INTERNATIONAL JOURNAL OF PHARMACEUTICAL, CHEMICAL AND BIOLOGICAL SCIENCES

Available online at www.ijpcbs.com

Research Article

FORMULATION AND EVALUATION OF IBRUPROFEN FLOATING TABLETS

Chandrasekhara Rao Baru[1]*, S. Vidyadhara[2], KV. Raghavendra Rao[3], K. Vanitha Prakash[1]and B.Umashankar[1]

[1]SSJ College of Pharmacy, V.N Pally, Gandipet, Hyderabad, Andhra Pradesh, India.
[2]Chebrolu Hanumaiah Institute of Pharmaceutical Sciences, Chowdavaram, Guntur, Andhra Pradesh, India.
[3]J&J Dechane Pharmaceuticals Pvt Ltd, Hyderabad, Andhra Pradesh, India.

ABSTRACT

The present study of Ibuprofen Floating tablets were to develop optimized gastric floating drug delivery system(GFDDS) by using various polymers like HPMC K4M and Carbopol 940 to enhance the bioavailability and therapeutic efficacy of ibuprofen Various approaches have been followed to encourage gastric retention of an oral dosage form. Floating systems have low bulk density so that they can float on the gastric juice in the stomach. The present work attempts have been made to prepare Ibuprofen by Direct compression method, 4 formulations (F1 to F4) floating tablets of Ibuprofen were prepared using variable concentrations of HPMCE5M and Carbopol940,buoyancy lag time and the total floating time was studied for all the formulations, The compatibility evaluations were performed by DSC analysis. Studies imply that polymers are compatible with each other. There was no interaction found between polymer and drug. The research was undertaken with the aim to formulate and characterize the sustained release floating tablets of Ibuprofen using HPMCK4M and Carbopol 940 as polymers.

Keywords: Ibuprofen, buoyancy lag time, HPMCK4M, Carbopol 940.

INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administered among all the routes that have been employed for the systemic delivery of drug via various pharmaceutical products of different dosage forms. The reasons that the oral route achieved such popularity may be in part attributed to its ease of administration. The retentive characteristics of the dosage form are not significant for the drugs that: They Are insoluble in intestinal fluids Act locally to overcome these limitations, various approaches have been proposed to increase gastric residence of drug delivery systems in the upper part of the gastrointestinal tract includes floating drug dosage systems (FDDS) swelling or expanding systems , mucoadhesive systems , modified-shape systems , high-density system , and other delayed gastric emptying devices. Among these systems, FDDS have been most commonly used.

When the dosage form administered it contact with gastric fluid and produce effervescent and evolved CO_2 gas. This support to penetrate the fluid in tablet and float, the low density polymer HPMC various grade provide low density system so it buy out efficiently in gastric fluid. The system is as design to float and shows sustains release for better patient compliance and reduces dose

frequency and adverse effect of drug Floating drug delivery offers several applications for drug shaving poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage form at the site of absorption and thus enhances the bioavailability.

MATERIALS AND METHOD

Ibuprofen obtained as a gift sample from Savan Pharma Pvt Ltd., Hyderabad, Carbopol 940 and HPMC K4M was supplied from Bio - Gen extracts Pvt Ltd., Bangalore, Citric acid, lactose and Sodium bicarbonate were obtained from Qualigens Fine Chemicals, Mumbai, India, Talc and Microcrystalline cellulose were obtained from Loba chemie pvt.,ltd., Mumbai, India. All the chemicals and reagents required for the present experimental work are of analytical grade.

METHOD OF PREPARATION OF IBUPROFEN FLOATING TABLETS

The ibuprofen floating tablets were prepared by blending the drug (ibuprofen),polymer s(HPMCK4M) and Carbopol940 in different proportions respectively. To this sodium bicarbonate, lactose, citric acid were added to mortar and pestle according to their geometric dilution and finally make up the total weight (515mg) of tablet using micro crystalline cellulose. The powder was passed through sieve no.60. The obtained samples were collected and re triturated. To this required amount of talc is added and compressed finally.

In the present work, 4 formulations (F1 to F4) floating tablets of Ibuprofen were prepared using variable concentrations of HPMCE5M and Carbopol940 as shown in the Table No.01**.**

IN – VITRO CHARACTERIZATION

a. Weight uniformity test[8]

If the drug forms greater part of the tablet, any variation in the tablet weight obviously indicates a variation in the active ingredient this test resembles weight uniformity test. 20 tablets were selected at random and average weights were determined. Then individual tablets weighed and the individual weight was compared with the average.

$$\text{Calculate the average weight of tablets} = \frac{\text{Total weight of tablets}}{\text{Number of tablets}}$$

$$\text{Average weight of tablets (X)} = (X1+X2+X3+\ldots+X20) / 20$$

b. Hardness uniformity studies[8]

The hardness of prepared formulation was measured by using Pfizer hardness tester. Five floating tablets were used for hardness uniformity studies. The hardness data used to calculate mean and standard deviation.

c. Thickness uniformity studies

The thickness uniformity studies were carried out by using Vernier callipers. Five tablets were used for thickness uniformity studies and denoted in millimeter. The data obtained was used to calculate mean and standard deviation.

d. Friability (F)

The friability of the tablet was determined using Roche Friabilator. It is expressed in percentage (%). 20 tablets were initially weighed (W initial) and transferred into the friabilator. The friabilator was operated at 25 rpm per min for 4 mins (100 revolutions). The tablets were weighed again (W final). The % friability was then calculated by

$$F = \frac{W_1 \text{initial} - W_2 \text{final} \times 100}{W_1 \text{initial}}$$

e. Thickness and diameter

Tablet thickness is important for tablet packaging; very thick tablets affect packaging

either in blisters or plastic containers. The tablet thickness is determined by the diameter of the die, the amount of fill permitted to enter the die and the force or pressure applied during compression. The thickness of the tablet may be measured manually or by automatic equipment. The thickness and diameter of the tablets was measured by Vernier Calipers. It is expressed in mm.

f. Content uniformity

Twenty tablets were taken and amount of drug present in each tablet was determined. The tablets were crushed in a mortar and the powder equivalent to 100mg of drug was transferred to 100ml standard flask. The powder was dissolved in a suitable solvent and make up the final volume with the suitable buffer solution. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and analyzed for drug content by UV spectrophotometer, using buffer solution as a blank.

g. In vitro buoyancy / floating study

In vitro buoyancy studies were performed for all the formulations. The randomly selected tablets from each formulation were kept in a 200ml beaker containing simulated gastric fluid, pH 1.2 as per USP. The time taken for the tablet to rise to the surface and float was taken as floating lag time (FLT). The duration of time the dosage form constantly remained on the surface of medium was determined as the total floating time (TFT).

h. Swelling Index[9]

The swelling behavior of a dosage unit was measured by studying its weight gain. The swelling index of tablets was determined by placing the tablets in the basket of dissolution apparatus using dissolution medium pH 6.8 buffer at 37 ± 0.5^{0}C. After 0.5, one, two, three, four, five, six, seven and eight hours, each dissolution basket containing tablet was withdrawn and blotted with tissue paper to remove the excess water and weighed on the analytical balance (Shimadzu, AX 120). The experiment was performed in triplicate for each time point. Swelling index was calculated by using the following formula.

Tablets were randomly selected and one tablet was introduced in each tube disintegration apparatus and placed in 1litre beaker containing water at 37^0± 2^{0}C and the time of disintegration was recorded. The study was done at room temperature without disc being added.

j. In vitro dissolution studies[8]

The release rate of aceclofenac from floating tablets was determined using United States Pharmacopeia (USP) Dissolution Testing Apparatus 2 (paddle method). The dissolution test was performed using 900 ml of pH 1.2 HCL buffer for 2 hrs followed by pH 6.8 Phosphate buffer for 8hrs. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µ membrane filter and diluted to a suitable concentration with of pH 1.2 HCL buffer for 2 hrs followed by pH 6.8 Phosphate buffer for 8hrs. Absorbance of these solutions was measured at 222 nm using a UV/Visible spectrophotometer.

l. Drug release kinetics[3,15]

The success of HPMC K4M with Carbopol940 in controlling the release of the drug was studied under the following heads to understand the order and probable underlying mechanism involved in the release pattern. To analyze the mechanism of drug release from the prepared formulations, the data obtained from *in vitro* release studies were subjected to Higuchi's model, Zero order model and Korsmeyer's model.

DSC

DSC curves: (*A*) ibuprofen, (*B*) physical mixture. DSC thermo gram of pure ibuprofen exhibited a single endothermic response corresponding to the melting of the ibuprofen at 77.5°C. As mixture did not show any fusion peak or phase transition, apart from a broad endotherm, as a result of dehydration, which

lies between 80°C and 120°C. For the PM, the endotherm broadened and was shifted slightly to a lower temperature (76.8°C), reflecting a partials change of ibuprofen crystal structure.

RESULTS AND DISCUSSION

In the preparation of gastro-retentive drug delivery systems. These include floating systems, swell able and expandable systems, high density systems, bioadhesive systems, altered shape systems, gel forming solution or suspension systems and sachet systems. Various approaches have been followed to encourage gastric retention of an oral dosage form. Floating systems have low bulk density so that they can float on the gastric juice in the stomach.

The prepared Ibuprofen FDDS were subjected to various evaluation studies done like Weight uniformity test, Hardness, Thickness, Friability (F)Thickness, Content uniformity, *In vitro* buoyancy / floating study, Swelling Index Disintegration studies , *In vitro* dissolution studies.

Evaluation of tablets

Weight Variation, Thickness, Hardness and Friability

The results showed that weight variation, thickness were lying within limits. Because of variation in the compressional forces there is a slight variation in hardness of tablets. As the proportion of polymers increases the hardness of the tablets was found to increase in case of HPMC. The friability loss was found to be within the limits in all the friability tablet was found to mechanically strong.

Buoyancy and total Flotation test

From the results, it was observed that as the buoyancy lag time and the total floating time was studied for all the formulations. F1, F2, F3 and F4 total floating time were found to be 12, 10, 5.5 and 7 hrs respectively as shown in Table No. 3. F1 showed optimum buoyancy lag time. for all the F1 and F2 formulations showed more total floating time when compared to F3 and F4 due to the presence of hydrophobic polymer which decreased the solubility. When compared in between F2 and F4, F4 showed less total floating time. Thus with an increase in the concentration of the hydrophilic polymer total floating time was found to be decreased due to increase in the solubility.

Results revealed that as the concentration of the hydrophilic polymer increases, the buoyancy lagging time decreases. The increase in the concentration of the hydrophobic polymer resulted in the increase of the buoyancy lag time. Thus polymer HPMCK4M and Carbopol 940 were found to have optimum floating characters for a longer period.as shown fig:1

Swelling thickness

As tabulated in Table no. 05 the extent of swelling was found out by measuring the thickness of the tablet before and after one hour stay of the tablet in pH 6.8 buffer at 37 ± 0.5 ^{0}C. FormulationF1 And F2 tablets were found to swell more and formulationF3 and F4 tablets were swelling to lesser extent.

Drug content

Drug content of all the formulations are within the acceptable range which shows the proper mixing of the drug with excipients as shown in Table No. 04.

In-vitro drug release

In-vitro drug release study for all the formulations was conducted and tabulated in Table No. 6. Formulations showed sustained release. Formulations with polymers showed high less which retards the drug release to a greater extent. Thus the HPMC Decreasing and Carbopol 940 Increasing concentration provide the optimum drug release.

Drug release kinetics

From the data of drug release, it was found that, all the tablet formulations follow diffusion mechanism for drug release. The Higuchi square root equation describes the release from systems where the solid drug is dispersed in an insoluble matrix and the rate of drug release is related to the rate of drug

diffusion. Results revealed that all the prepared formulations follow Higuchi Kinetics as shown in Table No-7

DIFFERENTIAL SCANNING CALORIMETRY (DSC) ANALYSIS

The DSC thermo grams of ibuprofen, physical mixture of ibuprofen and HPMC K4M and Carbopol940 are shown in (Fig-4). In order to investigate the possible interactions between the drug and polymers used, differential scanning calorimetric studies were carried out. DSC thermo gram of the formulation was compared with the DSC thermo gram of the pure drug. The DSC thermo gram obtained is reported in Figure-4. The pure ibuprofen displayed a sharp endothermic peak at 82^{0}C corresponding to the melting point of the drug and a similar peak was also observed in the formulation.

From the DSC thermo gram it was observed that the decomposition temperature of the pure drug and the formulation remained the same. Hence it can be concluded that there was no significant interaction between drug and the polymers used.

SUMMARY

In present work an attempt has been made to formulate sustained release floating drug delivery system of Ibuprofen tablets by using polymers. FDDS were prepared using polymers of HPMC K4M and Carbopol 940 by direct compression method. Ibuprofen meets all the ideal characteristics to formulate in the form a floating drug delivery system.

The compatibility evaluations were performed by DSC analysis. Studies imply that polymers are compatible with each other. There was no interaction found between polymer and drug.

All the formulations were characterized on the basis of their evaluation studies and in-vitro dissolution studies.

The compatibility evaluations were performed by DSC analysis. Studies imply that polymers are compatible with each other. There was no interaction found between polymer and drug.

The mechanism of drugs release from tablets was dissolution followed by USP Type-II. Two formulations F1 and F2 were able to release drug up to 13hrs and F3 and F4 released maximum drug F1 only compiles with the USP type-II, which maintained the release pattern as per mention. Rests of the formulations were unable to maintain release rate as per USP-typeII.

Table 1: Development of different formulations containing, varying proportions of polymers

Formulation code	Drug (mg)	HPMC (mg)	Carbopol (mg)	$NaHCo_3$ (mg)	M.C.C (mg)	Citric acid (mg)	Lactose (mg)	Mg stearate (mg)	Talc (mg)
F1	200	100	25	50	75	25	25	5	10
F2	200	75	50	50	75	25	25	5	10
F3	200	50	75	50	75	25	25	5	10
F4	200	25	100	50	75	25	25	5	10

Table 2: Weight Variation, Thickness, Hardness and Friability

Formula	Weight variations	Thickness	Hardness	Friability
F1	0.238	0.38±0.031	5.5	0.2
F2	0.246	0.40±0.011	6.0	0.4
F3	0.235	0.41±0.007	4.0	0.7
F4	0.245	0.43± 0.007	3.5	0.6

Table 3

Formulation Code	Buoyancy lag time (min)	Total floatation time (hrs)
F1	2.5min	12
F2	2.0min	10
F3	4.0min	5.5
F4	4.5min	7

Table 4: Data showing the drug content of various formulation of Ibuprofen

Formulation code	% Drug content
F1	96
F2	95
F3	91
F4	92

Table 5: Standard Curve of Ibuprofen

S. No.	Concentration(µg/ml)	Absorbance
1.	10	0.340
2.	20	0.748
3.	30	1.124
4.	40	1.486
5.	50	1.874

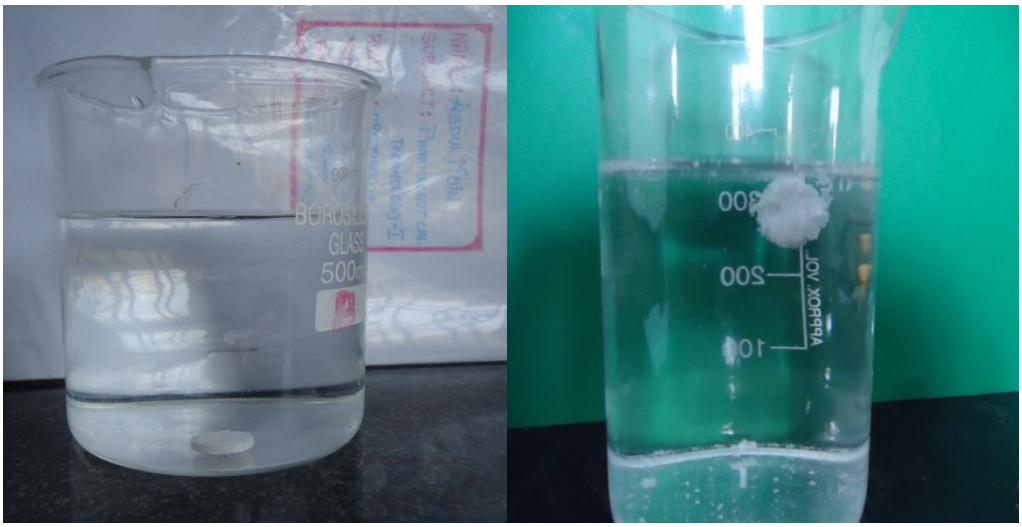
Table 6: Data showing comparative *In-Vitro* % drug release profiles for all the prepared formulations

Time(Hrs)	F1	F2	F3	F4
30(Mins)	1.00	2.36	2.98	4.26
1	1.08	6.48	6.30	7.25
2	3.61	7.63	8.15	9.08
3	9.95	9.15	10.0	10.98
4	13.66	11.05	11.97	12.0
5	15.61	13.87	13.97	13.93
6	18.48	15.82	20.38	18.58
7	21.38	16.89	23.3	22.38

8	22.51	19.77	30.75	30.72
9	25.45	25.38	37.38	37.35
10	27.52	29.25	48.58	47.87
11	31.41	36.76	51.8	54.48
12	35.36	43.45	70.35	75.76
13	40.45	54.71	80.1	90.97

Table 7: Data showing drug release kinetics for all the prepared formulations

Formulation Code	Zero order	First order	Higuchi	Korsmeyer	Hixson
F1	0.906	0.893	0.956	0.834	0.265
F2	0.866	0.886	0.866	0.787	0.265
F3	0.986	0.826	0.986	0.906	0.265
F4	o.986	0.826	0.986	0.906	0.265



BEFORE **AFTER 1 HOUR**

Fig. 1: Data of Buoyancy Lag Time and Total Floatation Time for All the Formulations of Ibuprofen

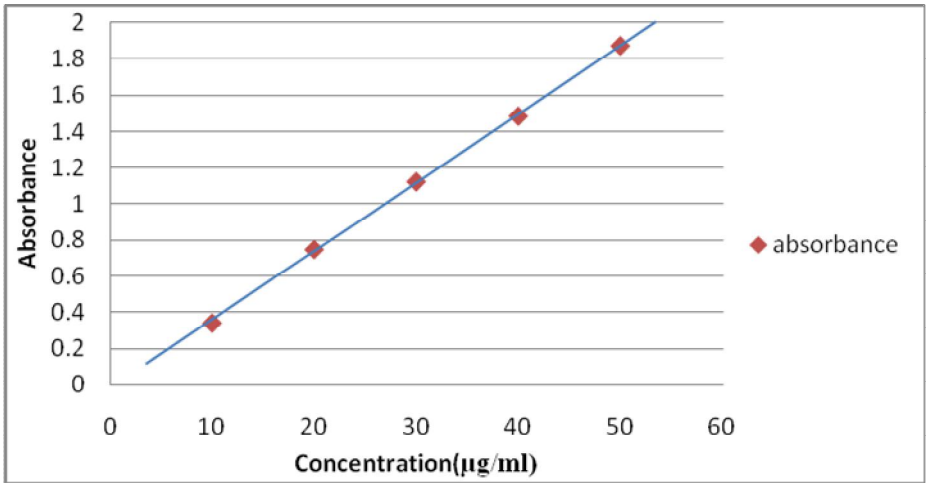


Fig. 2: Standard Graph of Ibuprofen

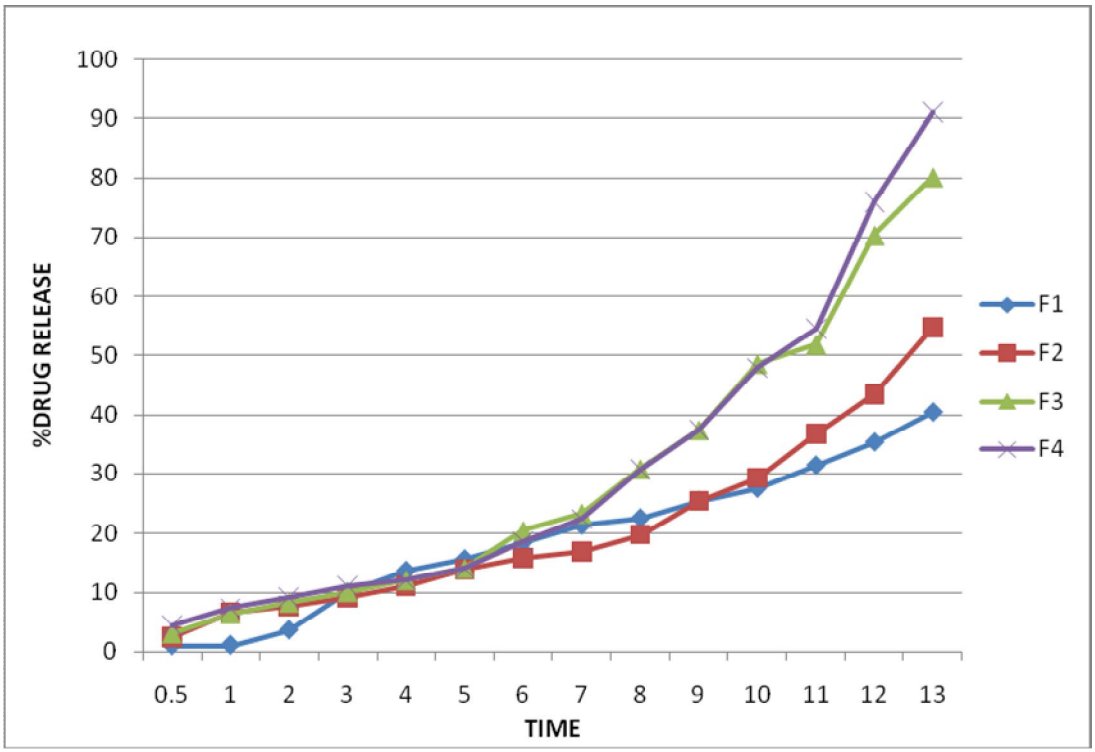


Fig. 3: Comparative In-Vitro % Drug Release Profiles for All the Prepared Formulations

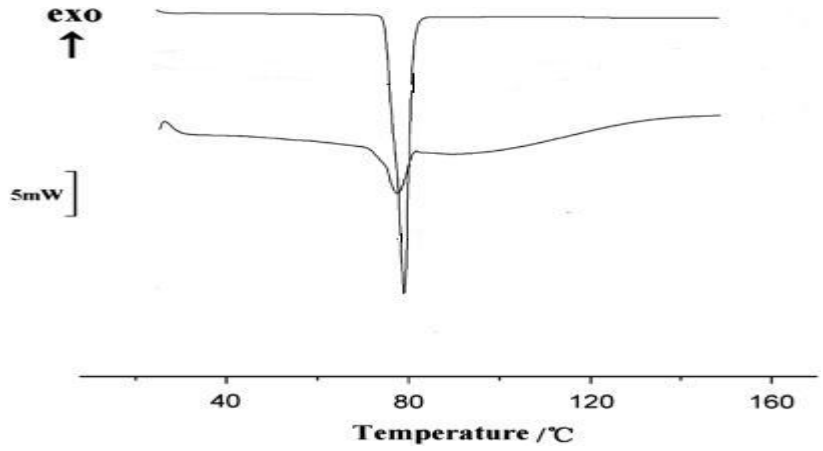


Fig. 4: DSC Thermograph

CONCLUSION

Development of Floating Drug Delivery System of sustained release oral dosage forms is beneficial for optimal therapy regarding efficacy, safety and patient compliance. In case of FDDS of sustained release (SR) dosage forms the release of the active agent, although, is lower than in the conventional formulations, however, it is still substantially affected by the external environments into which it is going to be released. The research was undertaken with the aim to formulate and characterize the sustained release floating tablets of Ibuprofen using HPMCK4M and Carbopol 940 as polymers. From results obtained, it was concluded that the formulation of sustained release tablet of Ibuprofen containing a combination of both polymers were taken as ideal or optimized formulation for 13 hours release as it fulfils all the requirement of Floating Drug Delivery System of sustained release dosage form.

Further work is required to stabilize the product; in-vivo studies estimate the amount of drug present in the various organs with disposition kinetics and establish appropriate dosage regimen to gauge the significant changes in the metabolism of the drug before further studies

REFERENCES

1. Rouge N, Buri P and Doelker E. "Drug absorption sites in the gastrointestinal tract and dosage forms for site specific delivery", International journal of pharmaceutics. 1996, 36, pp 117-139.
2. Soppimath KS, Kulkarni RA, Rudzinski WT and Aminabhavi TM. "Microspheres as floating drug delivery systems to increase gastric retention of drugs", Drug metabolism reviews, 2001, 33, pp 149-160.
3. Singh BN and Kim KH. "Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention", Journal of Control Release, 2000, 63, pp 235-239.
4. www.niro.com/niro/cmsdoc.nsf/webdoc/ndkw67hhfv.
5. http://pua.cc/PUASite/uploads/file/Pharmacy/fall2009/PHR312/week6/Microsoft_Word_-_Lecture_6_cont_09-10.pdf.
6. Vendruscolo CW, Andreazza IF, Ganter JL, Ferrero C and Bresolin TM. "Xanthan and galactomann matrix tablets based for oral controlled delivery of theophylline", International journal of Pharmaceutics, 2005, 296, pp 1-11.

7. Ziyaur R, Mushir A and Khar RK. "Design and Evaluation of bilayer floating tablets of captopril", Acta pharmaceutica, 2006, 56, pp 4957.
8. Reshu Gupta and kamala pathak. "Optimisation studies on floating multiparticulate gastro retentiva drug delivery system of famotidine", Drug development and industrial pharmacy, 2008, pp 1201-1208. Int. J. Drug Dev. & Res., April-June 2011, 3 (2): 290-300 Covered in Scopus & Embase, Elsevier 299 B. Samyuktha Rani et al: Aceclofenac Floating Tablets -A Promising Sustained Release Dosage Form Full Length Research Paper Covered in Official Product of Elsevier, The Netherlands.
9. Luy paert, zhang J and Massart M.H. "Feasibility study of the use of near Infrared spectroscopy in the quantitative analysis of green tea,camellia sinesis(l.)", Analytica chimica Acta, 2003, 478(2), pp 303-312.
10. Praneeth kumar S. "Formulation and evaluation of floating drug delivery of metoprolol succinate", Aaps pharmsci tech, 2009, 1, pp 1-315. Int. J. Drug Dev. & Res., April-June 2011, 3 (2): 290-300 Covered in Scopus & Embase, Elsevier.
11. Controll ed and novel drug delivery" by N.K.Jain. CBS Publications. Pg.no:256-257.
12. Controll ed dug delivery concepts and advances" by S.P.vyas, Roop K. Khar, Vallabh prakashan publishers. Pg.no:60-61.
13. Biophar maceutics and pharmacokinetics" – a treatise by D.M.Brahmankar, Sunil B. Jaiswal pg.no:398-399.
14. The theory and practice of industrial pharmacy" by Leon Lachmann, Varghese publishing house. Pg.no:430.
15. Novel drug delivery systems" by Yie W. Chien second edition. Pg.no:1.
16. Controll ed drug delivery concepts and advances" by S.P.Avyas and Roop K. Khar, Vallabh prakashan, pg.no:167.
17. Modern pharmaceutics" by Gilbert S. Banker and Christopher T. Rhodes, fourth edition pg.no:502.
18. Thomas Wai- Yip Lee, Joseph R Robinson, 'Controlled-Release Drug-Delivery Systems', Chapter-47 in Remington: "The science and practice of pharmacy", 20th edition, vol-1, pp 905-906, 910-913.
19. H.Popi and S.N.Sharma, "Trends in oral sustained release Formulations-I, The Eastern Pharmacist, August-1989, pp99-103.