IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
January 2023 Vol.:26, Issue:2

Formulation and *In Vitro* Evaluation of Ondansetron Oral Thin Films

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Dhendi Sandhya*[1], P. Jyothi[2]

[1]*Student, Department of Pharmaceutics, Holy Mary Institute of Technology and Science College of Pharmacy, Hyderabad, Telangana, India*

[2]*Department of Pharmaceutics, Faculty and HOD of Pharmaceutics, Holy Mary Institute of Technology and Science College of Pharmacy, Hyderabad, Telangana, India*

Submitted: 25 December 2022
Accepted: 31 December 2022
Published: 30 January 2023

Keywords: Ondansetron, Ludiflash, crospovidone, oral disintegrating thin patches.

ABSTRACT

Patients who have difficulties swallowing tablets/capsules may benefit from a fast-dissolving medication delivery method. The current study aims to create oral thin films of Ondansetron utilizing the solvent casting process. Oral thin patches were created by combining different super disintegrants such as ludiflash (1,2,3,4 and 5% w/w), crospovidone (1,2,3,4 and 5% w/w) concentrations with Gelatin and Polyvinyl alcohol as film-forming agents. The patch formulations were tested for film thickness, folding durability, in-vitro disintegration time, and in-vitro drug release pattern (in pH 6.8 phosphate buffer). Drug composition and drug-polymer interaction research (IR spectroscopy). The formulation (F5) created with 5% ludiflash has the highest drug release rate (98.34%) of all formulations tested.

INTRODUCTION

Fast fast - dissolving films have gained popularity as a novel delivery technique since they are simple to use and provide for rapid commencement of medication activity because they are administered sublingually. Because the sublingual mucosa is permeable due to its thin membrane and is strongly perfused, fast drug absorption and immediate bioavailability are achievable, resulting in a rapid commencement of pharmacological action. Because the medicine is absorbed directly into the systemic circulation, it avoids degradation in the gastrointestinal (GI) tract and the first-pass effect. 1 Furthermore, higher patient compliance is predicted since this approach does not need swallowing like a traditional tablet, which is advantageous in patients with dysphagia or trouble swallowing. The introduction of mucoadhesive polymers in the films allows them to stick to the sublingual mucosa, resulting in improved retention and medication absorption. 2.

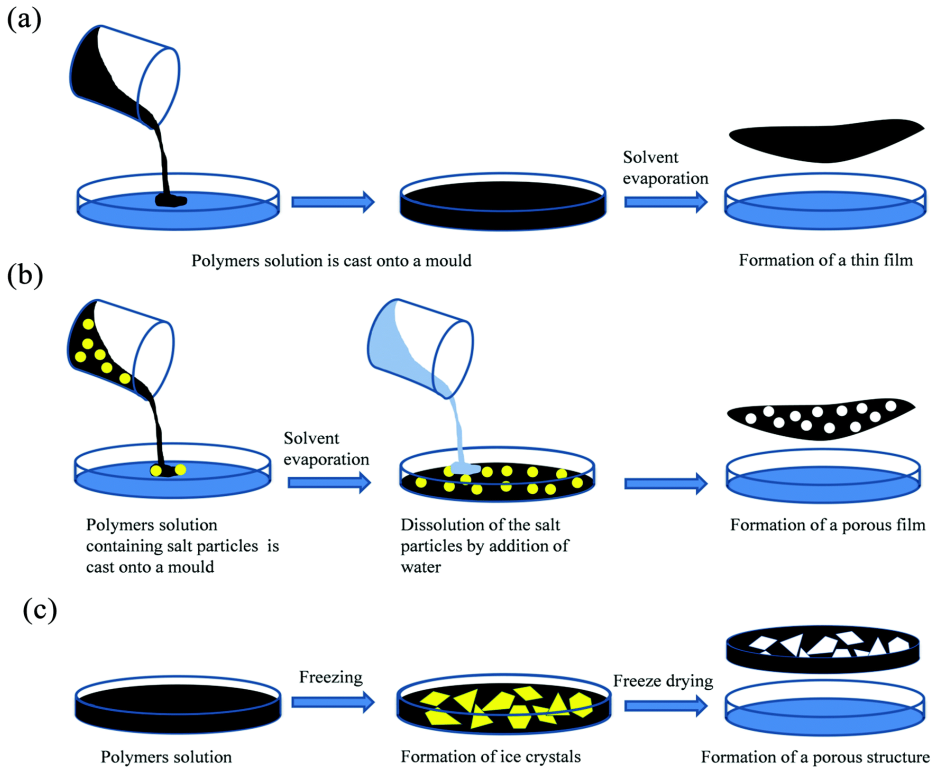

Figure no.1. Solvent Casting Technique

In recent decades, there has been a surge in the development and manufacturing of innovative dosage forms to enhance patient compliance and quality of life. The feasibility of employing oral solid dosage forms is a serious concern in various patient populations, such as children, geriatrics, and patients with nausea and vomiting, or swallowing difficulties. 3,4.ODFs are

oral strips comprised of hydrophilic polymers that include active ingredients and excipients. When these lms come into touch with saliva, they dissolve quickly and release the medicine promptly. 5,6. Simple fabrication and a less expensive manufacturing technique.6,7.as well as flexibility and a greater likelihood of patentability 8. The films make it simple to deliver medications to youngsters, the elderly, and patients who are immobile. A film's flavor, stability, and ease of handling are all desirable features. 9. A fast-dissolving oral thin film (FDF) is a solid dose medium; when put in the mouth without water or chewing, OTFs disintegrate or dissolve in 1 minute. 10. As saliva runs down into the stomach, pre-gastric uptake from the mouth, throat, and esophagus improved the drug's therapeutic efficacy as it decomposed in the mouth.11. Fast-dissolving films may prefer adhesive tablets because of their flexibility and comfort.12. There are numerous polymers available for the production of FDF. 13.

Polymers, active pharmaceutical additives, film stabilizing agents, sweeteners, flavors, textures, saliva-inducing agents, preservatives, surfactants, and other ingredients are used in the preparation of the film, but the polymer is the first and most important ingredient that aids in film formation. Oral thin films, compressed tablet-based uses, and lyophilized devices are the three categories of fast-dissolve technologies. 14.

Figure.2.Oral Thin Films

Ondansetron is a 5-HT3 serotonin receptor antagonist used to decrease nausea and vomiting during cancer treatment and after surgery. A competitive antagonist of the serotonin type 3 receptor. It is useful in treating nausea and vomiting produced by cytotoxic chemotherapy medicines such as cisplatin, and it has anxiolytic and neuroleptic characteristics. Ondansetron, which was developed by GlaxoSmithKline in the 1980s and has been licensed by the US FDA since January 1991, has a long history of usage and efficacy. Ondansetron, which is commonly formulated as oral tablets, orally disintegrating tablets (ODT), and injections, and is also available as a generic product, continues to see modern innovations in

its formulation and use, including the development of orally soluble films that are both discreet in administration and less of a burden in comparison to having patients take tablets.15Due to a substantial risk of QT prolongation, the FDA revoked authorization for the use of all intravenous medication containing products and over 16 mg of ondansetron HCl in a single dosage.16,17.Ondansetron was studied in single intravenous dosages of 8 mg, and 32 mg over 15 minutes.18,19.

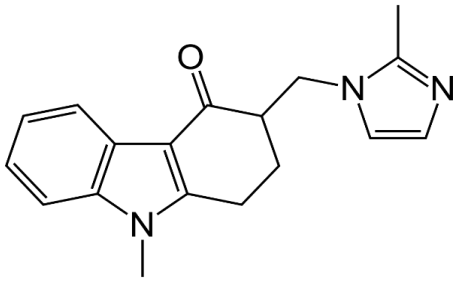

Figure no.3.Structure of Ondansetron

Ondansetron hydrochloride is efficiently absorbed through the buccal or sublingual mucosa, according to studies.20

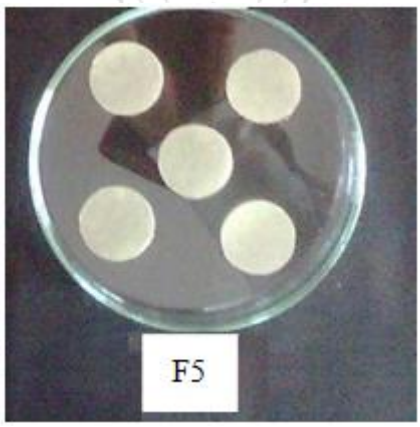

Figure.4: Picture depicting the best formulation F5

MATERIALS AND METHODS USED:

Ondansetron API was procured from Kekule Pharma Limited and P.V.A from INRchem. Mumbai, HPMC K4M from Hi Medialab. Pvt. Ltd.Mumbai, Povidone from Signet Chemical Corp., Mumbai, and PEG 400, Citric acid, Gelatin, and Ludiflash were procured from S.D Fine Chemicals, Mumbai.

Preparation Method:

Formulation of Oral Disintegrating Thin Films of Ondansetron:

From the preliminary physical observation of the films prepared the best compositions were used for the incorporation of Ondansetron. Gelatin and PVA polymers were dissolved in water with continuous stirring. The calculated amount of Ondansetron was dissolved in propylene glycol and add it to the polymeric solution, after complete dissolution of the drug; propylene glycol (plasticizer) was added and stirred to form a homogeneous solution and add disintegrants. The solution was cast onto a mercury substrate and then kept in a hot air oven at 40ºC for 2 hrs. The film thus formed was cut into a size of 2 cm diameter. Each film contains 10 mg of Ondansetron. The oral disintegrating thin films of Ondansetron were prepared by solvent casting technique. The ODT films were prepared using polymers like Gelatin, and PVA. Propylene glycol is used as a plasticizer. The calculated amount of polymer was dispersed in the three-fourth volume with continuous stirring using a magnetic stirrer and the final volume was adjusted with distilled water. The calculated amount of Ondansetron was incorporated in the polymeric solutions after levitation with the required volume of PEG. The solution was cast onto a mercury substrate and then kept in a hot air oven at 400c. The films were punched into size 2cm diameter containing 10mg of Ondansetron. By carrying out the trial and error method different concentrations of film-forming polymers were used like Gelatin and PVA. It has been found that 4.5%of gelatin and 3.5% of PVA show better films. These concentrations of films were prepared by dissolving different quantities of film-forming polymers in 10 ml of water.

Table 1: Formulation details of Ondansetron Oral disintegrating thin films

Formulation	*Ondansetron (mg)*	*Gelatin (%)*	*PVA (%)*	*Ludiflash (%)*	*povidone (%)*	*Citric acid (mg)*	*Trusil flavor (mg)*	*PG (mg)*
F1	90	4.5	--	1	--	4	8	30
F2	90	4.5	--	2	--	4	8	30
F3	90	4.5	--	3	--	4	8	30
F4	90	4.5	--	4	--	4	8	30
F5	90	4.5	--	5	--	4	8	30
F6	90	--	3.5	--	1	4	8	30
F7	90	--	3.5	--	2	4	8	30
F8	90		3.5	--	3	4	8	30
F9	90	--	3.5	--	4	4	8	30
F10	90	--	3.5	--	5	4	8	30

Evaluation of ODT Dissolving Oral Thin Films:

Post-formulation studies:

The Ondansetron ODT films were evaluated for the following properties.

a) Physical appearance and surface texture of the patch:

This parameter was checked simply with a visual inspection of films and an evaluation of texture by feel or touch.

b) Weight uniformity of films:

Three films of the size 2cm diameter were weighed individually using digital balance and the average weights were calculated.

c) The thickness of films:

The thickness of the films was measured using a screw gauge with a least count of 0.01mm at different spots of the films.

d) Folding endurance of films:

The flexibility of films can be measured quantitatively in terms of what is known as folding endurance. The folding endurance of the films was determined by repeatedly folding a small strip of the films (approximately 2x2 cm) at the same place till it broke. The number of times films could be folded at the same place, without breaking gives the value of folding endurance.

e) Surface pH of films:

Surface pH was determined by the films allowed in contact with 1 ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of the films and allowing equilibration for 1 min.

f) In vitro disintegration time of films:

The disintegration test was performed in the USP disintegration time testing apparatus. 0.1N HCl solution was used as a medium.

g) Drug content uniformity study of films:

The films were tested for drug content uniformity by a UV-Spectrophotometric method. Films of 2 cm diameter were cut from three different places from the casted films. Each patch was placed in a 100 ml volumetric flask and dissolved in 0.1N HCl solution and 0.2 ml is taken and diluted with water up to 10 ml.

h) In-vitro Dissolution Study:

In vitro dissolution of Ondansetron Oral disintegrating thin films was studied in USP XXIV dissolution test apparatus 900ml 0.1N HCL solution was used as dissolution medium. The stirrer was adjusted to rotate at 50rpm. The temperature of the dissolution medium was maintained at 37±0.5ºC throughout the experiment. One film was used in each test. Samples of dissolution medium (5ml) were withdrawn utilizing a syringe fitted with a pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 310 nm.

Drug Release Kinetics:

To analyze the mechanism of the drug release rate kinetics of the dosage form, the data obtained were plotted as:

• Zero order release rate kinetics:

To study the zero–order release kinetics the release rate data are fitted to the following equation.

$$F = K.t$$

• First Order Kinetics:

A first order release would be predicted by the following equation.

$$\text{Log } C = \log Co \qquad Kt\ 2.303$$

RESULTS AND DISCUSSION:

Solubility: The solubility of Ondansetron was carried out at 250C using 0.1 N HCL, 6.8 phosphate buffer, and purified water.

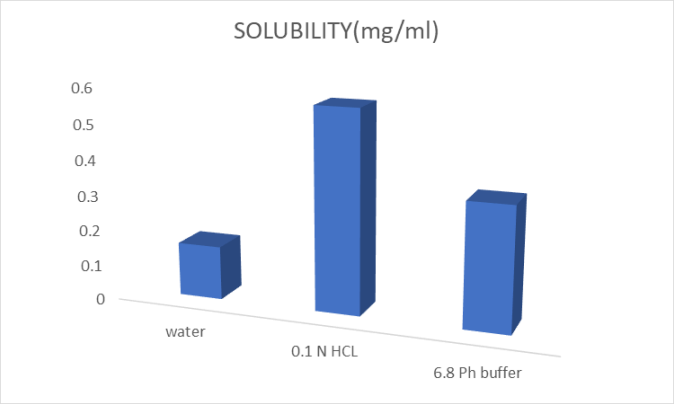

Figure .5.Solubility studies

Discussion: From the conducted solubility studies in various buffers, we can say that 0.1 N HCL solutions have more solubility when compared to other buffer solutions.

Uv spectrum of Ondansetron:

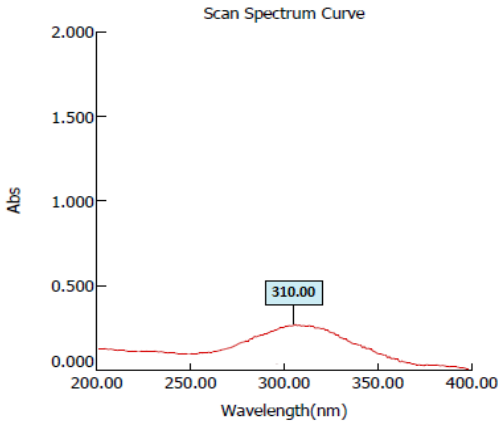

Figure .6. Absorption maxima of Ondansetron in 6.8 pH phosphate buffer

Standard Calibration Curve Of Ondansetron In 6.8 pH Phosphate Buffer:

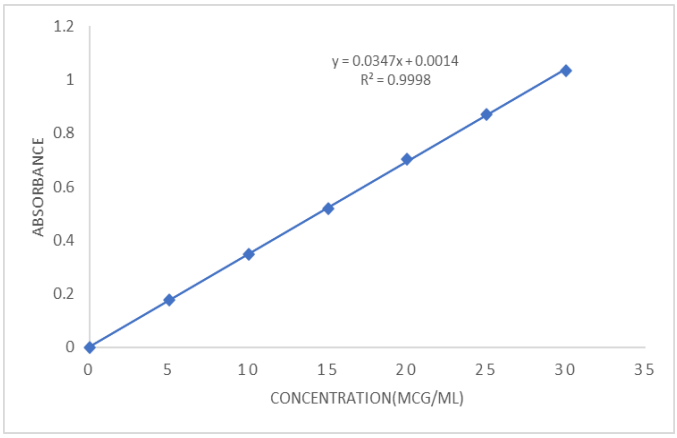

Figure .7.Calibration Curve

Compatibility Study: Compatibility studies were performed using an FT-IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and polymer were studied by making a KBr disc. The characteristic absorption peaks of Ondansetron were obtained at different wave numbers in different samples.

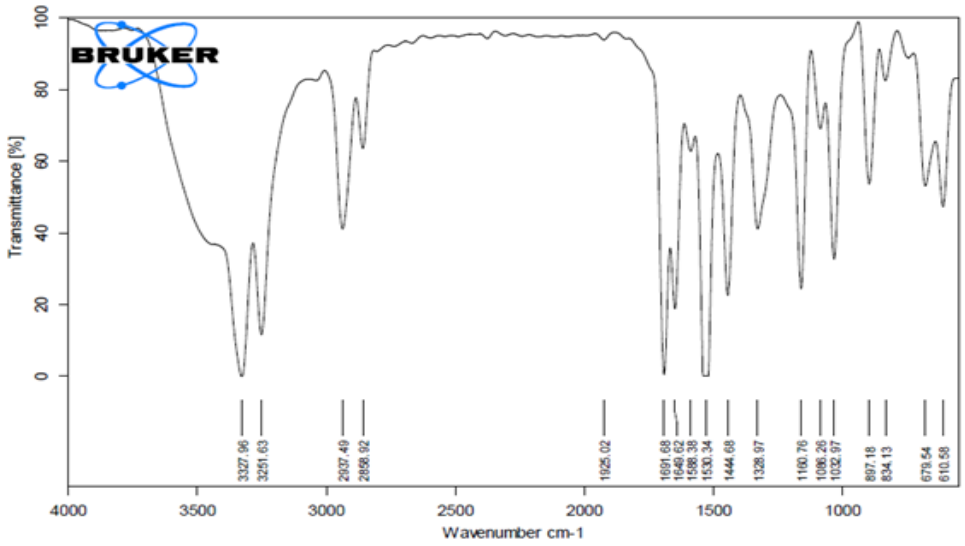

Figure .8.I.R. Spectra of pure drug

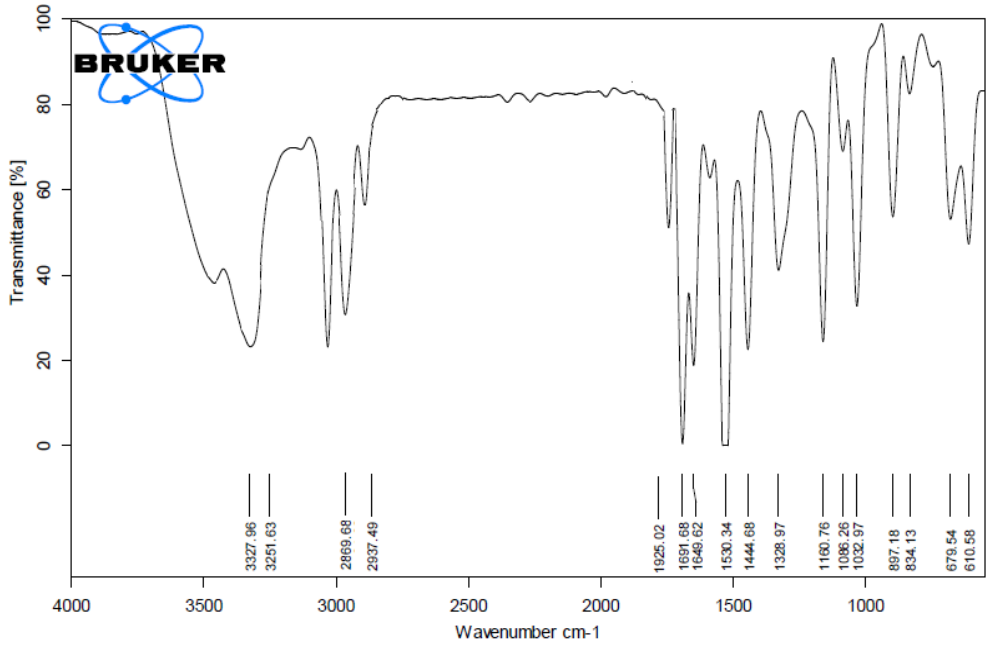

Figure .9.I.R. Spectra of optimized formulation

Evaluation of Oral Disintegrating Thin Films Formulations:

Table .2: Evaluation ofFastDissolving Films ondansetron

Formulation Code	Avg. Weight (mg)	Avg. Thickness (mm)	Avg. Folding Endurance
F1	58.50	0.120	232
F2	60.50	0.122	236
F3	62.50	0.124	238
F4	64.50	0.122	235
F5	66.50	0.120	233
F6	57.50	0.120	244
F7	59.50	0.120	248
F8	61.50	0.122	244
F9	63.50	0.124	245
F10	65.50	0.122	244

Table.3. Evaluation of ODT films of Ondansetron.

Formulation Code	Avg. Drug Content Uniformity	Avg. In Vitro Disintegration (sec)	Avg. Surface pH
F1	98.24	12	6.76
F2	96.22	10	6.00
F3	97.48	10	6.46
F4	98.20	8	6.23
F5	97.42	6	6.66
F6	98.88	17	6.06
F7	98.88	14	6.83
F8	98.26	12	6.06
F9	97.48	10	6.33
F10	97.55	11	6.76

In-Vitro Dissolution Study: The in-vitro drug release study of mouth dissolving films from each batch (F1 to F10) was carried out in 6.8 pH phosphate buffer solution for 30 mins and the values are shown in Table.

Table: 4. In vitro dissolution studies:

TIME(MIN)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
5	42.95	65.42	67.91	69.93	67.49	41.27	48.87	54.78	56.87	58.45
10	57.31	69.37	72.43	74.86	74.04	45.96	54.08	59.85	60.98	64.94
15	66.72	73.07	76.48	79.13	79.19	49.97	58.36	64.19	65.39	70.51
20	72.05	79.19	82.49	84.78	88.06	58.05	66.16	70.69	72.68	77.93
25	81.66	86.83	89.97	92.53	98.34	67.34	75.76	79.71	82.96	83.50
30	88.26	93.75	95.83	98.79		76.68	84.48	89.61	93.06	94.82

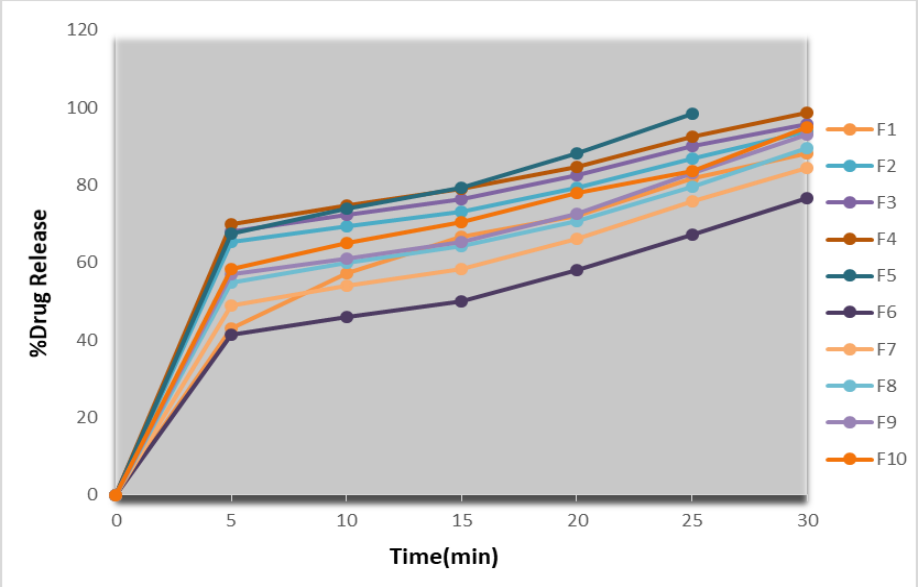

Figure .10.In-vitro drug release of formulationsDrug Release Kinetics Of Ondansetron:

Zero Order Release Kinetic Data:

First Order Release Kinetics Data:

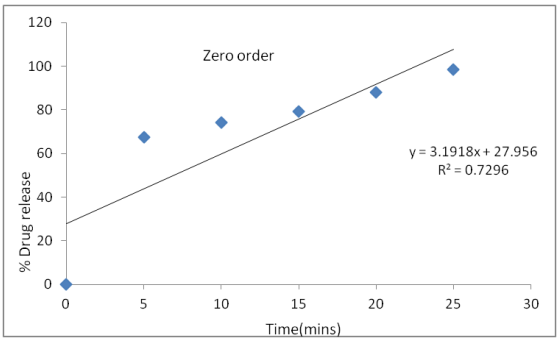

Figure .11.Zero order release profile of Ondansetron Best formulation (F5)

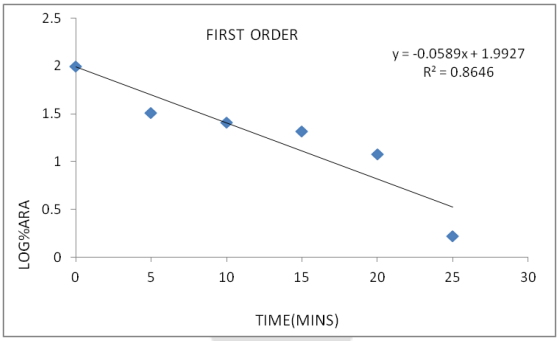

Figure .12.First order release profile of Ondansetron Best formulation (F5)

Table.5: Regression coefficients fit different drug release kinetics models of Ondansetron Best formulation (F5).

Formulation code	Zero-order	First order
	r2	r2
F5	0.729	0.864

The in-vitro dissolution data for best formulation F5 were fitted in different kinetic models i.e, zero order, first order. Optimized formulation F5 follows the first order.

SUMMARY AND CONCLUSION:

In the current study, Ondansetron oral disintegrating drug delivery system was successfully created in the form of oral disintegrating thin films, which provides a suitable and practical method in meeting the intended goal of quicker disintegration and dissolving characteristics with increased bioavailability. Crospovidone and ludiflash were used as super disintegrants to create oral disintegrating thin films of Ondansetron.

API characterization and drug-excipient compatibility tests were conducted as part of the pre-formulation investigations. The API characterization revealed that it complied with the drug's features. To construct the final formulation, the disintegrants, and other excipients were chosen based on the positive findings obtained during drug-excipient compatibility experiments.

The solvent casting procedure with polyvinyl alcohol and ludiflash as disintegrants yielded the final appropriate formulation (F5).revealed a quick disintegration time (6sec) and high in vitro drug release (98.34%).

When the findings of batches containing ludiflash and crospovidone as disintegrants were compared, it was established that the formulation F5 met the higher in-vitro correlation limits in less time than other formulations employing crospovidone as the disintegrating agent. It was also discovered that the solvent casting approach was the most appropriate way for quick drug release. Based on the foregoing factors, these formulations will be put into bioavailability studies, and if they meet all of the requirements of those studies, they will be marketed.

REFERENCES:

1.Jain NK. Controlled and novel drug delivery. 1st ed. India: CBS Publishers and Distributors; 2004. pp. 52–74.
2. Mashru RC, Sutariya VB, Sankalia MG, Parikh PP. Development and evaluation of fast dissolving film of salbutamol sulphate. Drug Dev Ind Pharm. 2005;31:25–34.
3.Arun Arya AC, Sharma V, Pathak K. Fast dissolving oral lms: An innovative drug delivery system and dosage form. Int J ChemTech Res. 2010;2:576-83.
4. Bhyan B, Jangra S, Kaur M, Singh H. Orally fast dissolving lms: Innovations in formulation and technology. Int J Pharm Sci Rev Res. 2011;9:50-57.
5.Koland M, Sandeep VP, R.Charyulu NR, Subrahmanyam EVS. The design and characterisation of sublingual lms of ondansetron hydrochloride. Int J Chem Sci. 2009;7:2927-38.
6.Panda BP, Rao MEB. Development of innovative orally fastdisintrgratinglm dosage forms. Int J Pharm Sci Nanotech. 2012;5:1666-74.
7. Parmar DUP, Bhimani B, Tripathi A, Daslaniya D, Patel G. Orally fast dissolving lms as dominant dosage form for quick release. Int J Pharm Res Bio-Sci. 2012;1:27-41.

8. Dixit R, Puthli S. Oral strip technology: Overview and future potential. J Control Release. 2009;139:94-107.
9.Drumond, N.; Stegemann, S. Better Medicines for Older Patients: Considerations between Patient Characteristics and Solid Oral Dosage Form Designs to Improve Swallowing Experience. Pharmaceutics2021, 13, https://doi.org/10.3390/pharmaceutics13010032.
10. Dwivedi, K.P.; Gupta, A.; Pandey, S.; Singh, A. Fast dissolving drug delivery system: an overview on novel drug delivery system. International Journal of Modern Pharmaceutical Research 2021, 5, 19-32.
11.Patoliya, N.;Joshi, B.; Upadhyay, U. FutureProspect of Oral Disintegration drug Delivery system: A Review.Research Journal of Pharmaceutical Dosage Forms and Technology 2021, 13, 66-71.
12.Shaikh, S.S.; Barrawaz, A. Quality by Design Approach in the Formulation of GlibenclamideMucoadhesiveBuccal Films. Analytical Chemistry Letters 2021, 11,497511,https://doi.org/10.1080/22297928.2021.1938217.
13. Vihar, B.; Rozanc, J.; Krajnc, B.; Gradisnik, L.; Milojevic, M.; CincCuric, L.; Maver, U. Investigating the Viability of Epithelial Cells on Polymer Based Thin-Films. Polymers 2021, 13,https://doi.org/10.3390/polym13142311.
14. Radicioni, M.; Caverzasio, C.; Rovati, S.; Giori, A.M.; Cupone, I.; Marra, F.; Mautone, G. ComparativeBioavailability Study of a New Vitamin D3 Orodispersible Film Versus a Marketed Oral Solution in Healthy Volunteers. Clinical drug investigation 2022, 1-11, https://doi.org/10.1007/s40261-02101113-
15.Gregory RE, Ettinger DS: 5-HT3 receptor antagonists for the prevention of chemotherapy-induced nausea and vomiting. A comparison of their pharmacology and clinical efficacy. Drugs. 1998 Feb;55(2):173-89.
16.Electronic Medicines Compendium: Zofran (ondansetron hydrochloride dihydrate) Tablets 4mg and 8mg Monograph.
17.Zofran Canadian Product Information .
18.Sandoz Ondansetron Canadian Product Information.
19.Ondansetron FDA 2016 Label.
20.Tripathi KD. Essentials of Medical Pharmacology. 5th ed. New Delhi: JP Medical Publishers; 2003. pp. 606–7.