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FORMULATION, OPTIMIZATION AND EVALUATION OF BUCCOADHESIVE PHARMACEUTICAL WAFERS CONTAINING ONDENSETRON HCL

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ABSTRACT

The aim of the work is to design Oral pharmaceutical wafer of Ondensetron HCl by using 3^2 factorial designs. The Total 9 experimental batches (F1…F9) of Ondensetron HCl containing wafers produced following design of experiment and optimized with the help of response surface methodology involving the factors as percentage of polymer and hydrophilic matrix forming, HPMC E 15 as a film forming material, Aspartame as a sweetener and PEG 4000 as a plasticizer. The prepared formulations were subjected for various evaluations such as Appearance, Size and Shape, thickenss, Weight variation, Folding endurance, Percentage moisture loss, Drug content uniformity, Disintegration test, Percent elongation, Surface pH, In-vitro drug release. The study reveals satisfactory results. Hence, the Buccoadhesive Pharmaceutical Wafers Containing Ondensetron HCl is expected to provide clinician with a new choice of safe and more bioavailable formulations.

KEYWORDS: Solvent casting, Fast Disintegrating, Buccoadhesive Wafers, Ondensetron HCL.

INTRODUCTION

Among the Novel Drug Delivery system, buccal drug delivery is the main and extensive acceptable drug delivery between the other delivery systems. Among fast dissolving drug delivery systems, Oral flash release wafer drug delivery system is an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experience in difficulties of swallowing traditional oral solid dosage forms. This technology has been used for local action, rapid release of products and for direct systemic circulation in the oral cavity to release drug in rapid fashion. And also this delivery protect drug from first pass metabolism and improve the dissolution. Oral thin Wafer drug delivery systems are solid dosage forms, which dissolve in a short period of time when placed in the mouth without drinking water or chewing. These are also referred as fast dissolving Oral Wafers, wafers, buccal films, Oral strips.[1]

The wafer quickly dissolves in the oral cavity, and the active ingredient can be absorbed into the blood - stream via the oral mucosa. The active ingredient, once absorbed by the oral mucosa, thus bypasses the liver's first-pass effect, which improves bioavailability. Depending on the selected wafer type, the active ingredient's release may also be delayed. In this case, it is absorbed after swallowing via the gastrointestinal tract.[2,3]

Ondensetron HCl is a drug that is used as an anti-emitting approved by USFDA on 2005 for the treatment of Nausea, and vomiting, caused by cancer chemotherapy, radiation therapy and surgery. It is also useful in gastroenteritis. Also use to controlling postoperative nausea and vomiting and vomiting. The need for Pharmaceutical Wafers thin films has been felt because of the variety of reasons like convenience of dosing and portability of oral thin films have led to wider acceptability of this dosage form by pediatric as well as geriatric population having difficulty in swallowing or chewing.

MATERIALS AND METHODS

MATERIALS

Ondensetron HCl was supplied as a gift sample by Shree swami Samarth Ayurveda Pharmacy (Allopathic division) Jalgaon. HPMC E15, sodium alginate, lactose, PEG-4000 and Aspartame etc. procured from Research-Lab Fine Chemicals Industries, Mumbai.

Development of Pharmaceutical Wafers

The pharmaceutical wafers prepared by using solvent casting method, the base film forming polymer (2% w/v of HPMC) was mixed with the required amount of sodium alginate as per the experimental design and kept for overnight soaking in distilled water containing a constant proportion of propylene glycol, glycerin as plasticizers. A calculated amount of Ondensetron HCl dissolved in aliquot of ethanol was added in the stirred suspension of the plasticized aqueous polymeric gel. Lactose was added in the suspension with continuous stirring followed by mixing aspartame (sweetener) and

peppermint. The stirring process of the total polymeric suspension was continued for 6 hrs. and 25mL of the solution was casted in polypropylene petri plates and kept overnight to remove the entrapped air bubbles. The suspension was dried at 45◦C, and wafers were cut with in-house fabricated hollow punch (dia. 2.2 cm) and kept in desiccators, maintained relative humidity (60 ± 5%) until further analysis. All the 9 experimental batches were designated as (F1…F9) with numerical suffix from 1 to 9 in accordance with the experimental design elaborated in Table 1.[4,5]

Table 1: Batches formulation of Pharmaceutical wafer.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ondensetron (%w/v)	0.134	0.134	0.134	0.134	0.134	0.134	0.134	0.134	0.134
HPMC E15 (% w/v)	1	1	1	1.5	1.5	1.5	2	2	2
Sodium Alginate(%w/v)	-	0.5	1	-	0.5	1	-	0.5	1
Polyethylene glycol (%w/v)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Glycerin (%w/v)	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6
Sorbitol (%w/v)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Aspartame (%w/v)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Peppermint (%w/v)	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Lactose (%w/v)	0.5	1	1.5	1.5	1	1.5	0.5	1	1.5
Ethanol (%v/v)	15	15	15	15	15	15	15	15	15
Water (Up to)	100	100	100	100	100	100	100	100	100

EVALUATION PARAMETERS[6-11]

Drug-Excipients Compatibility

FTIR and DSC studies conducted on pure drug and mixture of drug and excipients for evaluation of Drug-Excipients Compatibility.

General appearance and Thickness

The formulated wafers were checked for their appearance, shape and thickness. The Thickness of the wafer were measured by Vanier caliper micrometer at different locations (five locations; Centre& four corners) and mean thickness was calculated.

Weight variation

Three wafers randomly selected from each formulated batch of prepared wafers of Ondensetron HCl and the average weight variation were determined.

Folding endurance

It is measured by repeatedly folding a wafer at the same point until it breaks. Folding endurance value is number of times the wafer is folded without breaking. Higher folding endurance value depicts the more mechanical strength of a wafer.

Percentage moisture loss

Percentage moisture loss accurately weighed three wafers of area 2 cm x 2 cm and kept in desiccators for 3 consecutive days, wafers were removed and reweighed. The % moisture loss was calculated using the formula.

Percentage moisture loss=W_2-W_1/W_1×100

(Where, w_1=initial weight, w_2=final weight).

Drug content uniformity

To determine the Ondensetron HCl content percent in the wafers, in 100 ml phosphate buffer (pH 6.8), the wafer that contains 4 mg of the drug, was dissolved in a volumetric flask with the aids of ultra sonicator for 30 min, then it was left undisturbed at room temperature for 24 hours, then after the solution was filtered via filter paper and examined by UV spectrophotometer at wavelength of 310 nm and drug content was calculated.

Disintegration test

Disintegration test was performed in the USP disintegration apparatus. Disintegrating time is defined as the time (seconds) at which a wafer breaks when brought in contact with water or saliva. The wafers were placed in the tubes of the container and the disks were placed over it. The average disintegration time of three wafers from each formulation batch was noted.

Percent elongation

When stress is applied, a wafer sample stretches and this is referred to as strain. Strain is basically the deformation of wafer divided by original dimension of the sample. Generally elongation of film increases as the plasticizer content increases.

% Elongation = increase in length/original length X 100

Surface pH

The pH meter was employed to measure the surface pH of the wafer by bringing the electrode in contact with a swollen yet intact wafer after exposure to 1 mL of distilled water for 1 min at the room temperature. The pH was recorded after direct contact between the electrodes with the surface to equilibrate for 1 minute.

In -vitro drug release

In-vitro drug dissolution is performed by using USP paddle type apparatus. The studies were carried out at 37°C of stirring speed 75 rpm in 900 ml phosphate buffer (pH 6.8). 5 ml of the samples withdrawn at the predetermined time intervals and they are replaced

within the same volume of buffer. The samples were collected and the concentration were determined at the appropriate wavelength by using UV-visible spectrophotometer.

Stability studies

The purpose of the stability testing is to provide evidence on how the quality of the drug substance or the drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and the light, enabling the recommended storage condition, retest periods and the shelf life. The stability studies were carried out as per the International Conference of harmonization (ICH) Guidelines. The Stability studies were carried out at 40º C / 75% RH for 3 months. The optimized wafer formulations were packed in amber coloured bottles, which were tightly plugged with cotton and capped. They are stored at 40ºC / 75% RH for 3 months and these are evaluated for their physical appearance, drug content and in-vitro dispersion time at specified intervals of time.

Drug release kinetics

The mechanism and Kinetics of drug release from batch F8 formulation was evaluated based on the Higuchi equation, Zero order, First order, Hixoncrowell equation and Peppas model.

RESULTS AND DISCUSSION

Drug-Excipients Compatibility

FTIR studies conducted on pure drug and mixture of drug and excipients showed that there is no marked interaction between drug and excipients selected. All the characteristic peaks of Ondensetron HCL were present in spectra which are indicating that compatibility between drug and polymers. So there is no interaction between pure drug and polymers. It means that all the polymers are compatible with a drug. (Figure 1 and 2) DSC studies conducted on pure drug and mixture of drug and excipients showed that there is no marked interaction between drug and excipients selected since no change in the endothermic peak of the drug in its mixture. It means that the drug compatible with the excipients used. (Figure 3 and 4).

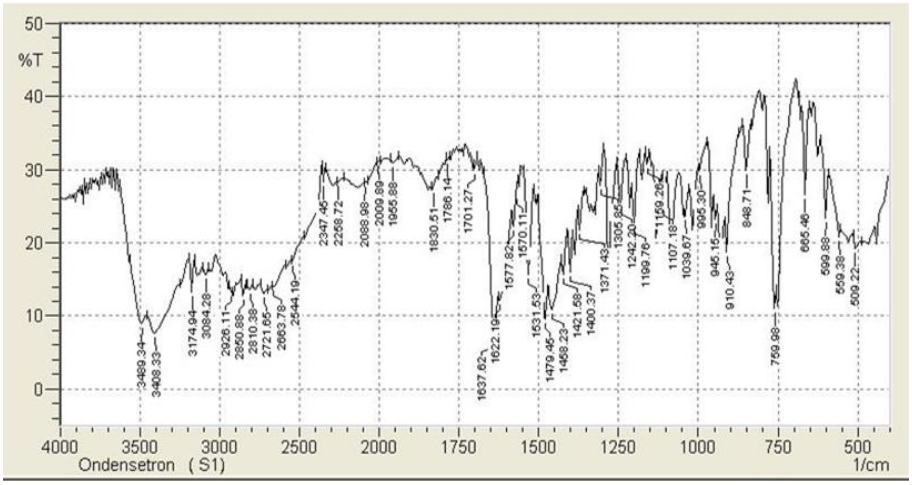

Figure 1: FTIR spectrum of drug (Ondensetron HCL).

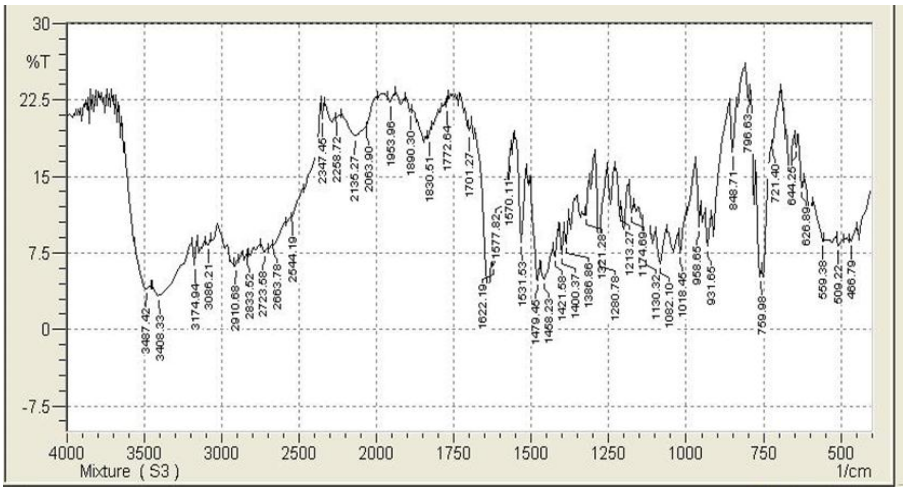

Figure 2: FTIR spectrum of Mixture (Drug& polymers).

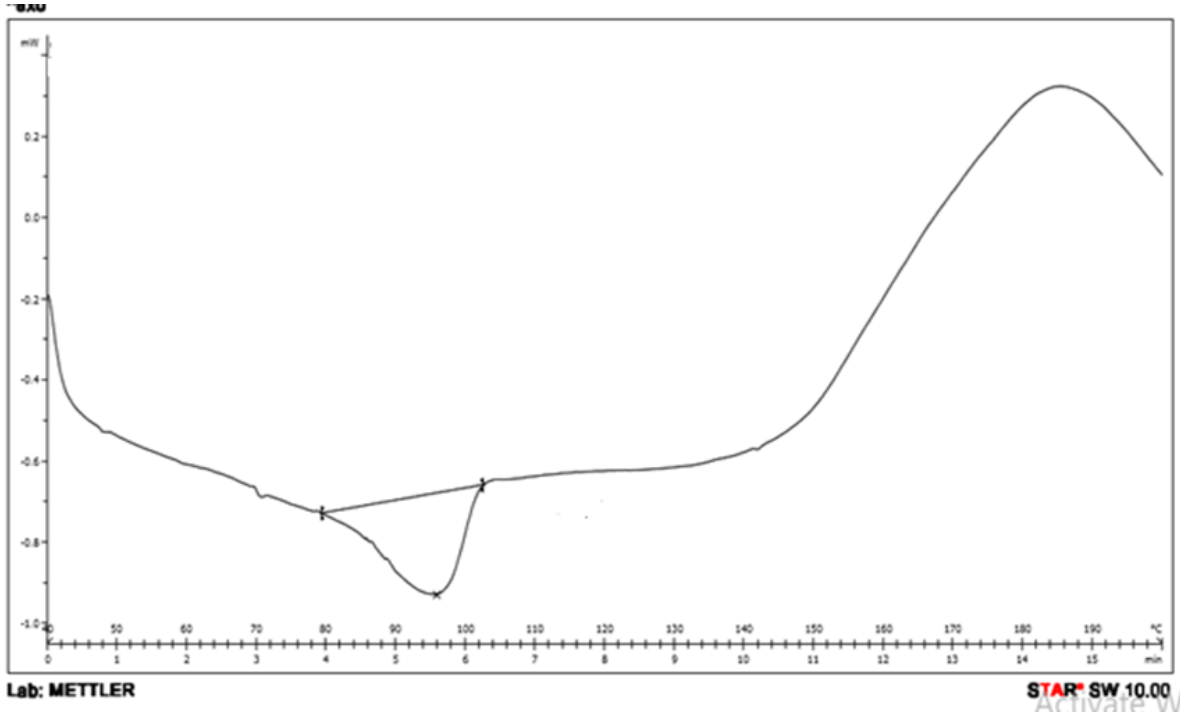

Figure 3: DSC spectra of drug.

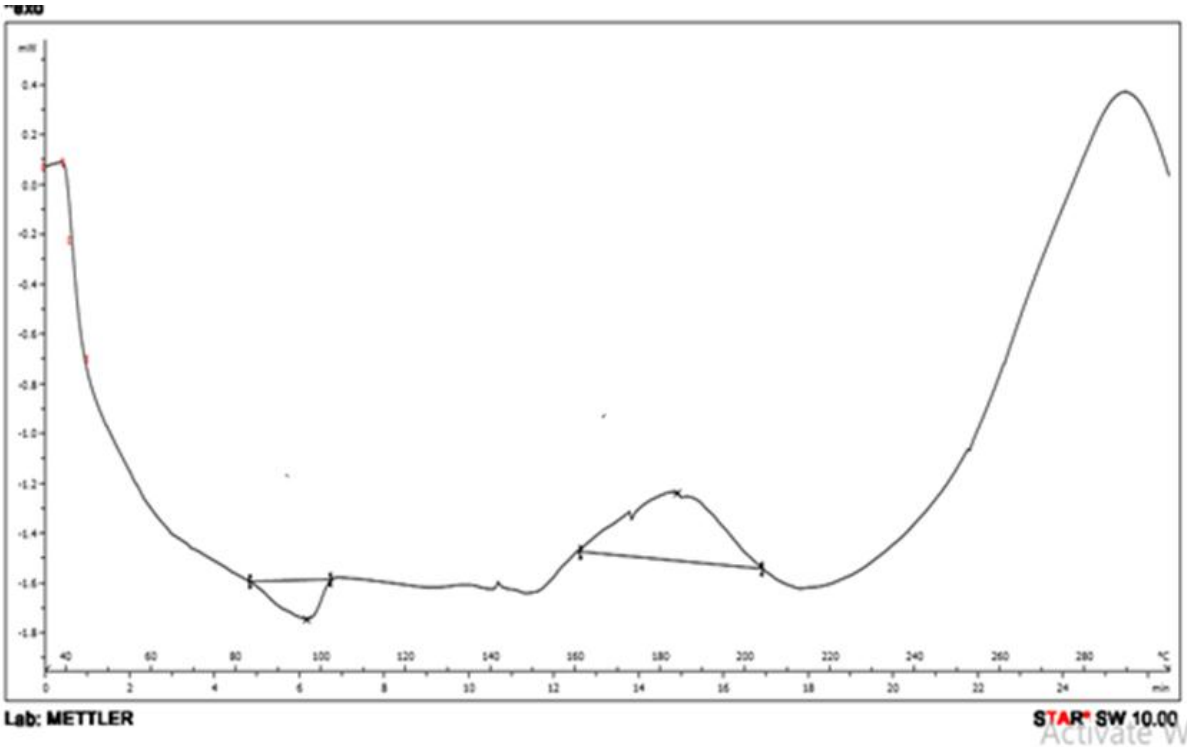

Figure 4: DSC spectra of a drug in its mixture.

General appearance and Thickness

All the prepared batches of pharmaceutical wafers are smooth, thin and semitransparent. Thickness of the wafers was measured with vernier caliper. The uniformity of the film thickness could be attributed to the accuracy of dose in the strip. As the concentration of the polymer and plasticizer increased, the thickness was gradually increased. The wafers thickness ranged from 0.366 to 0.533 mm. (Table 2)

Weight variation

The average weights of 10 wafers were determined and the results are given in the Table 2. The weight variation was in the range of 25.33± 0.57 to 38.6± 0.76 mg. As per

USP requirement, the formulations meet the criteria for weight variation.

Folding endurance

The value of folding endurance was in the range of 101± 0.57- 384± 1.52. It was observed that with increase in concentration of polymer and plasticizer, the folding endurance also increased. Higher the value of folding endurance, lower is the chance of wafer to rupture. (Table 2)

Percentage moisture loss

% moisture loss was determined and results are given in Table 2. It was determined to know about the wafers stability nature and ability of film to withstand its physicochemical properties under normal conditions. % moisture loss varied within the range of 1.1 to 3.48 %.

Drug content uniformity

The % drug content in various formulations ranged from 85.27 % – 98.4 %. As per USP requirement, the drug content was found to be within limit. (Table 2)

Disintegration test

Disintegrating time is defined as the time at which a wafer breaks when brought in contact with water or saliva. Typical disintegration time for wafer is 10.5-28.0 seconds. As the concentration of HPMC and plasticizer increased, the disintegration time also increased. (Table 2)

Percent elongation

The % elongation of wafers was determined and the results are as given in Table 2. The % elongation was ranged from 6.12-7.28. The nature of polymer affects the % elongation. It increased with the increase in the concentration of polymer and plasticizer. It gives an indication of elasticity of the wafers. (Table 2)

Surface pH

The surface pH was measured to determine the possibility of any in vivo side effects, as the acidic or alkaline pH may cause oral mucosal irritation. The surface pH of the strips was ranging from 6.92 to 7.00 as shown in Table. The surface pH values of wafers assured that there will be no irritation to the oral mucosal lining**.** (Table 2)

In -vitro drug release

Wafer formed by higher quantity of polymer and plasticizer had shown slower dissolution rate. It might be due to the increase in the concentration of polymer which results in the formation of high viscous gel layer that is caused by more intimate contact between the particles of polymer. It results in reduced mobility of drug in swollen and hence decreased release rate. As the viscosity of polymer increases, the drug release rate decreases. (Table 3)

Table 2: Evaluation of Different Parameters of Formulated Batches of Wafer.

Formulation Code	Appearances	Thickness (mm)	Weight variation (mg)	Folding endurance	% elongation	Tensile strength (kg/mm2)	% moisture loss	Surface pH	%Drug content	Disintegration time (Second)
F_1	Semitransparent, smooth, thin	0.36±0.05	25.3±0.57	313.0±1.52	6.12±0.19	1.11±0.04	2.23±0.15	6.95±0.01	87.70±0.90	20.6±1.15
F_2	Thin, smooth, semitransparent	0.43±0.05	28.3±0.50	321.0±1.00	6.23±0.10	1.11±0.03	1.1±0.1	6.95±0.00	85.70±0.73	16.3±0.57
F_3	Semitransparent, thin, smooth	0.36±0.05	25.6±0.57	350.3±0.57	6.24±0.43	1.12±0.03	1.02±0.06	6.96±0.00	90.80±0.79	14.3±0.57
F_4	Smooth, thin, Semitransparent	0.46±0.11	32.8±0.76	115.0±1.00	6.69±0.49	1.16±0.04	2.35±0.05	6.95±0.01	85.27±0.62	12.6±0.28
F_5	Thin, smooth, semitransparent	0.43±0.05	28.6±0.57	375.0±1.00	6.24±0.40	1.16±0.03	1.27±0.02	6.98±0.01	87.88±0.39	24.0±1.00
F_6	Smooth, thin, Semitransparent	0.46±0.05	34.8±0.66	361.3±0.57	6.28±0.61	1.11±0.02	2.12±0.10	6.98±0.00	98.03±0.76	18.5±0.50
F_7	Semitransparent, thin, smooth	0.36±0.05	28.0±0.50	139.6±1.52	6.46±0.30	1.13±0.05	1.89±0.03	6.96±0.02	95.75±0.45	14.5±0.50
F_8	Smooth, thin, Semitransparent	0.53±0.15	38.6±0.76	384.6±1.52	7.28±0.94	1.19±0.01	3.48±0.07	7.00±0.01	98.46±0.50	28.0±1.00
F_9	Thin, smooth, Semitransparent	0.46±0.11	30.5±0.50	101.3±0.57	6.75±1.83	1.19±0.17	1.54±0.04	6.99±0.01	97.83±0.87	10.5±0.50

Table 3: In vitro drug release for formulated batches of wafer.

Time (min)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	4.27	4.92	2.32	1.02	8.82	2.97	10.12	11.20	10.00
2	10.07	11.37	21.72	10.07	28.83	24.31	23.01	20.85	17.84
3	19.68	22.25	35.13	20.96	41.56	42.85	39.63	40.92	37.30
4	29.19	28.54	44.56	34.31	50.32	55.45	65.05	55.20	53.52
5	49.43	41.14	51.98	44.97	61.54	64.09	76.19	70.20	58.35
6	66.93	68.83	65.03	54.88	68.20	73.90	89.75	78.44	69.46
7	76.05	81.09	82.98	68.48	77.94	83.62	92.12	85.20	82.98
8	81.30	86.95	90.71	73.77	86.32	84.44	93.22	91.10	88.83
9	88.21	93.16	96.32	84.30	95.44	97.20	93.97	98.23	94.61

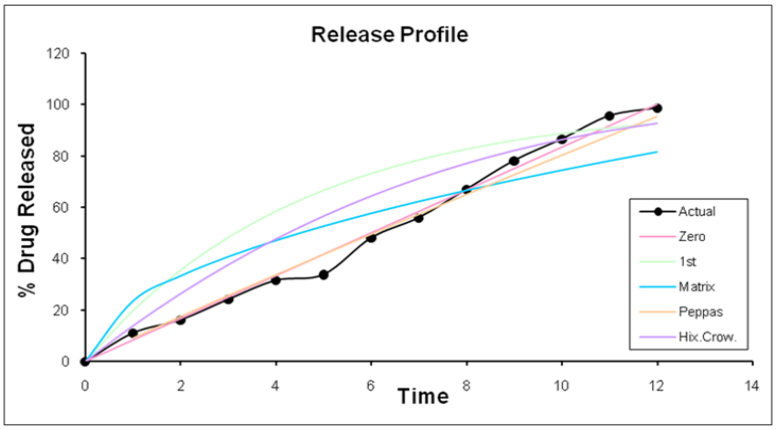

Figure 5: In vitro drug release.

Stability studies

The selected formulation F8 was subjected to stability study. Initial and third month studies were carried out and the results were mentioned in the Table 6 . The results showed that there were no significant changes for thickness, weight variation, % drug content, surface pH, disintegration time, folding endurance and in vitro drug release. So, the drug product was found to be stable. The stability study will be continued further up to 3 months. (Table 4)

Table 4: Stability study data at 40±2°C / 75% RH.

Parameters	Initial	After 90 d 40±2°C / 75±5% RH
Thickness	0.466 mm	0.466 mm
Weight variation	28.6 mg	27.5mg
% Drug content	98.46%	97.85%
Surface pH	7.00	7.0
Disintegration time	28 s	24s
Folding endurance	115	113

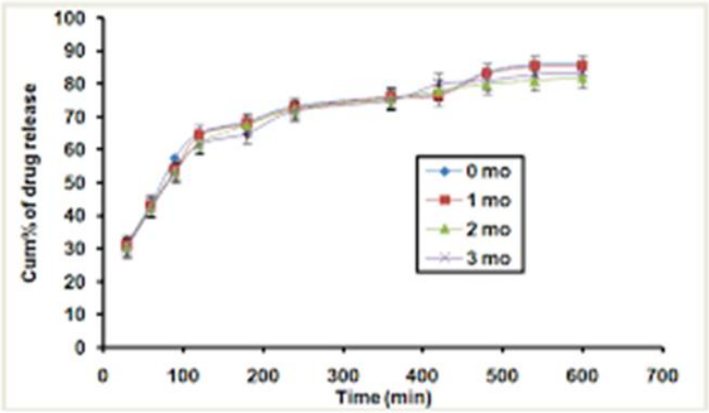

Figure 6: Stability studies.

Drug release kinetics

The mechanism and Kinetics of drug release from batch F8 formulation was evaluated based on the Higuchi equation, Zero order, First order, Hixoncrowell equation and Peppas model. Correlation coefficient (r2) and slope value for each equation in the range of (r2= to and n=) was calculated. The diffusion exponent 'n' values of Korsemeyer-Peppas model was found to be in the range of wafer. (Table 5)

Table5: Drug release kinetics.

Formulation code	Zero Order	First Order	Hixoncrowell	Higuchi	Korsmeyer Peppas	
	r^2	r^2	r^2	r^2	r^2	N
F8	O.97	0.91	0.85	0.93	0.99	1.9

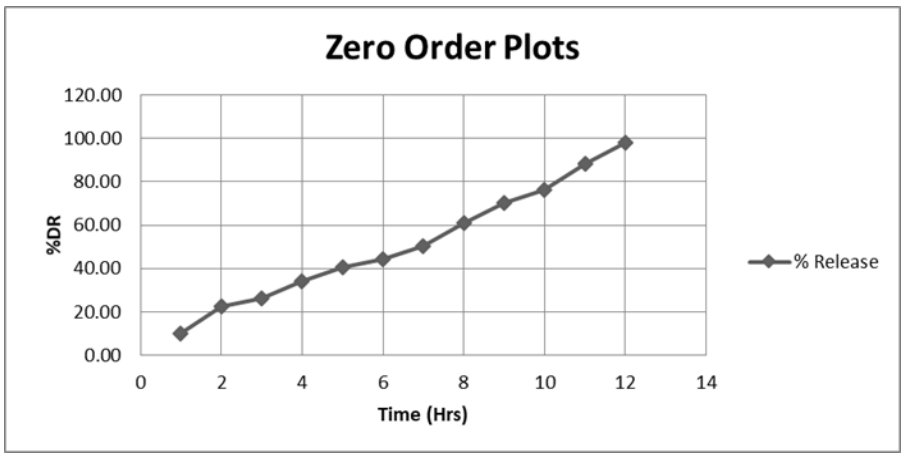

Figure 7: Zero order plot.

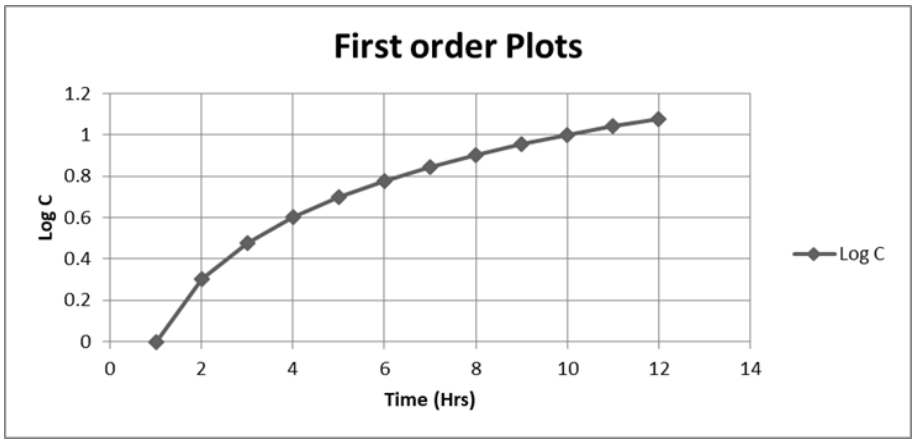

Figure 8: First order plot.

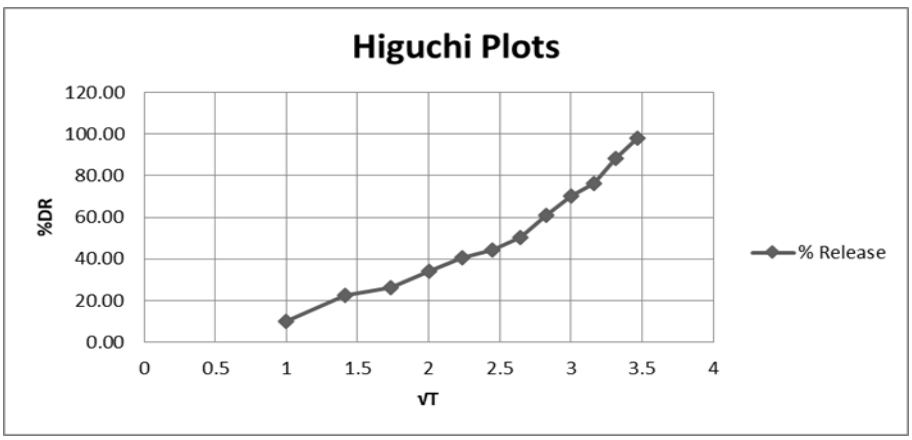

Figure 9: Higuchi plot.

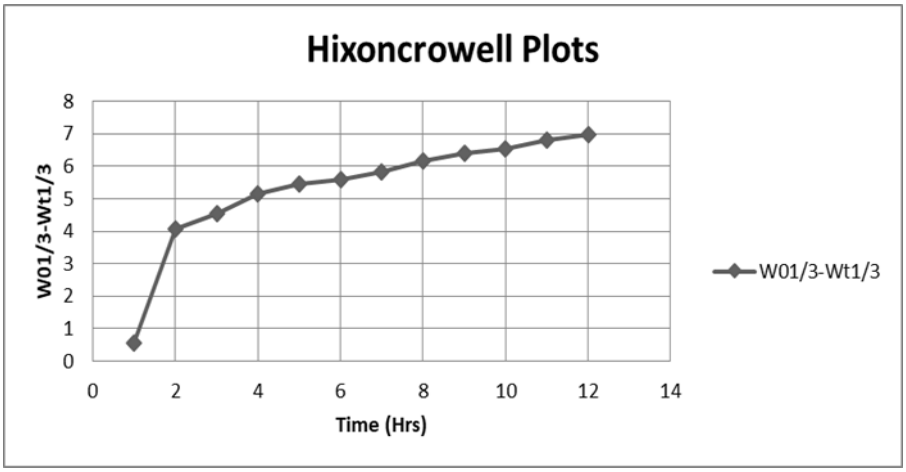

Figure 10: Hixoncrowell plot.

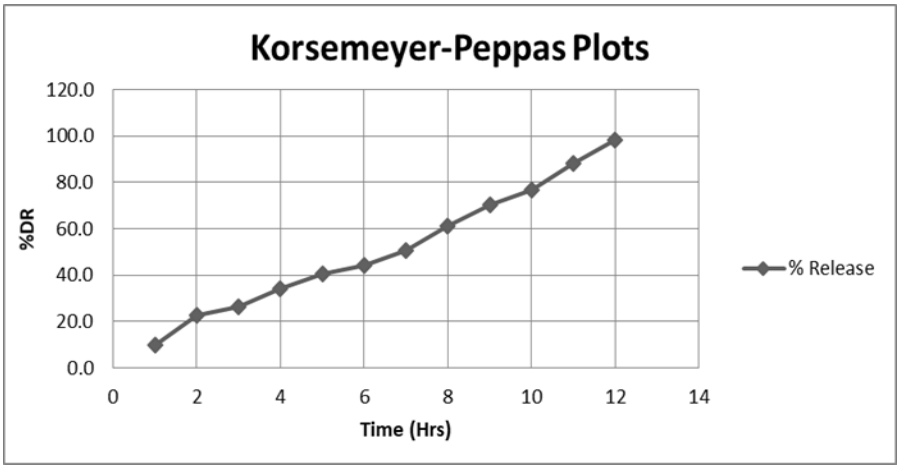

Figure 11: Korsmeyer Peppas plot.

CONCLUTION

In conclusion, we reported here the formulation of Ondensetron hydrochloride containing wafers produced following design of experiment and optimized with the help of response surface methodology involving the factors as percentage of polymer and hydrophilic matrix forming, HPMC E 15 as a film forming material, Aspartame as a sweetener and PEG 4000 as a plasticizer. The wafer formulation F 8 was found to be optimized with desirable properties. One of the advantages of oral wafer preparation was the ease in intake. The present wafer base preparation was found to be easily dissolving in saliva without producing insoluble materials. The constituents of the wafer base preparation had already been used in internal dosage additives and thus safe. Prepared wafer were found to be thin and fast disintegrating having desirable folding endurance as well as follow zero order kinetic model. Therefore, Ondensetron Hydrochloride can be conveniently administered orally in the form of wafers with lesser occurrence of its side effects and with improved bioavailability.

REFERENCES

1. S. Maheswari et al. Oral wafer in drug delivery: An emerging paradigm International Journal of Pharmacy & Technology, 2017; 9(2): 5886-5907.
2. Lade Milind et al. Polymer Based Wafer Technology: A Review International Journal of Pharmaceutical & Biological Archives, 2013; 4(6): 1060-1074.
3. Papola Vibhhooti, Kothiyal Preethi. Wafer's technology: a newer approach to smart drug delivery system. Indian Journal Research Pharm Biotechnology., 2013; 1: 428-9.
4. Snehal Jagtap, Abhijeet Kulkrani. A Novel Venture in Oral Formulation: Wafer. Journal of Emerging Technologies and Innovative Research (JETIR), 2020; 7(4): 345-359.
5. Dey et al. Wafers: An Innovative Advancement of Oro-Dispersible Films. International journal of applied pharmaceutics, 2016; 8(1): 1-7.
6. Indian Pharmacopoeia (IP), Government of India, Ministry of health and family welfare, Delhi Controller of publications, 1996; 2: 1034-1035.
7. United State Pharmacopoeia (USP) 24, NF 19, and Asian Rockville: United States Pharmacopoeia convention, 2004; 1623-1624.

8. Prithviraj Chakraborty, Surajit Dey. Design Expert Supported Mathematical Optimization and Predictability Study of Buccoadhesive Pharmaceutical Wafers of Loratadine. Hindawi Publishing Corporation Biomed Research International, 2013; 1-12.
9. Arun Arya, Amish Chandra, Vijay Sharma, Kamal Pathak. Fast dissolving oral films: An innovative drug delivery system & dosage. International journal of chem tech-research, 2010; 2(1): 576-583.
10. Upendra c. Galatia et al. Development of fast dissolving sublingual wafer by using films former: optimization and characterization. Journal of Chemical and Pharmaceutical Research, 2017; 9(4): 82-91.
11. Deepak Sharma et al. Fast Dissolving Oral Films Technology: A Recent Trend for an Innovative Oral Drug Delivery System. International Journal of Drug Delivery, 2015; 60-75.