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Oral Thin Films of Ondanetron HCL: Formulation and Performance Evaluation

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Abstract

This study had the goal to formulate oral polymeric thin film that would dissolve and disintegrate instantly, while also having high mechanical features. These are the most advanced forms of solid dosage forms. Solvent casting was the technique employed to create oral thin films. These are additionally referred to as buccal films/strip, mouth dissolving films, oral thin films, as well as oral strips of paper. These films are suitable for both elderly and young individuals because they dissolve instantly and do not require water. Their quick dissolution facilitates rapid drug absorption through the oral mucosa, enhancing bioavailability and enabling swift onset of action, which is particularly vital for medications requiring immediate effects or emergency situations. Advantages of these films include convenient dosing, no risk of chocking, patient compliance, site specific and local action. Special features of these films include dose accuracy, mucoadhesive, rapid release. For the manufacturing of oral thin film, ondansetron hydrochloride, an antiemetic drug categorized into BCS class II, was employed. Ondansetron is used for the prevention of the symptoms of chemotherapy-induced nausea and vomiting. It is an antagonist belonging to the serotonin 5-HT3 receptor class. To optimize the polymers HPMC E15, polymer content, plasticizer (glycerol, propylene glycol), and sweetener (aspartame), the formulations from the preliminary trial were investigated. The thickness, folding durability, drug content, swelling index, surface pH, in vitro disintegration time, along with in vitro dissolution investigations of the resulting films were investigated. Propylene glycol-prepared oral thin films responded better than the ones developed with glycerol plasticizer with regard to solubility and the breakdown capabilities. In less than 30 seconds, the optimal film (F2) began to break down, releasing more (92.23). By subjecting the data to statistical analysis (ANOVA) the observed f value is 1.36 and p value is 0.252.

Keywords: Oral thin films, ondansetron, polymers, solvent casting method, drug delivery systems.

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INTRODUCTION

An oral thin film is a type of medication delivery system containing active ingredients that quickly disintegrate, typically within seconds when placed on the tongue. It utilizes a water-soluble polymer, often a hydrocolloid, which may also serve as a bio adhesive. This feature enables the film to rapidly hydrate, adhere, and dissolve upon contact with the tongue or oral cavity, facilitating swift absorption for both local and systemic drug effects. The FDA prefers the term ‘soluble film’ due to its rapid dissolution, while the European Medicines Agency refers to it as ‘oro-dispersible film’.

Oral polymer thin films are the most advanced form of solid dosage forms due to their superior

flexibility and comfort. The mouth dissolves in less saliva than fast-dissolving tablets, and chewing or water is not necessary for administration, which enhances the effectiveness of active pharmaceutical ingredients in aphasia patients. dizziness, repeated vomiting and mental disorders that cannot swallow large amounts of liquid in dosage form. The advantages of convenient dosing and portability of oral film allow for wide application of this dosage form in pediatric and hospitalized patients.

The medication that is administered goes by the name Ondansetron, and its primary goal is to relieve nausea and vomiting which may ensue following radiation therapy, chemotherapy, or surgery. It is among the members of a category of medication designated as antagonists of the hormone serotonin 5-HT3 receptor [1]. Ondansetron suppresses the feeling of nausea and vomiting by functioning on the brain's vomiting area and blocking serotonin activity. It occurs in many kinds of forms, including injections, pills, and tablets which disintegrate in the mouths. Frequently, oral editions are taken as suggested by a healthcare medical professional, paired with or without food. For patients who could be experiencing trouble swallowing, the oral disintegrating tablets' immediate tongue dissolving without the need for water can be convenient.

Patients undergoing chemotherapy for cancer or certain kinds of surgery where nausea and vomiting are prominent side effects are frequently prescribed ondansetron. Despite it is typically well tolerated, adverse reactions are likely depending on the medication. Headache, constipation, restlessness, and dizziness frequently experienced negative side effects. Allergic reactions, cardiac arrhythmia and symptoms of serotonin syndrome are unusual but theoretically more hazardous negative consequences, especially after being administered with additional medications which impact serotonin levels.

HPMC[E15] polysaccharides are developed. A semisynthetic polymer that is composed of cellulose is designated as hydroxypropyl methylcellulose [2]. It frequently serves as a stabilizer, thickening agent, and film-forming agent in pharmaceutical formulations. HPMC E15 is frequently used throughout oral solid forms of administration, which include capsules and tablet forms, in pharmaceutical manufacturing. The synthetic polymer HPMC E15 is employed on account of its enhanced film-forming competencies, accelerated disintegration, and hydrolysis [3]. Whenever a hydrophilic polymer dissolves in water, its fundamental stages include the absorption of water on the polymer, polymer connection breakdown and concomitant establishment of water polymeric bonds, chain separateness, inflammation, and ultimately dissemination of the chains of polymers in the medium.

Manufacturing oral thin-film Ondansetron HCl for prompt disappearing in the oral cavity was the most important objective of this work [4]. The films underwent evaluation shortly after having been produced employing the solvent-based casting the process. This study optimizes the plasticizer's concentration and type additionally to optimizing the polymer's saturation [5].

Materials and Method

- *Materials:* Ondansetron (drug), HPMC E-15, ethanol, aspartame, propylene glycol, glycerol, distilled water. All reagents are of analytical grade [6].
- *Preparation of oral thin films:* They are different methods to prepare oral thin films, such as hot melt extrusion, solvent casting, rolling method, solid dispersion, semi solid casting oral thin films are developed adopting the solvent-based molding approach [7].
- *Solvent casting method:* Oral thin films were prepared by dissolving the polymer (HPMC[E15]) in solvent mixture (distilled water and ethanol), with continuous stirring drug, aspartame is added [8]. To the resulting solution plasticizers (glycerol, propylene glycol) are added subsequently and stirred for 15 minutes. These solutions were cast slowly on to a glass petri plates without formation of air bubbles [9]. (Each strip 2 x 2 cm^2 consists of 4 mg of drug). These plates were

kept aside for 48 hrs and dried films are carefully separated from the petri plate and cut into desired size, shape. Then films are evaluated [10]. Various formulations were prepared as per Table 1.

Table 1. Formulation of oral thin films.

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Drug (mg)	4	4	4	4	4	4
HPMC E15 (mg)	80	100	120	80	100	120
Propylene glycol (ml)	0.3	0.3	0.3	–	–	–
Glycerol (ml)	–	–	–	0.3	0.3	0.3
Aspartame (mg)	0.5	0.5	0.5	0.5	0.5	0.5
Ethanol (ml)	1	1	1	1	1	1
Distilled water	q.s	q.s	q.s	q.s	q.s	q.s

Evaluation of Oral Thin Films

- *Thickness:* To ensure consistency in film width, the outermost layer of the films has been measured using a micrometer for measurement at five distinct points. Following estimating an average thickness, sections exhibiting breadth fluctuations bigger than 5% had been excluded in the statistical evaluation.
- *Foldable tolerance:* To determine a film's foldable perseverance, identically sized films (4 by 4 cm) were then folded repeatedly unless the film shattered.
- *Enlargement score:* Swelling index investigation is implemented for estimating exactly how much the polymer (HPMC E-15) is accountable for the film's enlargement.
- *Medication composition:* For determination of the medicinal product information, disintegrate a 4 cm^2 film in 100 milliliters of 6.8 pH phosphate buffer. Before a component of the solution was adequately diluted, and the absorbance at 259 nm was considered.
- *The Surface the pH level:* A pH meter was implemented for determining the film's surface pH levels. With the support of moisture, OTF was saturated. By maintaining contact amongst the conducting electrode as well as the film's surface, the pH was established. It has been determined that conserving the outermost the pH level as similarly neutral as practicable is necessary in maintaining the pH of the film due an alkaline or buffered pH might irritation the mucous membrane of the mouth.
- *In vitro destruction time:* The preliminary a position incorporates two uncomplicated procedures: a 10-ml pipette comprising just one teaspoon of dissolution media outlets was dropped onto the securely fastened film. Disintegration time is the duration of period that it needed for water to get through the film.
- *In-vitro disintegrating investigations:* 900 milliliters of phosphate buffer was employed to serve as the disappearing media during an in-vitro dissolution investigation the fact that was performed in a USP II paddling disintegration apparatus. The ambient air temperature had been maintained at 37 ± 0.5° C using the 50-rpm frequency. Occasionally, a 1 milliliter amount of the disintegrating medium was drawn in. The corresponding volume of disintegrating medium has been added before every extraction [11]. Using a UV-visible spectrophotometer set at 310 nm, the absorbance was measured, and the quantity of medications released was quantified.

RESULTS AND DISCUSSIONS

Evaluation Parameters

- *Thickness:* The mean thickness of the oral thin films was found to be in the range of 0.083 mm to 0.092 mm.
- *Folding endurance:* A range of 40 to 150 had been chosen to correspond with the degree of folding tolerance of the orally thin films [12]. Better flexibility has been observed in the films of formulae F2, F3, F5, and F6. It becomes apparent because the remaining the equations are particularly vulnerable.
- *Swelling index:* The range of 97–146 has been determined to be the level of swelling associated

with the oral thin films. HPMC E15's polymer was having excellent swelling capabilities [13].

- *Medication composition:* A range of 95 ± 0.0 to 99.64% has been identified about the oral strip's drug content, corresponding to 4 cm^2. It has been determined that F2 encompasses a high drug content. The concentration of the medication has been determined to be around 87 & 105% as specified by USP [14].
- *Surface pH:* The surface pH of the drug was found to be 6.3–7.5.
- *In vitro disintegration test:* The duration of disintegration will be determined to provide an overall understanding regarding the oral dissolving film disintegration time. It was determined that the F2 composition broke down the fastest, taking 33 seconds, while the F4 formulation dissolved breakdown the slowest, consuming 84 seconds [15]. The low standard deviation among the formulated films demonstrated that the films that had been manufactured were virtually identical. Originally the films' disintegration periods were displayed in ascending order, they were F2 > F1 > F3 > F5 > F4. Oral film eventually fragmented as an outcome of water's ability to hydrate HPMC (Table 2) [16].

Table 2. The properties of formulation.

Formulation Code	Folding Endurance	Swelling Index	Disintegration Time
F1	65	99	57 sec
F2	145	142	33 sec
F3	112	97	65 sec
F4	56	102	84 sec
F5	127	113	49 sec
F6	119	124	54 sec

In Vitro Dissolution Studies

Formulation containing propylene glycol as plasticiser showed maximum drug release within 110 sec the release was found to be 92.23% F2, 82.02% F3, 88.42% F4, 86.23% F5,84.12% F6 from Table 3. The release of F5 is less than F2 this can be attributed due to change in plasticiser [17]. F1 shows still lesser due to less concentration. The formulation with propylene glycol and glycerine shows the following order of release F2 (92.23%) > F4 (88.42%) > F5 (86.23%). The equivalent amount of medication [18–20] was released by the other formulation nearly exactly. F1 had the lowest percentage of drug release (Figure 1).

Table 3. Time vs. percentage of drug released.

Time in Min	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	23.65	20.1	25.63	22.76	21.78	21.7
10	31.19	32.67	36.01	33.02	34.12	42.17
15	49.92	55.89	52.42	54.28	56.25	58.15
20	62.12	68.44	58.56	56.42	64.24	70.17
25	72.46	86.44	78.63	76.68	74.74	79.22
30	78.08	92.23	82.02	88.42	86.23	84.12

Statistical Analysis

F value is 1.36 suggests that group means are significantly same not much variation is observed. P value 0.25 indicates null hypothesis cannot be rejected. Variation in the group can be neglected (Table 4).

CONCLUSION

With the objective to achieve optimum therapeutic efficacy, promote patient compliance through decreased administration frequency, and take care of additional concerns connected with conventional parenteral formulation, Ondansetron Hcl oral dispersing films were successfully manufactured and investigated. According to the analysis of the study's conclusions, everything generated film demonstrated significant appropriate properties with respect to of the drug's integrity and dissemination. Each of the films had the same thickness and had resilient folding endurance (142), demonstrating that the films could stand exceptionally well to normal wear and tear. The formulations' fast the decomposition and surface pH equivalence to the oral cavity should encourage patient compliance by offering the medicinal product a pleasant sensation whenever wet by salivary and an instantaneous release of pharmaceutical after absorbing water. Maximum release has been demonstrated using formulation F2 (92.23%). By subjecting the data to statistical analysis (ANOVA) the observed f value is 1.36 and p value is 0.252.

Table 4. ANOVA analysis of drug release data.

Anova: Single Factor						
Summary						
Groups	***Count***	***Sum***	***Average***	***Variance***		
Time in Min	7	105	15	116.6667		
F1	7	317.42	45.34571	806.0568		
F2	7	355.77	50.82429	1195.926		
F3	7	333.27	47.61	862.2866		
F4	7	331.58	47.36857	954.8868		
F5	7	337.36	48.19429	948.7065		
F6	7	355.53	50.79	974.8441		
ANOVA						
Source of Variation	***SS***	***df***	***MS***	***F***	***P-value***	***F crit***
Between Groups	6833.981	6	1138.997	1.360722	0.252719	2.323994
Within Groups	35156.24	42	837.0533			
Total	41990.22	48				

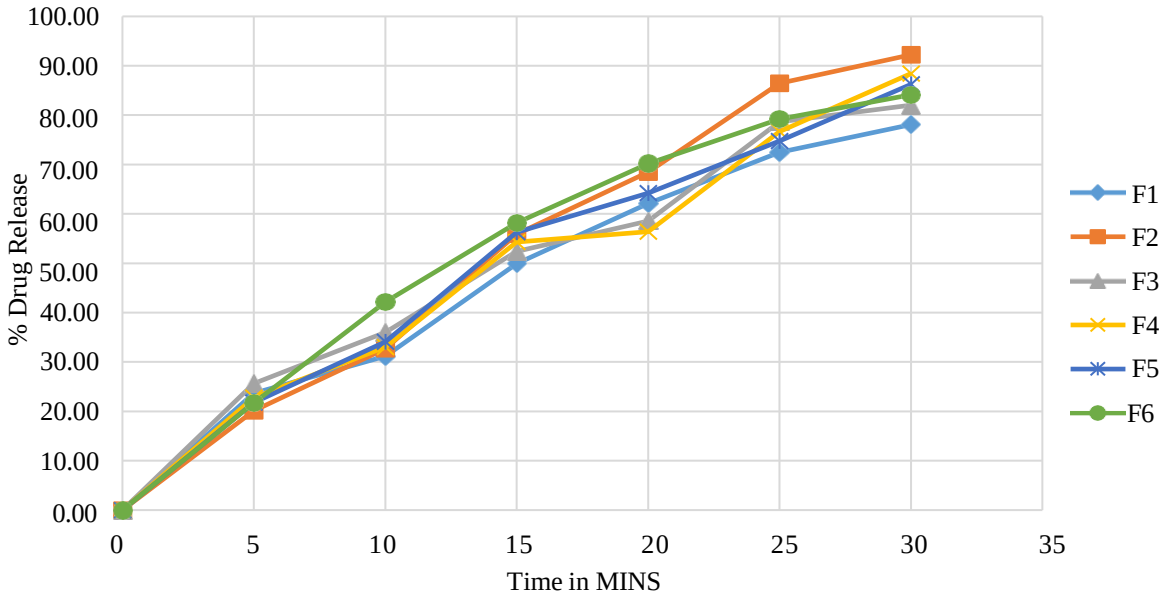

Figure 1. Time vs percentage of drug release of ondansetron Hcl PBS 6.8.

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