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Formulation and *In- vitro* Evaluation of Gastroretentive Itopride Hydrochloride Loaded Floating Matrix Tablet

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Abstract:
Itopride hydrochloride (ITH) is a novel gastro-prokinetic agent that stimulates gastrointestinal motility through synergistic effects of D2 receptor blocker and acetyl choline esterase inhibitor. In the present work, Floating matrix tablets containing ITH were prepared by using various polymers and excipients designed to enhance the drug's gastroretentive properties. Hydrophilic polymer HPMC K100M with other release retarding and matrix forming polymers (Eudragit RSPO 100, sodium alginate, ethyl cellulose, *psyllium husk*, xanthan gum and carbapol 971P) using polyvinyl pyrolidine K30 (dry binder) and gas forming agent sodium bicarbonate. FTIR study conducted to confirm compatibility between ITH and the excipients. No significant interactions were found, indicating the excipients are suitable for the formulation. All tablet formulations showed acceptable physical properties but, the formulation composition (F-3) containing HPMC K100 M and ethyl cellulose showed excellent floating behaviour and sustained drug release characteristics. F-3 formulation showed minimum floating lag time (0.2944 minutes) remained floated for 24 hours and cumulative % drug release 99.67%. Drug release from F-3 floating matrix tablet followed Higuchi kinetic model with R^2 value 0.9926.

Key words: Floating, gastro-prokinetic agent, matrix tablet, effervescent.

Introduction:

Itopride hydrochloride (ITH) is a novel prokinetic agent used to stimulate gastrointestinal motility through its dual action as a dopamine D2 receptor blocker and acetylcholinesterase inhibitor. Classified as a BCS Class III drug, ITH is a water-soluble benzamide derivative that is primarily absorbed in the upper part of the GIT (Gastrointestinal tract) [(1)]. Itopride hydrochloride having 5-6 hours elimination half-life ($t_{1/2}$) and bioavailability approximately 60%, necessitating frequent dosing (typically 50 mg three times a day) to maintain therapeutic plasma concentrations over time. For the development of SR (sustained release) dosage from ITH is a good drug, which prolonged the gastric retention and release drug slowly [(2-3)].

Researchers have explored various approaches (high density, swelling and expanding, bio adhesive, super porous hydrogel, magnetic and floating systems etc.) to enhance gastric retention of oral drug formulations. Enhancing gastric retention can significantly improve the bioavailability of certain drugs, reduce the frequency of drug administration, reduce drug waste, improve the solubility of drugs and prolong the duration of drug release. [(4)].

In the present research work, Itopride hydrochloride floating matrix tablets were developed using a combination of hydrophilic polymer HPMC K100M along with other release-retarding and matrix-forming polymers. The specific polymers used include Eudragit RSPO 100, sodium alginate, *psyllium husk*, ethyl cellulose, xanthan gum and carbopol 971P. The formulation also employed PVP K30 as a dry binder and gas generating agent sodium bicarbonate.

Materials and Methods:

Materials:

Itopride hydrochloride (D.K. Pharma, Mumbai), HPMC K-00M (Shreya life Sciences, Aurangabad), Eudragit (Evonik, Mumbai), Sodium alginate (DuPont, Mumbai), Ethyl cellulose, Xanthan gum, Sodium bicarbonate, Carbopol 971P (Research Lab Fine Chem Industries, Mumbai), *Psyllum husk* (Hamdard Laboratories Hariyana), Talc, Magnesium stearate, MCC, PVPK-30 (Shalina Laboratories Pvt Ltd, Mumbai).

Methods:

Formulation of Itopride Hydrochloride Floating Tablet:

ITH floating matrix tablets prepared by using direct compression method. HPMC K100M, eudragit RSPO 100, sodium alginate, ethyl cellulose, *psyllium husk*, xanthan gum and carbapol 971P were used as drug release retardant polymers. PVP K30 (binder), Sodium bicarbonate (gas forming agent), Microcrystalline cellulose (diluent), talc (glidant) and magnesium stearate (lubricant) formulation shown in table 1. ITH and all the ingredients

were passed through a #44 sieve to ensure uniform particle size. The polymers, binder (PVP K30), and MCC were mixed using the geometrical mixing method for 10 minutes. Itopride hydrochloride was then added to this mixture and mixed for an additional 5 minutes. Sodium bicarbonate, the gas-generating agent, was accurately weighed and mixed with the drug blend. This blend was transferred in a poly bag and mixed for 3 minutes to ensure homogeneity. For lubrication talc and magnesium stearate was added to the final powder blend and mixed for 2 minutes. Blend was compressed into tablets using 12 mm diameter punches. (Rotary tablet press: Fluid pack Accura D-4).

Table (1): Composition of Floating Itopride Hydrochloride Matrix Tablet

Sr.No.	**Ingredients(mg/tablet)**	**F-1**	**F-2**	**F-3**	**F-4**	**F-5**	**F-6**	**F-7**
1	Itopride Hydrochloride	150	150	150	150	150	150	150
2	HPMCK110M	60	60	60	60	60	60	60
3	PVPK30	17	17	17	17	17	17	17
4	Sodium Bicarbonate	100	100	100	100	100	100	100
5	Eudragit RSPO100	100	-	-	-	-	-	-
6	Sodium Alginate	-	100	-	-	-	-	-
7	Ethyl Cellulose	-	-	100	-	-	-	-
8	Psyllium Husk	-	-	-	100	-	-	-
9	Xanthan Gum	-	-	-	-	100	-	-
10	Carbopol 971P	-	-	-	-	-	100	-
11	MCC	53	53	53	53	53	53	53
12	Talc	10	10	10	10	10	10	10
13	Magnesium Stearate	10	10	10	10	10	10	10
	Total Weight(mg)	500mg						

Evaluation of Itopride Hydrochloride Floating tablets:

Precompression parameters[5-9]**:**

Angle of Repose (˚):

The angle of repose (˚) provides insight into powder's cohesiveness and flowability. Fixed funnel method was used to measure angle of repose. Powder sample was allowed to flow on butter paper through funnel, whose tip fixed at 2.5 cm from horizontal plane. A pile was formed on butter paper, whose tip touches to the lower tip of the funnel. Mark the circular base of the pile remove powder sample and measure average diameter and calculate radius of the circle. 2.5 cm was the height of pile from horizontal plain.

Formula:

$$\tan \theta = \text{heigh(h)} / \text{radius(r)}$$

$$\theta = \tan^{-1} [\text{height (h)} / \text{radius (r)}]$$

Where: ɵ = Angle of repose,

h= height from lower tip of funnel to the base of cone

r = Radius of base to cone.

Bulk Density:

Powder blend (15gm) was weighed and poured into 50ml measuring cylinder and volume was measured.

Formula:

Bulk Density (gm/ml) = Powder weight/Powder Volume

Tapped Density:

Powder blend (15gm) was weighed and poured into 50ml measuring cylinder. Then placed on density apparatus and volume measured after 100taps.

Formula:

Tapped Density = Powder weight/ Powder tapped volume

% Compressibility/Carr's Index:

Formula:

% Compressibility = [(Tapped Density - Bulk Density) / Tapped Density] × 100

Hausner's Ratio:

Formula:

Hausner's Ratio = Tapped Density/Bulk Density

Post Compression Parameters:

Weight Variation Test IP [10]**:** To determine uniformity of weight twenty tablets were selected randomly and weight of individual tablet was taken. Then twenty tablets average weight calculated. Individual weight of tablets compared with average weight. (Limit: Not more than two of the individual tablet weights deviate from the average weight by more than the % specified in table 2. Verified that none of the tablets deviate by more than twice the specified %.).

Table (2): Limits for weight variation as per IP

Average Weight (mg)	Deviation (%)
80	10
More than 80 but less 250	7.5
250 or more	5

Thickness:

To determine thickness six tablets from each formulation was taken and average thickness determined by using vernier caliper (Acculab).

Hardness:

To determine hardness six tablets from all formulation were taken and average hardness was calculated. Monsanto hardness tester was used to measure the tablet hardness. In the jaw of hardness tester tablet was placed. Scale was adjusted till it coincides with the pointer on the tester. Screw knob slowly turned by applying pressure till tablet breaks or any cracks observed on tablet.

Friability [10]**:**

To determine friability, tablets corresponding to weight 6.5gm were selected, and placed in the drum of Roche friabilator (Vigo FT-20). Drum was set for 100 rotations, after 100 rotations tablets were removed, dedusted and again weighed.

Formula:

%Friability = [(Initial weight of tablets - Final weight of tablets) / Initial Weight of tablets)] × 100

Tablet Density ([11-12]**:**

Solvent displacement method was used to determine densities of tablet. It is an apparent density of tablets. Initial weight of tablets was taken. Then placed in measuring cylinder containing measured volume of absolute hexane.

Formula:

Tablet Density = Mass of tablet (M)/ Displacement volume of hexane (V)

Swelling Index (SI) [13-14]**:**

The study of degree of swelling is essential as it influences a) tablet buoyancy b) ability of swellable polymer to remain intact in test fluid c) kinetics of drug release. The behavior of tablet formulation swelling based on the weight gain or water uptake ability. To determine swelling index weighed tablet (W_0) was placed in 200ml of 0.1NHCl in a beaker at temperature 37±0.5˚C. Then at selected time intervals tablet was withdrawn and excess of surface liquid removed by tapping with tissue paper and reweighed (Wt).

Formula:

SI (Swelling Index) = [Fully swollen tablet weight (Wt) - Initial weight of tablet(W_0)/ Initial weight of tablet(Wo)] ×100

Floating Lag Studies [13-14]**:**

The duration between the placement of the tablet in the dissolution medium and the movement it begins to float is called floating flag time. To determine floating lag time, beaker containing 100ml 0.1NHCl (temperature 37±2˚C) tablets were placed. The floating

lag time was measured as the time taken for the tablets to ascend to the surface and start floating was measured as floating lag time, recorded using a stopwatch.

Total Floating Time [14-15]**:**

In this study, the total floating time (the duration for which tablet remains floated on the 0.1NHCl was observed visually.

Floating Force (Resultant weight determination)[16-17]**:**

The floating force (F) of the dosage form must be sufficient to keep the dosage form buoyant on the surface of the gastric contents. Simply determining the density of the dosage form is not adequate to predict the floating force, as the dry content of the system interacts with gastric secretions to release their contents. To accurately determine the floating force, a precise method for measuring the resultant weight (RW) has been reported.

Resultant weight of tablet was calculated as:

$$RW = (Df- Ds) gV$$

Where:

g = Acceleration of gravity D_f = Gastric secretion density

D_s = Tablet density V = Volume of the tablet

Drug Content [18-19]**:**

Six tablets of each formulation were taken powdered and amount ≈ 150mg of ITH (Itopride hydrochloride) weighed. Then transferred into 100ml volumetric flask containing 10 ml 0.NHCl and mixed thoroughly, volume was adjusted to 100ml using 0.1NHCl.To solubilize Itopride hydrochloride,the above stock solution was sonicated for 15 min. This solution was filtered using whattman filter paper no.41 and diluted using 0.1NHCl.The absorbance of this solution was measured at 258nm on UV visible spectrophotometer, using 0.1 HCl as blank.

***In-vitro* Dissolution study** [15]**:**

Apparatus: USP dissolution test apparatus II/Paddle (Labindia)

Medium: 0.1NHCl (900ml)

Temperature:37±0.5˚C

RPM:75

Duration of study:24 hours

Sample points: 1 hour interval

Volume withdrawn: 5 ml

λmax: 258 nm

UV-Spectrophotometer: UV-Visible 3000+, Labindia.

All determinations were conducted in triplicate to ensure accuracy and reproducibility.

Drug Release Kinetics[20]**:**

Kinetic models applied to analyze the release pattern of drug. Different mathematical models were applied to drug release data of Itopride hydrochloride (ITH) tablet formulations as zero-order kinetics, first-order kinetics, Korsmeyer-Peppas, Higuchi, and Hixson-Crowell models. For describing drug release the kinetic model with highest regression coefficient (R^2) was considered for describing the drug release as the best fitting model.

Compatibility study[21]:

FTIR study was conducted on pure Itopride hydrochloride and the best formulation (F-3) to confirm the compatibility of Itopride with both natural and synthetic polymers used in tablet formulations. KBr pellets were prepared by mixing each formulation sample with KBr in a glass mortar and pestle, followed by compression into pellets using a KBr press. The prepared pellets of each sample was scanned over the transmission range of 4000-400 cm^{-1} using a Bruker ALPHA II FTIR spectrometer.

Results and Discussion:

Itopride hydrochloride floating matrix tablets were prepared using hydroxyl propyl methyl cellulose K100M (a hydrophilic matrix-forming polymer) along with other release-retarding polymers such as Eudragit RSPO (a copolymer of acrylates), sodium alginate, *Psyllium husk*, xanthan gum (natural biopolymers), ethyl cellulose (a hydrophobic cellulose derivative), and Carbopol 971P (a synthetic acrylic acid polymer). PVP K30 (binder), and $NaHCO_3$ (gas forming agent). Itopride hydrochloride (ITH) floating matrix tablet was prepared using effervescent approach and direct compression method.

Evaluation of Itopride hydrochloride floating matrix tablet formulations:

Pre-compression Evaluation:

All batches (F-1 to F-7) of Itopride hydrochloride (ITH) floating matrix tablets were evaluated for various parameters as shown in table 3. Angle of repose (˚) for the powder mixture was ranged between 28.58˚ and 33.77˚, indicating that the powder flow was good to excellent. Powder densities i.e. bulk and tapped found between 0.373g/cc and 0.841g/cc and 0.437g/cc and 0.989g/cc respectively.% compressibility and Hausner's ratio for the powder mixture were less than 14.93% and less than 1.17, respectively, which further confirmed good to excellent flowability of mixture.

Table (3): Pre-compression evaluation of powder mixture (Formulation F-1 to F-7)

Sr. No.	Formulations	Angle of Repose (°)	Bulk Density (gm/cc)	Tapped Density (gm/cc)	Percent (%) Compressibility	Hausner's Ratio
1	F1	28.95 ±0.63	0.505 ±0.004	0.580 ± 0.017	12.92 ± 2.5	1.14 ± 0.035
2	F 2	32.39 ±0.092	0.841 ±0.013	0.989 ± 0.038	14.93 ± 401	1.17 ± 0.061
3	F 3	32.5	0.373	0.437	14.48	1.16

		±0.238	± 0.005	± 0.021	± 4.8	± 0.06
4	F 4	32.30 ±1.15	0.769 ± 0.019	0.900 ± 0.041	14.53 ± 1.49	1.16 ± 0.023
5	F 5	33.77 ±0.5	0.408 ± 0.006	0.4737 ± 0.008	13.66 ±2.5	1.15 ± 0.035
6	F 6	33.10 ±0.73	0.8185 ± 0.025	0.948 ± 0.046	13.65 ± 2.8	1.15 ± 0.04
7	F 7	28.58 ± 0.66	0.616 ± 0.014	0.7070 ± 0.012	12.96 ± 2.82	1.1436 ± 0.035

Post -compression evaluation:

The results of the physical evaluation for all batches (Formulation F-1 to F-7) for the Itopride hydrochloride floating matrix tablets were presented in table 4. All formulations passed the weight uniformity test, with the percent deviation for each tablet being less than ±5%, meeting the official requirements. The average thickness (4.65mm to 4.89mm) and average diameter (11.96 mm to 12.03mm) was observed. The hardness between 4.75 Kg/cm² to 8.8 Kg/cm², indicating that the tablets have adequate resistance to mechanical stress. The percent (%) friability for all formulations was less than 1%, (0.12% to 0.62%) meeting pharmacopoeial specification and indicating good mechanical resistance during transportation.

Table (4): Evaluation of Itopride hydrochloride floating matrix tablet formulations (F-1 to F-7) for physical characterization

Sr. No.	Formulations	Weight Variation Test (mg)	Thickness (mm)	Diameter (mm)	Hardness (Kg/cm)	% Friability
1	F 1	500 ±1.11	4.65 ± 0.03	12.03± 0.01	7.82±0.34	0.28
2	F 2	499.9 ±2.17	4.66 ± 0.02	12.01± 0.03	6.6 ± 0.25	0.62
3	F 3	499.85 ± 2.34	4.89 ± 0.02	12.00± 0.1	4.75 ± 0.27	0.14
4	F 4	499.05 ± 1.84	4.77 ± 0.04	11.98± 0.09	5.75 ± 0.27	0.2
5	F 5	499.15 ± 2.4	4.73 ± 0.05	11.96± 0.05	8.8 ± 0.25	0.6
6	F 6	500.8 ± 3.1	4.62± 0.04	11.98± 0.11	8.67 ± 0.4	0.12
7	F 7	499.6 ± 2.4	4.68 ± 0.029	12.00± 0.02	8.00 ± 0.31	0.3

The results of floating and swelling studies are shown in table 5. The drug content for floating matrix formulations was uniform and found to be more than 96%, indicating consistent distribution of Itopride hydrochloride within tablets formulation.

Table (5): Itopride hydrochloride formulations F1-F7 evaluation

Sr. No.	Formulations	Drug content (%)	Tablet Density (gm/cc)	Floating Force (N)	Percent Swelling Index	Floating Lag Time (min)	Total Floating Time (h)
1	F 1	98.78 ± 1.86	0.499 ± 0.003	4.874 ± 0.043	81.51 ± 1.31	1.44 ± 0.14	>24
2	F 2	99.65 ± 0.88	0.497 ± 0.0036	4.968 ± 0.0034	99.06 ± 0.81	2.08 ± 0.07	>24
3	F 3	100.01 ± 1.23	0.504 ±0.005	4.893 ± 0.054	78.8 ±1.75	0.2944 ± 0.02	>24
4	F 4	96.87 ± 0.10	0.500 ± 0.002	4.935 ± 0.02	96.56 ± 0.81	1.11 ± 0.19	>24
5	F 5	99.54 ±0.18	0.518 ± 0.0037	4.759 ± 0.037	93.63 ± 1.6	1.12 ± 0.2	>24
6	F 6	99.12 ± 1.01	0.508 ± 0.002	4.857 ± 0.04	74.33 ± 1.242	1.13 ± 0.032	>24
7	F 7	98.71 ± 0.38	0.500 ± 0.002	4.959 ± 0.01	66 .00 ± 2.64	2.06 ± 0.11	>24

Tablet Density:

Tablet density was found between 0.497gm/cc to 0.518gm/cc (figure 1.), which was less than the density of gastric content (≈1.004gm/cc), ensures floating of tablet dosage form. Tablet density was not sufficient to predict buoyancy of formulations, floating force was determined, which was positive for all formulations ensure floating of all formulations (table 5).

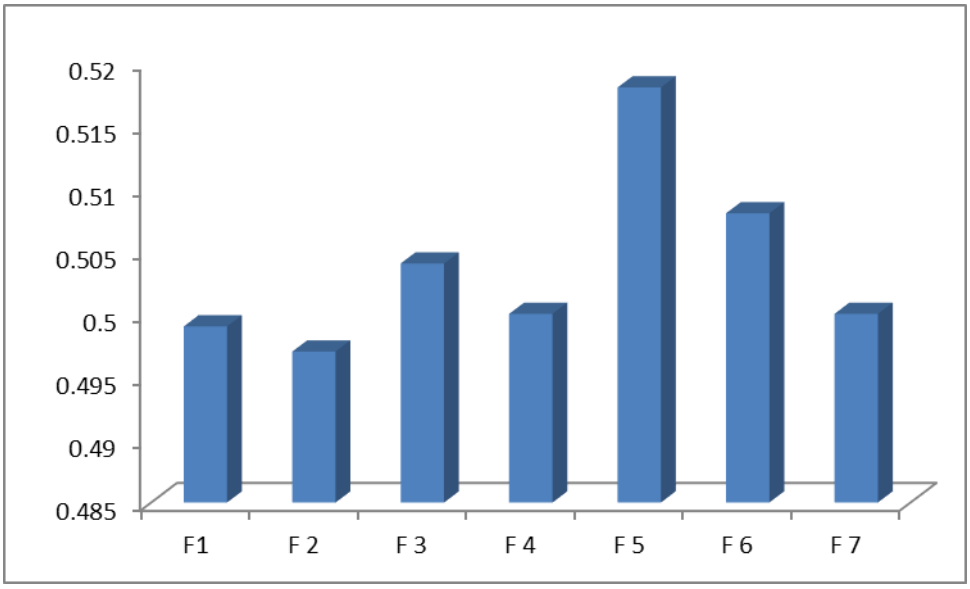


Figure (1): Tablet Density (Formulation F1 to F7)

Swelling Index (SI):

SI for all formulations range between 66% to 99.06% (figure 2) indicate that formulation containing only HPMC K100 M shows less swelling index, while formulation containing sodium alginate shows immediate swelling due to fast gelation of sodium alginate. Swelling of all formulation containing different polymers was in following order: Sodium alginate>

Psyllium husk> Xanthan gum> Eudragit RSPO> Carbpol 971P> Ethyl cellulose> HPMC K100M.

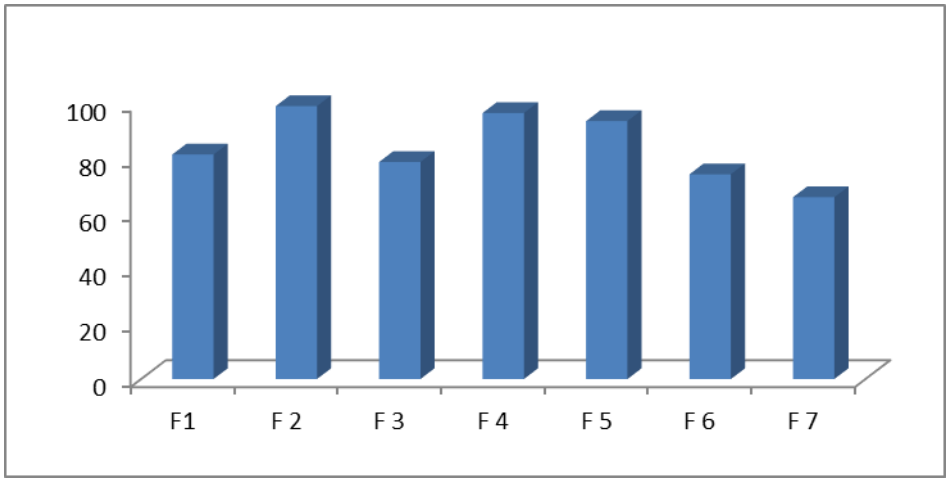


Figure (2) :% Swelling Index (Formulation F1 to F7)

Floating Studies:

Floating lag time (Flag) for all batches of Itopride hydrochloride floating matrix tablet was found in the range of 0.2944 min to 2.08 min (figure3 and 4). Formulation containing ethyl cellulose shows minimum floating lag time, it enhance the floating behavior of formulation. While other formulations take 1-2minutes to float. Formulations containing HPMC K100M and eudragit RSPO 100 take more time to float due to slow hydration of polymer and formation of gel layer. Floating time for all formulation was found to be more than 24 hours. Formulation containing sodium alginate, *psyllium husk* shows low mechanical strength, start to disintegrate faster. Formulation containing HPMC K100M, eudragit RSPO 100 and ethyl cellulose showed high mechanical strength, remained intact for 24 hours as compared to other polymers.

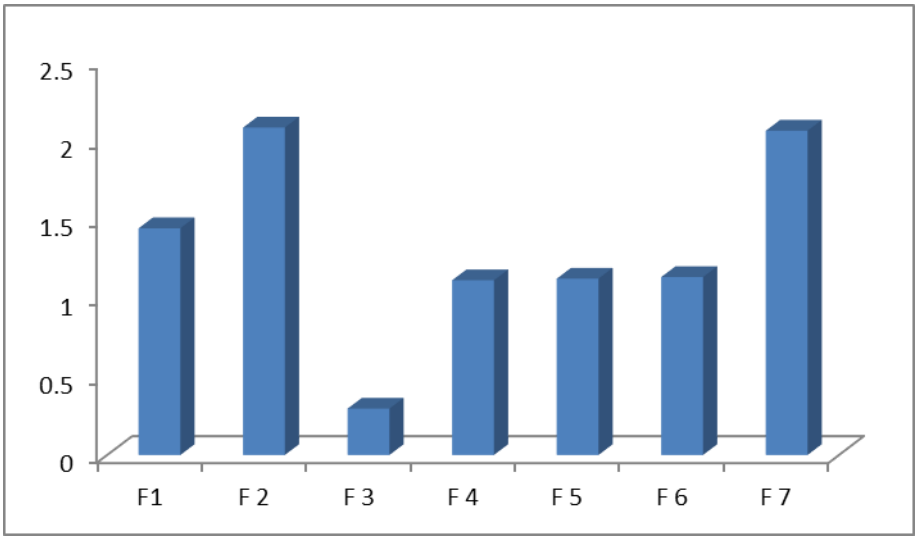


Figure (3) : Floating Lag Time

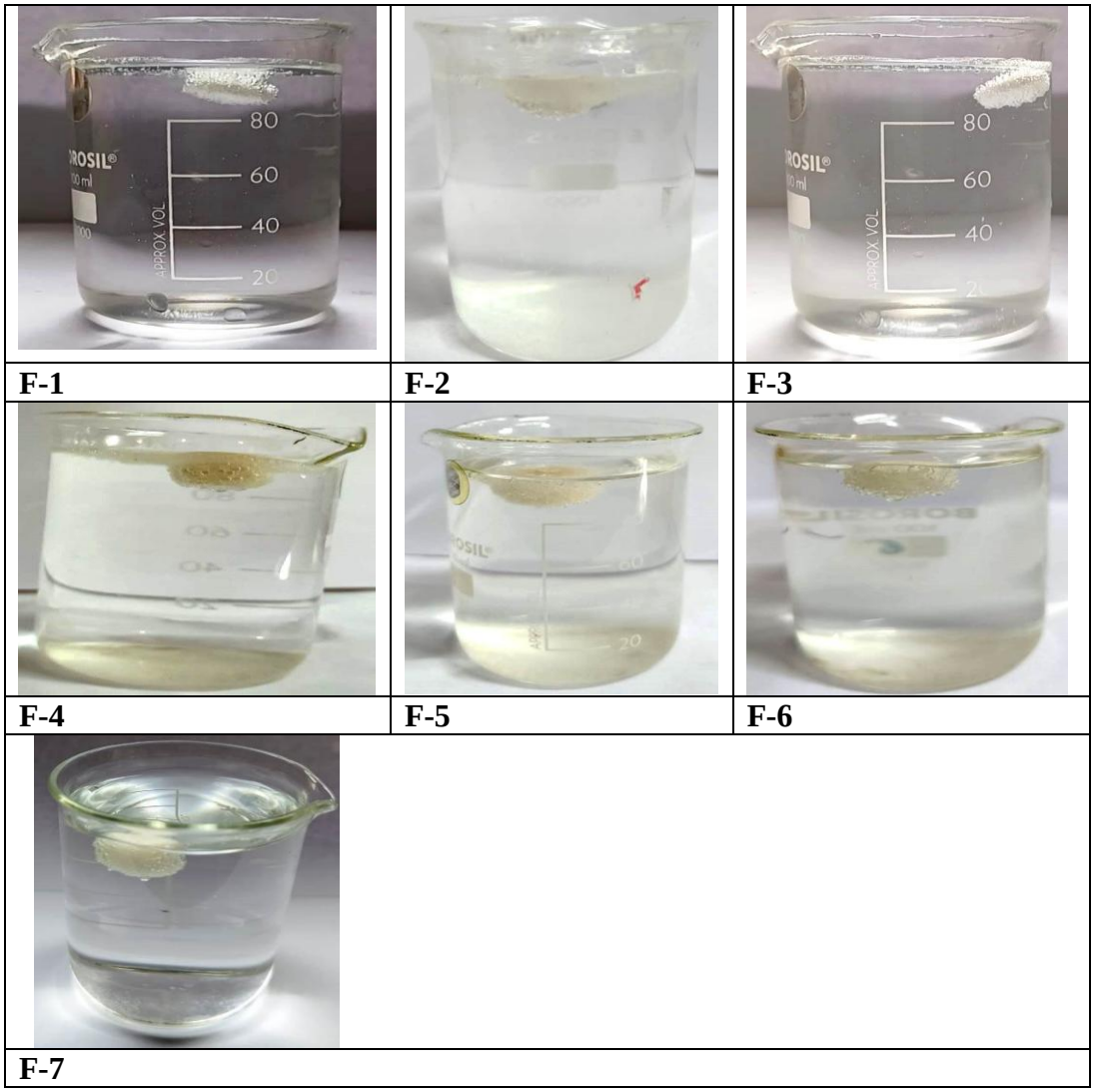


Figure (4) : Floating images

***In-vitro* Dissolution Study:**

The percent cumulative release of drug obtained by plotting % cumulative drug release on Y-axis and time t on X- axis for all formulations (table 6 and figure 5). The formulation containing sodium alginate showed 98.88% drug release in 8 hours due to the fast gelling and low mechanical strength of sodium alginate. Formulations F-4 and F-6 showed drug release 99.55% (16hours) and 96.57% (12 hours), indicating that *Psyllium husk* and Carbopol 971P could retard drug release for longer periods compared to sodium alginate, but not up to the desired limit. Formulations F-5 (containing xanthan gum) and F-7(containing HPMCK 100M) retarded drug release up to 18 hours, showing 98.05% and 98.73% drug release. Formulations containing Eudragit RSPO 100 (F-1) and ethyl cellulose (F-3) were able to retard release of drug up to 24 hours. The formulation containing ethyl cellulose in combination with HPMC K100M (F-3) showed the desired release of drug 99.67% in 24 hours. Therefore, F-3 formulation considered as the best formulation to achieve the desired release pattern.

Table (6) : Percent cumulative drug release (Formulation F-1 to F-7)

	F-1	F-2	F-3	F-4	F-5	F-6	F-7
2	23.43±0.57	8.08± 2.10	23.88±1.08	6.32±0.61	21.43±1.55	6.21±2.17	23.71± 1.04
4	35.54±0.98	33.22±1.28	32.97±1.35	15.76±1.22	37.53±1.19	24.15±1.10	36.98± 1.87
6	45.9± 0.14	78.41±3.25	44.03±1.77	34.08±0.53	48.65±0.53	51.75±1.11	45.84± 2.32
8	54.34±1.06	98.88±0.99	55.94±1.53	57.1±0.47	58.37±2.50	76.61±2.09	55.14± 0.97
10	62.67±0.75	-	61.71±2.41	72.6±1.26	70.82±3.07	91.33±1.41	65.22±0.17
12	72.40±1.57	-	69.34±3.04	83.3±1.15	78.51±2.25	96.57±1.56	78.05±1.57
16	81.43±1.95	-	78.88±1.60	99.55±1.89	90.77±1.18	-	90.21± 1.20
18	87.15±2.14	-	88.64±1.16	-	98.05±0.45	-	98.73± 0.98
24	97.9± 2.90	-	99.67±0.16	-	-	-	-

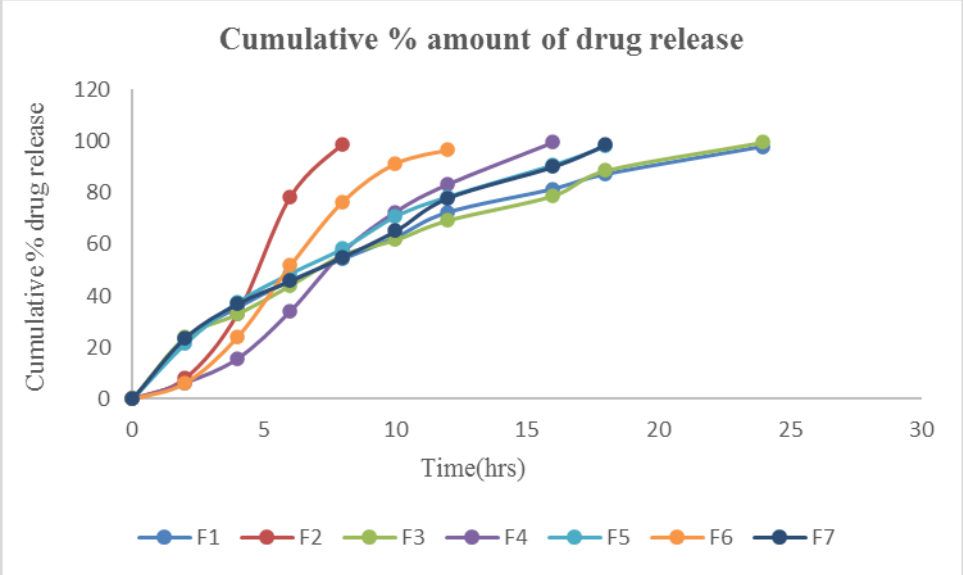
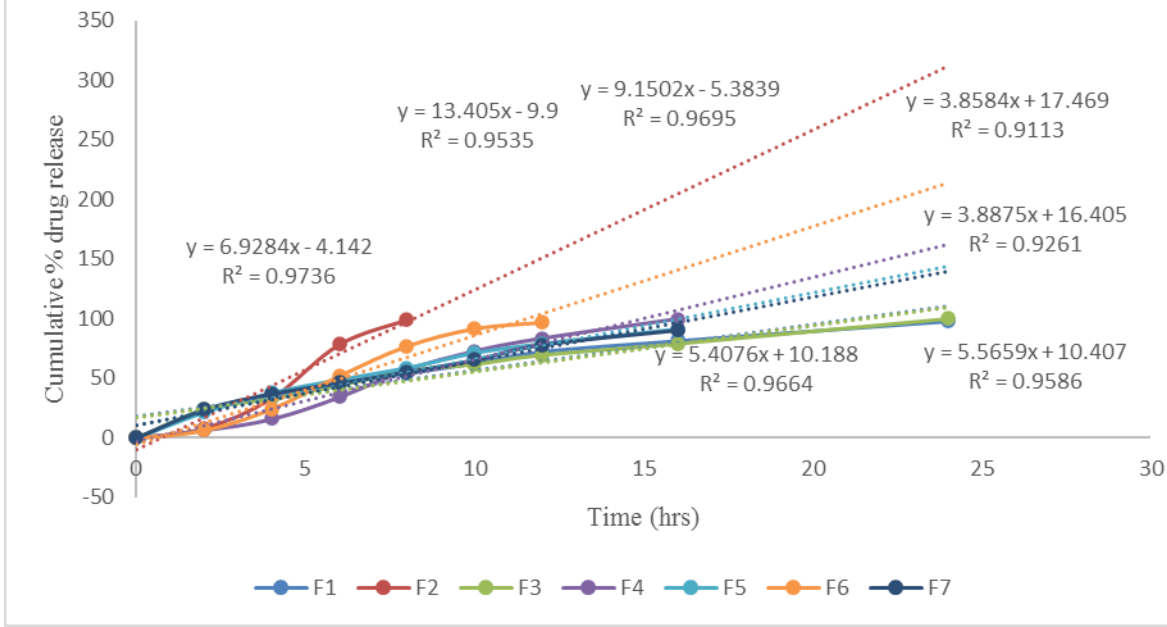


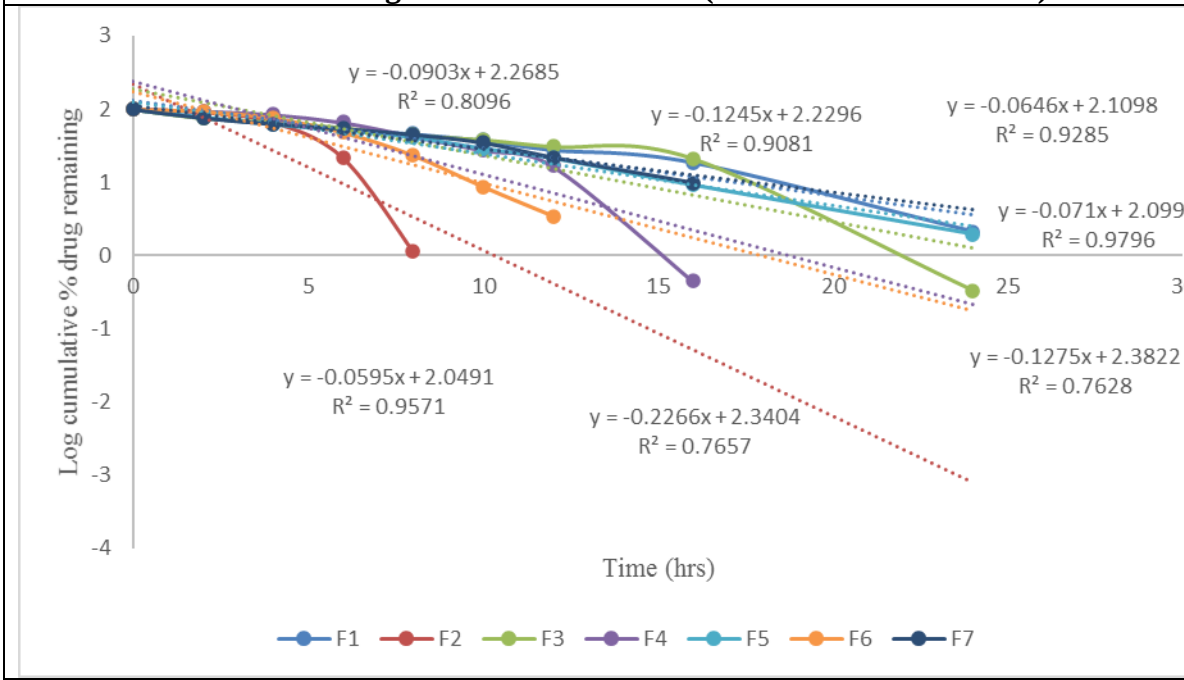
Figure (5): Cumulative percent (%) drug release (Formulation: F-1 to F-7)

***In- vitro* dissolution Kinetic Model Fitting:**

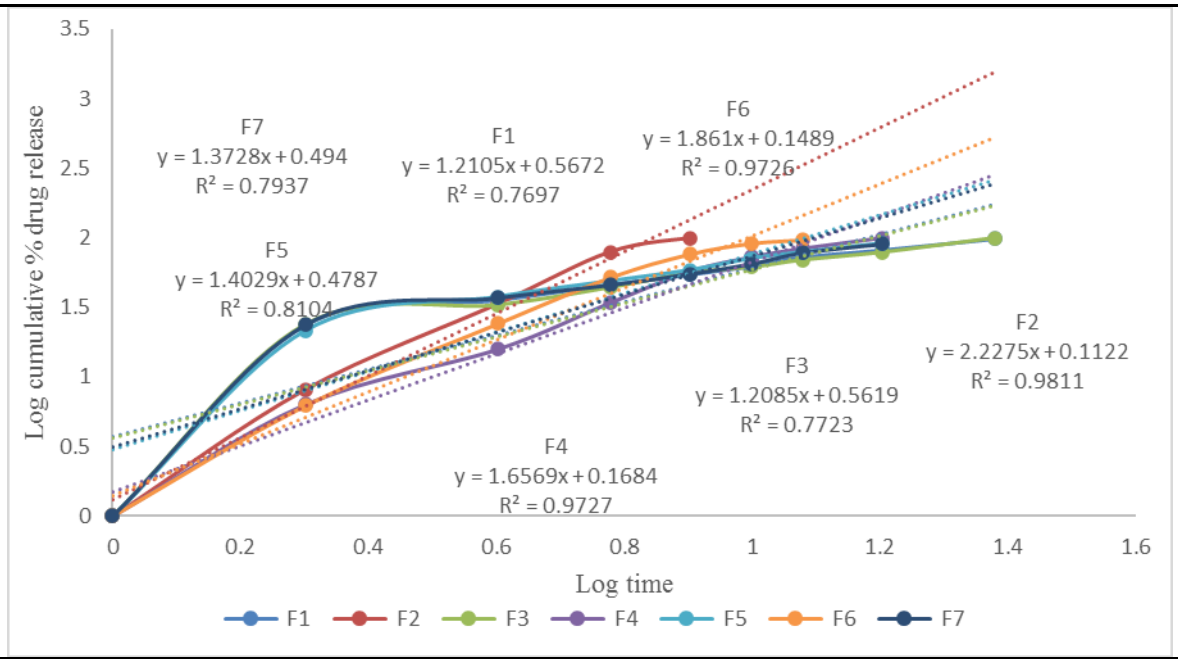
Various drug release kinetic models (zero-order, first-order, Korsmeyer-Peppas, Higuchi, and Hixson-Crowell models) were used to predict the best drug release kinetic mechanism from the matrix tablet formulations. The results are shown in figure 6 and table 7. Formulations F-2 and F-6 followed the Korsmeyer-Peppas kinetic model with R^2 value 0.9811 and 0.9726, respectively. Formulations F-1 and F-3 followed the Higuchi diffusion model(R^2 values close to 1), indicating release of drug was primarily governed by diffusion. Formulations F-5 and F-7 followed the Hixson-Crowell model, suggesting that the release of drug was influenced due to surface area and diameter of the tablets changes. Zero-order kinetics followed by formulation F-4 with an R^2 0.9736, indicating a constant drug release rate over time.



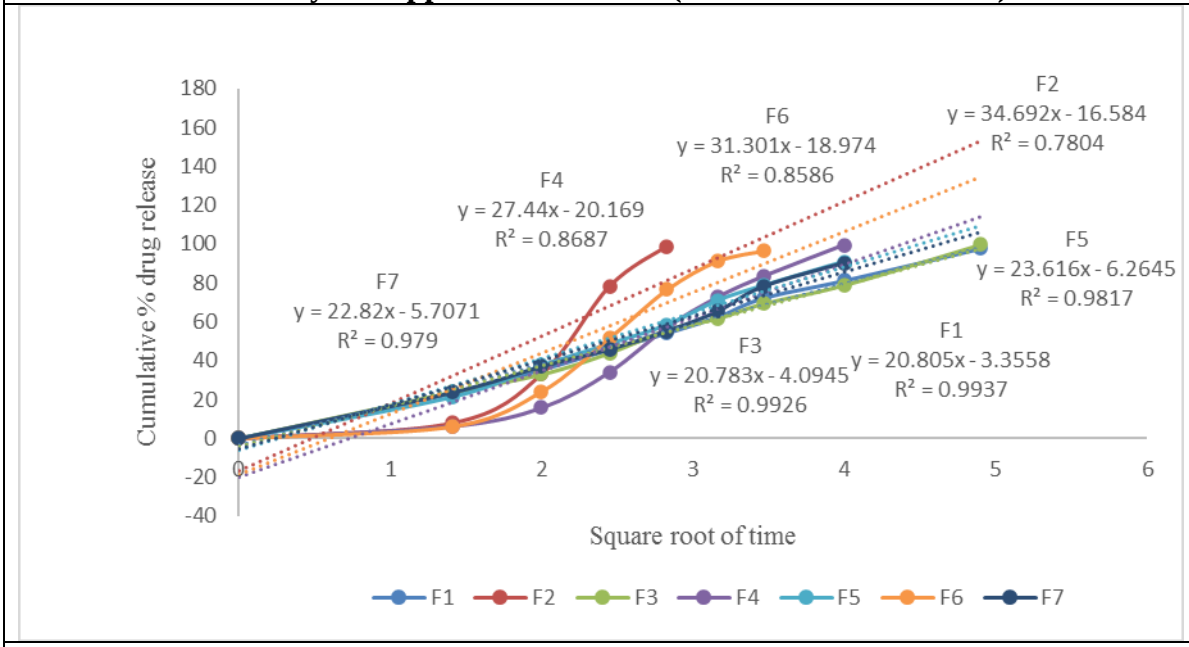
Zero order drug release kinetic model (Formulation F-1 to F-7)



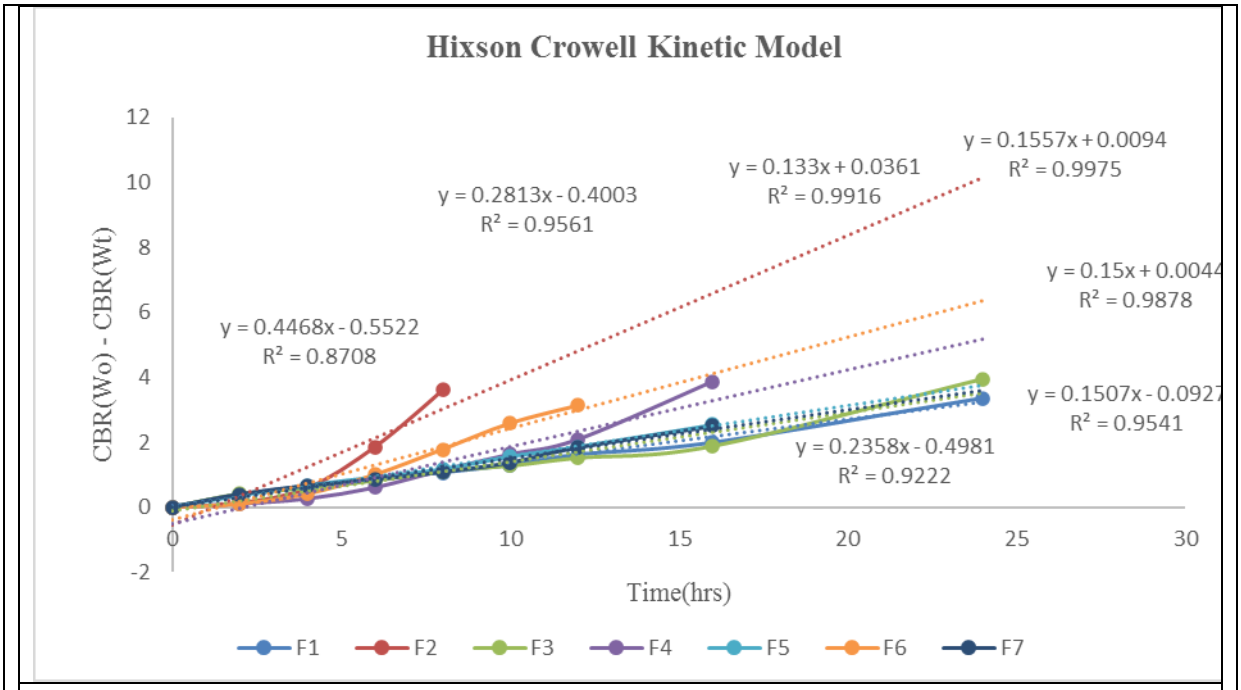
First order drug release kinetic model (Formulation:F-1 to F-7)



Korsmeyer- Peppas kinetic model (Formulation F-1 to F-7)



Higuchi kinetic model (Formulation F-1 to F-7)



Hixson Crowell kinetic model (Formulation F-1 to F-7)

Figure (6) : Kinetic drug release model fitting of Itopride hydrochloride floating matrix tablet (Formulation F-1to F-7)

Table (7): *In- vitro* Kinetic model fitting to drug release data of Itopride hydrochloride floating tablet formulations (F-1 to F-7)

Sr. No.	Kinetic Model	Parameters	F1	F2	F3	F4	F-5	F-6	F-7
1	Zero Order	R^2	0.9113	0.9535	0.9261	0.9736	0.9586	0.9695	0.9664
		Slope	3.858	13.405	3.8875	6.9284	5.5659	9.1502	5.4076
		Intercept	17.469	-9.9	16.405	-4.142	10.407	-5.3839	10.188
2	First Order	R^2	0.9285	0.7657	0.8096	0.7628	0.9796	0.9081	0.9571
		Slope	-0.0646	-0.2266	-0.0903	-0.1275	-0.071	-0.1245	-0.0595
		Intercept	2.1098	2.3404	2.2685	2.3822	2.0997	2.2296	2.0491
3	Korsmeyer-Peppas	R^2	0.7697	0.9811	0.7723	0.9727	0.8104	0.9726	0.7937
		Slope	1.2105	2.2275	1.2085	1.6569	1.4029	1.861	1.3728
		Intercept	0.5672	0.1122	0.5619	0.1684	0.4787	0.1489	0.494
4	Higuchi	R^2	0.9937	0.7804	0.9926	0.8687	0.9817	0.8586	0.979
		Slope	20.805	34.692	20.783	27.44	23.616	31.301	22.82
		Intercept	-3.3558	-16.584	-4.0945	-20.169	-6.2645	-18.974	-5.7071
5	Hixson-Crowell	R^2	0.9916	0.8708	0.9541	0.9222	0.9975	0.9561	0.9878
		Slope	0.133	0.4468	0.1507	0.2358	0.1557	0.2813	0.15
		Intercept	0.0361	-0.5522	-0.0927	-0.4981	0.0094	-0.4003	0.0044

Compatibility Study:

To investigate the drug and polymer interaction, FTIR spectra of Itopride hydrochloride and the best formulation, F-3 were taken. The FTIR scan of pure Itopride hydrochloride showed significant peaks at the following wavelengths: 1003.59 cm^{-1} (C-N stretching), 3277.12 cm^{-1} (N-H stretching), 1637.98 cm^{-1} (C=O stretching) 1503.12 cm^{-1} (C=C aromatic stretching), 1225.05 cm^{-1} (C-O-C asymmetric ether stretch) The same peaks, with slight

changes in intensity, were found in the F-3 formulation, as shown in the fourier transform infrared (FTIR) spectra of both the drug and formulation F-3 (figure 7 and figure 8). All characteristic bands of the drug were preserved in the F-3 formulation. Indicated compatibility of Itopride hydrochloride with polymers as there is no interaction between drug and polymers used.

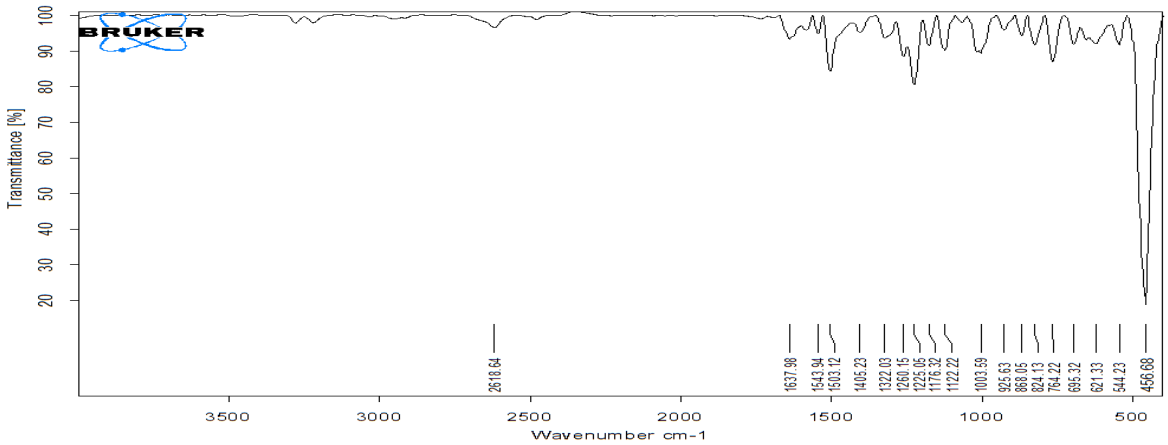


Figure (7): Fourier transform infrared (FTIR) spectra of pure Itopride hydrochloride

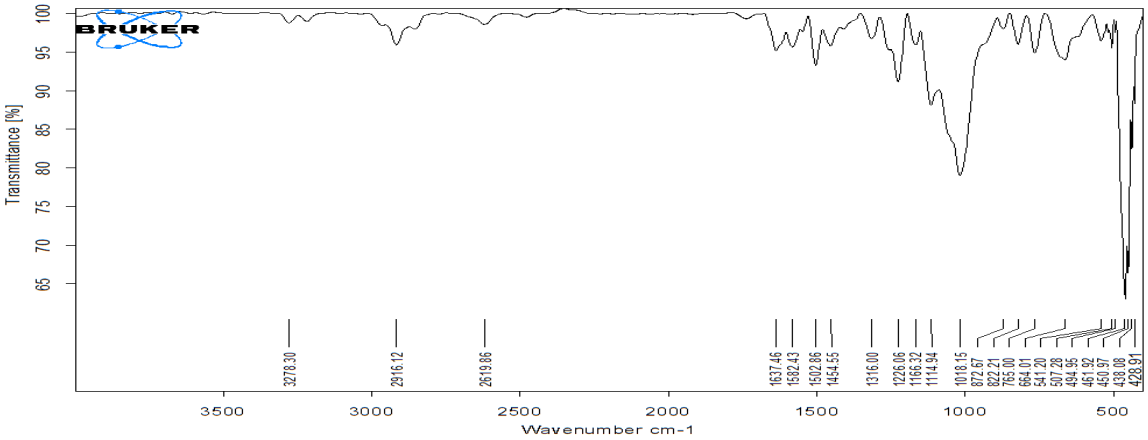


Figure (8): Fourier transform Infrared (FTIR) spectra Itopride hydrochloride floating matrix tablet F-3 formulation

Conclusion:

Direct compression method was used to prepare the Itopride hydrochloride floating matrix tablets. Matrixing agent HPMC K100M was used in combination with other natural and synthetic release-retarding polymers such as sodium alginate, xanthan gum, *psyllium husk*, Eudragit RSPO 100, ethyl cellulose, and Carbopol 971P, with PVP K30 as a dry binder. The floating tablets were formulated using the effervescence approach with $NaHCO_3$ as a gas-generating agent. Compatibility of drug and excipients used in formulation confirmed by FTIR studies.All tablet formulations exhibited acceptable physical properties. Among them, formulation F-3, containing HPMC K100M and ethyl cellulose, demonstrated excellent floating behaviour with sustained release characteristics. The F-3 formulation had a minimal

floating lag time (0.2944 minutes) and remained floated for 24 hours. The cumulative percentage of drug release for F-3 was 99.67%. Release of drug from the F-3 floating matrix tablet followed the Higuchi kinetic model, with an R^2 value 0.9926, indicating drug release by diffusion through the matrix.

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