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FORMULATION AND *IN VITRO* EVALUATION OF GASTRO RETENTIVE DRUG DELIVERY SYSTEM OF PROKINETIC AGENT (ITOPRIDE HYDROCHLORIDE)

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ABSTRACT

Itopride hydrochloride is gastroprokinetic drug, the site of action is stomach; and as the drug pH ranges from 3.5 to 5.5, the present work was aimed to formulate floating tablets of Itopride hydrochloride using an effervescent approach for gastroretentive drug delivery system. The present study concerns the development of floating tablets of Itopride hydrochloride, 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, natural polymers Guar gum, Xanthan gum, Sodium alginate, along with gas generating agent sodium bicarbonate. The floating tablet formulations were evaluated for physical characterization, in-vitro drug release, hardness, friability and weight variation and drug content. The results indicated that gas powered floating tablets of Itopride hydrochloride containing 60 mg Guar gum provides a better release action and improved bioavailability.

KEY WORDS

Gastroretentive drug delivery system, Gastroprokinetic agent.

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. [6-7] 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.[8,9, 10] The objective

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

A controlled drug delivery system is usually designed to deliver the drug at particular rate. Safe and effective blood levels are maintained for a period as long as the system continues to deliver the drug (Figure 1). Controlled drug delivery usually results in substantially constant blood levels of the active ingredient as compared to the uncontrolled fluctuations observed when multiple doses of quick releasing conventional dosage forms are administered to a patient.

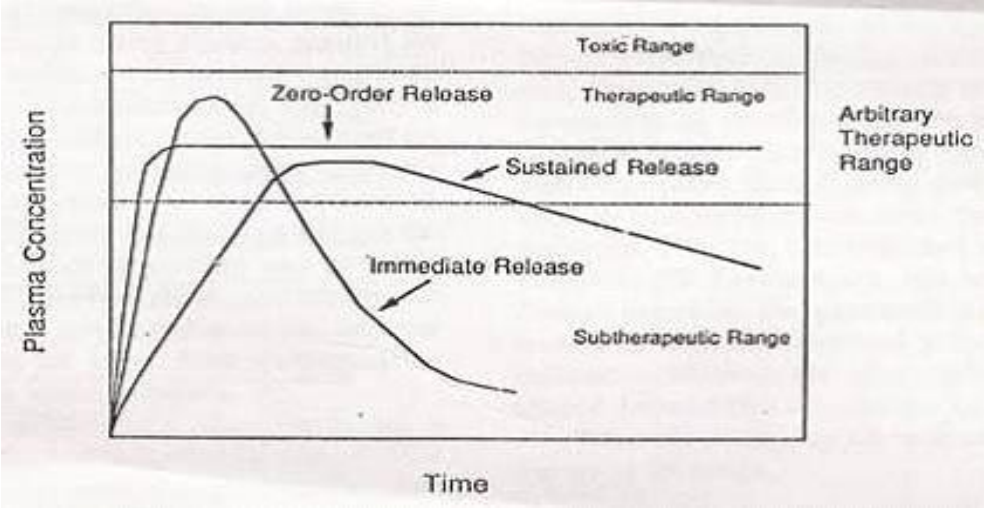

Figure 1: Drug level verses time profile showing differences between zero order, controlled releases, slow first order sustained release and release from conventional tablet

METHODOLOGY

MATERIALS

Table 1: List of Materials Used

Name of the material	Source
Itopride hydrochloric acid	SURA LABS
Xanthan gum	Merck Specialities Pvt Ltd, Mumbai, India
Guar gum	Merck Specialities Pvt Ltd, Mumbai, India
Sodium alginate	Merck Specialities Pvt Ltd, Mumbai, India
Talc	Merck Specialities Pvt Ltd, Mumbai, India
Magnesium stearate	Merck Specialities Pvt Ltd, Mumbai, India
Micro crystalline cellulose	Merck Specialities Pvt Ltd, Mumbai, India
Sodium bi carbonate	Merck Specialities Pvt Ltd, Mumbai, India

Determination of Lambda max of Itopride hydrochloric acid

A stock solution of Itopride hydrochloric acid (10 µg/ml) was prepared in 0.1N HCL. The UV spectrum was recorded in the range of 200-400 nm in UV-Visible spectrophotometer and lamda max was determined.

Preparation of standard graph of Itopride hydrochloric acid in 0.1 N HCl:

100mg of drug was dissolved in 100ml of 0.1N Hcl (stock solution-1000 µg/ml). The solutions of concentrations 5 to 25 µg/ml were prepared from above stock solution by appropriate dilution with 0.1 N HCL. The absorbance of each of solution was recorded using UV-Visible spectrophotometer at wavelength of maximum absorption (262nm). The standard graph was plotted by

taking concentration (µg/ml) on X-axis and absorbance on Y-axis.

Formulation of floating tablets of Itopride hydrochloric acid:

The composition of different formulations of Itopride hydrochloric acid floating tablets are shown in Table no 3**.** Itopride Hydrochloric acid, Na alginate, Xanthan gum, Guar gum were passed through sieve no. 80 separately. Sodium bicarbonate was passed through sieve no. 44. All the ingredients were mixed in the following proportions. The powder blends were lubricated with Magnesium stearate and Talc and mixed for two to three minutes. These lubricated blends were compressed into tablets using 12 mm punch on a multiple punch tablet machine. The compression force was adjusted to obtain tablets with hardness in the range of 4.5 to 6 kg/cm2. Each tablet contained 300 mg of Itopride hydrochloric acid.

Table 2: Optimization of gas generating agent

Ingredients	F1	F2	F3
Itopride hydrochloric acid	100	100	100
Guargum	100	100	100
NAHCO3	14	30	45
Mg.stearate	3	3	3
Talc	3	3	3
MCC pH 102	Q.s	Q.s	Q.s

Table 3: Composition of different floating tablet formulations of Itopride hydrochloric acid

Ingredients(mg)	F1	F2	F3	F4	F5	6	F7	F8	F9
Itopride hydrochloric acid	100	100	100	100	100	100	100	100	100
Guargum	30	60	90	-	-	-	-	-	-
Xanthane gum	-	-	-	30	60	90	-	-	-
Sodium alginate	-	-	-	-	-	-	30	60	90
$NaHCO_3$	45	45	45	45	45	45	45	45	45
Talc	3	3	3	3	3	3	3	3	3
Magnesium stearate	3	3	3	3	3	3	3	3	3
Microcrystalline cellulose	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s
Total weight	300	300	300	300	300	300	300	300	300

Evaluation of floating tabets of Itopride hydrochloric acid:

Preformulation studies (drug-excipient interaction studies, flow properties) were carried out for powder blends to detect any interaction between drug and excipients and to determine the flow properties of ingredients. Prepared tablets were evaluated for post compression parameters like various quality control tests such as Tablet thickness and Diameter, Hardness, Friability, uniformity of weight, content uniformity of drug, drug release and other specific evaluation tests for GFDDS like floating lag time and total floating time.

Pre-compression Parameters

a) Drug-Excipient Interaction Studies:

i) Fourier transform Infrared spectroscopy: The Infrared spectra of Itopride hydrochloric acid pure drug, exicipients, physical mixture of drug and excipients (Optimised formula F2) were recorded between 400 to 4000 cm^{-1}. The IR spectra were obtained using KBr disk method using an FTIR spectrophotometer.

b) Flow properties:

i) Angle of Repose: Angle of repose has been defined as the maximum angle possible between the surfaces of pile of powder and horizontal plane. It is performed to determine the flow rate of powder. It is done by funnel method. The powder mass was allowed to flow through the funnel orifice kept vertically to a plane paper kept on the horizontal surface, giving a heap angle of powder on paper. The angle of repose was calculated by substituting the values of the base radius 'R' and pile height 'H' in the following equation:

$$\Theta = \tan^{-1} H/R$$

Table No 4: Angle of repose values

S.No	Angle of repose	Flow
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	40 and above	Very poor

ii) Bulk Density: Bulk density was obtained by dividing the mass of powder by the bulk volume in cm^3. The sample of about 50 cm^3 of powder, previously been passed through a standard sieve no. 20, was carefully introduced into a 100 ml graduated cylinder. The cylinder was dropped at 2- second intervals on to hard wood surface three times from a height of 1 inch. The bulk density of each formulation was then obtained by dividing the weight of sample in grams by the final volume in cm^3 of the sample contained in the cylinder. It was calculated by using equation given below:

Df = M /Vp

Where, Df = bulk density; M = weight of sample in grams; Vp = final volume of powder in cm^3

iii) Tapped density: The tapped density was obtained by dividing the mass of powder by tapped volume in cm^3. The sample of about 50 cm^3 of powder, previously been passed through a standard sieve no.20, is carefully introduced in to a 100 ml graduated cylinder. The cylinder was dropped at 2- second intervals on to hard wood surface three times from a height of 1 inch. The tapped density of each formulation was then obtained by dividing the weight of sample in grams by the final tapped volume in cm^3 of the sample contained in the cylinder. It was calculated by using equation given below:

Do = M /Vp

Where, Do = bulk density; M = weight of sample in grams; Vp = final tapped volume of powder in cm^3

iv) Carr's index: Carr developed an indirect method of measuring powder flow from bulk densities. The percentage compressibility of a powder was a direct measure of the potential powder arch or bridge strength and stability. Carr's index of each formulation was calculated by

$$\% \text{ Compressibility} = \frac{Do - Df}{Do} \times 100$$

Where, Df = Fluff of poured bulk or bulk density; Do = Tapped or consolidated bulk density

Table No 5: Carr's index values

Compressibility (%)	Flow description
5-15	Excellent
12-16	Good
18-21	Fair
23-35	Poor
35-38	Very poor
>40	Extremely poor

V) Hausner's ratio: Hausner Ratio is the measure of the propensity of a powder to be compressed. As such, they are measures of the relative importance of inter particulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticle interactions and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Hausner Ratio, which are calculated using the following formula:

$$\text{Hausner ratio} = \frac{Do}{Df}$$

Where, Df = Fluff of poured bulk or bulk density; Do = Tapped or consolidated bulk density

Table No 6: Hausners ratio values

Hausners ratio	Type of flow
<1.25	Good
1.25-1.5	Moderate
>1.5	Poor

Post compression parameters:

The prepared floating tablets were evaluated for thickness, weight variation, hardness, friability, drug content, swelling index, in vitro buoyancy studies, in vitro drug release studies. All the studies were performed in triplicate, and results were expressed as mean ± SD.

i) Tablet thickness and Diameter: Thickness and diameter of tablets were important for uniformity of tablet size. Thickness and diameter were measured using Screw gauge.

ii) Hardness: This test is used to check the hardness of a tablet which may undergo chipping or breakage during storage, transportation and handling. In these six tablets were selected at random and the hardness of each tablet was measured with Monsanto hardness tester. The hardness is usually measured in terms of kg/cm^2.

iii) Friability: The friability test was carried out to evaluate the hardness and stability instantly. In Roche friabilator in which twenty tablets were weighed (Wo) initially and put in a tumbling and rotating apparatus drum. Then, they are subjected to fall from 6 inches height. After completion of 100 rotations i.e., 25 rpm for 4 minutes, the tablets were again weighed (w). The percent loss in weight or friability (F) was calculated by the formula

$$F = (1-W/Wo) \times 100$$

Where, F = friability; Wo = initial weight; W = final weight

iv) Uniformity of weight: This test is performed to maintain the uniformity of weight of each tablet which should be in the prescribed range, this is done by sampling and weighing 20 tablets at random and average weight is calculated. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the Table 14 and none deviate by more than twice the percentage. The mean and standard deviation were determined.

Table 7: Pharmacopoeial specifications for tablet weight variation

Average weight of tablets (mg) (I.P)	Average weight of tablets (mg) (U.S.P)	% ± deviation allowed
Less than 80	Less than 130	10
80 – 250	130 – 323	7.5
More than 250	More than 324	5

v) Content Uniformity: This test is performed to maintain the uniformity of weight of each tablet which should be in the prescribed range according to the Indian Pharmacopoeia. This test is performed by taking twenty tablets were selected randomly, weighed and powdered. A quantity of powdered tablet equal to 4 mg of Itopride hydrochloric acid was dissolved in 0.1 N HCL in 100ml volumetric flask. The so formed sample was diluted, and the absorbance was measured at 288 nm using 0.1 N HCL as blank and the % drug content was estimated using the following formula.

Note: The Regression equation for Itopride hydrochloric acid from standard graph is

$$\text{Concentration (mcg/ ml)} = \frac{\text{Absorbance - Intercept}}{\text{Slope}}$$

$$\text{Drug content (mg)} = \text{concentration} \times \text{dilution factor}$$

$$\text{\% Drug content} = \frac{\text{drug content (mg)}}{\text{label claim (mg)}} \times 100$$

vi.1) Floating Lag Time: The time taken by the tablet to emerge onto the surface of the liquid after adding to the dissolution medium simulated gastric fluid without pepsin, at pH 1.2, temperature 37 ± 0.5˚C paddle rotation at 50 rpm it is measured using stopwatch.

vi. 2) Total Floating Time: The time taken by the tablet to float constantly on the surface of the gastric fluid without pepsin, at pH 1.2, temperature 37 ± 0.5˚C, paddle rotation at 50 rpm. it is measured using stopwatch.

vii) In vitro dissolution studies: Dissolution test was carried out using USP XXIV (model DISSO, M/s. Lab india) rotating paddle method (apparatus 2). The stirring rate was 50 rpm. 0.1 N hydrochloric acid was used as dissolution medium (900ml). It was maintained at 37 ± 1˚C. Samples of 5ml were withdrawn at predetermined time intervals, filtered and replaced with 5ml of fresh dissolution medium. The collected samples were suitably diluted with dissolution fluid, wherever necessary and were analyzed for the Itopride hydrochloric acidat 288 nm by using a double beam UV

spectrophotometer (Labindia-3000). Each dissolution study was performed for three times and the mean values were taken.

ix) Kinetic Analysis of Dissolution Data: To analyze the in vitro release data various kinetic models were used to describe the release kinetics. The zero-order equation rate describes the systems where the drug release rate is independent of its concentration (Hadjiioannou *et al*., 1993). The first order Equation describes the release from system where release rate is concentration dependent. Higuchi (1963) described the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion Equation. The Hixson-Crowell cube root law Equation describes the release from systems where there is a change in surface area and diameter of particles or tablets (Hixson and Crowell, 1931).

There are several linear and non-linear kinetic models to describe release mechanisms

- Zero order kinetics
- First order kinetics
- Korsmeyer-Peppas model
- Higuchi model

Zero order kinetics: Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly (assuming that area does not change, and no equilibrium conditions are obtained) can be represented by the following equation

$$W_0 - W_t = K_0 t$$

Where W_0 is the initial amount of drug in the pharmaceutical dosage form, W_t is the amount of drug in the pharmaceutical dosage form at time t and k is proportionality constant. Dividing this equation by W_0 and simplifying

$$f_t = k_0 t$$

Where $f_t = 1 - (W_t / W_0)$ and f_t represents the fraction of drug dissolved in time t and k_0 the apparent dissolution rate constant or zero order release constant in this way, a graphic of the drug-dissolved fraction versus time will be linear if the previously established conditions were full filled. In this way a graphical relationship between f_t versus time to get the Zero order constant from the slope. This relation can be used to describe the drug dissolution of several types of modified release pharmaceutical dosage forms, as in the case of some transdermal systems as well as matrix tablets with low soluble drugs (Varelas et al., 1995), coated forms, osmotic systems, etc. the pharmaceutical dosage forms following this profile release the same amount of drug by unit of time and it is the ideal method of drug release in order to achieve a pharmacological prolonged action.

First order kinetics: This type of model to analyze drug dissolution study was first proposed by Gibaldi and Feldman 1967 and later by Wagner 1969(Wagner 1967). The relation expressing this model

$$\text{Log } Q_t = \text{Log } Q_0 + K_1 t/2.303$$

Where Q_t is the amount of drug released in time t, Q_0 is initial amount of drug in the solution and K_1 is the first order release rate constant. In this way a graphical relationship between log percent drug remaining versus time to get the First order constant from the slope. The pharmaceutical dosage forms following this dissolution profile, such as those containing water-soluble drugs in porous matrices release the drug in a way that is proportional to the amount of drug remaining in its interior, in such a way, that the amount of drug released by unit of time diminishes.

Korsmeyer Peppas model (power law): (Korsmeyer et al.,1983, Peppas 1985) Korsmeyer et al., (1983) developed a simple semi empirical model, relating exponentially the drug release to the elapsed time (t)

$$Q_t/Q_\alpha = K_k t^n$$

Where K_k is a constant incorporating structural and geometric characteristic of the drug dosage form and n is the release exponent, indicative of the drug release mechanism. For matrix tablets, an n value of ~0.5 indicates diffusion – controlled mechanism while an n value of ~1.0 indicates erosion (Ford et al., 1991). Hariharan et al., 1997 a suggested that if the value of n is 0.5, it indicates Fickian transport, a value of 0.5 and 1.0 non-fickian transport, and the values close to 1.0 indicate that the system is releasing drug in a zero-order manner regardless of the actual mechanism of release.

This type of analysis of release behavior is valuable is to the formulator for comparative purposes. The Release exponent can be obtained from the slope and the Constant (K_k) obtained from the intercept of the graphical relation between logarithmic versions of left side of the equation versus log t. This model is used to analyze the release from polymeric dosage forms, when the release mechanism is not well known or when there is a possibility of more than one type of release phenomenon being involved.

Table No 8: Release Mechanism –Korsmeyer Peppas Kinetic mode

Release exponent (n)	Drug transport mechanism	Rate as a function of time
0.5	Fickian diffusion	$t^{-0.5}$
0.5<n<1.0	Anomalous transport or non-Fickian	t^{n-1}
1.0	Case-II transport	Zero-order release
Higher than 1.0	Super Case-II transport	t^{n-1}

Higuchi Model (Higuchi 1961, Higuchi 1963)

$$Q_t = K_H t^{1/2}$$

Where Q_t = the amount of drug released at time t and K_H = the Higuchi release rate;

This is the most widely used model to describe drug release from pharmaceutical matrices. A linear relationship between the square root of time versus the concentration indicates that the drug release follows strict Fickian diffusion. For purpose of data treatment, the above equation is usually reduced to:

$$Q = Kt^{1/2}$$

Therefore, a plot of amount of drug released versus the square root of time should be linear if drug release from the matrix is diffusion controlled. Alternatively, the drug release rate is proportional to the reciprocal of the square root of time. An important advantage of the above equations is its simplicity.

The following plots were made using the *in-vitro* drug release data:

- Cumulative % drug release vs time (Zero order kinetic model);
- Log cumulative of % drug remaining vs time (First order kinetic model);
- Cumulative % drug release vs square root of time (Higuchi model);
- Log cumulative % drug release vs log time (korsmeyer – peppas model);

RESULTS AND DISCUSSION

Standard graph of Itopride hydrochloric acid in 0.1N HCl:

The scanning of the volumetric solution of Itopride hydrochloric acid in the ultraviolet range (200-400nm) against 0.1 N HCl blank gave the λ_{max} as 262 nm. The standard concentrations of Itopride hydrochloric acid (5-25 µg/ml) prepared in 0.1N HCl showed good linearity with R^2 value of 0.998, which suggests that it obeys the Beer-Lamberts law.

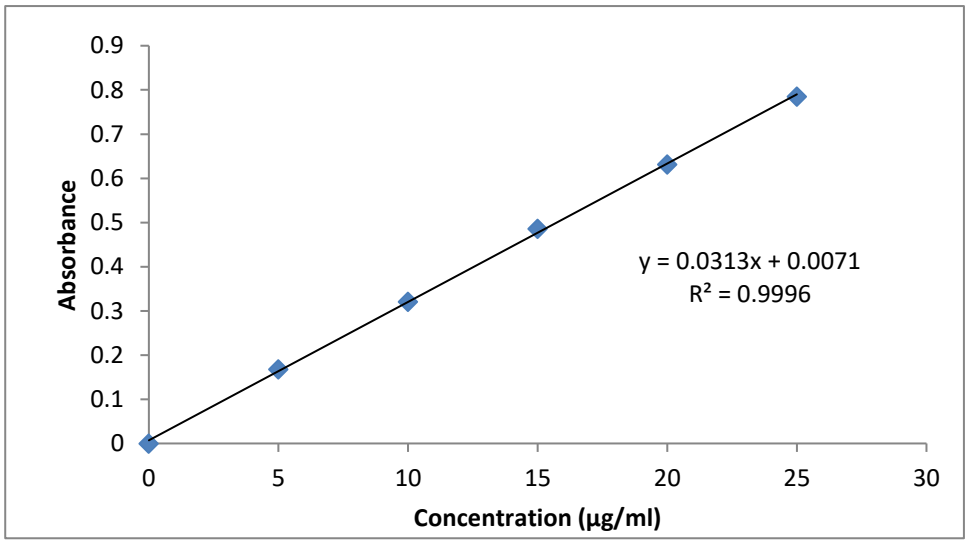

Fig No. 2: Standard curve of Itopride hydrochloric acid

Drug-Excipient Interaction Studies:

Fourier Transform Infrared spectroscopic studies (FTIR)

The FTIR spectra of drug, excipients, drug loaded formulation were recorded. The characteristic peaks of the optimized formulation followed the same trajectory as that of the drug alone with minor differences. Thus, there may be no drug-excipient interactions. The FTIR spectra were given in Figure 3 And 4.

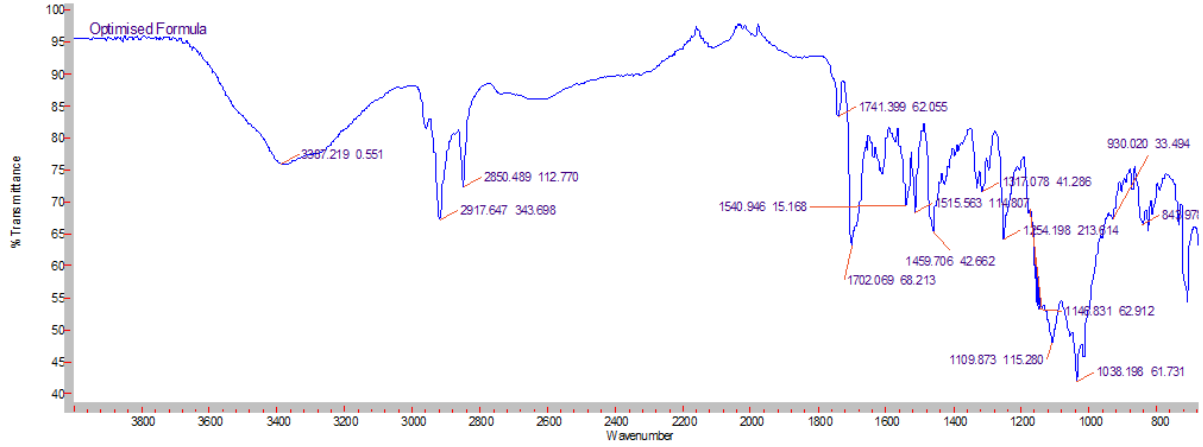

Fig No 3 : FTIR spectra of Itopride hydrochloric acid

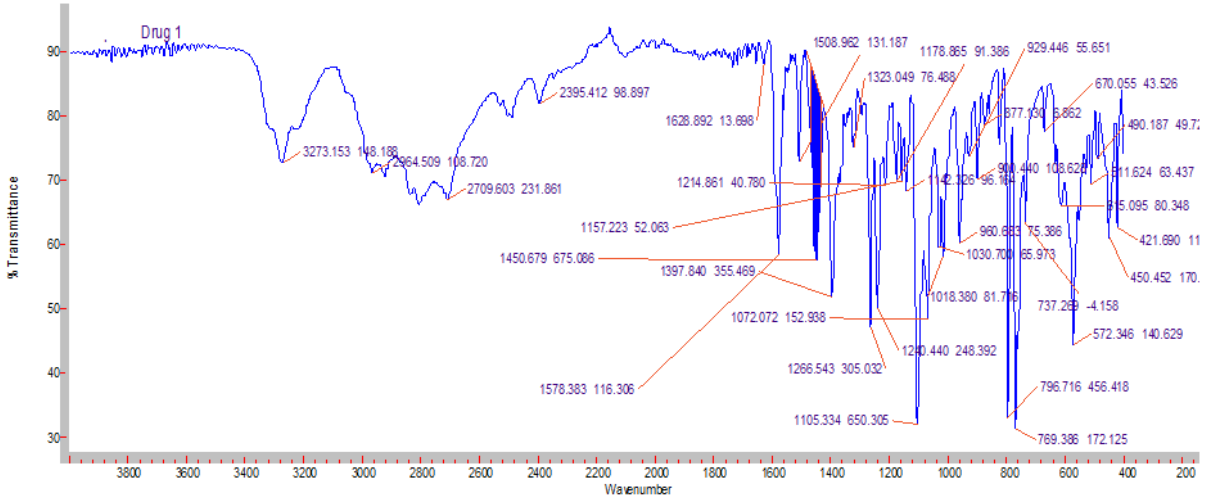

Fig. No 4: FTIR spectra of optimized formulation

Flow properties of floating tablet blends:

Table 9: Results of Precompression Flow Properties of Itopride hydrochloric acid

Formulation code	Angle of repose (Θ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's index (%)	Hausner ratio (HR)
F1	23.01	0.46	0.51	09.80	1.10
F2	22.8	0.52	0.57	10.52	1.09
F3	21.74	0.56	0.61	8.19	1.08
F4	26.33	0.55	0.60	11.67	1.10
F5	28.24	0.54	0.61	11.47	1.12
F6	24.12	0.58	0.64	09.32	1.11
F7	23.08	0.56	0.65	13.84	1.16
F8	22.12	0.47	0.52	10.78	1.10
F9	26.45	0.55	0.59	08.54	1.07

The powder blends of floating tablets were evaluated for their flow properties, the results were shown in Table 9. Angle of repose was in the range from 22.1 to 28.24 which indicates good flow of the powder for all formulations. The values of bulk density were found to be in the range from 0.46 to 0.58 gm/cc; the tapped density was in the range of 0.51to 0.65 gm/cc. The Carr's index was found to be in the range from 08.54 to 13.84, the Hausner ratio was found to be in the range less than < 1.20. These values indicate that the powdered blend exhibited good flow properties and have good compressibility.

Post compression parameters of floating tablets of Itopride hydrochloric acid

Table 10: Results of Post Compression Properties Itopride hydrochloric acid -of Floating Tablets

Formulation Code	Thickness (mm)	Hardness (kg/cm2)	Friability (%)	Drug Content (%)	Weight Variation (mg)
F1	5.56	4.5	0.53	100.89	299.6
F2	5.76	4.3	0.54	99.93	293.0
F3	5.34	4.4	0.48	103.63	289.8
F4	5.45	4.5	0.64	98.56	299.8
F5	5.23	4.6	0.48	97.96	314.7
F6	5.13	4.3	0.69	102.5	319.8
F7	5.17	5.1	0.42	97.7	320.05
F8	5.15	4.9	0.64	98.54	317.85
F9	5.79	4.7	0.55	97.5	320.5

The thickness of floating tablets was measured by vernier calipers and was ranged between 5 and 5.79 mm. The weight variation for different formulations (F1 to F9) showed satisfactory results as per United States Pharmacopoeia (USP) limit (average weight). The hardness of the floating tablets was measured by Monsanto tester and was found to be ranged from 4.1 to 5.1 kg/cm. The friability was found in be ranged from 0.42 to 0.69 which was below 1% for all the formulations, which is an indication of good mechanical resistance of the tablet. The percentage of drug content for F1 to F9 was found to be in between 95 to 105 of Itopride hydrochloric acid. The results are shown in Table 10.

Table 11: Results of *In vitro* Buoyancy study of Itopride hydrochloric acid Floating Tablets

Formulation code	Buoyancy Lag Time (sec)	Total Floating Time (hrs)
F1	92	8
F2	84	>12
F3	88	6
F4	83	>8
F5	92	>12
F6	101	>12
F7	96	6
F8	88	>8
F9	103	>12

All the tablets were prepared by effervescent approach. The results of floating study were shown in table 11. On immersion in 0.1N HCL solution pH (1.2) at 37˚C, the tablets floated, and remained buoyant without

disintegration. Sodium bicarbonate was used as the effervescent base. When the floating matrix tablets containing gas generating agent were exposed to 0.1N HCl, hydrochloric acid reacted with sodium bicarbonate in the floating tablet inducing CO_2 formation. The generated gas was entrapped into the matrix of swollen polymer matrix and was well protected by gel formed by hydration of polymers, which led to floating of the dosage forms. All the prepared batches show the total floating time more than 12 hours except the F1, F3, F4, F7 and F8.

Table No. 12: *In vitro* drug release profile of Itopride hydrochloric acid

Time	Percentage of drug release								
(Hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	34.12	31.12	23.18	51.2	35.8	32.4	16.56	29.8	11.04
3	54.25	42.27	34.28	61.5	57.2	56.4	31.56	45.6	28.57
4	61.35	46.29	38.28	63.4	69.3	62.4	41.52	51.3	31.32
5	67.28	55.28	44.20	68.6	78.2	69.7	50.16	58.8	35.62
6	76.23	61.16	48.18	73.8	86.2	71.4	51.96	61.4	42.96
7	79.26	66.32	55.19	80.8	92.3	76.4	61.08	69.9	53.4
8	85.73	73.16	60.18	88.9	94.9	81.6	61.68	71.3	59.04
9	93.18	78.26	63.18	96.8		82.3	63.72	77.8	62.08
10	100.34	84.29	69.19			86.7	67.92	81.4	63.76
11		95.32	76.27			91.3	73.92	88.9	79.8
12		99.47	83.14			92.4	78		89.5

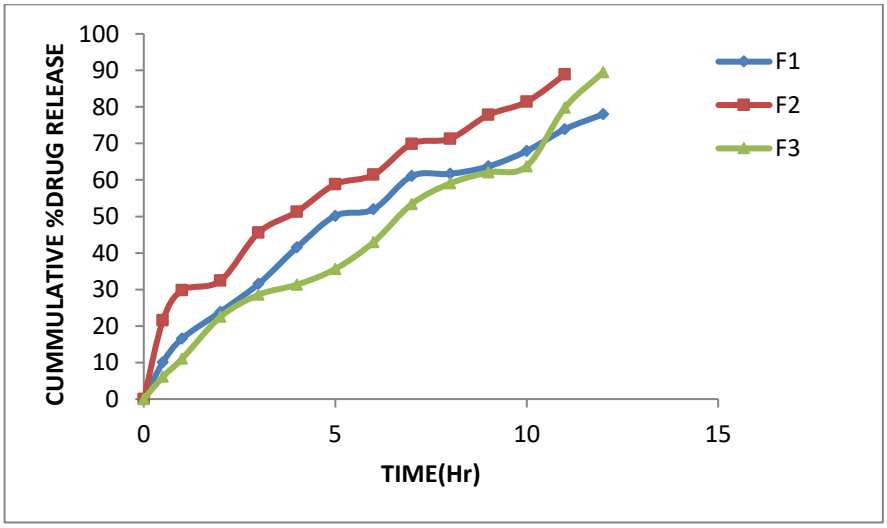

Fig No 5 *: Invitro* drug release data from formulation with Guar gum

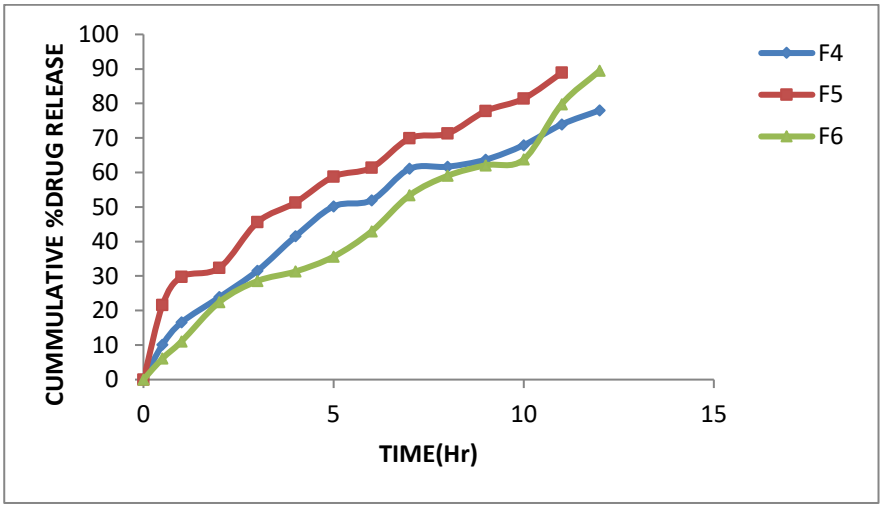

Fig No 6: *Invitro* drug release data from formulation with Xanthane gum

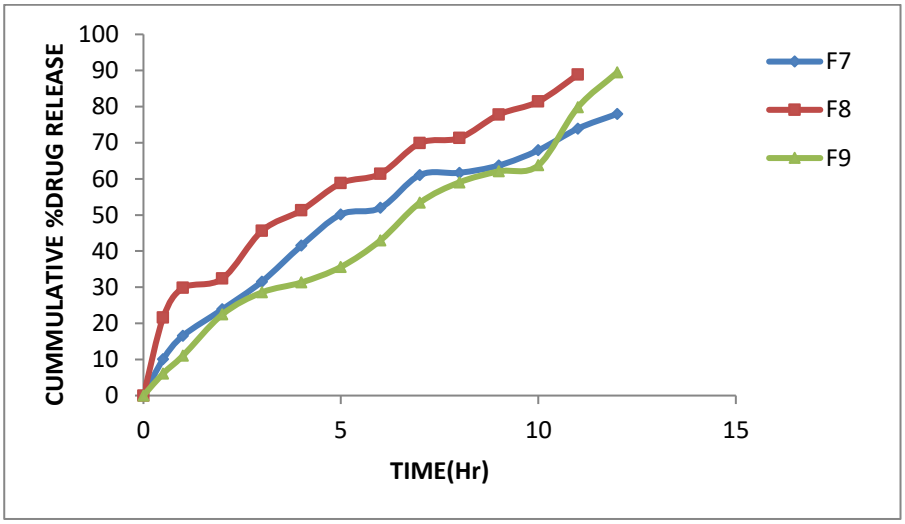

Fig No 7: *Invitro* drug release data from formulation with Na Alginate

In vitro dissolution studies of all the formulations of Itopride hydrochloric acid were carried out in 0.1 N HCl. Percentage drug release was calculated at one-hour time intervals for 12 hours. The variation in drug release was due to different types of polymers and different concentrations of polymer in all the formulations. Among these formulations, formulation F2 gave desired release in first hour for loading dose and also retarded the drug release for 12 hours (99.47%). Hence, the formulation F2 was considered as most promising formulation among all the formulations.

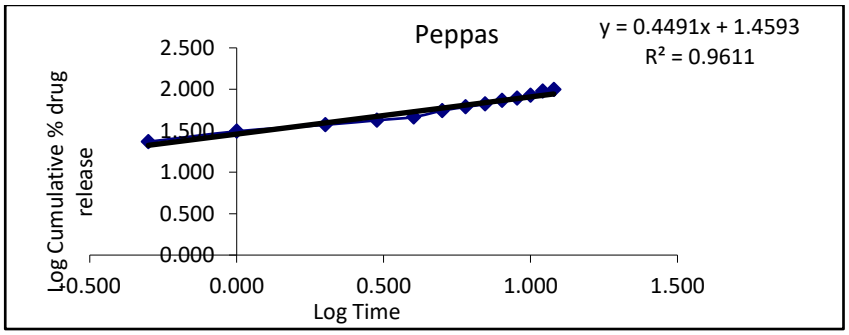

Fig No 8 : Kinetic release plot - Korsemeyers peppas plot

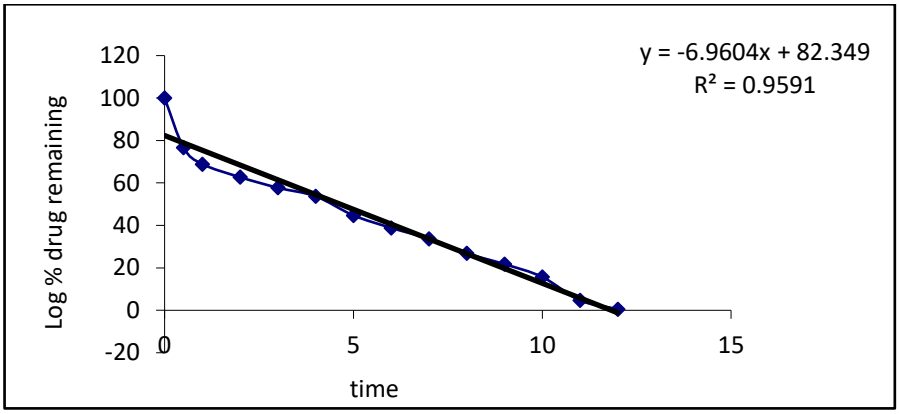

Fig No 9 : Kinetic release plot - First order plot

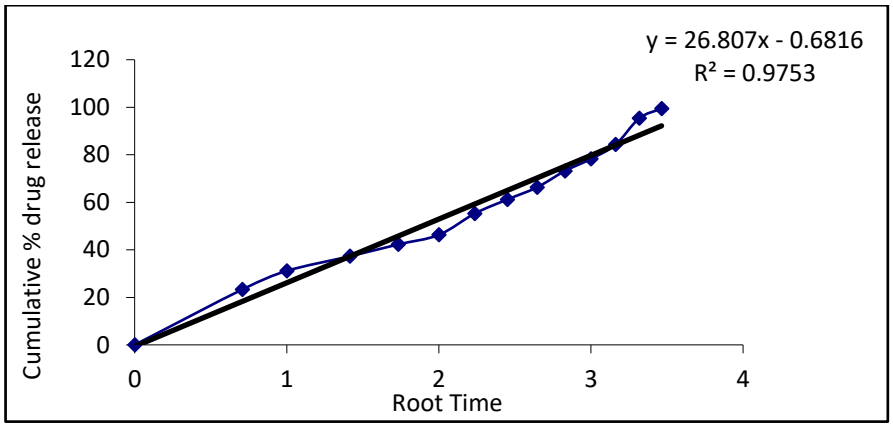

Fig No 10: Kinetic release plot - Higuchi plot

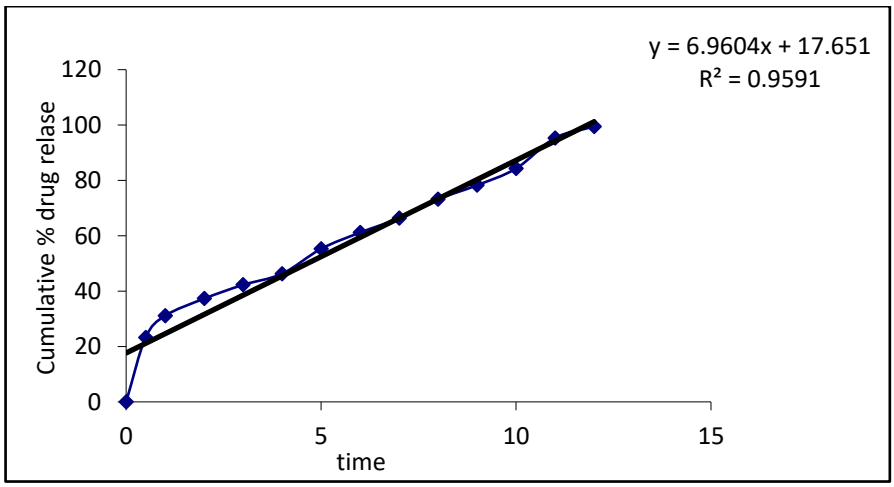

Fig No 11: Kinetic release plot - Zero order plot

The *In vitro* dissolution data were fitted in different kinetic models viz. zero order, first order, Higuchi and Korsemeyer - Peppas equation. Correlation coefficients of formulation F2 showed higher correlation with Higuchi (R^2 = 0.975).

CONCLUSION

This study was conducted to develop gastro retentive floating tablets for Itopride hydrochloric acid used in the treatment of anti-cholinergic agent. which has rapid and complete absorption after oral administration**.** The floating tablets were prepared by direct compression

method by using natural polymers as floating agents so as to maintain in buoyancy condition for about 12 hours to achieve maximum bioavailability and to produce local bioavailability. The prepared formulations were evaluated for various post compression parameters like hardness, friability, thickness, weight variation, floating lag time floating buoyancy studies and invitro dissolution studies. Among all the formulations F2 formulation which contains guar gum has shown desired percentage drug release in 12 hours. The In vitro dissolution data were fitted in different kinetic models viz. zero order, first order, Higuchi and Korsemeyer - Peppas equation. Correlation coefficients of formulation F2 showed higher correlation with Higuchi $R^2 = 0.975$.

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