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ONDANSETRON-LOADED ORODISPERSIBLE FILMS: A FAST-DISSOLVING DRUG DELIVERY STRATEGY FOR ANTIEMETIC THERAPY

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Abstract

Objective: The objective of the present study was to formulate and evaluate mouth dissolving films (MDFs) of Ondansetron Hydrochloride for the rapid management of nausea and vomiting, especially in pediatric and geriatric patients.

Methods: MDFs were prepared by the solvent casting technique using Hydroxypropyl Methylcellulose (HPMC E15) as the film-forming polymer and Polyethylene Glycol 400 (PEG 400) as a plasticizer. Excipients like sucralose, citric acid, and peppermint flavor were incorporated for improved palatability and disintegration. Preformulation studies including UV spectroscopic identification, solubility analysis, melting point determination, and FTIR compatibility were carried out. The films were evaluated for various parameters such as thickness, folding endurance, weight variation, surface pH, disintegration time, drug content uniformity, and in vitro drug release. FTIR spectra were used to assess drug–excipient compatibility.

Results: The formulated films were transparent, smooth, and flexible with rapid disintegration time (20–22 seconds). Drug content was found to be uniform (~99%), and all physical parameters were within acceptable limits. In vitro dissolution studies revealed that over 85% of the drug was released within 5 minutes and ~97% within 10 minutes. FTIR studies confirmed no significant chemical interaction between drug and excipients.

Conclusion: The study demonstrated that mouth dissolving films of Ondansetron Hydrochloride can serve as a promising alternative to conventional oral dosage forms, offering rapid onset of action and ease of administration, particularly for patients with swallowing difficulties.

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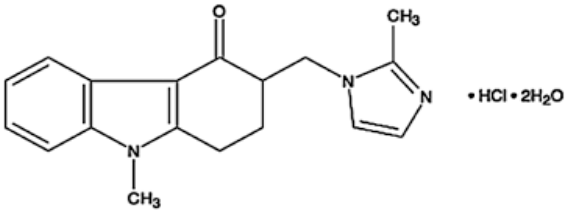
Introduction

Nausea and vomiting are protective reflexes that can be triggered by a wide range of physiological and pathological stimuli, such as motion sickness, pregnancy, gastroenteritis, and notably, chemotherapy and radiotherapy. Chemotherapy-induced nausea and vomiting (CINV) remains one of the most distressing side effects of cancer treatment, often leading to poor adherence to therapy and deteriorated quality of life. The emetic response is primarily mediated by the stimulation of serotonin (5-HT3) receptors in the gastrointestinal tract and central nervous system. Thus, 5-HT3 receptor antagonists have become the mainstay of antiemetic therapy in oncology care [1]. Ondansetron hydrochloride is a potent and selective 5-HT3 receptor antagonist approved for the prevention and treatment of nausea and vomiting associated with chemotherapy, radiotherapy, and postoperative recovery.



It is typically administered via oral or intravenous routes. However, conventional oral dosage forms such as tablets and syrups may be less effective or unsuitable during active emesis or for patients with dysphagia, particularly in pediatric and geriatric populations. This necessitates the exploration of patient-friendly alternative delivery systems [2,3].Mouth dissolving films (MDFs) are thin, flexible, and rapidly disintegrating polymeric strips designed to dissolve on the tongue without the need for water. They provide several advantages over traditional oral solid dosage forms, including ease of administration, rapid onset of action, improved patient compliance, and bypass of first-pass metabolism. Recent

technological advancements have made MDFs a promising vehicle for delivering drugs like Ondansetron, especially where fast therapeutic action is essential [4].

Figur-1: Mouth Dissolving Films (MDFs)

Need and Rationale for the Study

Despite the increasing popularity of MDFs, there are limited optimized formulations of Ondansetron as a mouth dissolving film available in the market. Challenges such as achieving uniform drug distribution, improving taste masking, enhancing mechanical strength, and ensuring rapid disintegration still persist. Additionally, during episodes of vomiting, retaining a tablet is difficult, making a fast-dissolving film a more practical and efficient choice. Thus, there is a pressing need to develop an optimized Ondansetron MDF formulation that ensures therapeutic efficacy and patient acceptability [5,6].

Research Gaps and Objectives

A review of recent literature reveals several gaps in the current research landscape:

- Limited exploration of natural or mucoadhesive polymers in MDFs for Ondansetron.
- Inadequate attention to pediatric-specific dose adjustment and taste masking.
- Scarce in vivo or pharmacokinetic correlation studies.
- Lack of comprehensive FTIR compatibility studies between the drug and excipients [7,8].

To address these gaps, the present study is undertaken with the following objectives:

Objectives of the Study

- To formulate mouth dissolving films of Ondansetron Hydrochloride using HPMC and PEG 400.
- To evaluate the physicochemical properties such as thickness, folding endurance, disintegration time, and drug content.
- To assess drug-excipient compatibility using FTIR spectroscopy.
- To conduct in vitro drug release studies and evaluate formulation performance.

This study aims to develop a patient-friendly, fast-acting, and pharmaceutically acceptable dosage form of Ondansetron for effective management of nausea and vomiting.

Materials and Methods

Table 1: Materials

S. No.	Material	Category	Supplier/Manufacturer	Source
1.	Ondansetron Hydrochloride	Active Pharmaceutical Ingredient (API)	Loba Chemie Pvt. Ltd., Mumbai	Collected from CPS Bam.
2.	HPMC E15	Film-forming Polymer	Loba Chemie Pvt. Ltd.	Collected from CPS Bam.
3.	PEG 400	Plasticizer	Loba Chemie Pvt. Ltd.	Collected from CPS Bam
4.	Sucralose	Sweetener	Loba Chemie Pvt. Ltd.	Collected from CPS Bam.
5.	Citric Acid	Saliva Stimulant / Acidifier	Loba Chemie Pvt. Ltd.	Collected from CPS Bam.
6.	Peppermint Flavor	Flavoring Agent	Loba Chemie Pvt. Ltd.	Collected from CPS Bam.
7.	Distilled Water	Solvent	Laboratory Prepared	CPS Bam.Laboratory
8.	Ethanol	Co-solvent / Solvent	Loba Chemie Pvt. Ltd.	Collected from CPS Bam.

Pre-formulation Studies

Preformulation studies were performed to evaluate the physicochemical properties of Ondansetron Hydrochloride and to assess its compatibility with selected excipients before formulating the mouth dissolving films. [15]

Drug Identification (UV Spectroscopy) (Shimadzu 1800)

Preparation of Standard Calibration Curve

1. **Stock Solution**
   Weigh accurately 10 mg of Ondansetron HCl and dissolve in 100 mL of phosphate buffer (pH 6.8) to get a concentration of 100 µg/mL (stock solution).
2. **Serial Dilution**
   From the stock solution, prepare dilutions of 2, 4, 6, 8, and 10 µg/mL.
3. **Measurement**
   Measure the absorbance of each solution at 310 nm using phosphate buffer as the blank.
4. **Plotting**
   Plot a graph of absorbance vs. concentration to obtain the calibration curve.
5. **Regression Equation**
   Use the graph to calculate the regression equation:

$$\text{Absorbance} = m \times \text{Concentration} + c$$

This equation is used to calculate the drug content in unknown samples.

Solubility Studies

Procedure

An excess quantity of Ondansetron Hydrochloride was added to 10 mL of different solvents: distilled water, ethanol, phosphate buffer (pH 6.8), and 0.1 N HCl. The mixtures were shaken for 24 hours at room temperature and filtered. The drug concentration in the filtrate was determined using UV spectrophotometry. [16]

Melting Point Determination

Procedure:

The melting point of Ondansetron Hydrochloride was determined using a digital melting point apparatus by capillary method. A small amount of drug was placed in a capillary tube and the temperature was gradually increased until the drug melted [17].

FTIR Compatibility Study

To evaluate any potential chemical interaction between Ondansetron Hydrochloride and excipients used in the mouth dissolving film formulation. FTIR spectra of pure Ondansetron Hydrochloride, polymers (HPMC, PEG 400), and the physical mixture were recorded using an FTIR spectrometer (Bruker Alpha II) in the range of 4000–400 cm^{-1}. Samples were mixed with KBr and compressed into a disc for analysis [18]

Formulation Procedure (Solvent Casting Method) [19]

1. **Preparation of polymer solution**:
   - Dissolve HPMC E15 and PVA in 70 mL distilled water with continuous stirring (use magnetic stirrer for 30–45 minutes until a clear solution is obtained).
2. **Plasticizer addition**:
   - Add 0.5 mL of glycerol or PEG 400 to the polymer solution and stir.
3. **Drug solution preparation**:
   - Dissolve Ondansetron HCl in 5 mL ethanol.
4. **Combine**:
   - Add the drug solution slowly to the polymer solution under constant stirring.
5. **Add additives**:
   - Mix in citric acid, sweetener (sucralose), and flavor (peppermint oil). Stir thoroughly to ensure uniform distribution.
6. **Final volume**:
   - Make up the volume to 100 mL with distilled water.
7. **Degassing**:
   - Allow the solution to stand for 30 minutes to remove air bubbles.
8. **Casting**:
   - Pour the solution onto a leveled glass plate or petri dish (use a calibrated area for dose uniformity) and spread uniformly.
9. **Drying**:
   - Dry in a hot air oven at 40–45°C for 24 hours.
10. **Cutting**:

- Cut into 2x2 cm films, each containing 4 mg Ondansetron.

Table 2: Formulation Table for One Batch of Mouth Dissolving Films

Category	***Ingredients***	***Quantity per batch (for 100 mL casting solution)***
API	Ondansetron Hydrochloride	40 mg *(4 mg per 2x2 cm film × 10 films)*
Polymer	HPMC E15	2.5 g
	PVA (as co-polymer)	0.5 g
Plasticizer	Glycerol or PEG 400	0.5 mL
Solvent	Distilled Water	q.s. to 100 mL
	Ethanol (Cosolvents)	5 mL
Others	Citric Acid	0.1 g
	Sucralose (sweetener)	0.1 g
	Peppermint flavor	0.1 mL

Evaluation Procedures of Mouth Dissolving Films of Ondansetron Hydrochloride

The prepared mouth dissolving films (MDFs) were subjected to a series of physicochemical evaluations to ensure uniformity, quality, and performance characteristics. All tests were conducted in accordance with established pharmacopeial and scientific protocols.

Physical Appearance

The films were visually inspected for parameters such as transparency, uniformity, surface smoothness, and presence of air bubbles or cracks. A good-quality MDF should be translucent or transparent, uniform, and free from any physical defects [20].

Film Thickness

Film thickness was measured using a digital Vernier caliper at three different positions (center and both ends) of the film, and the average was calculated. Uniform thickness indicates homogeneous distribution of the polymer and drug [21].

Unit: Millimeters (mm)

Weight Variation

Each film (2×2 cm) was individually weighed using a high-precision digital balance, and the mean weight along with standard deviation (SD) was recorded. Acceptable weight uniformity reflects consistent casting and composition [21].

Unit: Milligrams (mg)

Folding Endurance

Folding endurance was assessed by repeatedly folding a film at the same location until it broke. The number of folds required to break the film reflects its mechanical strength and flexibility, crucial for packaging and handling [22].

Unit: Number of folds

Surface pH

To avoid mucosal irritation, the surface pH of the films was determined by allowing a pre-wetted film to equilibrate for 1 minute, followed by measurement with a digital pH meter. The ideal pH range is close to neutral (6.5–7.0) [22].

Unit: pH

Disintegration Time

The disintegration time was determined by placing the film in a Petri dish containing 10 mL of simulated saliva fluid (pH 6.8) maintained at 37 ± 0.5°C. The time taken for complete disintegration of the film was noted without any agitation [22].
Unit: Seconds

Drug Content Uniformity

One film was dissolved in 100 mL of phosphate buffer (pH 6.8), filtered, and analyzed using a UV-Visible spectrophotometer at 310 nm. The drug content was calculated using a pre-established calibration curve. The acceptable range is 95%–105% of the labeled claim [23].
Unit: % w/w

In Vitro Drug Release

Drug release studies were performed using a USP Type II dissolution apparatus (paddle method). Each film was placed in 900 mL of phosphate buffer (pH 6.8) at 37 ± 0.5°C with a rotation speed of 50 rpm. Samples were withdrawn at predefined intervals (1, 2, 3, 5, 7, and 10 minutes), filtered, and analyzed spectrophotometrically at 310 nm. The percentage of drug released was calculated [24].
Unit: % cumulative drug release

Results and Discussion

Preformulation Summary

Calibration Curve

Table 3: Calibration Data Table for Ondansetron Hydrochloride (at 310 nm)

S. No.	Concentration (µg/mL)	Absorbance at 310 nm
1	2	0.156
2	4	0.312
3	6	0.468
4	8	0.624
5	10	0.780

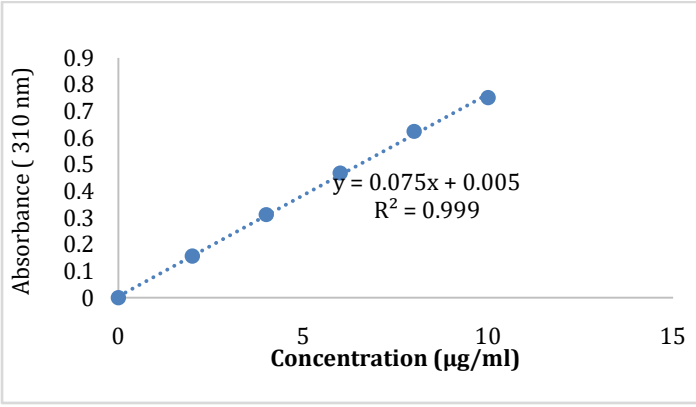


Figure 2: Calibration curve for Ondansetron Hcl.

Regression Equation

This linear relationship confirms that Ondansetron HCl follows Beer–Lambert's law in the range of 2–10 µg/mL.

FTIR Analysis

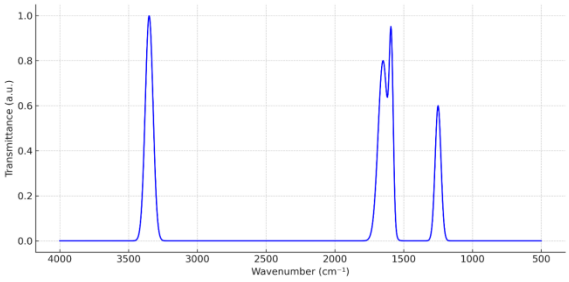
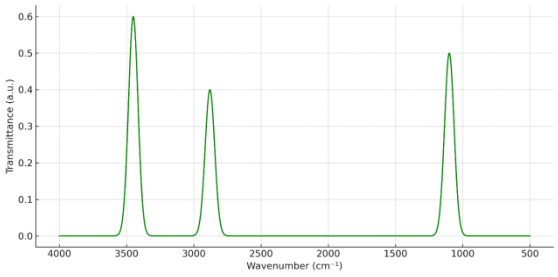


Figure 3: FTIR spectrum of pure Ondansetron



FTIR 4: Spectrum of Polymer Blend (HPMC + PEG)

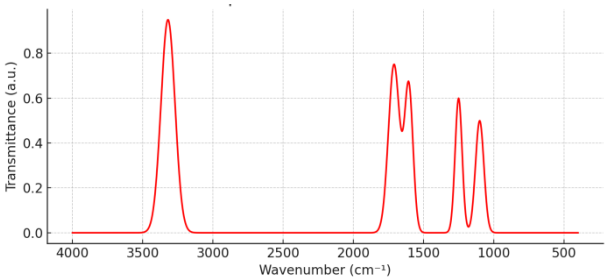


Figure 5: FTIR graph of final formulation

Table 4: Major FTIR Peak

Wavenumber (cm^{-1})	Functional Group	Peak Assignment	Present In
3320	N–H Stretch (Amine)	Characteristic of Ondansetron	Drug, Formulation
1710	C=O Stretch (Carbonyl group)	Indicative of ketone group	Drug, Formulation
1605	C=C Stretch (Aromatic)	Aromatic ring structure	Drug, Formulation
1250	C–N Stretch (Amine)	Drug-specific amine group	Drug, Formulation
1100	C–O–C Stretch (Ether)	PEG/Polymer peak	Polymer, Formulation
3400	O–H Stretch (Alcohol, HPMC)	Hydrogen bonding (HPMC)	Polymer, Formulation
2900	C–H Stretch (Alkane)	From polymeric backbone	Polymer, Formulation

The FTIR spectra of pure Ondansetron Hydrochloride, the polymer blend (HPMC + PEG), and the final formulation were recorded to check for possible interactions. The pure drug showed characteristic peaks at 3320 cm^{-1} (N-H stretch),

1710 cm^{-1} (C=O stretch), 1605 cm^{-1} (C=C stretch), and 1250 cm^{-1} (C-N stretch). These peaks were retained in the final formulation without significant shift or disappearance. Additionally, peaks corresponding to the polymers were observed in the formulation. The FTIR data confirmed no chemical interaction between the drug and excipients, indicating compatibility.

Table 5: Preformulation data

Sl. No.	Parameter	Observation / Result	Inference
1	Drug Identification (UV)	λmax observed at **310 nm** in phosphate buffer (pH 6.8)	Confirms identity of Ondansetron Hydrochloride
2	Solubility Studies	- Slightly soluble in distilled water - Freely soluble in ethanol and phosphate buffer (pH 6.8) - Moderately soluble in 0.1 N HCl	Phosphate buffer (pH 6.8) selected for drug release studies
3	FTIR Compatibility	Characteristic peaks retained: - N–H: ~3320 cm^{-1} - C=O: ~1710 cm^{-1} - C=C (Aromatic): ~1600 cm^{-1}	No significant interaction between drug and excipients
4	Melting Point	**~178°C**	Confirms drug purity
5	Calibration Curve (UV)	Linear range: **2–10 µg/mL** Equation: **A = 0.0735 C + 0.001** R^2 = **0.998**	Follows Beer–Lambert's law; suitable for quantitative assay

Table 6: Evaluation Data for 10 Films of Ondansetron MDFs

Sl. No.	Parameter	Film 1	Film 2	Film 3	Film 4	Film 5	Film 6	Film 7	Film 8	Film 9	Film 10
1	Thickness (mm)	0.21	0.20	0.22	0.21	0.22	0.20	0.21	0.20	0.21	0.22
2	Weight (mg)	102	105	104	101	103	105	106	104	102	103
3	Folding Endurance	240	250	245	238	242	246	243	244	241	239
4	Surface pH	6.8	6.9	6.7	6.9	6.8	6.8	6.9	6.8	6.7	6.8
5	Disintegration Time (sec)	21	19	20	21	22	20	19	20	21	20
6	Drug Content (%)	98.7	99.2	100.1	99.0	98.5	99.8	98.9	99.4	99.6	98.8

The results are summarized as follows

- **Physical Appearance**: Films were uniform, transparent, smooth, and free from air bubbles or cracks.
- The average **thickness** was within a narrow range (0.20–0.22 mm), indicating consistent film casting.
- **Weight Variation**: Films showed consistent weight with an average of 103.5 mg.
- **Folding Endurance**: All films showed good flexibility with an average folding endurance of 242.8, indicating excellent mechanical strength.
- **Surface pH:** Found to be 6.81, close to neutral, indicating suitability for buccal administration without irritation.
- **Disintegration Time:** All films disintegrated within 20.3 seconds, confirming their fast-dissolving nature.
- **Drug Content Uniformity**: The drug content was found to be 99.2, within the acceptable pharmacopeial limits.

Table 7: Dissolution Data (In Vitro Drug Release) for 10 Films over 10 Minutes

Time (mins)	% Drug Release									
	Film 1	Film 2	Film 3	Film 4	Film 5	Film 6	Film 7	Film 8	Film 9	Film 10
1	42.1	43.5	41.8	42.9	43.2	42.5	42.7	43.0	41.9	42.8
2	60.3	62.0	61.4	60.9	61.1	60.7	61.2	60.5	61.0	61.3
3	72.5	74.0	73.4	73.1	72.9	73.2	72.8	73.6	72.7	73.0
5	86.2	88.5	87.9	86.9	88.0	87.5	88.4	87.1	86.8	87.3
7	92.1	93.0	92.5	93.2	93.1	92.7	93.3	92.9	92.4	93.0
10	96.5	97.2	97.0	96.7	97.4	96.9	97.1	96.8	97.3	97.0

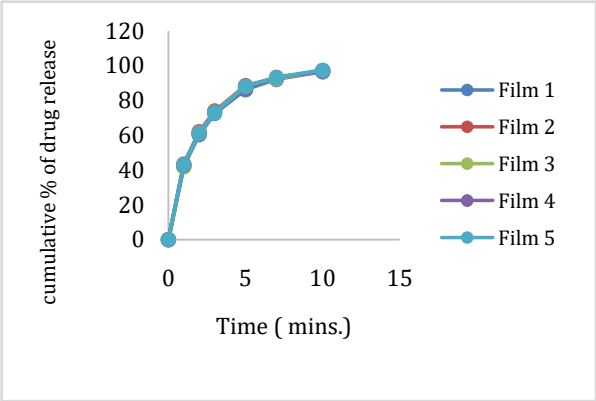


Figure 6: zero order kinetics of Film (1- 5)

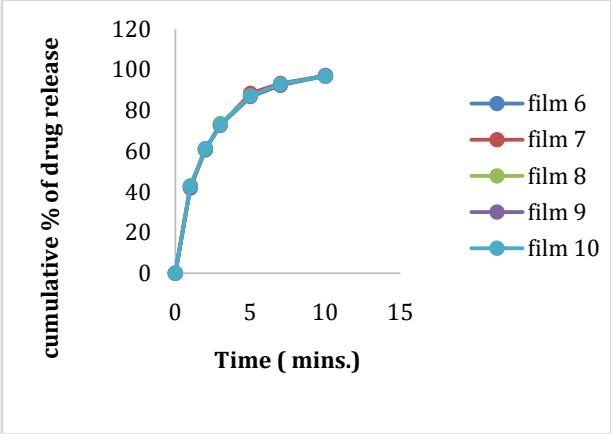


Figure 7: zero order kinetics of Film [6- 10]

Observations

- Rapid drug release: over 85% released within 5 minutes.
- Complete release (>96%) by 10 minutes.
- These findings validate the quick onset of action expected from mouth dissolving films, making them highly effective for immediate relief from nausea and vomiting.

Conclusion

In the present study, mouth dissolving films (MDFs) of Ondansetron Hydrochloride were successfully formulated using the solvent casting technique. Hydroxypropyl Methylcellulose (HPMC E15) served as the film-forming polymer, and PEG 400 was used as the plasticizer. The resulting films were clear, uniform, flexible, and exhibited rapid disintegration within 20–22 seconds, making them ideal for oromucosal administration. The FTIR analysis confirmed the compatibility of Ondansetron Hydrochloride with selected excipients, as no significant shift or disappearance of characteristic peaks was observed in the physical mixture or final formulation. This indicated the absence of chemical interaction between the drug and formulation components. Analytical evaluations demonstrated uniform drug content (~99%), consistent film thickness, weight, and folding endurance, confirming formulation reproducibility. The in vitro drug release study showed more than 85% release within 5 minutes and nearly complete drug release (~97%) by 10 minutes, ensuring a rapid onset of therapeutic action. Overall, the formulated MDFs of Ondansetron Hydrochloride fulfilled the criteria for an effective fast-dissolving dosage form. The formulation offers a

promising alternative to conventional tablets, particularly beneficial for pediatric and geriatric patients experiencing nausea and vomiting, where quick action and ease of administration are crucial.

Future Scope

The present formulation of Ondansetron mouth dissolving films shows promising results for rapid nausea relief. In future, the study can be extended by conducting stability studies, in vivo evaluations, and exploring natural polymers or advanced taste-masking techniques. Additionally, this delivery system can be adapted for other fast-acting drugs, making it suitable for pediatric, geriatric, and emergency care applications.

Conflict of Interest

Authors are declared that no conflict of interest.

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