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FORMULATION AND EVALUATION OF SOTALOL GASTRORENTENTIVE TABLETS

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ABSTRACT

The objective of this study was to formulate floating tablets (GRDDS) of Sotalol using direct compression method to increase its bioavailability and the gastric residence time of the dosage form. The Sotalol tablets were prepared by direct compression method. The tablets werepreparedby using different types of polymers i.e.; Sodium CMC, Chitosan and Psyllium Husk which act as a release retardant polymer. Sodium bi carbonate ($NaHCO_3$) was used as a gas degenerating agent and MCC (Micro crystalline cellulose) was used as a diluent. The prepared formulation were subjected to some evaluation parameters like hardness, friability, weight variation, drug content, buoyancy property, drug release study etc. In the FT-IR study it was revealed that there is no interaction between the drug and excipients. The formulation which containing Chitosan polymer and Sodium bicarbonate shows good drug release pattern with less floating lag time and good floating duration. The *in vitro* drug release pattern of Sotalol floating tablets was fitted to different kinetic models which showed the highest regression for Higuchi order kinetics. Thus, it can be concluded that the floating drug delivery system of Sotalol using the appropriate polymers in right amount may enhance the activity of the drug by prolonging the gastric residence time or reducing the floating lag time.

KEYWORDS: Sotalol, Sodium CMC, Chitosan, Psyllium Husk and Floating Tablets.

INTRODUCTION

Oral drug delivery systems have dominated other drug delivery systems for human administration due to their various advantages including ease of administration, flexibility in formulation, cost-effectiveness, easy storage and transport, and high patient compliance. However, oral drug delivery systems face challenges such as low bioavailability due to the heterogeneity of the gastrointestinal system, pH of the commensal flora, gastric retention time of the dosage form, surface area, and enzymatic activity.[1] Conventional drug delivery systems may not overcome the issues imposed by the gastrointestinal tract (GIT) such as incomplete release of drugs, decrease in dose effectiveness, and frequent dose requirement. Therefore, the failure of conventional drug delivery systems to retain drugs in the stomach may lead to the development of GRDDS. These systems offer several benefits such as prolonged gastric residence time (GRT) of dosage forms in the stomach up to several hours, increased therapeutic efficacy of drugs by improving drug absorption, and suitability for targeted delivery in the stomach. In addition, GRDDS can enhance the controlled delivery of drugs by continuously releasing the drug for an extended period at the desired rate and to the desired absorption site until the drug is completely released from the dosage form.[1,2]

GRDDS are feasible for drugs that have low absorption in the lower part of the GIT, are unstable and poorly soluble at alkaline pH, have a short half-life, and show local activity at the upper part of the intestine for eradication of *Helicobacter pylori*.[3,4,5,6,7,8,9,10,11,12,13,14,15] Several formulation strategies have been used to design successful controlled release GRDDS including superporous hydrogel, bio/mucoadhesive, raft-forming, magnetic, ion-exchange, expandable, and low- and high-density systems.[3,4,5,6,7,8,9]

Various formulation-related factors such as polymer types (nonionic, cationic, and anionic polymers), polymer composition in dosage form, viscosity grade, molecular weight of the polymer, and drug solubility can affect the quality of the gastroretentive dosage form.[9] Moreover, the physicochemical nature of excipients plays an important role in various GRDDS. For instance, density of excipients and composition of effervescent agents are critical factors in effervescent floating systems. In the case of superporous hydrogel systems, high swelling excipients such as crospovidone and sodium carboxymethylcellulose are required to form a superporous hydrogel.[9,16] Likewise, process variables can also influence the quality of the gastroretentive dosage form, as the density of a tablet can be altered by the compression pressure during tableting.[9]

The aim of the present work is to formulate & evaluate gastro retentive floating tablets of Sotalol using various polymers. Sotalol is a medication used to treat and

prevent abnormal heart rhythms. It is only recommended in those with significant abnormal heart rhythms due to potentially serious side effects. Evidence does not support a decreased risk of death with long term use. It is taken by mouth or injection in to a vein. Sotalol is rapidly and efficiently absorbed after oral administration and requires multiple dosing for maintaining therapeutic effect throughout the day. In fact there is a need to develop a dosage form to deliver Sotalol in the stomach and to increase the efficiency of the drug, providing targeted action. The objective of this study was to prepare floating matrix tablets of Sotalol using Sodium CMC, Chitosan and Psyllium Husk. The purpose of this project was to prepare a floating drug delivery system of Sotalol. Floating drug delivery system makes the dosage form to float on the gastric fluid. These can remain in the gastric part for several hours and hence significantly prolong the gastric residence time of the Sotalol.

MATERIALS

Sotalol Provided by SURA LABS, Dilsukhnagar, Hyderabad. Sodium CMC from Degussa India Ltd. (Mumbai, India), Chitosan from Arvind Remedies Ltd, Tamil nadu, India, Psyllium Hus, Sodium bicarbonate, Micro crystalline cellulose from Merck Specialities Pvt Ltd, Mumbai, India, Citric acid from Laser Chemicals, Ahmedabad, India were purchased.

METHODOLOGY

Characterization of SotalolOrganoleptic properties

Take a small quantity of sample and spread it on the white paper and examine it visually for color,odour and texture.

Determination of Sotalol Melting point

The melting point of Sotalol was determined by capillary tube method according to the USP. A sufficient quantity of Sotalol powder was introduced into the capillary tube to give a compact column of 4-6 mm in height. The tube was introduced in electrical melting point apparatus and the temperature was raised. The melting point was recorded, which is the temperature at which thelast solid particle of Sotalol in the tube passed into liquid phase**.**

Determination of Sotalol Solubility

Determination of solubility of drug by visual observation. An excess quantity of Sotalol was taken separately and adds in 10 ml of different solutions. These solutions were shaken well for few minutes. Then the solubility was observed and observations are shown in the Table.

Analytical method development

Preparation of 0.1N HCl

Diluted 8.5mL of Concentrated Hydrochloric acid to 1000mL of Purified water and mixed.

Determination of absorption maxima

A solution containing the concentration 10 µg/ mL drug was prepared in 0.1N HCL UV spectrumwas taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the rangeof 200 – 400 nm.

Preparation calibration curve

10mg Sotalol pure drug was dissolved in 10ml of methanol (stock solution1) from stock solution 1ml of solution was taken and made up with10ml of 0.1N HCL (100µg/ml). From this 1ml was taken and made up with 10 ml of 0.1N HCL (10µg/ml). The above solution was subsequently diluted with 0.1N HCL to obtain series of dilutions Containing 2, 4, 6, 8, 10 µg /ml of per ml of solution. The absorbance of the above dilutions was measured at 230 nm by using UV- Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking Concentrationon X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis.

Formulation development of floating Tablets

Procedure for direct compression method

1) Drug and all other ingredients were individually passed through sieve no □ 60.
2) All the ingredients were mixed thoroughly by triturating up to 15 min.
3) The powder mixture was lubricated with talc.
4) The tablets were prepared by using direct compression method by using 7mm punch.

FORMULATION OF TABLETS

Table 1: Formulation composition for Floating tablets.

INGREDIENTS (MG)	FORMULATION CODE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Sotalol	40	40	40	40	40	40	40	40	40
Sodium CMC	40	80	120	-	-	-	-	-	-
Chitosan	-	-	-	40	80	120	-	-	-
Psyllium Husk	-	-	-	-	-	-	40	80	120
Citric acid	10	10	10	10	10	10	10	10	10
Sodium bicarbonate	15	15	15	15	15	15	15	15	15
Micro crystalline	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

cellulose									
Magnesium Stearate	4	4	4	4	4	4	4	4	4
Talc	5	5	5	5	5	5	5	5	5
Total Weight	250	250	250	250	250	250	250	250	250

All the quantities were in mg

***In vitro* drug release studiesDissolution parameters**
Apparatus -- USP-II, Paddle Method
Dissolution Medium -- 0.1 N HCL
RPM -- 75
Sampling intervals (hrs) -- 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 12
Temperature -- 37°C ± 0.5°C

As the preparation was for floating drug release given through oral route of administration, different receptors fluids are used for evaluation the dissolution profile.

Procedure
900ml 0f 0.1 HCL was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°C ± 0.5°C. Tablet was placed in the vessel and the vessel was covered the apparatus was operated for 12 hours and then the medium 0.1 N HCL was taken and process was continued from 0 to 12 hrs at 50 rpm. At definite time intervals of 5 ml of the receptors fluid was withdrawn, filtered and again 5ml receptor fluid was replaced. Suitable dilutions were done with media and analyzed by spectrophotometrically at 230 nm using UV-spectrophotometer.

RESULTS AND DISCUSSION

Analytical Method

a. Determination of absorption maxima

The standard curve is based on the spectrophotometry. The maximum absorption was observedat 230 nm.

b. Calibration curve

Graphs of Sotalol was taken in 0.1N HCL (pH 1.2)

Table 2: Observations for graph of Sotalol in 0.1N HCL.

Conc. [µg/mL]	Abs
0	0
2	0.126
4	0.231
6	0.344
8	0.469
10	0.581

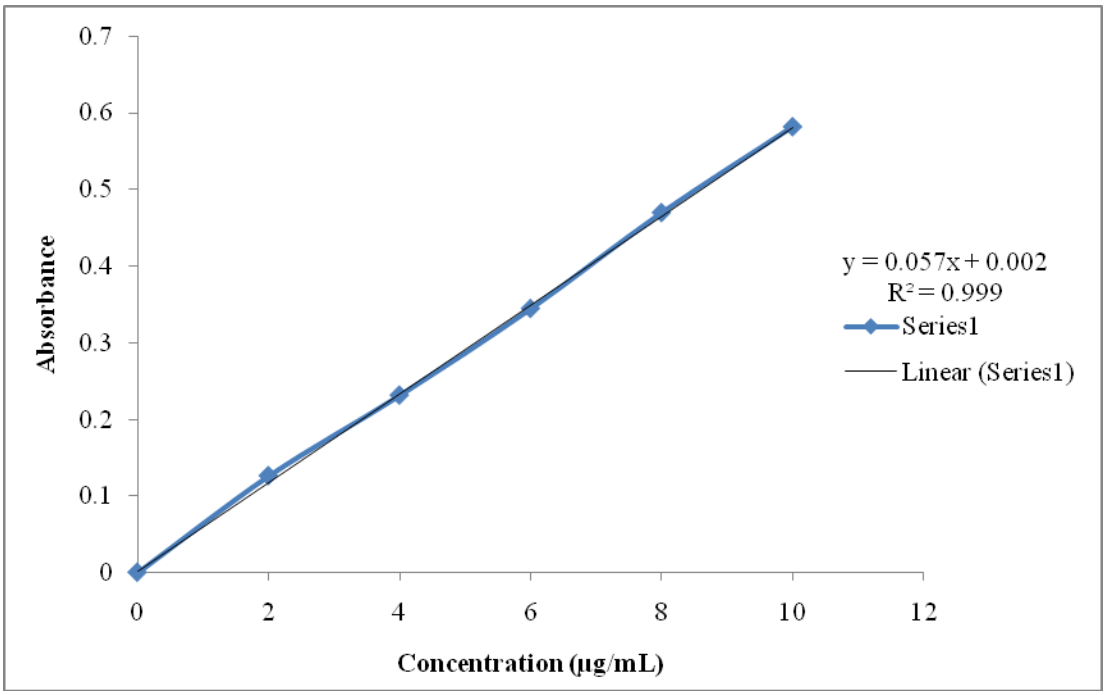

Fig 1: Standard graph of Sotalol in 0.1N HCL.

Standard graph of Sotalol was plotted as per the procedure in experimental method and its linearity is shown in Table 5.1 and Fig 5.1. The standard graph of Sotalol showed good linearity with R^2 of 0.999, which indicates that it obeys "Beer- Lamberts" law.

Preformulation parameters of powder blend

Table 3: Pre-formulation parameters of blend.

Formulation Code	Angle ofRepose	Bulk density (gm/mL)	Tapped density (gm/mL)	Carr's index (%)	Hausner'sRatio
F1	30.45±0.43	0.312±0.12	0.354±0.01	11.86±0.04	1.134 ±0.13
F2	29.89±0.23	0.314±0.21	0.358±0.12	12.29±0.16	1.140±0.07
F3	30.25±0.26	0.315±0.13	0.362±0.12	12.98±0.09	1.149±0.02
F4	28.6±0.24	0.314±0.11	0.360±0.14	12.77±0.07	1.146±0.15
F5	29.45±0.34	0.318±0.12	0.366±0.13	13.11±0.11	1.150±0.06
F6	30.23±0.24	0.326±0.11	0.365±0.14	13.42±0.05	1.155±0.12
F7	26.82±0.34	0.449±0.13	0.530±0.11	15.28±0.14	1.180±0.04
F8	29.81±0.32	0.452±0.14	0.536±0.14	15.67±0.06	1.185±0.11
F9	30.42±0.36	0.453±0.11	0.538±0.11	15.79±0.17	1.187±0.03

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.312 to 0.453 (gm/ml) showing that the powderhas good flow properties. The tapped density of all the formulations was found to be in the range of 0.354 to 0.538 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 20 which show that the powder has good flow properties. All the formulations has shown the Hausners ratio ranging between 1.134 to 1.187 indicating the powder has good flow properties.

Quality Control Parameters For tablets

Tablet quality control tests such as weight variation, hardness, and friability, thickness,Drug content and drug release studies were performed for floating tablets.

Table 4: In vitro quality control parameters.

Formulation codes	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lagtime (sec)	Total Floating Time(Hrs)
F1	249.50	5.6	0.31	3.64	99.61	53	5
F2	248.32	5.0	0.28	3.36	98.29	47	7
F3	245.20	5.4	0.25	3.66	99.87	63	8
F4	248.75	5.1	0.29	3.19	97.62	45	6
F5	246.86	5.9	0.24	3.54	99.46	36	8
F6	247.21	5.7	0.20	3.82	99.90	49	8
F7	249.36	5.3	0.37	3.91	98.67	51	5
F8	248.03	5.2	0.31	3.37	99.83	56	6
F9	247.89	5.8	0.25	3.49	98.41	49	8

All the parameters for tablets such as weight variation, friability, hardness, thickness, drug content were found to be within limits.

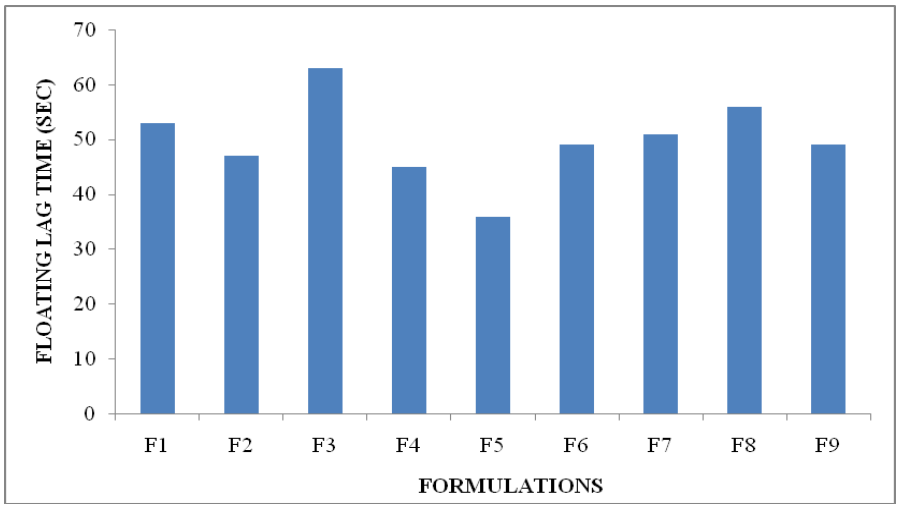

Fig 2: Floating lag time (sec)

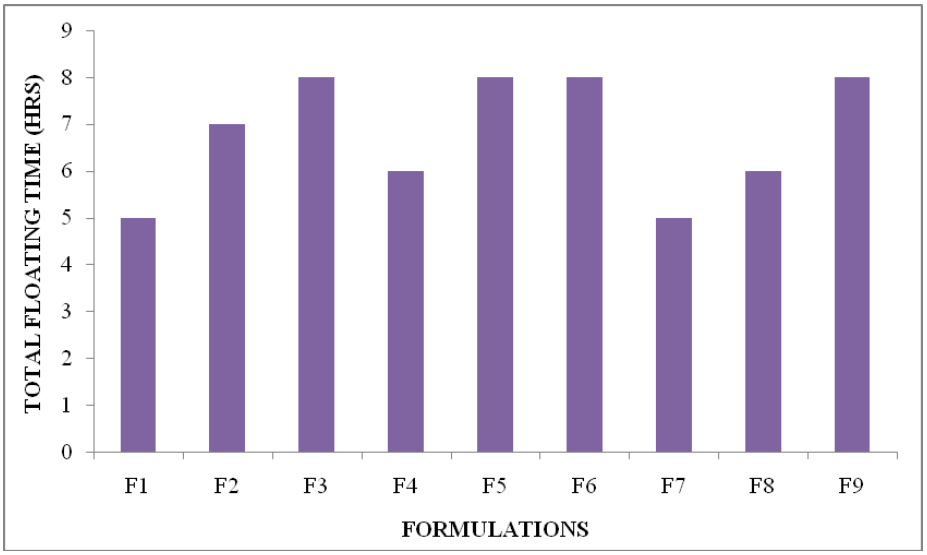

Fig 3: Total Floating Time (Hrs)

***In Vitro* drug release studies**

Freshly prepared dissolution medium i.e. 900ml 0.1N HCl in each dissolution vessel of dissolution paddle apparatus maintained at temperature 37±0.5°C and rotated at 75 rpm. The tablets of Sotalol were placed in dissolution medium. About 5ml of the dissolution medium was pipette out for every 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12hrs and the volume was adjusted using by replacing with 5ml of 0.1N HCl. The above samples i.e., 5ml were collected in a volumetric flask and make up the volume to 10ml with 0.1N HCl. Finally, the absorbance of the solution was taken using UV spectrometer at 230 nm.

Table 5: Dissolution data of Floating Tablets.

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	25.28	19.75	15.36	29.93	26.81	18.62	30.04	27.78	19.57
1	33.45	23.24	20.91	35.42	30.15	21.93	37.99	33.88	25.81
2	48.36	32.99	27.06	40.89	35.90	28.10	49.76	42.65	32.29
3	57.47	49.31	32.14	48.10	42.73	34.54	55.36	50.22	49.39
4	63.33	55.08	40.75	53.59	48.29	42.37	62.24	56.42	55.12
5	70.21	60.72	47.22	59.36	52.46	50.84	77.96	61.67	61.58
6	75.98	66.55	53.89	65.14	57.73	54.36	84.48	67.91	65.66
7	81.65	71.37	57.34	71.80	64.12	60.11	92.71	72.55	70.73
8	98.12	87.28	65.82	89.25	70.97	68.29	97.99	88.26	78.81
9		92.36	73.93	96.87	77.30	74.43		94.43	82.98
10		97.51	81.11		84.12	80.19		98.79	89.15
11			86.39		95.79	87.23			91.44
12			92.74		99.84	95.91			95.22

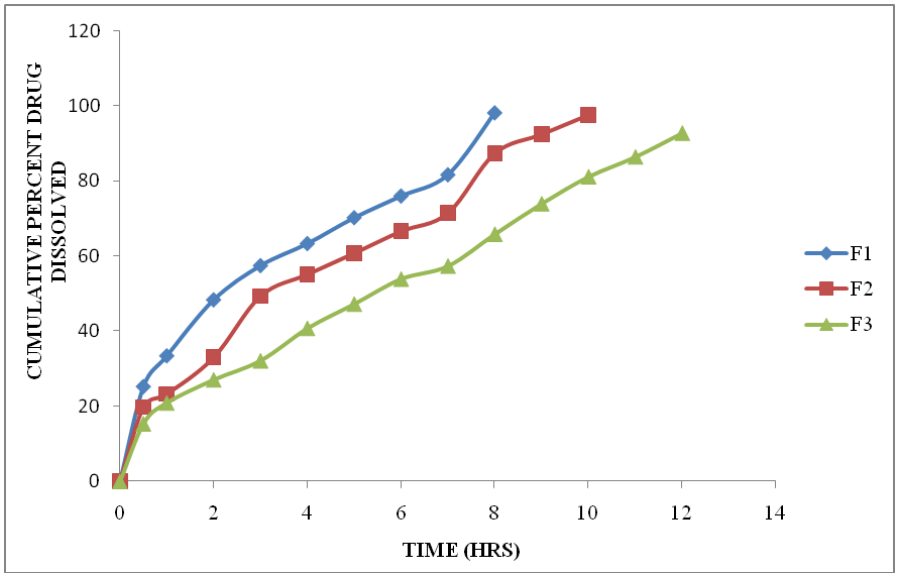

Fig 4: Dissolution data of Sotalol Floating tablets containing Sodium CMC.

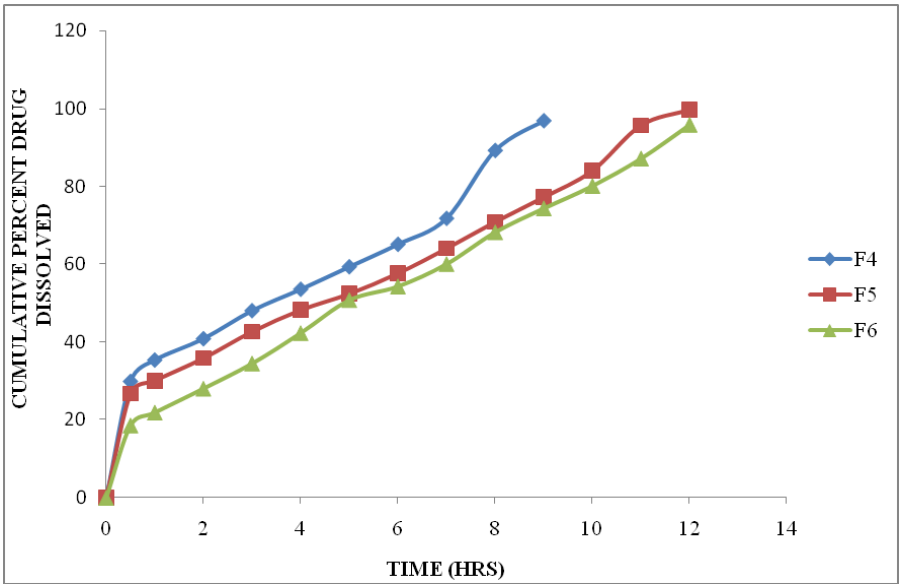

Fig 5: Dissolution data of Sotalol Floating tablets containing Chitosan.

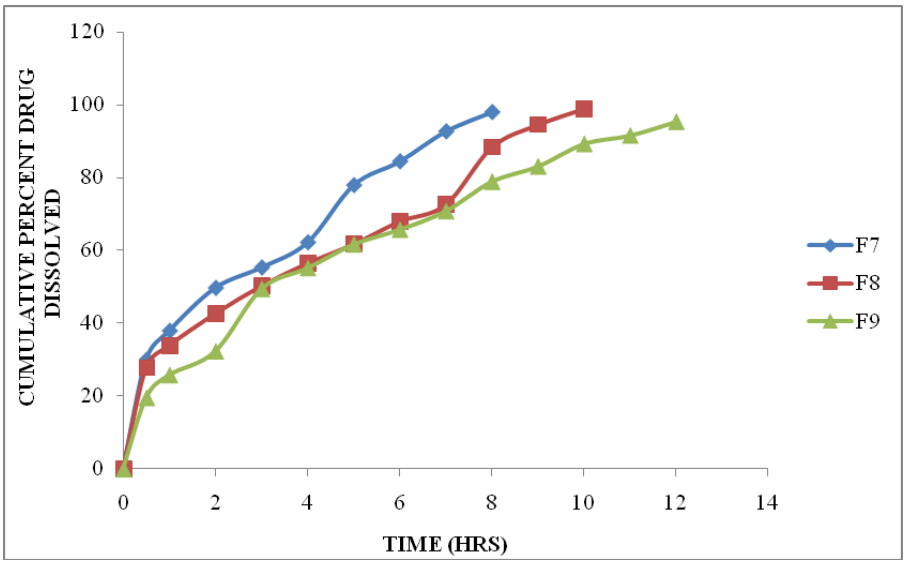

Fig 6: Dissolution data of Sotalol Floating tablets containing Psyllium Husk.

From the dissolution data it was evident that the formulations prepared with Sodium CMC as polymer were retarded the drug release 12 hours.

Whereas the formulations prepared with higher concentration of Chitosan retarded the drug release up to 12 hours in the concentration 120mg. In lower concentrations the polymer wasunable to retard the drug release up to 12hrs.

Whereas the formulations prepared with Psyllium Husk were retarded the drug release in the concentration of 120 mg (F9 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 95.22 % in 12 hours with good retardation.

Hence from the above dissolution data it was concluded that F5 formulation was considered as optimised formulation because good drug release (99.84%) in 12 hours.

Application of Release Rate Kinetics to Dissolution Data for optimised formulation: Table no 5.7 Application kinetics for optimised formulation

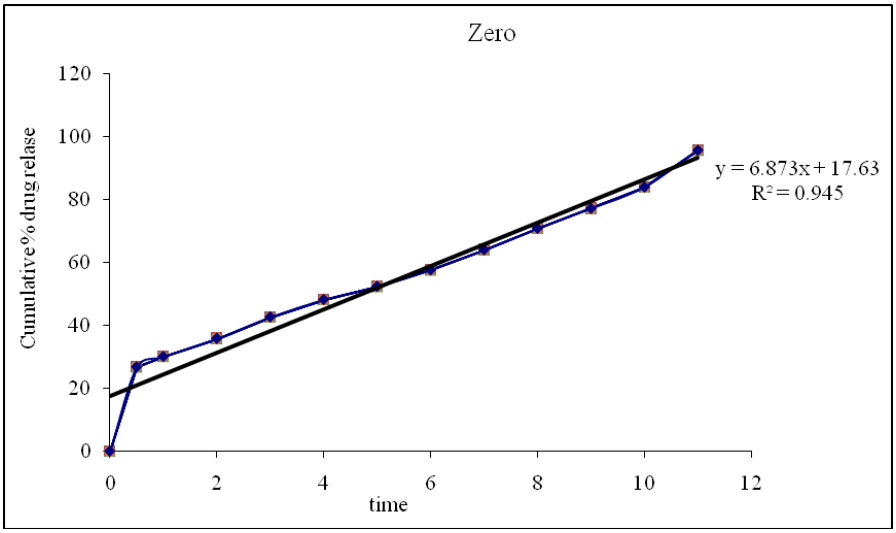

Fig 7: Zero order release kinetics.

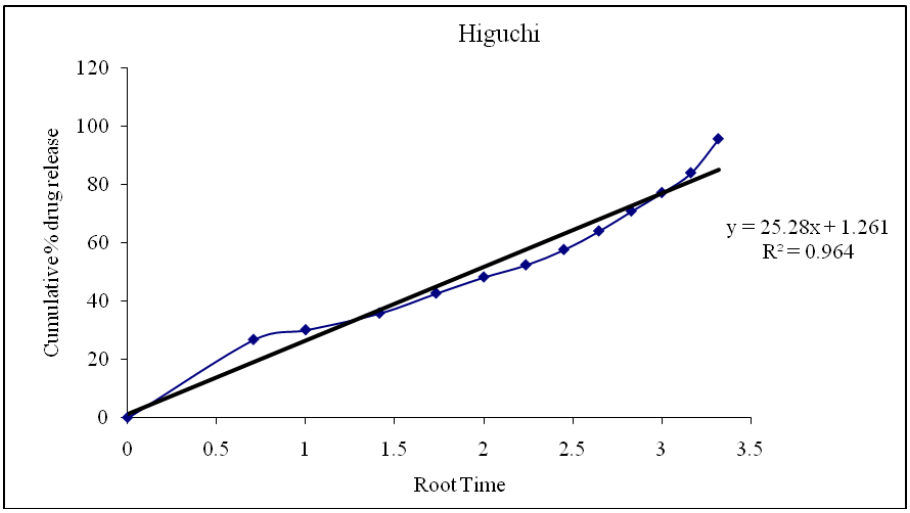

Fig 8: Higuchi release kinetics.

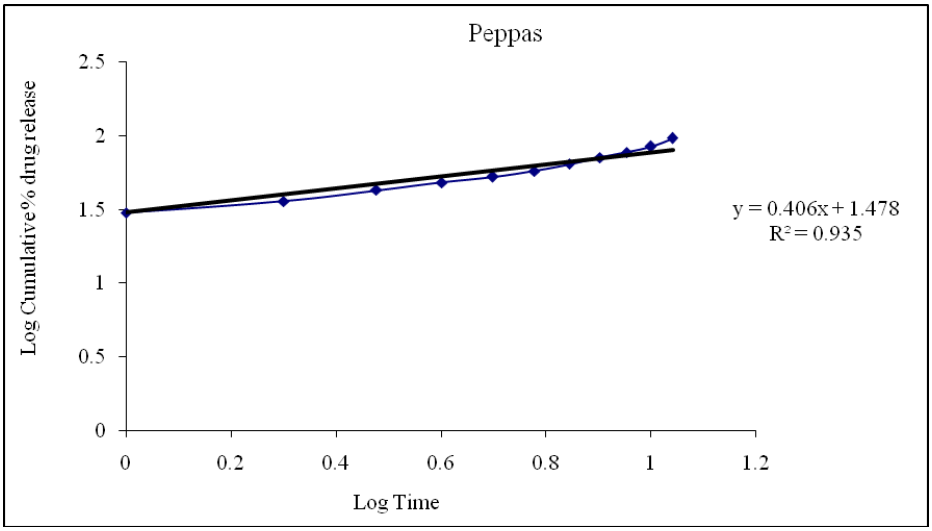

Fig 9: Kors mayer peppas release kinetics.

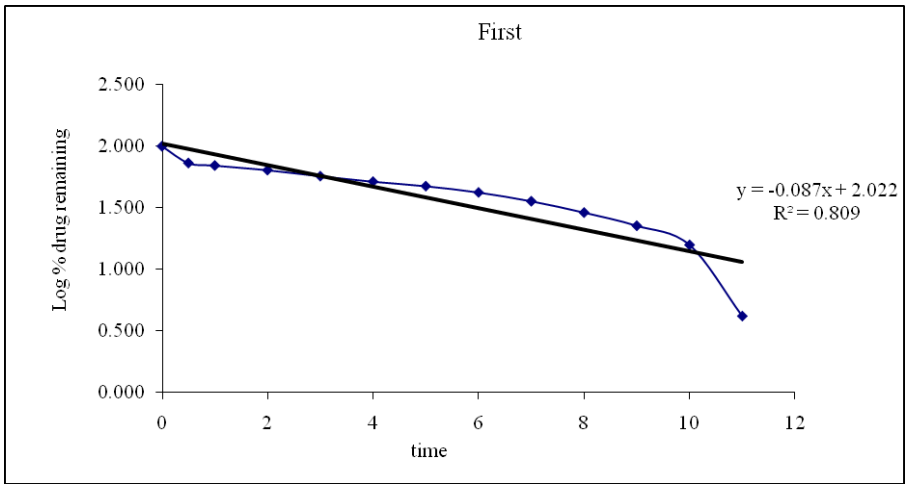

Fig 10: First order release kinetics.

Optimised formulation F5 was kept for release kinetic studies. From the above graphs it wasevident that the formulation F5 was followed Higuchi release kinetics mechanism.

Drug – Excipient compatibility studiesFourier Transform-Infrared Spectroscopy

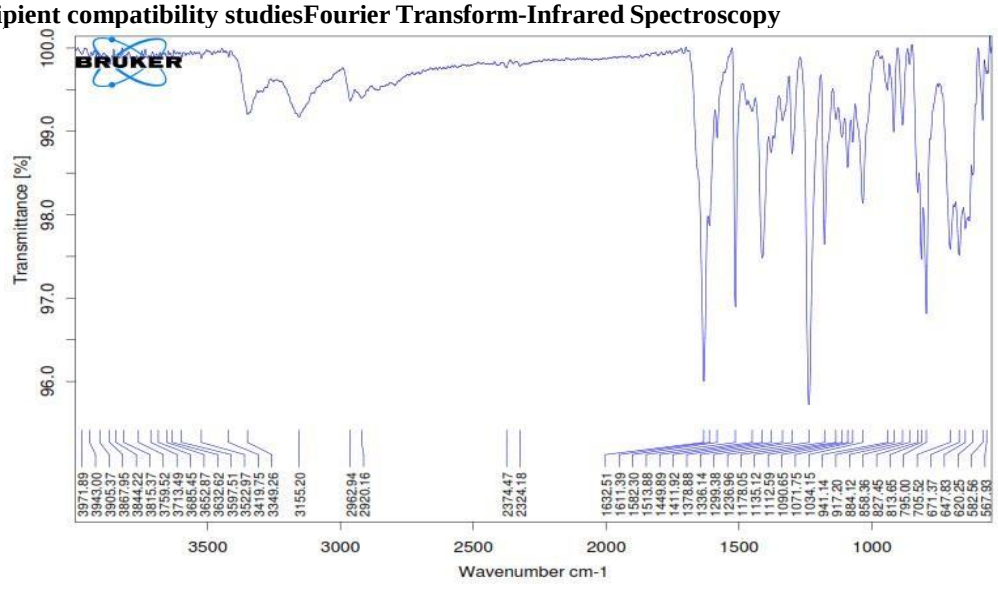

Fig 11: FTIR Spectrum of pure drug.

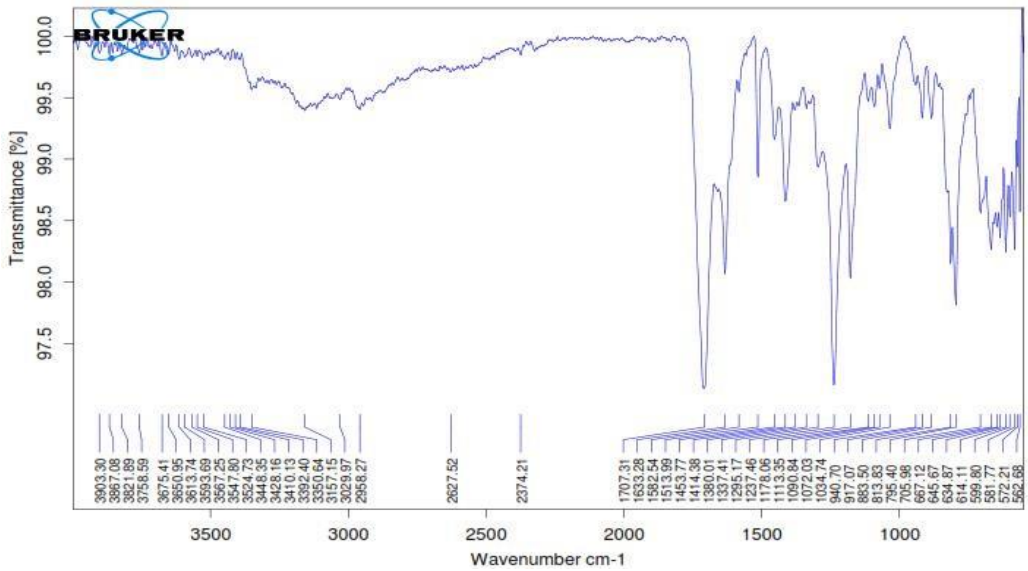

Fig 12: FTIR Spectrum of optimised formulation.

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

Sotalol are also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

ACCELERATED STABILITY STUDIES

The stability study of the optimised tablets were carried out according to ICH guidelines at 40±2^{o}C/75±5% RH for three months by storing the samples in (Lab-care, Mumbai) stability chamber. The results from stability studies are shown in table.

Table 6: Stability dissolution profile of F5 for 1st, 2nd & 3rd monthsDissolution Profile.

ACCELERATED STABILITY 40^{o}C/70%RH				
TIME(HRS)	**F9 (Initial)**	**F9 (1st Month)**	**F9 (2nd Month)**	**F9 (3rd Month)**
0	0	0	0	0
0.5	26.81	26.10	25.89	25.81
1	30.15	30.12	30.01	29.79
2	35.90	35.01	34.83	34.57
3	42.73	42.12	42.03	42.01
4	48.29	48.00	47.90	47.49
5	52.46	52.41	52.21	51.89
6	57.73	57.13	57.00	56.91
7	64.12	63.98	63.92	63.76
8	70.97	70.51	70.43	70.10
9	77.30	77.24	77.10	76.81
10	84.12	84.03	83.86	83.67
11	95.79	95.51	95.13	94.95
12	99.84	99.65	99.51	99.13

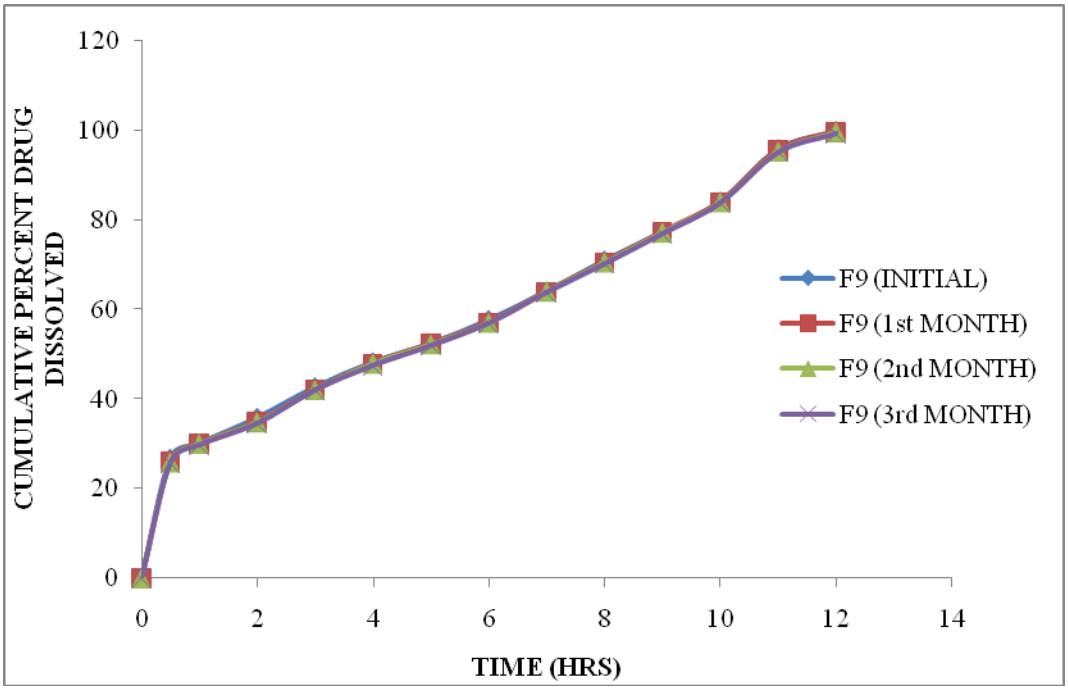

Fig 13: Drug release profile of formulation F5 during stability.

Table 7: Physicochemical parameters of most satisfactory formulation during stability studies for optimised formulation.

Time Period (Month)	Hardness(kg/cm^2)	Drug Content(%)
Initial	5.9	99.46
1	5.9	99.25
2	5.8	99.12
3	5.8	98.89

There was no major change in the various physicochemical parameters evaluated like hardness, drug content, *In vitro* dissolution pattern at the various sampling points. There was no statistically significant difference between the initial values and the results obtained during stability studies.

SUMMARY

Compounding drugs having narrow absorption window in a unique pharmaceutical dosage form with gastro retentive properties would enable an extended absorption phase of these drugs. After oral administration, such a dosage form is retained in the stomach and releases the drug in a controlled and prolonged manner, so that the drug is supplied continuously to its absorption sites in the upper gastrointestinal tract. In the present study an attempt was made to formulate Sotalol as floating drug delivery system in order to enhance its bioavailability and to localize drug at the absorption site. Floating tablets of Sotalol were formulated using sodium bicarbonate as gas generating agent and polymer by direct compression technique. FT-IR spectral studies revealed that the drug and polymer used were compatible. These formulations were subjected to various evaluation parameters like weight variation, thickness, hardness, friability, drug content, floating test, in-vitro release studies and stability studies. Evaluation parameters viz. tablet weight variation, thickness; friability and drug content were within acceptable limits for all seven formulations. Results of in-vitro release using USP dissolution apparatus Type II method indicated that the drug release of formulations F5 satisfactory. The results of kinetic drug release of formulation F5, in the R2 values was highest for Higuchi release kinetics mechanism. Stability studies showed F5 to be stable at room temperature, 40oC/70%RH for a period of 90 days. F5 formulations were stable at 40oC storage conditions up to a period of 90 days. However F5 showed a decrease in hardness after a period of 90 days, with subsequent increase in friability and in-vitro drug release, for samples stored at prevailing room temperature at 40oC/70%RH. No significant change was observed in F5 formulation stored in 40oC/70%RH. This suggested that the most suitable storage temperature for Sotalol floating tablets is 40oC/70%RH.

CONCLUSION

Hydrodynamically balanced tablets of Sotalol can be formulated with an approach to increase gastric residence and thereby improve drug bioavailability. An attempt to develop floating tablets of Sotalol, using sodium bicarbonate as gas generating agents and Chitosan as polymer by direct compression technique was achieved. The formulated tablets showed compliance for various

physiochemical parameters viz. tablet dimensions, total floating time and drug content. The dissolution studies formulations of F5 were good release and F5 formulation was excellent. Data obtained from kinetic treatment revealed F5 formulations follow Higuchi release kinetics mechanism model. The results of stability studies indicated that the most suitable storage temperature for Sotalol floating tablets was 40oC/70%RH for a period of 90 days.

REFERENCES

1. Lopes C.M., Bettencourt C., Rossi A., Buttini F., Barata P. Overview on gastroretentive drug delivery systems for improving drug bioavailability. Int. J. Pharm., 2016; 510: 144–158. [PubMed] [Google Scholar]
2. Rouge N., Buri P., Doelker E. Drug absorption sites in the gastrointestinal tract and dosage forms for site-specific delivery. Int. J. Pharm., 1996; 136: 117–139. doi: 10.1016/0378-5173(96)85200-8. [CrossRef] [Google Scholar]
3. Fujimori J., Machida Y., Tanaka S., Nagai T. Effect of magnetically controlled gastric residence of sustained release tablets on bioavailability of acetaminophen. Int. J. Pharm., 1995; 119: 47–55. doi: 10.1016/0378-5173(94)00368-F. [CrossRef] [Google Scholar]
4. Hwang K.-M., Cho C.-H., Tung N.-T., Kim J.-Y., Rhee Y.-S., Park E.-S. Release kinetics of highly porous floating tablets containing cilostazol. Eur. J. Pharm. Biopharm, 2017; 115: 39–51. doi: 10.1016/j.ejpb.2017.01.027. [PubMed] [CrossRef] [Google Scholar]
5. Kim S., Hwang K.-M., Park Y.S., Nguyen T.-T., Park E.-S. Preparation and evaluation of non-effervescent gastroretentive tablets containing pregabalin for once-daily administration and dose proportional pharmacokinetics. Int. J. Pharm., 2018; 550: 160–169. doi: 10.1016/j.ijpharm.2018.08.038. [PubMed] [CrossRef] [Google Scholar]
6. Klausner E.A., Lavy E., Friedman M., Hoffman A. Expandable gastroretentive dosage forms. J. Control. Release, 2003; 90: 143–162. doi: 10.1016/S0168-3659(03)00203-7. [PubMed] [CrossRef] [Google Scholar]
7. Sarkar D., Nandi G., Changder A., Hudati P., Sarkar S., Ghosh L.K. Sustained release gastroretentive tablet of metformin hydrochloride based on poly (acrylic acid)-grafted-gellan. Int. J. Biol. Macromol, 2017; 96: 137–148. doi: 10.1016/j.ijbiomac.2016.12.022. [PubMed] [CrossRef] [Google Scholar]
8. Sarparanta M.P., Bimbo L.M., Mäkilä E.M., Salonen J.J., Laaksonen P.H., Helariutta A.K., Linder M.B., Hirvonen J.T., Laaksonen T.J., Santos H.A. The mucoadhesive and gastroretentive properties of hydrophobin-coated porous silicon nanoparticle oral drug delivery systems. Biomaterials, 2012; 33: 3353–3362. doi: 10.1016/j.biomaterials.2012.01.029. [PubMed] [CrossRef] [Google Scholar]
9. Thapa P., Jeong S. Effects of Formulation and Process Variables on Gastroretentive Floating Tablets with A High-Dose Soluble Drug and Experimental Design Approach. Pharmaceutics, 2018; 10: 161. doi: 10.3390/pharmaceutics10030161. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
10. Chavanpatil M.D., Jain P., Chaudhari S., Shear R., Vavia P.R. Novel sustained release, swellable and bioadhesive gastroretentive drug delivery system for ofloxacin. Int. J. Pharm, 2006; 316: 86–92. doi: 10.1016/j.ijpharm.2006.02.038. [PubMed] [CrossRef] [Google Scholar]
11. Sawicki W. Pharmacokinetics of verapamil and norverapamil from controlled release floating pellets in humans. Eur. J. Pharm. Biopharm, 2002; 53: 29–35. doi: 10.1016/S0939-6411(01)00189-8. [PubMed] [CrossRef] [Google Scholar]
12. Bardonnet P., Faivre V., Pugh W., Piffaretti J., Falson F. Gastroretentive dosage forms: Overview and special case of Helicobacter pylori. J. Control. Release, 2006; 111: 1–18. doi: 10.1016/j.jconrel.2005.10.031. [PubMed] [CrossRef] [Google Scholar]
13. El-Zahaby S.A., Kassem A.A., El-Kamel A.H. Design and evaluation of gastroretentive levofloxacin floating mini-tablets-in-capsule system for eradication of Helicobacter pylori. Saudi Pharm. J., 2014; 22: 570–579. doi: 10.1016/j.jsps.2014.02.009. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
14. Jiménez-Martínez I., Quirino-Barreda T., Villafuerte-Robles L. Sustained delivery of captopril from floating matrix tablets. Int. J. Pharm, 2008; 362: 37–43. doi: 10.1016/j.ijpharm.2008.05.040. [PubMed] [CrossRef] [Google Scholar]
15. Sethi S., Mangla B., Kamboj S., Rana V. A QbD approach for the fabrication of immediate and prolong buoyant cinnarizine tablet using polyacrylamide-g-corn fibre gum. Int. J. Biol. Macromol, 2018; 117: 350–361. doi: 10.1016/j.ijbiomac.2018.05.178. [PubMed] [CrossRef] [Google Scholar]
16. Awasthi R., Kulkarni G.T. Decades of research in drug targeting to the upper gastrointestinal tract using gastroretention technologies: Where do we stand? Durg Deliv, 2016; 23: 378–394. doi: 10.3109/10717544.2014.936535. [PubMed] [CrossRef] [Google Scholar]