, particularly in the perioperative setting and during the first 24 h of emetogenic chemotherapy, when delayed gastric emptying and swallowing difficulties frequently compromise the utility of conventional oral dosage forms. The inclusion of β-cyclodextrin served a dual purpose: effective reduction of the intensely bitter taste of ondansetron, thereby improving acceptability in paediatric and geriatric cohorts, and potential enhancement of the effective surface area for dissolution through molecular dispersion of the drug within the hydrophilic oligosaccharide shell.

The binary superdisintegrant strategy was predicated on the complementary mechanisms of crospovidone and croscarmellose sodium. Crospovidone, being highly porous and hygroscopic, exhibits exceptional wicking capacity, rapidly drawing aqueous fluid into the tablet core via capillary action. This initial influx of water promotes hydration of croscarmellose sodium, which undergoes substantial swelling and gelation, generating internal hydrodynamic stresses that mechanically rupture interparticulate bonds and disperse the matrix. In isolation, concentrations of either superdisintegrant below 4% were insufficient to achieve the target disintegration time of under 30 s (F1, F2, F4). Increasing crospovidone to 6% (F3) achieved adequate disintegration but did not capitalise on the synergistic swelling contributed by croscarmellose sodium. The binary combination in F5 (4% crospovidone + 2% croscarmellose sodium) achieved the optimal balance, yielding a disintegration time of 18 s while preserving tablet hardness above 3.5 kg/cm² and friability below 0.5%. At higher combined loadings (F9), the tablet became overly fragile, reflecting the disruption of coherent bonding by excessive swelling capacity.

The dissolution kinetics confirmed a Fickian diffusion mechanism (n = 0.428), which contrasts with the anomalous transport typically reported for hydrophilic prolonged-release matrices. This distinction is mechanistically sound: FDTs are explicitly designed to minimise gel layer persistence and maximise matrix dispersion. Rapid water ingress, immediate disintegration, and subsequent diffusion of dissolved drug from the β-CD complex into the bulk medium dominate the kinetic profile, producing first-order–predominant release with an inherently rapid initial phase. The clinical relevance of this profile lies in the potential for faster attainment of plasma therapeutic levels compared to conventional tablets, thereby improving antiemetic coverage during the critical early phase of emetogenic stimulation.

The taste panel results substantiated the necessity of inclusion complexation. The marginal reduction in bitterness provided by sweeteners alone (score 3.2 versus 3.8 for pure drug) underscores the limitation of conventional flavouring strategies for intensely bitter actives. By contrast, the β-CD complex reduced the bitterness score to 0.8, well within the acceptable threshold for orodispersible dosage forms. The cooling effect of mannitol further complemented the orosensory appeal, and the absence of a gritty or chalky mouthfeel suggests that the particle size of the complex and the choice of diluent were appropriate.

Accelerated stability data reinforced the robustness of the optimised formulation. The marginal lengthening of disintegration time (from 18 s to 21 s) over 90 days under stress conditions is unlikely to be clinically meaningful, and the consistently high f_2 values (>82) provide strong assurance that the product will maintain its qualitative and quantitative dissolution performance throughout its proposed shelf life. The absence of significant changes in hardness, friability, or assay further supports the suitability of direct compression as a

commercially viable manufacturing process for this formulation.

5. CONCLUSION

This study successfully developed a fast dissolving tablet of ondansetron hydrochloride (4 mg) by systematically optimising a binary superdisintegrant system comprising crospovidone and croscarmellose sodium in conjunction with a β-cyclodextrin inclusion complex for taste masking. Formulation F5, containing 4% w/w crospovidone and 2% w/w croscarmellose sodium, achieved the most desirable performance profile: disintegration within 18 s, wetting within 15 s, and near-complete drug release (98.5%) within 10 min, governed by Fickian diffusion kinetics. The tablets met all pharmacopoeial quality specifications, demonstrated acceptable palatability in human volunteers, and exhibited excellent physicochemical stability under accelerated ICH conditions. The developed formulation offers a clinically relevant, patient-friendly alternative for the rapid management of nausea and vomiting, with particular utility in paediatric, geriatric, dysphagic, and postoperative populations. These findings support the further development and bioavailability assessment of the optimised FDT as a commercially viable antiemetic product.

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