Int J Pharm Bio Sci 2013 Oct; 4(4): (P) 288 – 295

Research Article **Pharmaceutics**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

FORMULATION AND EVALUATION OF FLOATING BIOADHESIVE TABLETS OF ONDANSETRON

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ABSTRACT

The aim of present work was to formulate, evaluate and optimize gastro-retentive tablet of Ondansetron HCl which would be advantageous, that can provide prolong gastric retention and increase efficacy of the dosage form. The objective of the present study is to developed a Floating bioadhesive tablets of Ondansetron hydrochloride. Systematic studies were conducted using different concentration of rate releasing polymer HPMC and Sodium carboxy methyl cellulose for extending the drug release in upper GIT. Preformulation studies were done to find the micromeritic properties to assess flow ability, compressibility. All the formulations gave good results for above studies. Formulated tablets gave satisfactory results for various physical tablet evaluation parameters like tablet dimensions, hardness, friability, weight variation, buoyancy, content uniformity, all the formulations were found within the permissible range.

KEY WORDS: Ondansetron HCL, Floating tablet HPMC K4M, Sodium carboxy methyl cellulose.

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INTRODUCTION

It is widely known that gastric residence time (GRT) is one of the important factors affecting the drug bioavailability of pharmaceutical dosage forms[1].Variable and short gastric emptying time results in incomplete drug release from the drug delivery system (DDS) above the absorption zone leading to a diminished efficacy of the administered dose[2, 3].Oral delivery of the drug is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in the formulations. From immediate release to site specific delivery, oral dosage form has really progressed. It is evident from the recent scientific and patented literature that an increased interest in novel dosage forms that are retained in the stomach for prolong and predictable period of time exist today in academic and industrial research groups. Various attempts have been made to develop Gastro retentive delivery systems. Over the past three decades, the pursuit and exploration of devices designed to be retained in the upper part of the Gastro Intestinal Tract (GIT) has advanced consistently in terms of technology and diversity, encompassing a variety of systems and devices such as floating systems, rate systems, expanding systems, swelling systems, bioadhesive systems and low-density systems. This technology benefits drugs that have a narrow window of absorption in the stomach and upper GI tract. Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestine. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients[4,5]. Therefore, control of placement of a Drug Delivery Systems (DDS) in a specific region of the GIT offers advantages for a variety of important drugs characterized by a narrow absorption window in the GIT or drugs with a stability problem[6]. These considerations have led to development of a unique oral controlled release dosage form with gastro retentive properties. One of the most feasible approaches for achieving a prolonged and predictable drug delivery in the GIT is to control the Gastric Residence Time (GRT), i.e. Gastro Retentive Dosage Form (GRDF).Floating systems or hydro dynamically balanced systems, are low-density systems that have sufficiently buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time and a better control of the fluctuations in plasma drug concentrations. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hallow micro spheres[7]. Floating drug delivery systems are designed to prolong the study of the dosage form in the gastro intestinal tract and aid in enhancing the absorption. Such systems are best suited for drug having a better solubility in acidic environment and also having specific site of absorption in upper part of the small intestine. To remain in the stomach for a prolonged period of time the dosage form must have a bulk density of less than 1. It should stay in the stomach, maintain its structural integrity, and release drug constantly from the dosage form[8].Ondansetron hydrochloride (OND) is a selective serotonin 5HT3 receptor antagonist used for the prevention of nausea and vomiting. Half life and bioavailability of Ondansetron are 5.5 hrs and 60% respectively[9]. Solubility of OND decreases with increasing pH. Ondansetron HCl is widely prescribed to control or prevents nausea and vomiting, particularly in patients undergoing chemotherapy and radiation treatments. Chemotherapy and radiotherapy may cause release of 5-HT in the small intestine initiating a vomiting reflex by activating vagal afferents via 5-HT3 receptors. Ondansetron blocks the initiation of this reflex. This drug is mainly absorbed in stomach[9, 10].

Hence, the focus of present work is to prepare and evaluate gastro-retentive floating tablet of the Ondansetron HCl to increase its residence time in the stomach to achieve prolonged therapeutic action. Once day Ondansetron HCl gastro retentive tablets offer better patient compliance through less frequent administration and thus would lower the cost of total therapy. Gastroretentive tablet of Ondansetron HCl will be prepared to give sustained therapeutic effect for up to 24 hrs.

MATERIALS AND METHODS

Ondansetron obtained as gift sample from Alkem (pvt.ltd) Mumbai, Lactose Monohydrate, Sodium Carboxy Methyl Cellulose, PVP K-30 & Isopropyl Alcohol purchased from Sd Fine – Chem (pvt.ltd) Mumbai, HPMC K4M obtained from (Loba Chemical Pvt. Ltd, Mumbai), Sodium bi carbonate obtained from (SDFCL) Pvt. Ltd (Mumbai), Magnesium stearate & Talc obtained from (Loba Chemical Pvt. Ltd, Mumbai).

Method

Preparation Procedure of Floating Bioadhesive Tablets Of Ondansetron:

Drug and polymer (HPMC K4M) pass through 40 # mesh separately and then transfer it to poly bag and mix it for 3 minutes. Binder (PVPK-30) dissolved in isopropyl alcohol which is used as a granulating agent. Above drug-polymer blend is granulated by using binder solution. Add diluents and other excipients to the above mixture. Finally add the Glidant (Magnesium Stearate) and Lubricant (Talc) to the above blend mix it for 2min. Compressed the above lubricated blend by using 8mm round punches. [Table-1]

Table1

COMPOSITION OF ONDANSETRON FLOATING TABLETS

S.No.	Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)
1	Ondansetron	32	32	32	32	32
2	HPMC K4M	80	90	100	110	120
3	Sodium carboxy methyl cellulose	55	45	35	25	15
4	Sodium bicarbonate	35	35	35	35	35
5	PVPK-30	20	20	20	20	20
6	Lactose monohydrate	35	35	35	35	35
7	Iso propyl alcohol	q.s	q.s	q.s	q.s	q.s
8	Mg.stearate	2	2	2	3	2
9	Talc	1	1	1	1	1
Total Weight		**260**	**260**	**260**	**260**	**260**

RESULTS AND DISCUSSION

Calibration of Standard Graph of Ondansetron

Standard graph of Ondansetron in 0.1 N HCl

The construction of standard calibration curve of Ondansetron was done by using 0.1N HCl as the medium. Ondansetron was found to have the maximum absorbance at 250.5 nm. The standard graph of Ondansetron in 0.1 N HCl was constructed by making the concentrations of 1µg/ml, 2µg/ml, 3 µg/ml, 4 µg/ml, 5 µg/ml solutions. The absorbance of solutions was examined under UV-spectrophotometer at an absorption maximum of 250.5 nm. The standard graph of Ondansetron was constructed by taking the absorbance on Y-axis and concentrations on X-axis.

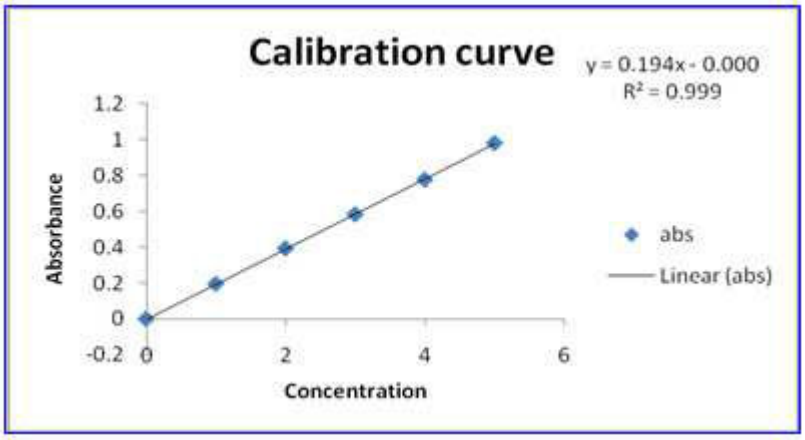

Figure 1
Standard graph of Ondansetron

Evaluation of Preformulation parameters

The properties like compressibility index, angle of repose and hausner ratio were calculated.

Table 2
Micromeritic properties of Active Pharmaceutical Ingredient

S.No	Parameter	Results
1	Angle of repose	26.45± 0.1
2	Bulk Density	0.95±0.3 gm/ml
3	Tapped Density	1.02±0.2gm/ml
4	Compressibility Index	7.36±0.5%
5	Hausner's ratio	1.07±0.29

Conclusion:based on the above pre-formulation results it was observed that the flow is good.

Table 3
List of Micromeritic properties of directly compressible powder

parameter	F1	F2	F3	F4	F5
Angle of repose	25.43±0.1	26.46±0.2	23.31±0.17	27.29±0.17	29.14±0.13
Bulk density	0.725±0.3	0.734±0.4	0.717±0.22	0.724±0.28	0.96±0.24
Tapped density	0.829±0.18	0.854±0.23	0.832±0.16	0.843±0.21	1.03±0.27
%Compressibility	12.54	14.05	13.82	13.63	7.29
Hausner's ratio	1.14	1.16	1.16	1.16	1.07

Evaluation of the Prepared Tablets for Physical Parameters[11,12]

All formulations were tested for Physical parameters like Hardness, thickness, Weight Variation, Friability and found to be within the Pharmacopoeia limits. The results of the tests were tabulated. The drug content of all the formulations was determined and was found to be within the permissible limit. This study indicated that all the prepared formulations were good.

Table 4
Results for Evaluation parameters of all formulations

parameter	F1	F2	F3	F4	F5
Weight variation	260.9±2	260.1±2	260.8±2	260.7±2	260.1±2
Thickness (mm)	5.5±0.4	5.9±0.4	5.3±0.4	5.6±0.4	5.5±0.4
Hardness (kg/cm^2)	8.9±1.4	7.4±1.2	8.2±1.2	6.9±0.9	8.4±1.9
Friability	0.12%±0.2	0.16%±0.23	0.15%±0.19	0.15%±0.26	0.15%±0.22
Content uniformity	95.01%±0.2	96.4%±0.4	98.7%±0.3	98.8%±0.2	99.8%±0.3
Floating lag time (min)	15	12	13	11	<1

Floating lag time

The floating tablets of Ondansetron were prepared by using HPMC K4M, Sodium Carboxy methyl cellulose. five different formulations were prepared using different ratios of polymers. The prepared tablets were evaluated for floating lag time and buoyancy time. Sodium bicarbonate induced carbon dioxide generation in presence of dissolution medium (0.1 N HCl). The floating lag time of the optimized formulation f5 was 31 sec.

Figure 2
Floating tablet of Ondansetron

In vitro dissolution studies

Dissolution study was carried out using USP dissolution test apparatus type II. The dissolution medium used was 900 ml of 0.1N HCl buffer at 37±0.5oC. The paddle speed was kept at 50 rpm throughout the study. Aliquot of 5 ml was withdrawn at predetermined time interval and equivalent amount of fresh medium was replaced to maintain a constant volume. After each sampling, suitably diluted with 0.1N HCl buffer and analyzed spectrophotometrically at 250.5 nm against suitable blank using UV-Visible spectrophotometer (1800, Shimadzu, Kyoto, Japan). [Table-5, Figure-3]

Table 5
Results of Dissolution profile for F1-F5:

%Drug Release					
Time in Min.	**F1**	**F2**	**F3**	**F4**	**F5**
0	0	0	0	0	0
30	12.45	21.36	14.67	15.67	18.95
60	27.94	34.92	26.91	23.68	35.78
120	54.68	67.93	51.24	56.98	46.48
240	74.98	84.72	73.97	79.97	73.18
360	96.59	95.92	89.92	92.15	82.94
600	98.95	97.83	99.13	98.99	94.56

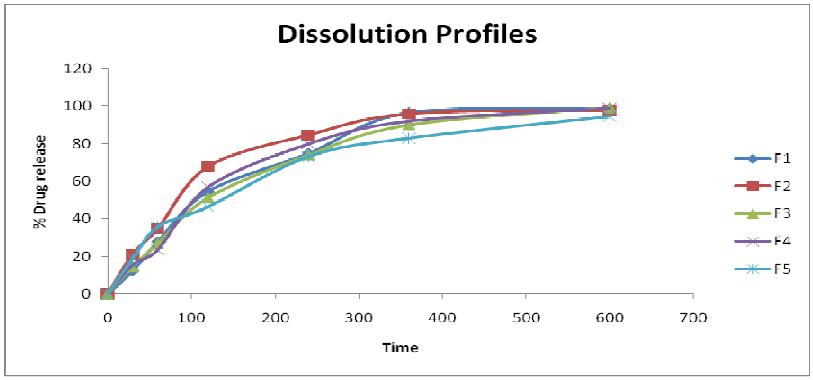

Figure 3
Results of Dissolution profile for F1-F5

Fourier transforms infrared spectroscopy (FTIR) studies

The pure drug Ondansetron, physical mixtures and optimized formulations (F1 & F5) were subjected for FTIR analysis. The samples were prepared on KBr-press (Startech Lab, India). The samples were scanned over a range of 4000-400 cm-1 using Fourier transformer infrared spectrophotometer (8600, Shimadzu Corporation, Japan). Spectra were analysed for drug polymer interactions.

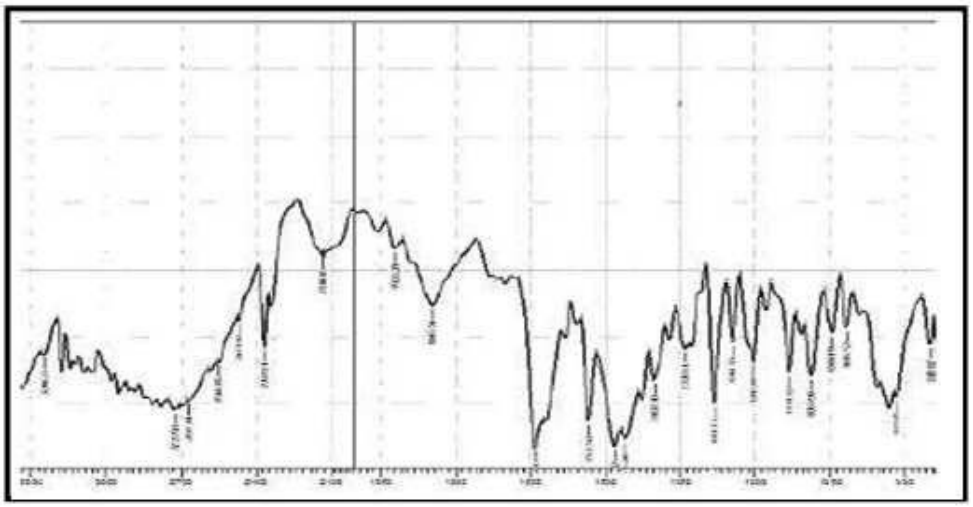

Figure 4
FTIR of Pure Drug (ONDANSETRON)

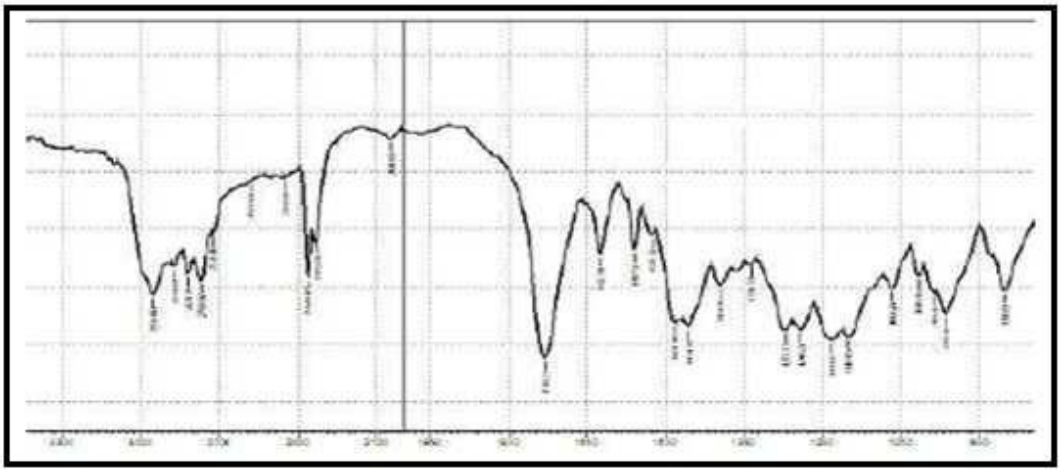

Figure 5
FTIR of Best Formulation (F5)

CONCLUSION

The objective of the present study is to develop a Floating bioadhesive tablets of Ondansetron hydrochloride. In this present study an attempt was made to increase the GI residence time of Ondansetron, as the drug is having less gastric residence time, by formulating in to Floating tablets. Systematic studies were conducted using different concentration of rate releasing polymer HPMC and Sodium carboxy methyl cellulose for extending the drug release in upper GIT. All the prepared systems were evaluated for the different properties. Before the preparation of tablets, preformulation studies to find out the micromeritic properties to assess flow ability, compressibility properties and solubility studies. And all the formulations gave good results for above preformulation studies. Formulated tablets gave satisfactory results for various physical tablet evaluation parameters like tablet dimensions, hardness, friability, weight variation, buoyancy, content uniformity, all the formulations were found within the permissible range. Finally it was concluded that: Among all the formulations (F1-F5), it was observed that formulation-5 has shown better buoyancy and dissolution profile. So Formulation-5 was found to be the best formulation among others.

ACKNOWLEDGMENT

The authors are thankful to COMPRIME Lab Pvt. Ltd. Hydernagar, Hyderabad, A.P. for completion of this work.

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