AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Formulation and Evaluation of Sustained Release Matrix Tablet of Ondansetron Hydrochloride

Santosh Girani[1]*, Mayudin shumra[1], Vishwanath Arakeri[1], Manjunath halkeri[1], Mahantesh kavatekar[1], Ajay Shahpur[1]

1. Department of Pharmaceutical Technology, BLDEA's College of Pharmacy, BLDEA's Hospital Campus, Bijapur, Karnataka, India.

ABSTRACT

In the present study, an attempt was made to prepare and evaluate matrix tablets of Ondansetron HCl using HPMC, EC and Eudragit for Sustained release of Ondansetron HCl. The matrix tablets were prepared by wet granulation method. All the formulations are evaluated for the Hardness, Friability, Weight variation, Drug Content, *In-Vitro* Drug Release. The weight variation and drug contents of all the tablets were found to be uniform with the low SD values. The FTIR study indicated that the drug is stable in the formulations. The prepared matrix tablets were capable of releasing the drug for 12 hours depending upon the formulation variables. The tablets prepared with HPMC and Eudragit combination have shown higher drug release Drug release mechanism followed non-Fickian transport from both the polymers matrices. The drug released from the formulation is depends on the concentration of the polymers.

Keywords: Sustained Release, Matrix tablet, Ondansetron HCl, HPMC K-100, EC, Eudragit.

*Corresponding Author Email: santoshgirani@gmail.com
Received 22 May 2015, Accepted 30 July August2015

Please cite this article as: Girani S.*et al*., Formulation and Evalution of Sustained Release Matrix Tablet of Ondansetron Hydrochloride. American Journal of PharmTech Research 2015.

INTRODUCTION

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance, and cost-effective manufacturing process. Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitation such as Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance[1,2]. In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits[3]. Introduction of matrix tablet as sustained release (SR) has given a new breakthrough for novel drug delivery system (NDDS) in the field of Pharmaceutical technology Matrix tablets composed of drug and polymer as release retarding material offer the simplest approach in developing a sustained-release drug delivery system[4]. Ondansetron HCl one of the serotonin 5-HT3 receptor blocking agent. It is also a potent antiemetic drug used in the treatment of emesis produced during chemotherapy or radiotherapy. .The main drawback of conventional dose of Ondansetron hydrochloride is its oral bioavailability, which is about 60% with peak plasma concentrations 1.5 hr after an oral dose. The elimination half-life is 3-3.5 hr. Therefore, it was excogitated to use permeation enhancer in delivering ODN through buccal mucosa[5].

MATERIALS AND METHOD

Ondansetron HCl were received as gift sample from Morvel Laboratories Pvt. Ltd. Mehsana, Gujarat, HPMC K 100 and Eudragit RL 100 were purchased from yarrow chemicals Mumbai, Ethyl cellulose, Magnesium stearate, Talc, PVP K 30 were purchased from Loba Chemical Pvt. Ltd. Mumbai.

Standard calibration curve for Ondansetron HCl in 6.8 Ph

Solution 1st:

100 mg of Ondansetron HCl was accurately weighed and dissolved Methanol in a 100 ml volumetric flask then the volume was made up to 100 ml with 6.8 phosphate buffer. This was 1st stock solution containing 1000 µg/ml.

Solution2nd:

From this 1st stock solution, 1 ml was pipetted out and transferred in to a 100 ml volumetric flask and volume was made up to 100 ml with 6.8 phosphate buffer which contained the concentration of 10 µg/ml (2nd stock solution). From 2nd stock solution aliquots equivalent to 1-5 µg (1, 2, 3, 4 and 5 ml) were pipette out in to a series of 10 ml volumetric flask and volume was made up to 10 ml with 6.8 phosphate buffer. The absorbance of these solutions was measured against the 6.8 phosphate buffer as blank at 310nm using UV-Visible double beam spectrophotometer. Then a calibration curve was plotted taking concentration in µg/ml on X-axis and absorbance on Y-axis[6,7].

Preparation of Matrix Tablets

In the present work, wet granulation technique, has been employed to prepare matrix tablets of Ondansetron HCl using HPMC K-100, Ethyl Cellulose, Eudragit RL100 as polymers. A non-aqueous granulation process was adopted to prepare Ondansetron HCl tablets. Granules were prepared as follows. Proportion of excipients with drug was as given in Table 1(Formulation Chart). All ingredients were sifted through sieve no. 60. PVPK 30 was dissolved in Alcohol (5% w/v) and used for wet granulation of the final blend. The wet mass was passed through sieve no. 12 and wet granules were dried at 50°C in an oven for 30 mints. Dried granules were sized by passing it through sieve no.22 and 44 lubricated with magnesium stearate and talc for 1 min. Tablets were compressed using 10 station Rotary tablet punch machine with 6 mm (diameter) punch[8].

Table 1: Formulation Chart

Ingredients/ Formulation code	**F1 (mg)**	**F2 (mg)**	**F3 (mg)**	**F4 (mg)**	**F5 (mg)**	**F6 (mg)**	**F7 (mg)**	**F8 (mg)**	**F9 (mg)**	**F10 (mg)**	**F11 (mg)**	**F12 (mg)**
Ondansetron HCl	8	8	8	8	8	8	8	8	8	8	8	8
HPMC	20	30	-	-	-	-	15	25	15	25	-	-
Ethyl cellulose	-	-	20	30	-	-	25	15	-	-	15	25
Eudragit RL100	-	-	-	-	20	30	-	-	25	15	25	15
Lactose	89	79	89	79	89	79	69	69	69	69	69	69
Mg. Stearate	1	1	1	1	1	1	1	1	1	1	1	1
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Total	120	120	120	120	120	120	120	120	120	120	120	120

Pre compression evaluation of powder

Bulk density and tapped density: Both loose bulk density and tapped bulk density were determined. A 2gm of granules from each formula, previously light Shaken for the break of any agglomerates formed, was introduced into the 10ml of measuring cylinder. After noting its initial volume, cylinder was allowed to fall down its own weight from the hard surface from a height of 2.5cm at 2 sec Intervals[9].

$$LBD = \frac{\text{Weight of the powder}}{\text{Volume of the packing}}$$

$$TBD = \frac{\text{Weight of the powder}}{\text{Tapped volume of packing}}$$

Percentage Compressibility or Carr's index

$$\text{Carr's Index (\%)} = \frac{TBD - LBD}{TBD} \times 100$$

Angle of repose:

The fixed funnel and free standing cone methods employ a funnel that is secured with its tip at a given height, h, which was kept above graph paper that is placed on a flat horizontal surface. With r being the radius, of base of conical pile, angle of repose can be determined by following equation:

$\theta = Tan^{-1} (h/r)$

POST COMPRESSION PARAMETERS

Hardness test:

The hardness of the tablets were determined using Pfizer Hardness tester. It is expressed in kg/cm2. Six tablets were randomly picked from each formulation and standard deviation values were calculated. [10,11.]

Friability test:

A friability test was conducted on the tablets using an Electro lab friabilator. Twenty tablets were selected from each batch and any loose dust was removed with the help of a soft brush. The tablets were initially weighed (W initial) and transferred into friabilator. The drum was rotated at 25 rpm for 4 minutes after which the tablets were removed. Any loose dust was removed from the tablets as before and the tablets were weighed again (W final). The percentage friability was then calculated by,

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} x100$$

% Friability of tablets less than 1% is considered acceptable.[12]

Weight variation test:

20 tablets were randomly selected and weighed individually than average wt. of the tablets was calculated All the tablets passed weight variation test as the % weight variation was within the Pharmacopoeial limits of±5% of the weight. The weights of all the tablets were found to be uniform with low standard deviation values[13].

Drug Content:

Ten tablets were randomly selected and allowed to equilibrate with 6.8 pH phosphate buffer solution overnight and the solution were filtered (0.45µ, millipore). After 12 hours, suitable dilution were made with 6.8 pH buffer solution to get the concentration in Beer's Range. Absorbance of the solution was noted at 310nm using 6.8 buffer solution as blank and drug content per tablet was calculated[10].

***In vitro* drug release study**

Dissolution tests were performed in a USP XXII dissolution apparatus type II (Electrolab, Mumbai, India) at 37 ± 0.5°C. The Paddles were rotated at a speed of 100 rpm. The prepared tablets of (Ondansetron HCl) tablets were placed in the dissolution vessel containing 0.1 N HCl solutions (pH 1.2) for 2 hrs. For the next 10 hrs the dissolution were conducted in ph 6.8 phosphate buffer. 5 ml sample were withdrawn every hour for 12 hours and the same volume of fresh medium was replaced every time. Sample were filtered through 0.45 µm filter paper and the content of Ondansetron HCl was determined spectrophotometrically at a wavelength of 310 nm for first 2 hr and then after take in 310 nm. The release studies were conducted and results were noted in respective tables.

Fourier Transform Infrared Spectroscopy:

The samples were crushed with KBr to make pellets under hydraulic pressure of 10 tons, and then the FTIR spectra were recorded between 400 and 4000 cm-1. It was used to study the interactions between the drug and polymer. The drug and polymer must be compatible with one another to produce a stable product. Drug and polymer interactions were studied by using FTIR. IR spectral analysis of pure Ondansetron HCL and mixture of Ondansetron HCL with HPMC, EC, Eudragit were carried out[15].

Differential Scanning Calorimetry (DSC):

Thermal properties of the pure Ondansetron HCl and the physical mixture of drug and excipients were analyzed. The samples were heated in a hermetically sealed aluminium pans. Heat runs for each sample were set from 30 to 3500C at a heating rate of 100C/ min, using nitrogen as blanket gas[16].

RESULTS AND DISCUSSION

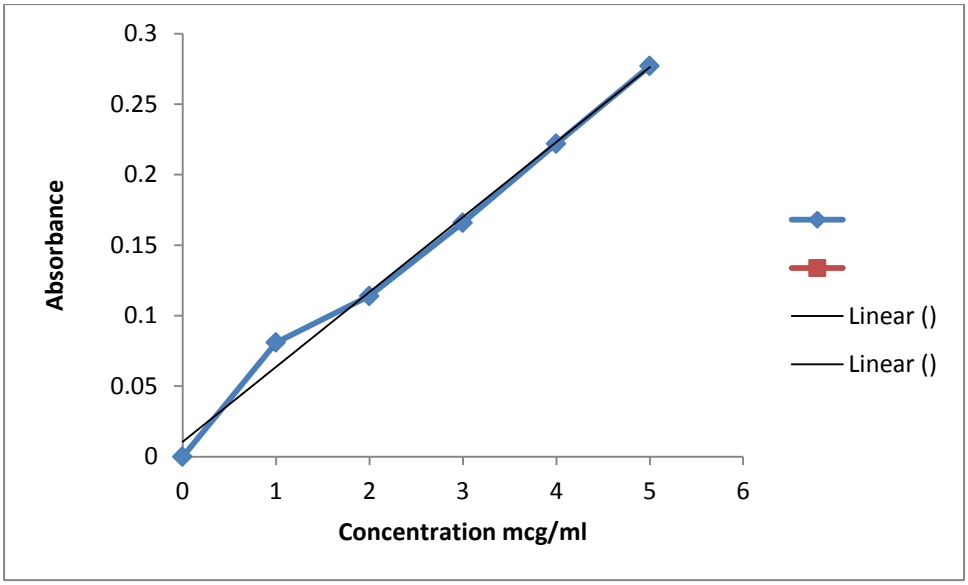

Figure 1: Calibration curve for Ondansetron HCl in phosphate buffer pH 6.8

Table 3: Evaluation of pre-compression matrix tablets

Tablets	Bulk density	Tap density	Carr's Index	Hausner ratio	Angle of repose*
F1	0.29	0.33	11.78	1.13	31.38˚
F2	0.35	0.39	9.87	1.10	29.68˚
F3	0.30	0.33	8.92	1.09	29.66˚
F4	0.29	0.31	6.5	1.07	29.24˚
F5	0.53	0.60	12.82	1.14	27.40˚
F6	0.41	0.45	8.83	1.09	27.92˚
F7	0.49	0.57	14.03	1.16	30.0˚
F8	0.55	0.63	12.69	1.14	27.92˚
F9	0.49	0.56	13.35	1.15	27.40˚
F10	0.39	0.45	13.33	1.15	28.81˚
F11	0.38	0.42	9.13	1.10	28.36˚
F12	0.40	0.47	14.89	1.17	29.24˚

*The values represent mean ± SD, n=3.

Table 4: Post-compression Evaluation of tablets

Formulation Code	Weight (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug Content (%)
F1	116	2.909	5.8	0.7	92.22
F2	119	2.960	5.4	0.5	94.25
F3	120	2.833	5.7	0.8	97.29

F4	120	2.868	6.2	0.5	95.27
F5	119	2.970	5.4	0.8	96.28
F6	119	3.059	5.7	0.7	93.75
F7	121	2.943	6.2	0.5	95.77
F8	121	2.988	6.0	0.7	92.73
F9	120	3.039	5.2	0.5	91.21
F10	119	3.008	5.6	0.3	94.76
F11	118	3.301	5.7	0.0	96.79
F12	119	3.281	5.0	0.1	91.21

I R spectrometry of Drug and Polymer

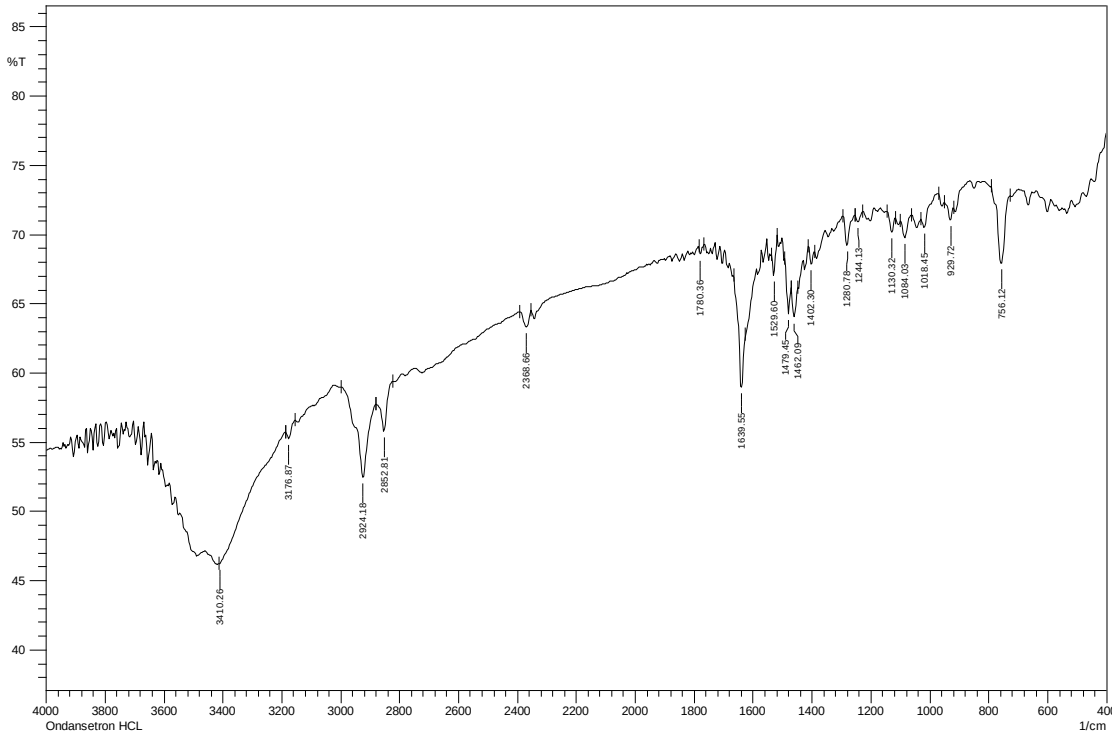

Figure 2: (A) Ondansetron HCL

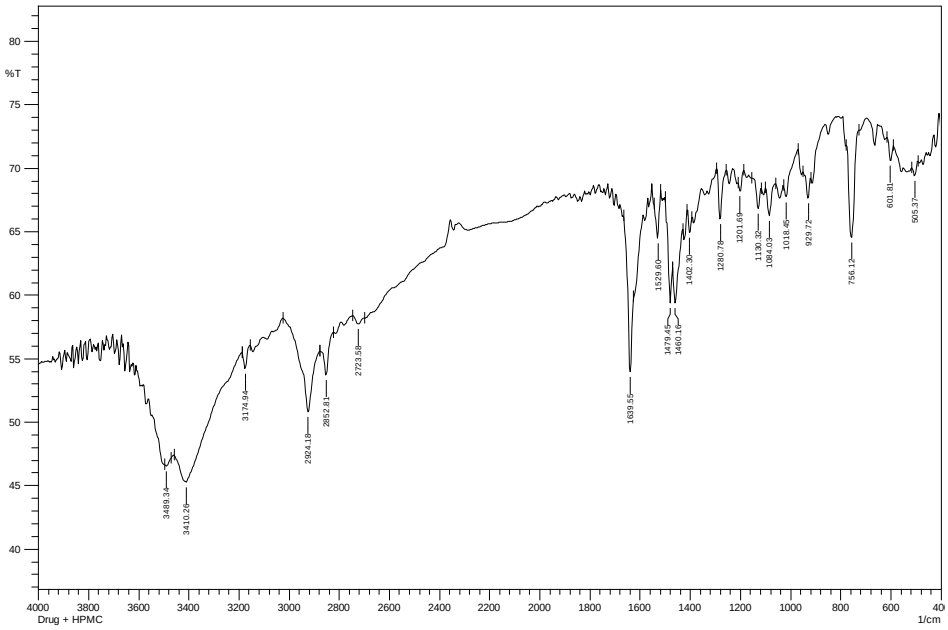

Figure 3: (B) Ondansetron HCL+HPMC

***In Vitro* Dissolution Studies**

Table 5: Percentage drug release of formulationsF1 toF6

Time In (Hrs)	*Formulations*					
	F1	***F2***	***F3***	***F4***	***F5***	***F6***
0	0	0	0	0	0	0
0.5	10.45	9.83	9.39	9.46	9.31	9.33
1	16.61	16.55	16.74	16.61	16.37	16.40
1.5	21.37	21.38	21.09	21.12	20.71	20.62
2	30.74	31.83	29.95	28.66	27.58	27.80
3	33.67	34.92	33.17	31.73	30.28	30.56
4	37.73	38.92	36.92	35.53	33.76	33.89
5	42.39	43.88	41.76	40.32	38.29	38.31
6	47.35	49.20	47.02	45.63	43.34	43.46
7	52.82	54.92	52.74	51.30	48.86	48.92
8	58.74	61.15	58.93	57.39	54.79	54.75
9	65.37	67.68	65.59	63.90	61.09	60.89
10	72.36	75.02	72.62	70.61	67.60	67.29
11	79.55	82.46	79.75	77.38	74.26	73.90
12	86.89	90.07	87.04	84.41	81.03	80.72

Table 6: Percentage drug release of formulationsF7 toF12

Time In (Hrs)	Formulations					
	F7	**F8**	**F9**	**F10**	**F11**	**F12**
0	0	0	0	0	0	0
0.5	9.50	9.59	9.71	9.80	9.75	9.82
1	16.65	16.76	16.81	16.56	16.48	16.59
1.5	21.16	21.31	21.40	21.46	21.27	21.37
2	29.09	29.74	30.38	29.95	29.37	30.17

3	32.18	33.07	33.81	33.59	33.06	33.71
4	35.77	36.87	37.82	37.65	37.27	38.03
5	40.19	41.40	42.50	42.12	41.69	42.71
6	45.45	46.76	47.96	47.79	47.52	48.43
7	51.12	52.64	54.05	54.09	53.71	54.83
8	57.16	58.89	60.50	60.91	60.74	62.06
9	63.77	65.60	67.42	68.14	68.08	69.56
10	70.54	72.78	74.65	75.58	75.58	77.28
11	77.77	80.28	82.20	83.28	83.34	85.17
12	85.32	88.09	90.16	91.35	91.30	93.19

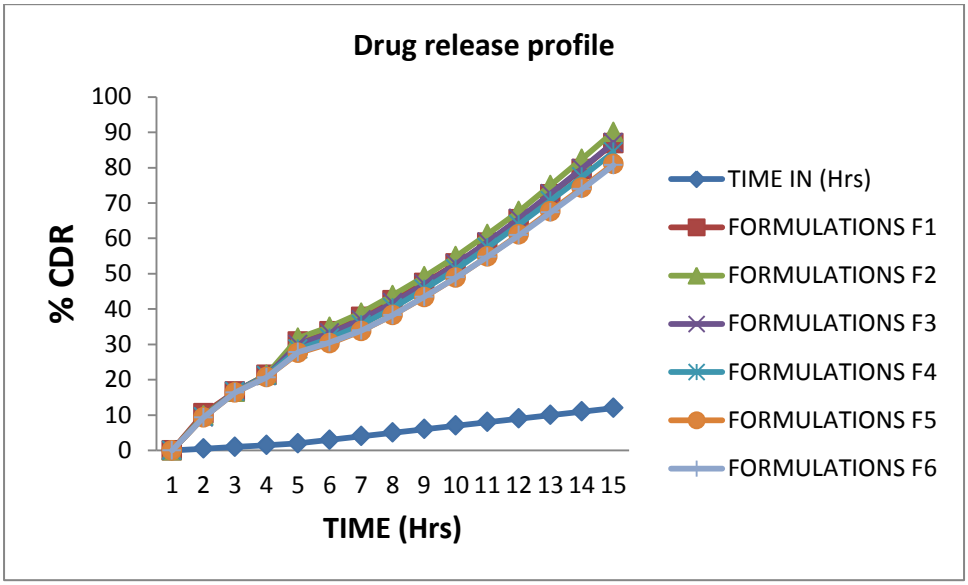

Figure 4: *In Vitro* Dissolution Profile of F-1 to F-6 Formulations

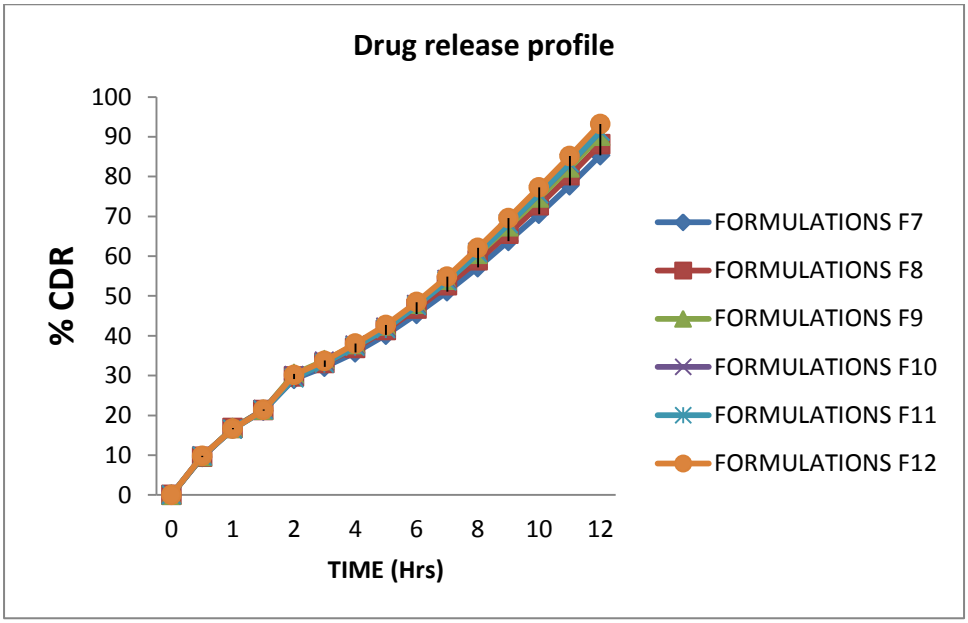

Figure 5: *In Vitro* Dissolution Profile of F-7to F-12 Formulations

DSC STUDY:

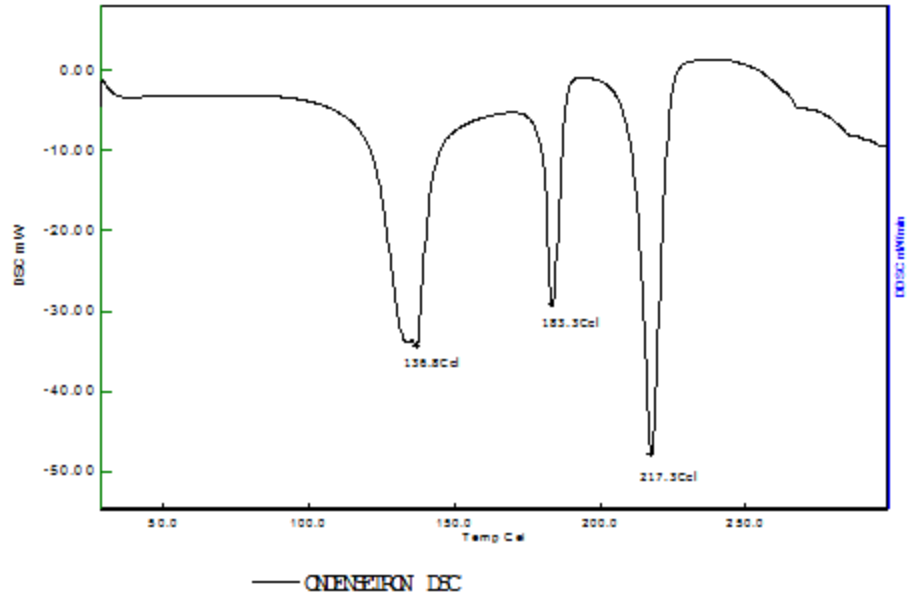

Figure 6: DSC Chromatogram of Ondansetron Hcl

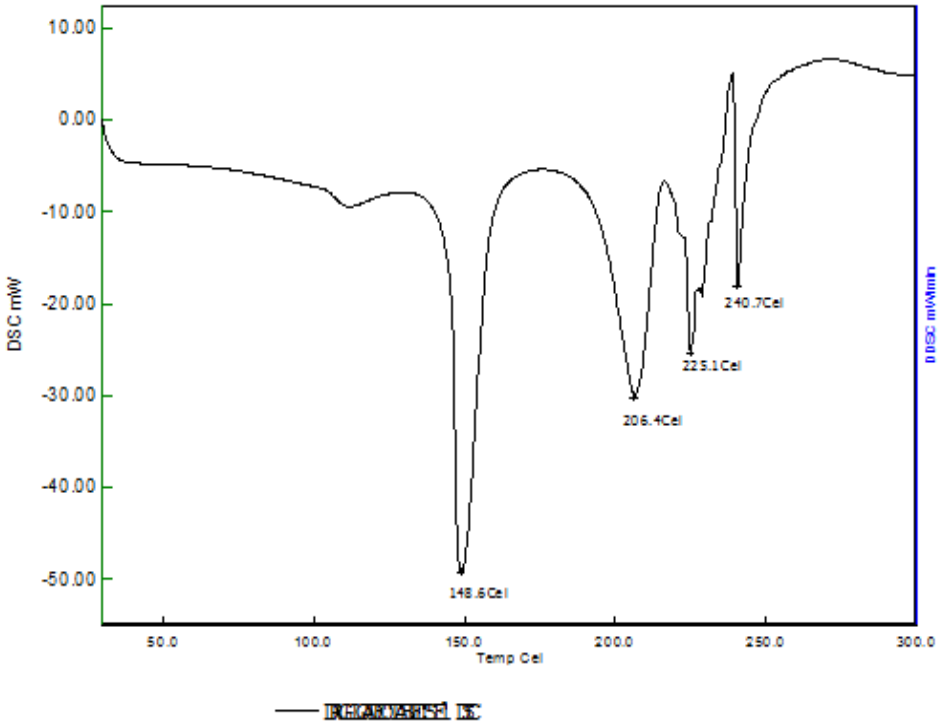

Figure 7: DSC Chromatogram of Drug Loaded Tablets F1

Table 7: Stability study of Ondansetron HCl matrix tablets

Sl. No.	Time (month)	Percentage of drug remaining											
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	0	92.22	94.25	97.29	95.27	96.28	93.75	95.77	92.73	91.21	94.76	96.79	91.21
2	1	91.18	92.22	96.98	93.32	94.82	91.15	93.27	90.81	89.92	90.76	94.45	89.64

The present research work was carried out to develop sustained release matrix tablets of Ondansetron HCL by wet granulation method. By using HPMC k 100, ethyl cellulose, Eudragit RL 100, by wet granulation method for controlled release. The results of granule evaluation suggested that all the prepared granules exhibited good flow properties, as the angle of repose values were less than 30^{o}. A good packing ability of the granules was indicated by carr's compressibility index and Hausner ratio (Table 10).The weight, thickness and drug contents of all the tablets were found to be uniform with their low standard deviation values. The hardness was in the range of 5.0 to 6.2 kg/cm^2andfriability was in the range of 0.1 to 0.8 % and drug content was in the range of 91.29 % to 97.29 % (Table 3, 4). The pure drug has shown characteristics peaks at 3489,3410,2924,1639, 1520, 1280, 756 cm^{-1} due to –OH, -NH, -CH, =C=O, groups. The similar peaks with little alterations were also observed in the spectra of mixture of drug and other polymers indicating chemical stability of the drug. The DSC thermogram of pure drug have shown an endothermic peak at 183^{0}C. which is due to melting point of the drug. whereas drug tablets F1, did not show the peak at 183^{0}C.This indicates the uniform dispersion of drug in an amorphous form in the tablets. The *in-vitro* drug release study was performed using dissolution rate test apparatus in 0.1 N HCl (pH 1.2) for 2 hours and in phosphate buffer (pH 6.8) till end of the study. The dissolution data are presented in Tables 5-10. The results indicate that the prepared tablets were capable of releasing drug up to 12 hours depending upon the formulation variables. Among all the formulations F10 and F12 formulation were optimized on the basis of its drug release profile. The tablets (F12) prepared with Ethyl cellulose and Eudragit RS100 has shown a maximum drug release of 93.19 % and F10 shows drug release 91.35% at the end of 12^{th} hour. Based on the result of evaluation data of all 12 formulations, F12 and F10 were optimized because of their sustained release property.

CONCLUSION

It can be concluded from this study that, the prepared tablets gave promising results with respect to sustained release of Ondansetron from the dosage form. Further work can be extended as *in-vivo* study can be carried out in animals for better prediction of *in- vivo* behaviour of the system. Bioavailability studies can be conducted to assess the relative usefulness of these formulations in targeting the drugs to human.

REFERENCE

1. Robinson JR, Lee VHL. Controlled Drug Delivery: fundamentals and Applications". 2^{nd} ed. New York: Marcel Dekker 1978;1-13.

2. Brahmankar DM, Jaiswal SB. Biopharmaceutics and pharmacokinetics treatise. 1st ed. New Dehli: Vallabh Prakashan., 1995: 335-337w.
3. Chein YW. Novel drug delivery systems. 2nded. New York : Marcel Dekker., 1992: 43-47.
4. Modi SA, Gaikwad PD, Bankar VH, Pawar SP. sustained release drug delivery system. Int. J. Pharm. Res. Dev 2011; 2(12): 147-160.
5. Kumar MP. Prasad MR. Pramod M, Reddy VP. Effect of permeation enhancer on *ex-vivo* permeation of Ondansetron HCl buccal tablets. Int. J. Pharm. Sci. Res 2011; 2(11): 2841-2845.
6. Chandira M, Mehul, Debjit, Chiranjib, Kumudhavalli, B Jayakar. Formulation, Design And Development Of Buccoadheshive Tablets Of Verapamil Hydrochloride. Int. J. Pharm. Tech.2009; 1(4): 1663-1677.
7. Basavaraj, Rao SB, Kulkarni SV, Patil P, Surpur C. Design and Characterization of Sustained Release Aceclofenac Matrix Tablets Containing Tamarind Seed Polysaccharide. Asian J. Pharm. Tech. 2011; 1(1): 17-21.
8. Hadi M A., Babu L V., Pal N. Formulation and evaluation of sustained release matrix Tablets of Glimipride based on combination of hydrophilic and hydrophobic polymer. J. Applied. Pharm. Sci.2012;02 (6): 101-107
9. Prajapati B G, Patel KR. Design and *in-vitro* evaluation of Nicorandil sustained release matrix tablets based on combination of hydrophilic and hydrophobic matrix system. Int. J. Pharm Sci. Rev. and Res.2010; 1(1): 33-38.
10. Tabandeh H, Mortazavi SA, Guilani TB. Preparation of Sustained Release Matrix Tablet of Aspirin with Ethyl cellulose, Eudragit RS 100 and EudragitS100 and studying the release profiles and their sensitivity to Tablet Hardness. Iranian J Pharma Res 2003. 201-206.
11. Harish NM, Charyulu NR, Shenoy KRP. Formulation Design and Optimization of Sustained Release Tablets of Terbutaline Sulphate. Ind J Pharm Edu Res 2011;45(3).
12. Chithaluru K, Tadikonda R, Gollapudi R, Kandula KK. Formulation and in-vitro evaluation of sustained release matrix tablets of losartan potassium. Asian J Pharm Clin Res, 2011; 4(3): 18-22.
13. Smith AA, Kottai MA, Rao WBP, Manavalan R. Formulation Development and Evaluation of Ondansetron Hydrochloride sustained release Matrix tablets. J. Pharm. Sci. Res. 2009; 4: 48-54.
14. Parsuram RR, Kharkate PR, Thangavel S. Formulation of Aceclofenac sustained release matrix tablet using hydrophilic natural gum. Int. J. Res. Ayurveda Pharm. 2011; 2(3): 851-

857.

15. Nayak RK, Manjunath B, Swamy VBN, Senthil A, Thakkar HK, Kumar DM, Mahalaxmi R. Design and Evaluation of sustained release floating tablets of Loratadine. Asian J. Pharm. Res. 2011; 3(1): 105-124