Formulation And Optimization of Fast Dissolving Tablets of Ondansetron Hydrochloride

Tejas Subhash Mashalkar[1], Deepak Dnyaneshwar Ghotale[2]
[1,2]*Department of Pharmaceutics, BSS's Tatyaraoji More College of Pharmacy, Omerga, Dist. Dharashiv, Maharashtra, India*

***Abstract*—Fast dissolving tablets (FDTs) have emerged as an innovative oral drug delivery system that disintegrates rapidly in the oral cavity without the need for water. Ondansetron Hydrochloride, a selective serotonin (5-HT$_3$) receptor antagonist, is widely used for the prevention and treatment of chemotherapy-induced, radiotherapy-induced, and postoperative nausea and vomiting. The present study aims to formulate and optimize fast dissolving tablets of Ondansetron Hydrochloride (4 mg) using Crospovidone and Croscarmellose Sodium as super disintegrants at varying concentrations (2–10 mg) by the direct compression method. Five formulations (F1–F5) were prepared and evaluated for pre-compression and post-compression parameters. Pre-compression studies revealed good powder flow properties across all batches. Post-compression evaluation showed acceptable hardness (3.1–3.6 kg/cm^2), low friability (<1%), and drug content uniformity (96.2–99.6%). Disintegration time progressively decreased from 48 seconds (F1) to 18 seconds (F5) with increasing super disintegrant concentration. In vitro dissolution studies demonstrated that F5 achieved 99.2% drug release within 10 minutes. FTIR spectroscopy confirmed the absence of drug–excipient interactions. DSC analysis revealed reduced crystallinity in solid dispersions. Formulation F5 was identified as the optimized batch, exhibiting the best disintegration, dissolution, and overall tablet performance. The study concludes that direct compression using a combination of Crospovidone and Croscarmellose Sodium is an effective approach for developing patient-compliant FDTs of Ondansetron Hydrochloride.**

***Index Terms*—Fast Dissolving Tablets, Ondansetron Hydrochloride, Superdisintegrants, Crospovidone, Croscarmellose Sodium, Direct Compression, Disintegration Time, In Vitro Dissolution.**

I. INTRODUCTION

The oral route of drug administration remains the most preferred route due to its convenience, cost-effectiveness, and high patient compliance. Among various oral dosage forms, tablets are the most popular because of their accurate dosing, stability, and ease of manufacturing. However, conventional tablets have certain limitations for patients who experience difficulty in swallowing (dysphagia), particularly pediatric, geriatric, and bedridden patients. During conditions such as nausea and vomiting, administering conventional tablets with water becomes highly inconvenient [1].

Fast Dissolving Tablets (FDTs), also known as Orally Disintegrating Tablets (ODTs) or Orodispersible Tablets, are solid dosage forms that disintegrate or dissolve rapidly in the oral cavity—typically within 60 seconds or less—without requiring water. The USP defines ODTs as solid dosage forms that disintegrate rapidly when placed on the tongue, while the European Pharmacopoeia defines them as uncoated tablets that disperse quickly in the mouth before swallowing [2]. Drug absorption may begin at the oral mucosa and continue in the gastrointestinal tract, resulting in faster onset of therapeutic action compared to conventional tablets.

Ondansetron Hydrochloride is a potent selective serotonin (5-HT$_3$) receptor antagonist used extensively for the prevention and treatment of chemotherapy-induced nausea and vomiting (CINV), postoperative nausea and vomiting (PONV), and radiation-induced nausea. It exerts its antiemetic action by blocking 5-HT$_3$ receptors both centrally in the chemoreceptor trigger zone (CTZ) and peripherally in the

gastrointestinal tract, thereby preventing the vomiting reflex [3]. Since patients experiencing nausea may find it difficult to swallow conventional tablets, formulation into FDTs offers a significant clinical advantage.

Superdisintegrants such as Crospovidone (CP), Croscarmellose Sodium (CCS), and Sodium Starch Glycolate (SSG) play a crucial role in achieving rapid tablet disintegration through mechanisms of swelling, wicking (capillary action), and deformation recovery. The selection and optimization of superdisintegrant type and concentration is critical to achieving the desired balance between rapid disintegration, adequate mechanical strength, and acceptable mouthfeel [4].
The present study focuses on the formulation and optimization of fast dissolving tablets of Ondansetron Hydrochloride using Crospovidone and Croscarmellose Sodium by the direct compression method, and systematic evaluation of their physicochemical properties, disintegration behavior, and in vitro drug release profile [5].

II. LITERATURE REVIEW

Gosai A.R., Patil S.B., and Sawant K.K. (2008) formulated orodispersible tablets of Ondansetron Hydrochloride by direct compression using sodium starch glycolate and croscarmellose sodium. Tablets showed rapid disintegration (3–5 seconds) and faster drug release compared to pure drug and conventional tablets [6].

Rakesh Dayaram Tiwle and Dr. Mohamed Mutahar R.K. (2024) developed and optimized fast-dissolving tablets of Ondansetron HCl using microcrystalline cellulose (MCC) and lactose by direct compression with a two-factor, three-level factorial design. The optimized formulation met all pharmacopoeial specifications [7].

Suthar R.M. and Chotai N.P. developed FDTs of Ondansetron Hydrochloride using solid dispersion technique. The optimized batch (F3) containing crospovidone showed fastest disintegration (3.22 sec) and maximum drug release (97.98% in 30 min) [8].

Asha Maharjan, H.S. Keerthy, and Gururaj S. Kulkarni (2023) formulated fast disintegrating tablets using natural superdisintegrants—spray-dried banana powder and ispaghula husk—by direct compression, demonstrating that natural polymers can effectively enhance tablet disintegration [9].

Pratik B. Aru and Nandakishor B. Deshmukh (2025) formulated orodispersible tablets using Acacia gum as natural superdisintegrant. The optimized batch (F3) showed 22 seconds disintegration time and 99.31% drug release within 30 minutes [10].

III. AIM AND OBJECTIVES

Aim: To formulate and optimize fast dissolving tablets (FDTs) of Ondansetron Hydrochloride using suitable superdisintegrants by the direct compression method to achieve rapid disintegration, improved drug release, and enhanced patient compliance.

Objectives:

1. To carry out preformulation studies of Ondansetron Hydrochloride and selected excipients.
2. To select and optimize suitable superdisintegrants (Crospovidone and Croscarmellose Sodium) for FDT formulation.
3. To prepare fast dissolving tablets (F1–F5) by direct compression with varying superdisintegrant concentrations.
4. To evaluate pre-compression parameters: angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio.
5. To evaluate post-compression parameters: hardness, thickness, friability, weight variation, drug content, wetting time, and disintegration time.
6. To perform in vitro dissolution studies and FTIR/DSC compatibility studies.
7. To select the optimized formulation based on minimum disintegration time and maximum drug release.

IV. DRUG PROFILE

Ondansetron Hydrochloride is a carbazole derivative and selective 5-HT_3 receptor antagonist classified as an antiemetic agent.

Table 1: Drug Profile of Ondansetron Hydrochloride

Parameter	Details
Drug Name	Ondansetron Hydrochloride
Category	Antiemetic (5-HT_3 Receptor Antagonist)
Chemical Name	(RS)-9-Methyl-3-[(2-methyl-1H-imidazol-1-yl) methyl]-1,2,3,9-tetrahydro-4H-carbazol-4-one hydrochloride
Molecular Formula	$C_{18}H_{19}N_3O \cdot HCl$
Molecular Weight	329.82 g/mol
Melting Point	~186–187°C
Solubility	Freely soluble in water; sparingly soluble in alcohol
Bioavailability	~60%
Half-life	3–5 hours
Protein Binding	~70–76%
Metabolism	Hepatic (CYP3A4, CYP2D6, CYP1A2)
Dose	4–8 mg (adults)
pKa	~7.4
Storage	Cool, dry place; protect from light; below 25°C

V. MATERIALS AND METHODS

A. Materials

Table 2: List of Materials Used

Material	Source/Company
Ondansetron Hydrochloride	Yarrow Chem Products, Mumbai
Crospovidone (CP)	Signet Chemical Corporation
Croscarmellose Sodium (CCS)	FMC Biopolymer
Mannitol	Merck Ltd.
Microcrystalline Cellulose (MCC)	FMC Corporation
Aspartame	NutraSweet Company
Magnesium Stearate	SD Fine Chemicals
Talc	Loba Chemie Pvt. Ltd.
Peppermint Flavor	Givaudan India Pvt. Ltd.

B. Formulation Design

Five formulations (F1–F5) were prepared with progressive increase in Crospovidone and Croscarmellose Sodium concentrations (2 mg to 10 mg each), while maintaining total tablet weight at 144 mg. Mannitol was used as the primary diluent and was adjusted to maintain constant tablet weight across all batches.

Table 3: Formulation Chart of Ondansetron HCl FDTs (F1–F5)

Ingredient (mg/tab)	F1	F2	F3	F4	F5
Ondansetron HCl	4	4	4	4	4
Crospovidone	2	4	6	8	10
Croscarmellose Sodium	2	4	6	8	10
Mannitol	80	76	72	68	64
MCC	45	45	45	45	45
Aspartame	3	3	3	3	3
Talc	3	3	3	3	3
Magnesium Stearate	3	3	3	3	3
Peppermint Flavor	2	2	2	2	2
Total Weight (mg)	144	144	144	144	144

C. Method of Preparation – Direct Compression

All ingredients were accurately weighed using a digital weighing balance. The drug and excipients (excluding magnesium stearate and talc) were passed through sieve #60 to ensure uniform particle size. Ondansetron Hydrochloride was blended with MCC and mannitol to achieve uniform drug distribution. Crospovidone and Croscarmellose Sodium were added and blended thoroughly. Aspartame and peppermint flavor were incorporated and mixed uniformly. Finally, magnesium stearate and talc were added as lubricant and glidant and blended gently for 2–3 minutes to avoid over-lubrication. The prepared blend was evaluated for pre-compression parameters, then compressed into tablets of 144 mg weight using a single-punch tablet compression machine [11].

D. Evaluation Parameters

Pre-Compression Parameters:

Powder blend was evaluated for angle of repose (tan θ = h/r), bulk density (mass/bulk volume), tapped density (mass/tapped volume), Carr's Index [(TD–BD)/TD × 100], and Hausner's ratio (TD/BD). These parameters indicate the flow and compressibility of the powder blend [12].

Post-Compression Parameters:

Tablets were evaluated for hardness (Monsanto hardness tester, kg/cm²), thickness (Vernier caliper, mm), friability [% F = (Iw – Fw)/Iw × 100, acceptable < 1%], weight variation (IP limits), drug content uniformity (UV spectrophotometry at 221 nm), wetting time (Petri dish method), and disintegration time (disintegration test apparatus, phosphate buffer pH 7.2 at 37°C) [13].

In Vitro Dissolution Study:

Dissolution was performed using USP Type II (paddle) apparatus in 900 mL phosphate buffer pH 7.2 at 37 ± 0.2°C, 100 rpm. Samples (5 mL) were withdrawn at 2, 4, 6, 8, and 10-minute intervals and analyzed spectrophotometrically at 221 nm (λmax). The calibration curve of Ondansetron Hydrochloride in ethanol followed Beer-Lambert's law in the concentration range of 5–25 µg/mL [14].

FTIR Spectroscopy:

KBr pellet method was used to analyze pure Ondansetron Hydrochloride, superdisintegrants, and solid dispersion (1:3 ratio) in the range 4000–400 cm^{-1} to confirm drug–excipient compatibility [15].

DSC Analysis: Differential Scanning Calorimetry was performed on pure drug and solid dispersions by heating samples at 10°C/min over 30–300°C range to assess thermal behavior and crystallinity changes [16].

VI. RESULTS AND DISCUSSION

A. Pre-Compression Parameters

All five formulations exhibited good powder flow characteristics suitable for direct compression. Angle of repose values ranged from 25.2° to 29.5°, indicating good to passable flow. Carr's index values (12.9–16.0%) and Hausner's ratio (1.13–1.19) confirmed acceptable compressibility. F5 demonstrated the best flowability with lowest angle of repose (25.2°) and Carr's index (12.9%).

Table 4: Pre-Compression Parameters of Formulations F1–F5

Parameter	F1	F2	F3	F4	F5
Angle of Repose (°)	29.5	28.8	27.6	26.4	25.2
Bulk Density (g/mL)	0.42	0.44	0.45	0.46	0.47
Tapped Density (g/mL)	0.50	0.51	0.52	0.53	0.54
Carr's Index (%)	16.0	13.7	13.4	13.2	12.9
Hausner's Ratio	1.19	1.15	1.15	1.14	1.13

B. Post-Compression Parameters

All formulations showed acceptable hardness (3.1–3.6 kg/cm²), uniform thickness (~3.0–3.2 mm), and friability well within the acceptable limit of <1% (0.65–0.89%). Weight variation was within IP limits for all batches. Drug content uniformity ranged from 96.2% (F1) to 99.6% (F5), indicating uniform drug distribution. Wetting time progressively decreased from 42 seconds (F1) to 18 seconds (F5), and disintegration time decreased from 48 seconds (F1) to 18 seconds (F5), indicating the positive effect of increasing superdisintegrant concentration on rapid tablet breakdown.

Table 5: Post-Compression Parameters of Formulations F1–F5

Parameter	F1	F2	F3	F4	F5
Hardness (kg/cm²)	3.1	3.2	3.4	3.5	3.6
Thickness (mm)	3.0	3.1	3.1	3.2	3.2
Friability (%)	0.89	0.82	0.76	0.71	0.65
Weight Variation (mg)	143	144	145	144	144
Drug Content (%)	96.2	97.5	98.4	99.1	99.6
Wetting Time (sec)	42	35	28	22	18
Disintegration Time (sec)	48	39	31	24	18

C. In Vitro Dissolution Study

In vitro dissolution profiles of all five formulations were determined in phosphate buffer pH 7.2 using USP Type II apparatus. Drug release increased progressively with higher superdisintegrant concentration. F5 exhibited the fastest and most complete drug release—99.2% within 10 minutes—attributed to the synergistic effect of Crospovidone (wicking action) and Croscarmellose Sodium (swelling mechanism) at optimum concentration. F1 released only 86.4% drug in the same period. The results confirm that increasing superdisintegrant concentration significantly enhances dissolution performance.

Table 6: In Vitro Drug Release (%) of Formulations F1–F5 in Phosphate Buffer pH 7.2

Time (min)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
2	28.5	36.2	45.4	52.6	58.3
4	45.2	58.4	68.6	75.2	82.5
6	61.8	72.5	82.3	88.4	92.8
8	75.6	84.3	92.6	95.1	97.4
10	86.4	91.5	95.8	97.2	99.2

D. FTIR Spectroscopy

FTIR spectra of pure Ondansetron Hydrochloride showed characteristic peaks at 1638.1 cm^{-1} (N–H bending), 1280.62 cm^{-1} (C–N stretching), and 760.1 cm^{-1} (ortho-substituted phenyl C–H bending). The spectra of solid dispersion (1:3 drug:polymer ratio) retained all characteristic peaks of the pure drug without significant shifts or disappearance, confirming no chemical interaction between Ondansetron Hydrochloride and the selected excipients. The formulation components are compatible [15].

E. Differential Scanning Calorimetry (DSC)

DSC thermogram of pure Ondansetron Hydrochloride exhibited a sharp endothermic peak at 186.7°C, confirming its crystalline nature. Thermograms of solid dispersions showed a slight shift to lower temperatures (174–185°C) with reduced peak intensity and broadening, suggesting partial amorphization of the drug within the solid dispersion matrix. This reduction in crystallinity is directly correlated with improved wettability and enhanced dissolution rate of the optimized formulation [16].

F. Optimized Formulation

Based on the comprehensive evaluation of pre- and post-compression parameters, in vitro dissolution, FTIR, and DSC results, Formulation F5 was identified as the optimized formulation. F5 exhibited: minimum disintegration time (18 sec), fastest wetting (18 sec), highest drug content (99.6%), maximum drug release (99.2% within 10 min), acceptable hardness (3.6 kg/cm²), and lowest friability (0.65%). The combination of Crospovidone (10 mg) and Croscarmellose Sodium (10 mg) acting synergistically through wicking and swelling mechanisms respectively was responsible for the superior performance of F5.

VII. CONCLUSION

The present study successfully accomplished the formulation and optimization of fast dissolving tablets of Ondansetron Hydrochloride using the direct compression method with Crospovidone and Croscarmellose Sodium as superdisintegrants. All five formulations demonstrated acceptable pre-compression flow properties and post-compression physicochemical characteristics within

pharmacopoeial limits. A clear correlation was established between increasing superdisintegrant concentration and decreasing disintegration time and wetting time, with concurrent improvement in drug release profile.

Formulation F5—containing 10 mg each of Crospovidone and Croscarmellose Sodium—emerged as the optimized formulation with the fastest disintegration (18 seconds), maximum drug release (99.2% within 10 minutes), and satisfactory mechanical strength. FTIR analysis confirmed drug–excipient compatibility, and DSC analysis indicated partial amorphization in solid dispersions contributing to enhanced dissolution. The developed FDT formulation of Ondansetron Hydrochloride represents a promising, patient-friendly oral drug delivery system particularly suitable for pediatric, geriatric, and dysphagic patients requiring rapid antiemetic action without the need for water.

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