AMERICAN JOURNAL OF PHARMTECH RESEARCH

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

Development and Evaluation of Floating Drug Delivery System of Itopride Hydrochloride

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ABSTRACT

Gastroretentive dosage forms have potential for use as controlled-release drug delivery systems. The use of floating dosage forms is one method to achieve prolonged gastric residence times, providing opportunity for both local and systemic drug action. The present work was aimed to formulate floating tablets of Itopride hydrochloride using an effervescent approach for gastroretentive drug delivery system. The present investigation concerns the development of floating tablets of Itopride hydrochloride, a novel prokinetic drug, which after oral administration are designed to prolong the gastric residence time and thereby increase drug bioavailability, and drug release rate. This would help in promoting gastrointestinal transit and speed up gastric motility, and thereby it will relieve the symptoms associated with it. Floating tablets were fabricated; using direct compression method; containing Itopride hydrochloride, polymers HPMC K100M, HPMC K15M and HPMC K4M, along with gas generating agent sodium bicarbonate. The floating tablet formulations were evaluated for physical characterization, assay, swelling index, in-vitro drug release, hardness, friability and weight variation.

Keywords: Itopride Hydrochloride, Gastroretentive drug delivery system, Swelling study, HPMC.

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Received 1 March 2012, Accepted 10 March 2012

Please cite this article in press as: Karen HD *et al.*, Development and Evaluation of Floating Drug Delivery System of Itopride Hydrochloride American Journal of PharmTech Research 2012.

INTRODUCTION:

Gastroretentive dosage forms developed to exhibit a prolonged gastric residence time (GRT), have been a topic of interest in terms of their potential for controlled drug delivery. A conventional dosage form in humans is affected by numerous factors and the time taken shows wide inter-and intra-subject variation. This variability leads to unpredictable time to_achieve peak plasma drug levels and bioavailability, since many drugs are absorbed to the greatest extent in the upper part of the small intestine. A drug that is released from a dosage form in a controlled manner in the stomach will empty together with fluids and have the whole surface area of the small intestine available for absorption. Topical drug delivery to the gastric mucosa for example, antibiotic administration for helicobacter pylori eradication in the treatment of peptic ulcer disease, would also be facilitated.[1-5]

Several methods of gastro retention have been proposed. Of these, floating dosage forms (FDFs) have achieved some success, since their earliest description in 1975. The FDFs are expected to remain buoyant on gastric contents due to their having a lower density than gastric fluids. [6-8]

Itopride hydrochloride is a novel prokinetic agent, widely absorbed from the stomach and upper part of the small intestine and absorption becomes less as the drug passes from it. It has half life of 6 hr, so necessity to frequent administration and bioavailability can be improved by making the drug completely absorbed in the stomach and upper part of the small intestine.[9, 10,11]

Now a day the use of hydrophilic polymers, in particular cellulose derivatives, has attracted considerable attention for the development of controlled release technology in the formulation of pharmaceutical products, due to their ability to form gels in aqueous medium.

The objective of present investigation was to developed floating tablet of itopride hydrochloride by using a gas generating agent. Prepared formulation retain in the stomach and subsequently to provide sustained release of the drug over the period of time of GRT.

MATERIALS AND METHOD

Materials

Itopride hydrochloride was received as a gift sample from, Zydus Cadila Healthcare ltd. Ahmedabad, India. Hydroxypropylmethylcellulose (HPMC) K4M, k15M and K100M were purchased from yarrow chem, Mumbai, India. All other materials and chemicals used were of either pharmaceutical or analytical grade.

Methods

Tablet preparation

Itopride hydrochloride tablets were prepared by direct compression method. Drug and all the other ingredients were passed through 60# sieve and mixed thoroughly. The prepared blend was compressed using 10 station tablet compression machine (Rimek, Ahmedabad, India), equipped with 12mm flat faced punches. The composition of formulation is given in table 1.

Table: 1 Formulation composition of Itopride HCl

Batch	Itopride HCl(%)	HPMC K4M (%)	HPMC K15M (%)	HPMC K100M (%)	MCC (%)
P1	30	30	-	-	27
P2	30	50	-	-	7
P3	30	-	30	-	27
P4	30	-	50	-	7
P5	30	-	-	30	27
P6	30	-	-	50	7

All ingredients are in percentage.

Each batch containing 10% $NaHCO_3$, 2% talc and 1% magnesium stearate.

The total weight of tablet is 500 mg.

Evaluation of tablets

All prepared matrix tablets were evaluated for weight variation, thickness, buoyancy and *in vitro* release characteristics. Friability was determined using Roche friabilator (EF-02, Electrolab, India). Hardness was measured by using Pfizer hardness tester (Janki, India). [12].

Buoyancy lag time and the duration of buoyancy

The *in vitro* buoyancy lag time and the duration of buoyancy of the tablets were studied at 37±0.5 ◦C, in 100 ml of simulated gastric fluid at pH 1.2 without pepsine (USP). The time of duration of tablet floatation was observed visually. [13]

Drug release study

The *in vitro* dissolution study of itopride hydrochloride tablets was performed using USP apparatus (model TDT-08L, Electrolab, Mumbai, India) fitted with paddle (50 rpm) at 37^0C ± 0.5^0C using SGF (pH 1.2; 900 mL) as a dissolution medium. At the predetermined time intervals, 10-mL samples were withdrawn, filtered through a 0.45μm membrane filter and assayed at 258 nm using a Shimadzu UV 1800 double-beam spectrophotometer (Shimadzu, Kyoto, Japan). Cumulative percentage drug release was calculated using an equation obtained from a calibration curve.

Swelling study

The swelling behaviour of a dosage form was measured by studying its weight gain or water uptake. Water uptake was measured in terms of percent weight gain, as given by the equitation.

$$\text{Swelling index} = \frac{(W2-W1)}{W1} \times 100$$

W2= weight of dosage form at time t

W1=initial weight of dosage form

Fourier transforms infrared spectroscopy

Fourier transform infrared (FTIR) spectra of Itopride HCl, HPMC K100M and a physical mixture of Itopride HCl:HPMC K100M were recorded using KBr mixing method on FTIR instrument available at central instrument laboratory of the institute (FTIR-8400 S, Shimadzu, Kyoto, Japan).

RESULT AND DISCUSSION

Different grade of HPMC was selected as a matrixing agent considering its widespread applicability and excellent gelling activity in sustained release formulations. Sodium bicarbonate generates CO_2 gas in the presence of hydrochloric acid present in dissolution medium. The gas generated is trapped and protected within the gel formed by hydration of HPMC, thus decreasing the density of the tablet. As the density of tablet fall below 1 (density of water), the tablet becomes buoyant. Six batches P1 to P6 prepared by using different grade of HPMC with two different proportions (30% and 50 %).

The evaluation parameters diameter, friability, buoyancy time, weight variation of all the formulation shown in table 2. FTIR spectra of analytical reports conformed that there was no interaction between drug and excipients used shown in figure 1.

Table: 2 Evaluation data of floating tablet of Itopride HCl

Batch	Buoyancy Lag Time (min)	Friability (%) (n=10)	Hardness (Kg/cm^2) (n=10)	Average Weight(mg) (n=20)
P1	1.33 ±0.5	0.27	6.2 ± 0.60	496.74 ± 2.81
P2	1.37± 0.4	0.42	5.9 ± 1.00	509.45 ± 2.65
P3	1.28± 0.7	0.31	6.3 ± 0.50	505.09 ± 2.00
P4	1.24± 0.5	0.48	5.3 ± 1.20	495.62 ± 3.50
P5	2.27± 0.6	0.20	6.7 ± 0.89	504.23 ± 2.00
P6	2.29± 0.5	0.56	5.5 ± 0.55	497.30 ± 2.74

Swelling study was performed on all the batches for 5 hr. From the results it was concluded that swelling increases as the time passes because the polymer gradually absorb water due to hydrophilicity of polymer. The hydration swelling release process is repeated towards new exposed surfaces, thus maintaining the integrity of the dosage form.

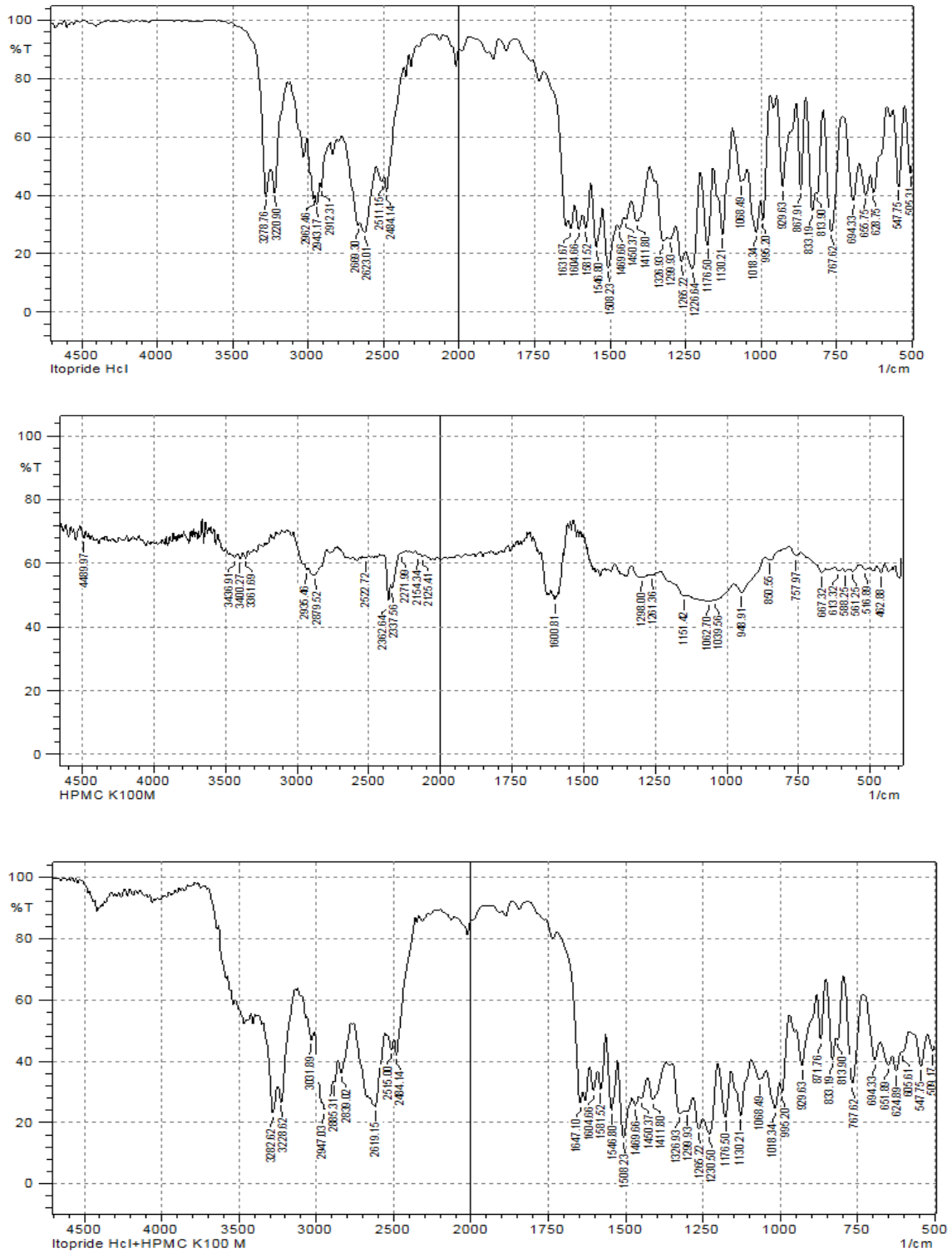

Figure. 1: IR spectra of a) Itopride HCl b) HPMC K100 C) Itopride HCl and HPMC K100

Effect of different grade of HPMC on *in vitro* release from itopride HCl tablet was shown in figure 2. This study was shown that HPMC K4M and K15M given retardant effect up to 18hrs. But HPMC K100M had given sustained drug release up to 24 hrs.

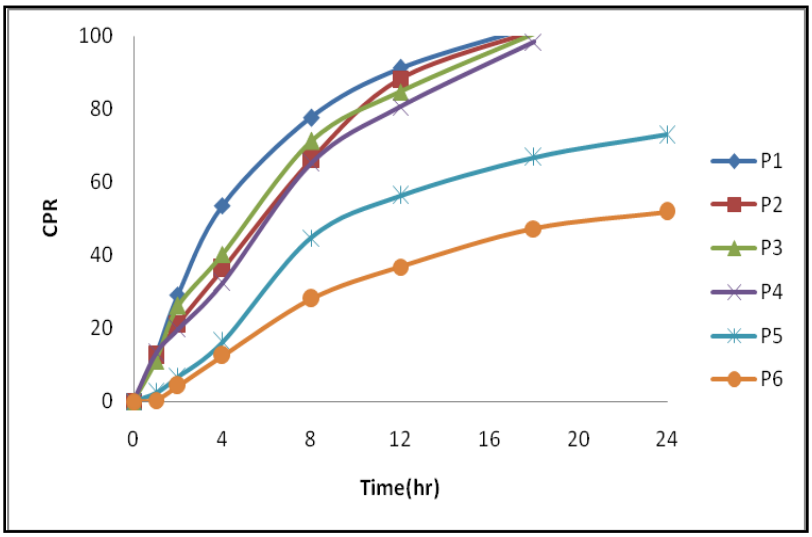

Figure.2: Release profile of Itopride HCl in 0.1N HCl

CONCLUSION

From the present investigation it was concluded that the drug release from the matrix tablet was slow and spread over 24 hour. Among three grades of HPMC polymer HPMC K100M is suitable for design of once a daily sustained release formulation of itopride hydrochloride.

ACKNOWLEDGEMENT

Authors are thankful to Zydus Healthcare ltd. Ahmedabad, India for providing gift sample off itopride hydrochloride. The authors also thankful to Shri Sarvajanik Pharmacy College, Mehsana, for providing all other ingredients and required infrastructure for the conduct of this research work.

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