International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 6(2): March-April 2016

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences

Research Article……!!!

Received: 09-03-2016; Revised: 18-04-2016; Accepted: 19-04-2016

FORMULATION AND EVALUATION OF FLOATING TABLET OF METFORMIN HCL

Shivendra Agarwal*, Sunil Rana, Saurabh Sharma, Amit Saxena

Vivek College of Technical Education, Bijnor, (U.P) India.

Keywords:

Metformin HCL, Gastroretentive floating drug delivery systems, Xanthan Gum, Gaur Gum

For Correspondence:

Amit Saxena

Vivek College of Technical Education, Bijnor, (U.P) India

E-mail:

saxenampharm@gmail.com

ABSTRACT

Gastrorententive floating drug delivery systems of Metformin HCL, an antihyperglycemic agent which improves glucose tolerance in patients with type 2 diabetes, lowering both basal and postprandial plasma glucose. It is absorbed from the small intestine, and has and oral bioavailability of only 50% to 60%. It has a half life of about 2 hours. Its duration of action is about 6-8 hours. Therefore, it is selected as a suitable drug for for the design of a gastro- retentive floating drug delivery system (GFDDS) with a view to improve its oral bioavailability. Natural polymers Xanthan Gum and Gaur Gum in different concentrations were used as the polymers and sodium bicarbonate as gas generating agent to reduce floating lag time. In the present study, floating tablets of Metformin HCl were prepared by using different concentrations of Xanthan Gum and Gaur Gum along with a gas generating agent, sodium bicarbonate. The tablets were prepared by direct compression method. Estimation of Metformin HCL in the prepared tablet formulations was carried out by extracting the drug with 0.1N HCL and measuring the absorbance at 233 nm. The prepared formulations were further evaluated for hardness, friability, weight variation, drug content uniformity, swelling index, *in vitro* drug release pattern and drug excipient interactions. The best formulation F5 containing 75 mg Xanthan Gum, 75 mg Gaur Gum and 50 mg $NaHCO_3$ has displayed first order release kinetics with a floating lag time of only 3.25 minutes and released more than 90% drug in 10 hours.

INTRODUCTION

Gastroretentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment[1]. These are primarily controlled release drug delivery systems, which gets retained for longer period of time in stomach, thus helping in absorption of drug for the intended duration of time, which in turn improves bioavailability by reducing drug wastage, and improving solubility of drugs that are less soluble at high pH environment. It also helps in achieving local delivery of drug in the stomach and proximal small intestine. G.R.D.D devices can be useful for the spatial and temporal delivery of many drugs. Floating systems are one of the important categories of drug delivery systems with gastric retentive behavior[2]. In this work, direct compression method has been employed to prepare tablets with xanthan gum and gaur gum. Tablets were compressed on a single punch tablet machine using 12mm flat round punches. Metformin HCL, an antihyperglycemic agent which improves glucose tolerance in patients with type 2 diabetes, lowering both basal and postprandial plasma glucose. It is absorbed from the small intestine, and has and oral bioavailability of only 50% to 60%. It has a half life of about 2 hours. Its duration of action is about 6-8 hours. Therefore, it is selected as a suitable drug for for the design of a gastro-retentive floating drug delivery system (GFDDS) with a view to improve its oral bioavailability.

EXPERIMENTAL

Materials:

Metformin HCL was obtained as Gift sample from Micro labs Bangalore. Xanthan Gum was procured from Loba Chem pvt. Ltd. Mumbai, Sodium Bicarbonate was procured from Alpha – Chem. Pvt. Ltd. Haryana, PVP- K30 was procured from Loba Chem pvt. Ltd. Mumbai, Hydrochloric Acid was procured from Thermo Fisher Scientific, India pvt. Ltd. Mumbai, Gaur Gum and Lactose were procured from Merck ltd. Mumbai.

Method:

In this work, direct compression method has been employed to prepare tablets with xanthan gum and gaur gum. All the ingredients were accurately weighed and passed through mesh #60. In order to mix the ingredients thoroughly drug and polymer were blended geometrically

in a mortar and pastel for 15 minutes then sodium bicarbonate and PVP-K30 were mixed one by one. After thoroughly mixing these ingredients, the powder blend was passed through #44 mesh[3]. Tablets were compressed on a single punch tablet machine using 12mm flat round punches.

TABLE- 1: DESIGNED FORMULATIONS (FORMULATION TABLE FOR 1TABLET)

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
Metformin HCL (mg)	500	500	500	500	500	500	500	500	500
Xanthan Gum(mg)	125	75	50	125	75	50	125	75	50
Gaur Gum (mg)	125	125	125	75	75	75	50	50	50
Sodium Bicarbonate (mg)	50	50	50	50	50	50	50	50	50
PVP-K30(mg)	38.5	38.5	38.5	38.5	38.5	38.5	38.5	38.5	38.5
Lactose	-	50	75	50	100	125	75	125	150

FACTORIAL DESIGN METHOD [4-5]

Formulations has been designed by using 3^2 full factorial design, where amount of Xanthan Gum (X_1) and amount of Gaur Gum (X_2) were taken as independent variables.

TABLE- 2: FACTORIAL DESIGN BATCHES OF FORMULATIONS

Variable	Batch								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
X1	-1	0	+1	-1	0	+1	-1	0	+1
X2	-1	-1	-1	0	0	0	+1	+1	+1

TABLE- 3: CODED VALUES AND ACTUAL VALUES FOR THE INDEPENDENT VARIABLES

Coded Values	Actual Values (mg)	
	X1(Xanthan Gum)	X2 (Gaur Gum)
-1	125	125
0	75	75
+1	50	50

EVALUATION

Hardness test:

The hardness or crushing strength (kg/cm^2) of tablets was determined by using Monsanto hardness tester[6]. In all the cases, means of six replicate determinations were taken.

Friability test:

This test was determined by weighing 10 tablets after dusting, placing them in the friabilator and rotating the plastic cylinder vertically at 25 rpm for 4 min[7]. After dedusting, the total

remaining weight of the tablets was recorded and the percent friability was calculated according to:

$$\text{Percent friability} = \frac{\text{Weight(final)} - \text{Weight(original)}}{\text{Weight (original)}} \times 100$$

Weight Variation:

The weight of each of 20 individual tablets was determined by de dusting each tablet off and placing it in an electronic balance. The weight data from the tablets were analyzed for sample Mean and percent deviation.

Drug Content:

5 tablets were weighed and taken in a mortar and crushed to powder. A quantity of powder weighed equivalent to 500 mg of Metformin HCL was taken in a 100ml volumetric flask and 0.1N HCL was added with vigorous shaking on a mechanical gyratory shaker (100 rpm) for 1 hour. It was then heated at 60^0 C for 30 min. The solution was filtered using membrane filter and then further appropriate dilution was made and absorbance was measured at 233nm against blank (0.1N HCL). The amount of drug was calculated using standard graph [8].

Floating Lag-Time:

It is determined in order to assess the time taken by the dosage form to rise to the surface to float on the top of the dissolution medium, after placed in the medium[8].

Floating Time:

Floating time was determined by using USP dissolution apparatus-II at 50 rpm using 900ml of 0.1N HCL and temperature was maintained at 37+/-0.5^0C, throughout the study. The duration of floating (floating time) is the time the tablet floats in the dissolution medium (including floating lag time) is measured by visual observation[8].

FIGURE-1 FLOATING LAG TIME OF TABLET

Swelling Index:

The individual tablets were weighted accurately and kept in 50 ml of water. Tablets were taken out carefully after 60 minutes, blotted with filter paper to remove the water present on

the surface and weighed accurately. Percentage swelling (swelling index) was calculated by using the formula[9].

Swelling index=wet weight – dry weight/dry weight x 100

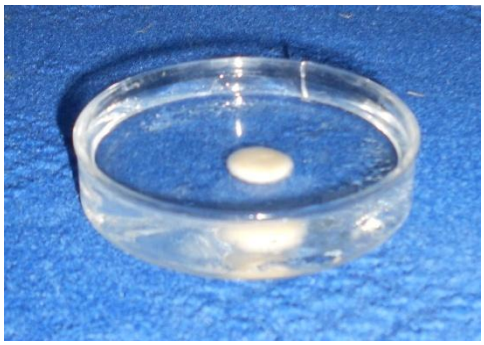


FIGURE-2 SWELLING OF TABLET

Density of Tablet:

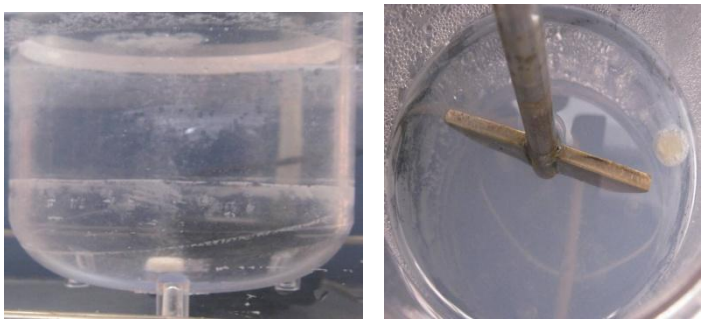
Density was measured by the displacement method using Benzene as displacement medium.

In vitro drug release study:

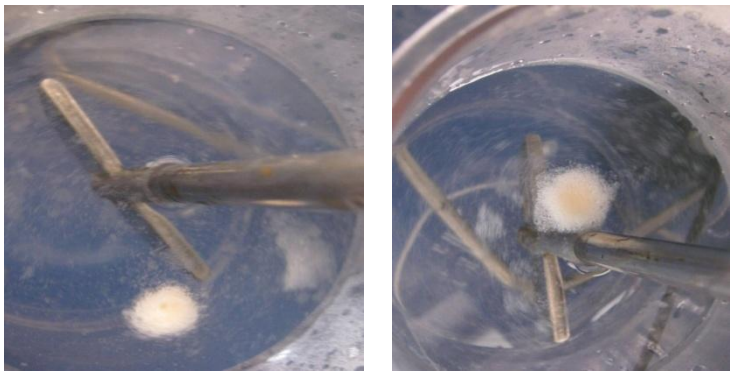
In vitro drug release studies of floating tablet of metformin HCL were carried out in USP tablet dissolution test apparatus-II, employing a paddle stirrer at 50 rpm using 900ml of 0.1N HCL at 37±0.5^{0}C as dissolution medium. One tablet was used in each test. At predetermined time intervals 5ml of the sample were withdrawn by means of a syringe fitted with a pre filter. The volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium maintained at 37±0.5^{0}C. the samples were analyzed for drug release by measuring the absorbance at 233nm using UV- spectrophotometer after suitable dilution. All the studies were conducted in triplicate.

The result of *in vitro* release profiles obtained for all the HBS formulations were fitted into .Four models of data treatment as follows:

1. Cumulative percent drug released versus time. (zero- order kinetic model).
2. Log cumulative percent drug remaining versus time. (first- order kinetic model).
3. Cumulative percent drug released versus square root of time (Higuchi's model).
4. Cube root of cumulative drug remaining versus time (Hixcon- Crowell cube –root model).
5. Log cumulative percent drug released versus log time (korsmeyer-Peppas equation).



AT INITIAL **AFTER 5 MINUTES**



AFTER 8 HOURS **AFTER 12 HOURS**

FIGURE-3 FLOATING TABLET AT DISSOLUTION TIME

Drug Polymer Interaction Studies:

There is always a possibility of drug polymer interaction in any formulation due to their intimate contact. The technique employed in the present study for this purpose in IR-spectroscopy. IR- spectroscopy is one of the most powerful analytical techniques, which offers the possibility of chemical identification. The IR spectra of Metformin HCL, and formulation F1, F2, F3, F4, F5, F6, F7, F8 and F9 were obtained by KBr pellet method employing Shimadzu FTIR and are shown in figure number 64 to 73.

TABLE 4: EVALUATION OF FORMULATIONS

Formulation Code	Mean Hardness Kg/cm^2	Friability % w/w	Average Weight (mg)	Mean Drug Content % +- SD	Floating Lag Time (min.)	Floating Time (hrs)
F1	5.0	0.35	0.840	96.62±0.50	5.5	24
F2	4.8	0.95	0.845	92.68± 1.12	4.0	24
F3	4.6	0.40	0.841	98.77± 0.9	3.5	9
F4	4.9	0.68	0.843	99.66± 0.9	3.5	24
F5	4.7	0.40	0.848	97.49± 1.34	3.25	24
F6	4.9	0.58	0.850	100.17± 2.45	4.3	8
F7	5.1	0.64	0.846	98.55±1.6	3.7	24
F8	4.9	0.74	0.841	90.11±1.36	4.75	8
F9	4.7	0.67	0.844	100.74±0.93	3.25	8

TABLE 5. FOR SWELLING INDEX:

Swelling index studies of Formulations

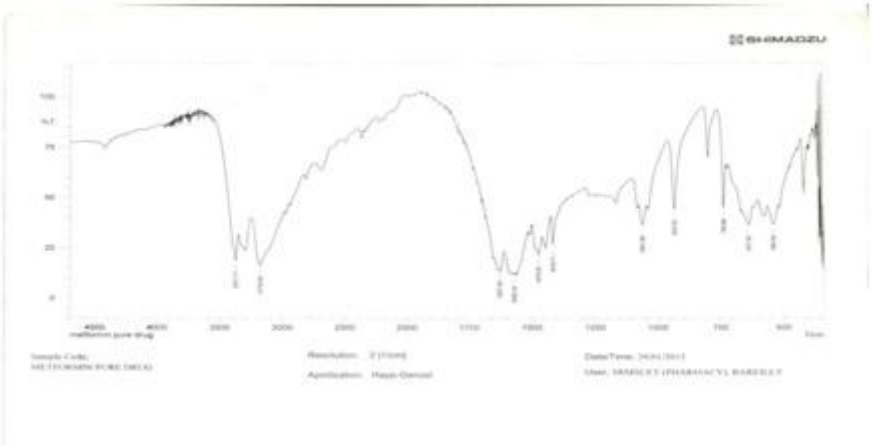
Time (hrs)	Swelling Index								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	43.66	48.05	48.72	47.48	50.92	46.97	54.71	54.17	48.80
2	47.35	51.61	52.01	52.76	55.72	52.07	58.89	56.77	52.04
3	52.68	54.44	56.04	56.46	57.52	55.97	59.92	57.51	53.74
4	57.21	58.51	58.76	59.14	59.19	58.07	61.19	59.18	55.43
5	61.37	61.19	60.35	61.54	60.64	59.27	62.29	60.82	56.92
6	65.33	63.29	61.70	63.38	61.84	60.94	63.19	61.43	58.35
7	67.88	64.97	62.87	65.21	62.94	61.65	64.37	62.13	59.47
8	68.26	65.15	63.96	66.73	63.68	62.18	65.11	62.73	60.28
9	67.23	65.43	64.23	66.67	64.43	62.98	65.35	61.65	61.87

Mechanism of Drug release

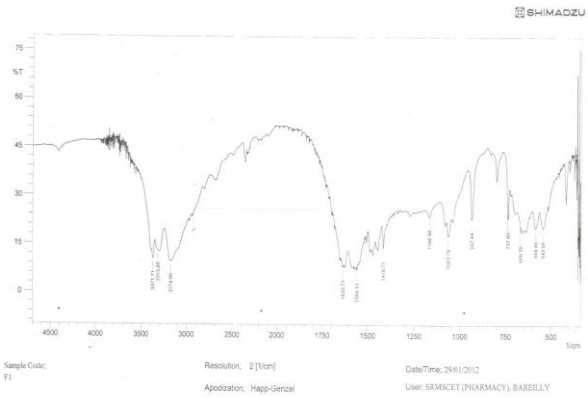
TABLE- 6. MECHANISM OF DRUG RELEASE

S.No.	R^2 Value					n Value
	Zero order	First order	Higuchi model	Hixson crowell cube root model	Korsmeyer peppas model	
F1	0.993	0.973	0.978	0.989	0.983	0.740
F2	0.980	0.947	0.967	0.975	0.959	0.587
F3	0.927	0.978	0.980	0.976	0.983	0.551
F4	0.959	0.984	0.989	0.979	0.990	0.560
F5	0.922	0.993	0.986	0.993	0.987	0.543
F6	0.886	0.981	0.941	0.930	0.957	0.458
F7	0.982	0.965	0.979	0.980	0.982	0.646
F8	0.875	0.980	0.953	0.933	0.977	0.476
F9	0.903	0.970	0.940	0.910	0.989	0.485

Figure-4: FTIR OF METFORMIN DRUG



FTIR OF FORMULATION



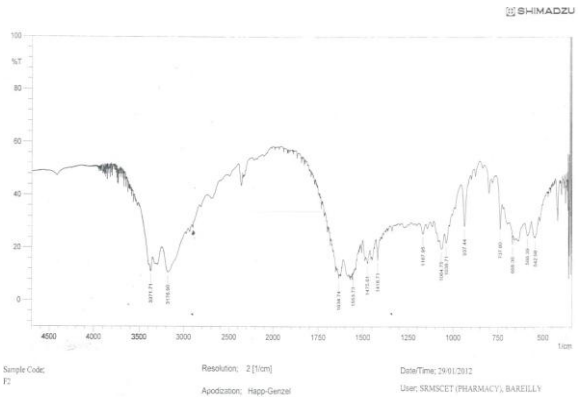
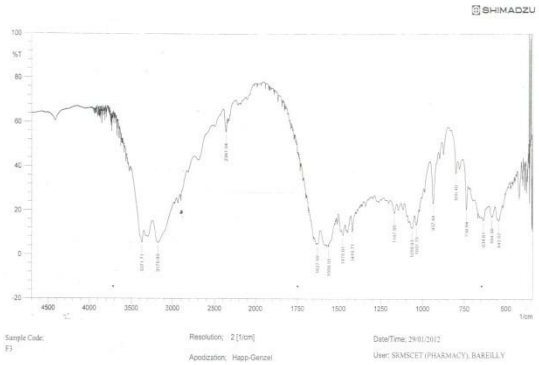


FIGURE-5: FTIR OF FORMULATION F1 FIGURE-6: FTIR OF FORMULATION F2



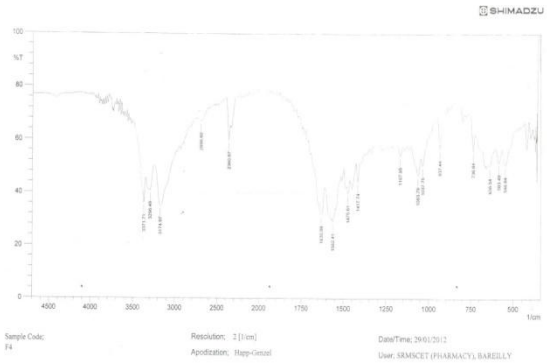
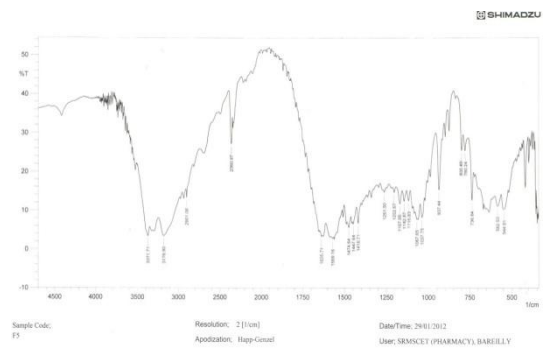


FIGURE-7: FTIR OF FORMULATION F3 FIGURE-8: FTIR OF FORMULATIONF4



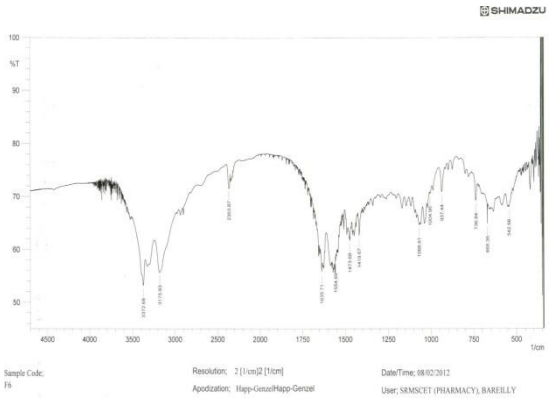


FIGURE-9: FTIR OF FORMULATION F5 FIGURE-10: FTIR OF FORMULATION F6

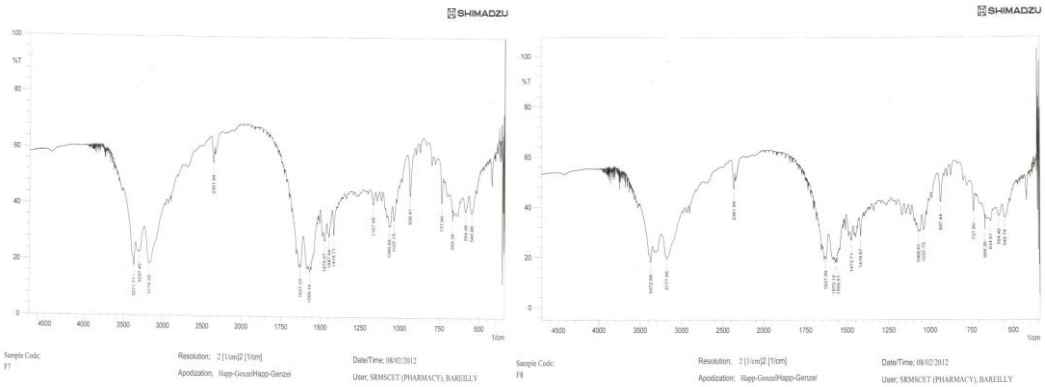


FIGURE-11: FTIR OF FORMULATION F7 FIGURE-12: FTIR OF FORMULATION F8

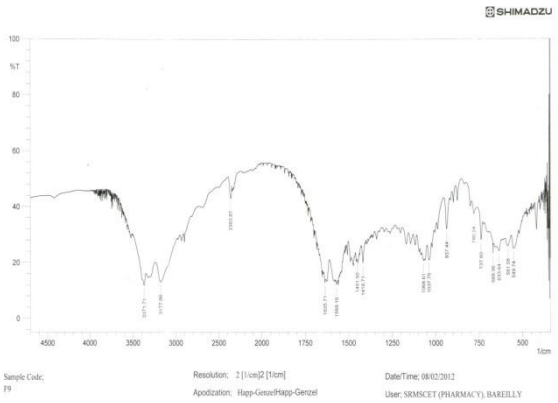


FIGURE-13: FTIR OF FORMULATION F9

RESULTS AND DISCUSSION

In the present study, floating tablets of Metformin HCl were prepared by using different concentrations of Xanthan Gum and Gaur Gum along with a gas generating agent, sodium bicarbonate. The prepared formulations were evaluated for hardness, friability, uniformity of weight, drug content, swelling index, floating lag time and in-vitro drug release. The hardness of the prepared formulations was found to be in the range of 4.73 to 5.1 kg/cm^2. The friability of all formulations was less than 1% i.e., in the range of 0.35 to 0.95%. The percentage deviation from the mean weight of all the batches of prepared formulations was found to be within the prescribed limits as per IP. The swelling index of the tablets increases as the polymer content. Lag time, for all the formulations was in the range of 3.25 to 5.5 min. The formulations with higher concentration of polymer remain buoyant up to 24 hours.

CONCLUSION

From the above results it has been concluded, that F5 is more effective among all the formulations by prompting good results. F5 revealed first order release kinetics with a floating lag time of 3.25 minutes and drug release more than 90% in 10 hours.

REFERENCES

1. Sarawade A.,* Ratnaparkhi M. P., Chaudhari S., Floating Drug Delivery System, An Overview International Journal of Research and Development in Pharmacy and Life Sciences 2014; Vol. (3); No.5, pp 1106-1115

2. Priyanka V.*, Reddy S. P. , Sowmya1 C. , Singh R. K. , Floating Tablet and It's Technology: ANOVERVIEW, International Journal of Pharmaceutics and Drug Analysis, 2014; Vol. (2); Issue:8 653-657

3. Salve P.S., Development and in vitro evaluation of gas generating floating tablets of metformin hydrochloride, Asian Journal of Research Pharmacutical Science, 2011; Vol. (1); Issue 4, 105-112.

4. Siddiqui A.I., Bakde B.V., Tappar K. K. , Floating Strategy For Low Absorption Window Diltiazem Hydrochloride, International Journal of pharmacy and technology ,2011 ; Vol. (3); Issue No.1, 1893-1903.

5. Kavitha K., Puneeth K.,P., Tamizh Mani T., Development and Evaluation of Rosiglitazone Maleate Floating Tablets using Natural Gums, International Journal of Pharmatech Research CODEN (USA), 2010 Vol.(2); No.3, pp 1662-1669 .

6. Lachman.L., Liberman, H.A., Kanig, J.L., The Theory and Practice of Industrial Pharmacy, Varghese Publishing House, Mumbai, 3rd Edition. 1991: 297-303.

7. Rosa J.C.M., Zia H., Rhodes. C, Design and testing in vitro of a bio-adhesive and floating drug delivery systems for oral application, International Journal of Pharmaceutics, 1994; Vol. (105); 65-70.

8.Ichikawa M., Watemblc S., Miyake V.A., Multiple unit oral floating dosage systems Preparation and in-vivo evaluation of' floating and sustained release characteristics, Journal of Pharmaceutical Sciences, l99l; Vol. (80); l062-1066.

9. Kumar R., Patil M.B., Patil S.R., Paschapur M.S., Formulation and evaluation of effervescent floating tablet of famotidine, International journal of Pharma Tech Research, 2009;Vol. (1); 754-763.