ISSN: 2321-3760

Research Article

International Journal of Current Trends in Pharmaceutical Research

IJCTPR, 2014, Vol. 2(6): 687-694

www.pharmaresearchlibrary.com/ijctpr

Formulation and Evaluation of Floating Tablet of Levofloxacin

Sravan Kumar. P *, Sabareesh Reddy. M, Umasankar. K, Alagu Sundaram. M, P. Jaya Chandra Reddy

Krishna Teja Pharmacy College, Chadalawada Nagar, Tirupathi-517506, Andhra Pradesh, India

Received: 24 August 2014, Accepted: 27 October 2014, Published Online: 15 November 2014

Abstract

In the present study, the tablets were prepared by melt granulation method, using the polymer, hydroxy propyl methyl cellulose (HPMC K4M),Carbopol with different amounts and other excipients and sodium bicarbonate and citric acid as gas generating agents. The present study is to develop a floatable drug delivery system of Levofloxacin hemihydrate for sustained drug delivery and gastric retentive property with special stress on optimization of formulations for floating tablets. Thus the study aims to improve the oral bioavailability of the drug and to achieve extended retention in the stomach which may result in prolonged absorption of drug. Tablets were evaluated by different parameters such as weight uniformity, content uniformity, thickness, hardness, IR spectral analysis, *in vitro* release studies, Buoyancy determination and kinetic analysis of dissolution data, stability studies Levofloxacin floating tablet drug delivery system showed improved in-vitro bioavailability and extended drug release which may favour the reduced dose frequency and patient compliance**.**

Keywords: Levofloxacin Hemihydrate**,** Floating tablets, gas generating *in vitro* release study, Buoyancy determination

Contents

***Corresponding author**
Sravan Kumar. P
Krishna Teja Pharmacy College,
Chadalawada Nagar, Tirupathi,
Andhra Pradesh, India-517506
Manuscript ID: IJCTPR2302

PAPER-QR CODE

1. Introduction

From many years the treatment of an acute diseases or illness like chronic or acute has been treated by drug delivery to patients in various pharmaceutical dosage forms like tablets, capsules, creams, suppositories, ointments, suspensions and injections etc. Even today these conventional drug delivery systems are the pharmaceutical products commonly seen in the prescription and available in the market as primary pharmaceutical products. Several technical advancements are developed for new techniques for drug delivery. These techniques are capable of controlling the rate of drug delivery, extending the duration of therapeutic activity and targeting the delivery of drug to the needed area [1]. The important of any drug delivery system is to release promptly a therapeutic amount of drug to the proper site of action, and then to maintain the desired therapeutic concentration of the drug to show desired pharmacological action, also it minimizes the unwanted adverse side effects severity. To achieve this goal, the dosage frequency may be minimized once or at most twice daily. An approximately designed extended release dosage form (e.g. sustained drug delivery, floating drug delivery) can be a major advance in this direction [2]. The main objectives of sustained/controlled drug delivery are safety, efficacy of drug and improve the patient compliance. These objectives are achieved by better control of plasma drug levels and less frequent dosing. Past three decades the innovation formulations of GI drugs to be retained in the upper part of the GI tract. Then these are advanced in terms of technology and diversity. variety of systems and devices such as floating systems, expanding systems, swelling systems, bioadhesive systems and low density systems [3].

2. Materials and Methods

The instruments and chemicals that are the best possible pharma grade and AR grade available were used as supplied by the manufacturers.

Table: 1 Chemicals used in the present work

S.No	Chemicals	Source
1	Levofloxacin hemihydrates	Promed Research Centre, New Delhi
2	HPMC K4M	Micro labs Limited, Hosur.
3	Sodium bicarbonate	Oxford laboratory reagent
4	Bees Wax	Oxford laboratory reagent
5	Ethyl cellulose	Micro labs Limited, Hosur
6	Talc	Nice chemicals pvt ltd
7	Magnesium Stearate	Qulikems laboratories

3. Standard Curve

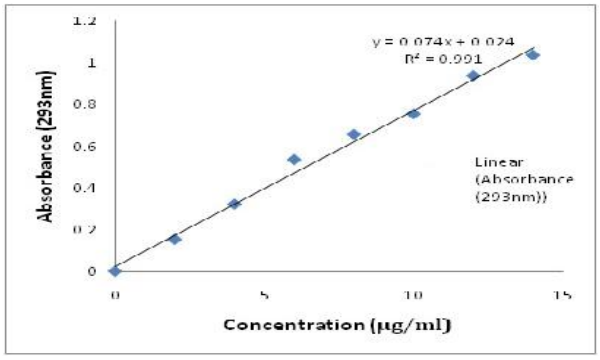


Figure 1: Plot-1 Standard curve of Levofloxacin Hemihydrate

Table 2: Standard curve of Levofloxacin hemihydrate in 0.1N HCl

S.No	Concentration (µg/ml)	Absorbance (293 nm)
1	0	0
2	2	0.152
3	4	0.321
4	6	0.534
5	8	0.656
6	10	0.753
7	12	0.930
8	14	1.035

Table 3: Preparation of Levofloxacin Floating Tablet

Formulation Code	Levofloxacin (mg)	HPMCK4M (mg)	Carbopol (mg)	Ethyl Cellulose (mg)	Sodium Bicarbonate (mg)	Citric acid (mg)	Bees Wax (mg)	Talc (mg)	Magnesium Stearate (mg)
F1	250	152	-	12.5	24	12.5	36	9	4
F2	250	139.5	-	25	24	12.5	36	9	4
F3	250	127	-	37.5	24	12.5	36	9	4
F4	250	114.5	-	50	24	12.5	36	9	4
F5	250	102	-	62.5	24	12.5	36	9	4
F6	250	90	-	74.5	24	12.5	36	9	4
F7	250	-	152	12.5	24	12.5	36	9	4
F8	250	-	136	25	24	12.5	36	9	4
F9	250	-	120	44.5	24	12.5	36	9	4
F10	250	-	100	64.5	24	12.5	36	9	4

4. Experimental Studies

4.1 Preparation of Levofloxacin Floating Tablets

Five formulations of Levofloxacin floating tablets were prepared. Beeswax was melted in a china dish, and the required quantity of Levofloxacin was added to the molten mass. Previously prepared geometric mixture of HPMC K4M and /or Ethyl cellulose and sodium bicarbonate was added to the molten Levofloxacin-Beeswax mixture and stirred well to mix. The mass was removed from the hot plate and subjected to scraping until it attained room temperature. The coherent mass was passed through a 36 mesh sieve, and the resulting granules were resifted on a 100-mesh sieve to remove the fines. Then the granules were mixed with 9mg of talc and 4mg of magnesium stearate.

5. Methodology

5.1 Evaluation of Levofloxacin Floating Granules

Preformulation studies

The Preformulation studies including Compatibility study, Bulk density, Tapped density, Hausner's ratioand Angle of repose was performed for the levofloxacin granules [4].

Angle of repose

Flow property of the granules was evaluated bydetermining the angle of repose and the compressibility index. Static angle of repose was measured according to fixed funnel method and free standing cone method of Banker and Anderson4. The angle of repose was calculated using the equation, Tan _ = h/r ….(1) whereis the angle of repose [5].

Bulk density

Loose bulk density (LBD) and Tapped bulk density (TBD) were determined for the prepared granules.

LBD and TBD was calculated using the formula,

LBD = Wt of Powder / Vol. of Powder ……..(2)

TBD = Wt of Powder / Tapped Vol. of Powder….(3)

Compressibility Index

Carr's Compressibility Index5 for the prepared granules was determined by the equation, Carr's Index (%) = TBD – LBD/TBD x 100 … …(4)

Hausner's ratio

Hausner's ratio can be determined by the following equation,

Hausner's ratio = TBD / LBD[6-8]

Table 4: Evaluation of Levofloxacin Hemihydrate Floating Granules

Formulations	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Bulkiness (ml/gm)	Angle of repose (Θ)	Compressibility index (%)	Hausner's ratio
F 1	0.36 ±0.002	0.40±0.02	2.75±0.03	32°26'±1.5	12.97±1.02	1.15±0.01
F 2	0.34±0.004	0.39±0.04	3.10±0.12	32°58'±0.59	13.54±0.76	1.15±0.02
F 3	0.34±0.004	0.37±0.06	2.75±0.03	33°67'±0.15	13.75±0.54	1.14±0.02
F4	0.32±0.005	0.40±0.01	3.03±0.08	32°46'±0.78	13.94±0.49	1.15±0.01
F 5	0.32±0.005	0.39±0.01	3.07±0.04	32º48'±0.72	14.08±0.2	1.14±0.02

F 6	0.33± 0.002	0.37± 0.14	3.01± 0.10	34º17'±1.11	13.95±0.52	1.14± 0.04
F 7	0.34± 0.011	0.40± 0.01	3.07±0.12	30º16'±1.08	14.12±1.24	1.15± 0.07
F 8	0.35± 0.001	0.37± 0.01	3.08± 0.06	33º17'±0.12	13.68± 0.93	1.16± 0.01
F 9	0.32± 0.002	0.39± 0.06	3.06± 0.04	34º18'±0.12	14.45± 1.15	1.17± 0.01
F 10	0.33±0.004	0.38±0.06	2.95±0.03	33°67'±0.15	13.75±0.54	1.14±0.02

5.3 Evaluation of Levofloxacin Floating Tablets

The formulated Levofloxacin hemihydrate Floating tablets were evaluated for various physico- chemical parameters.

5.3.2 Hardness

Oral tablets normally have a hardness of 4 – 10 kg/cm^2. The hardness of the tablets was tested using Monsanto hardness tester .The hardness of the tablets of all formulations was within the range of 4-5 kg/cm^2

5.3.3 Friability: Friability was carried out using Roche Friabilator on 10 pre-weighed tablets with revolution adjusted to 100 revolutions. After 100 revolutions, the tablets were dusted and reweighed. A maximum weight loss of not more than 1% of the weight of the tablet being tested during the friability test is considered generally acceptable [9-11].

5.3.4 Drug content Uniformity: The drug content of the tablets were evaluated by using UV-Visible Spectrophotometric method.. As per the IP the content uniformity should be in the range 90 – 110.

5.3.5 Weight Variation Test

Twenty tablets of each formulation were selected randomly and weighed individually. Not more than two tablets should go more than the prescribed deviation. The percentage deviation is ± 5% for more than 500 mg tablet. Here the actual weight of one tablet is 500 mg.

5.3.6 Buoyancy Determination: Floating time was determined by using Rolex dissolution apparatus at 100 rpm using 900 ml of 0.1N HCl and temperature was maintained at 37ºC ±0.5ºC throughout the study. Duration of Buoyancy (DB) of all the 5 formulations is more than 12 hours. The Buoyancy Lag Time (BLT) is in between 4 and 11.6minutes [11-14].

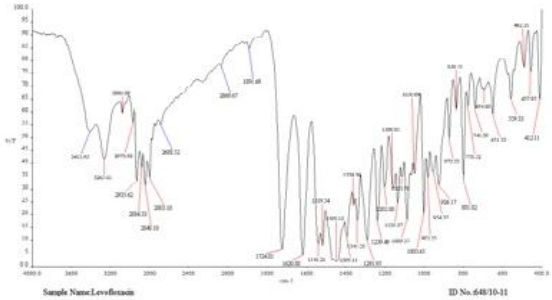
5.4 Evaluation of Levofloxacin Floating Tablets

Table 5: Evaluation of Levofloxacin Floating Tablets

Formulation	Hardness (Kg/cm2)	Friability (%)	Uniformity of Weight(mg)	Drug content (%)	Thick ness (mm)	Buoyancy Lag Time (minutes)	Duration of Buoyancy (Hours)
F 1	5.2	0.27	500± 2.3	96.9± 0.54	4.3	8.1	>12
F 2	4.5	0.71	500± 1.89	99.1± 0.21	4.5	6.6	>12
F 3	4.5	0.58	501± 1.8	97.1± 0.74	4.2	7.1	>12
F 4	4.5	0.41	502± 1.8	98.1± 0.65	4.3	5.6	>12
F 5	4.5	0.38	500± 4.3	97.3± 0.81	4.5	6.2	>12
F 6	4.3	0.34	501± 0.19	99.1± 0.12	4.5	7.1	>12
F 7	4.8	0.67	500± 0.94	98.9± 0.10	4.3	6.3	>12
F 8	4.5	0.54	500± 1.32	99.2± 0.18	4.6	8.0	>12
F 9	4.6	0.81	500± 0.3	97.9± 0.54	4.2	6.1	>12
F 10	4.2	0.66	500± 2.3	96.9± 0.54	4.3	7.6	>12

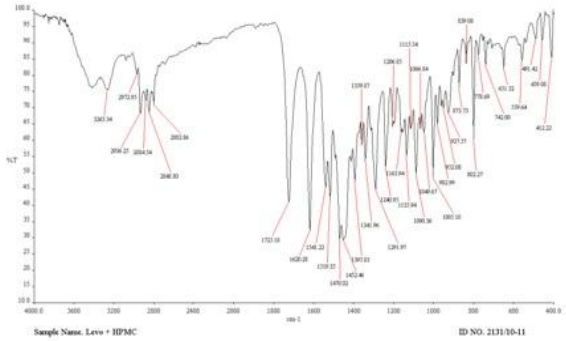
6. Results

IR Spectra of Levofloxacin



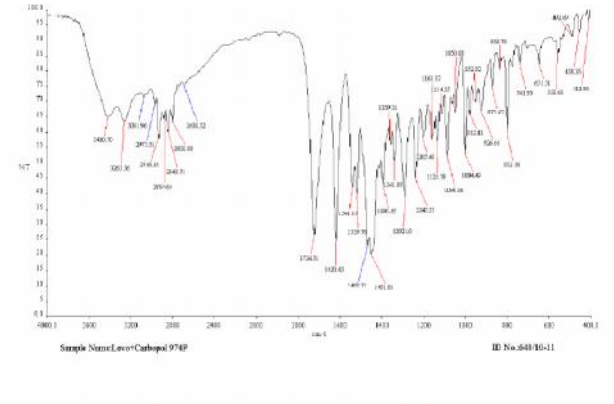
Graph 1: IR Spectra of Levofloxacin

IR Levofloxacin + HPMC (Physical Mixture)



Graph 2: IR Levofloxacin + HPMC

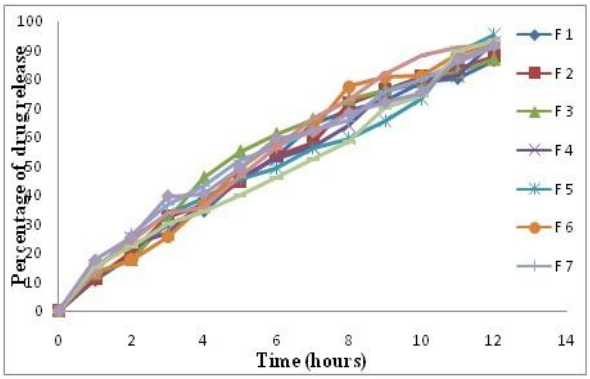
IR Levofloxacin + Carbopol (Physical Mixture)



Graph 3: IR Levofloxacin + Carbopol

Table: 6 In-Vitro Dissolution profiles of Levofloxacin formulations 1 To 10 in 0.1 N HCl

S.No	Time of Sampling (hour)	Percentage Drug Release									
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	0	0	0	0	0	0	0	0	0	0	0
2	1	10.53	11.32	12.91	15.25	14.32	13.30	13.31	14.30	15.44	17.46
3	2	19.21	20.60	17.74	23.20	24.93	17.56	26.64	24.19	22.39	25.56
4	3	30.34	32.55	31.56	26.78	33.27	25.66	36.57	34.11	30.11	39.55
5	4	34.41	36.59	45.93	38.08	38.92	36.85	43.38	36.02	34.51	40.34
6	5	45.35	44.63	54.90	46.03	45.54	48.98	52.12	46.39	39.82	49.43
7	6	53.14	53.60	60.95	52.35	49.35	57.95	56.45	56.35	45.87	59.51
8	7	64.43	58.15	65.98	56.60	56.13	62.51	62.12	66.41	52.43	61.87
9	8	69.18	71.58	73.04	64.11	59.45	77.58	65.75	72.91	58.39	68.26
10	9	72.43	76.17	76.15	75.73	65.62	80.71	75.64	81.94	69.94	71.91
11	10	79.11	80.77	79.28	79.31	73.25	81.32	79.84	88.52	74.34	75.39
12	11	80.23	83.90	82.41	81.42	79.16	88.46	85.83	91.26	89.51	86.89
13	12	86.45	87.95	86.80	92.81	95.20	92.32	90.97	92.17	93.31	91.51



Plot-2: In-Vitro Dissolution profile of Levofloxacin formulations 1 To 10 in 0.1 N HCl

6.1 Pharmacokinetic Studies

Table 7: Kinetic studies of formulation F5

Time (hrs)	√t	Log t	Cumulative % drug release	Cumulative % drug remain	Log cumulative % drug release	Log cumulative % drug remain
0	0	0	0	100	0	2
1	1.0	0	14.32	85.68	1.155	1.932
2	1.414	0.301	24.93	75.07	1.396	1.875
3	1.732	0.477	33.27	66.73	1.522	1.824
4	2.0	0.602	38.92	61.08	1.590	1.785
5	2.236	0.698	45.54	54.46	1.658	1.736
6	2.449	0.778	49.35	50.65	1.693	1.704
7	2.645	0.845	56.13	43.87	1.749	1.642
8	2.828	0.903	59.45	40.55	1.774	1.607
9	3.0	0.954	65.62	34.38	1.817	1.536
10	3.162	1.0	73.25	26.75	1.864	1.427
11	3.316	1.041	79.16	20.84	1.898	1.318
12	3.464	1.079	95.20	4.80	1.964	0.892

Kinetic plots of formulation F5

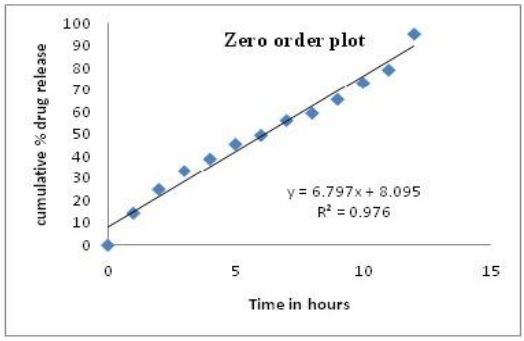


Figure 2

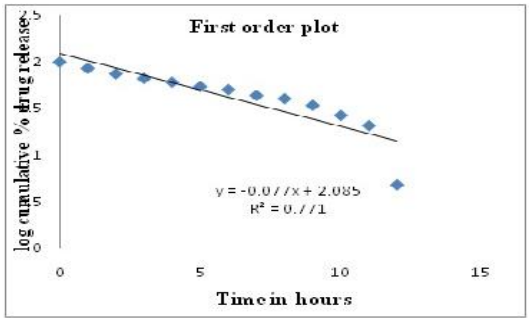


Figure 3

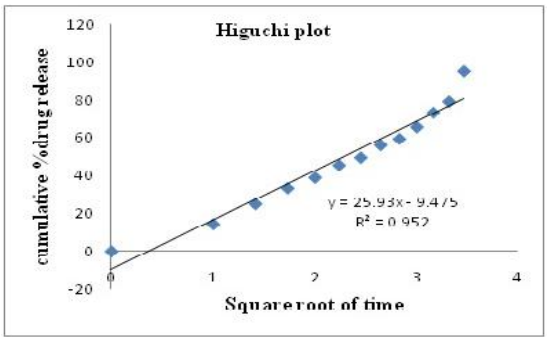


Figure 4

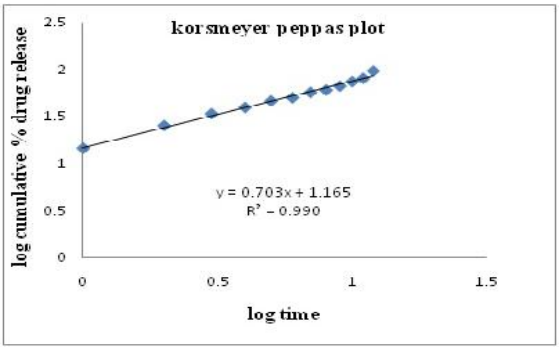


Figure 5

Table 8: Result of model fitting to formulation F 5

Model	R^2 value
Zero order	0.976
First Order	0.771
Higuchi	0.952
Korsmeyer-Peppas	0.990

6.2 Stability studies

Table 9: Stability Studies of Levofloxacin Hemihydrate Formulations

S.No	Parameters	Observation (40 ± 2ºC / 75 ± 5% RH)		
		At 15 Days	At 30 Days	At 45 Days
1	Physical Appearance	No change	No change	No change
2	Weight Variation (mg)	500 ± 4.3%	501 ± 1.8 %	500 ± 4.0%
3	Thick ness (mm)	4.3±0.02	4.4±0.08	4.3±0.08
4	Hardness (Kg/cm2)	4.4 ± 0.04	4.5 ± 0.18	4.4 ± 0.6
5	Friability (%)	4.4 ± 0.04	4.5 ± 0.18	4.4 ± 0.6
6	Drug Content (mg/tab)	99.2 ± 0.18	99.0 ± 0.2	99.0 ± 0.1
7	Buoyancy lag time (Mins)	6.5 ± 0.2	5.2 ± 0.2	5.2 ± 0.1
8	Duration of Buoyancy(Hrs)	>12	>12	>12

7. Discussion

The aim of the study is to make the formulation remain for a longer period of time in the stomach and to release the drug (Levofloxacin) in controlled rate.The use of polymer was to control the release and also to make the formulation buoyant. Bees wax was taken as a hydrophobic meltable material to impart sufficient strength to the tablets. Sodium bicarbonate generates carbon-di-oxide gas in the presence of HCl present in dissolution medium. Ethyl cellulose was used as a floating enhancer. The formulation was prepared by melt granulation method. The granules of different formulations were evaluated for angle of repose, bulk density, tapped density, compressibility index, Hauser's ratio (table 6) and drug content (table 7). The results show that the angle of repose (31-35). Compressibility index values ranges from 11-16 and Bulk density, Tapped density values favor the good flow property of the granules.

All tablets the formulations were subjected to many in-process parameters such as hardness, friability, thickness, content uniformity and weight variation. The hardness values of approximately 4-4.3 kg/cm^2. The weight loss was less than 1% in the friability test (0.38-0.5) was considered as acceptable value for conventional tablet. This indicates the tablet could withstand the mechanical shock while doing handling. Good uniformity in drug content was found among different preparations of the tablet and the percentage drug content was more than 93%. All the formulations showed the thickness in the range of 4.2- 4.6 mm. All tablets showed buoyancy lag time in between 5 to 11 minutes and duration of buoyancy was Equal to/greater than 12 hours.

Levofloxacin release from tablets was slow and extended over longer periods of time. The results of dissolution studies of all formulations (F1-F10) were shown in the table19. Formulations F1, F2, F3, showed more than 80% of drug release in 12hrs of dissolution study. Formulations F4, F5, F6, F7, F8 ,F9 and F10showed more than 90%. F5 showed 95.89 % of the drug release in 12hrs.So formulation-5 is considered as better formulation compared to other formulations (F1, F2, F3, F4, F6, F7, F8, F9 and F10).

8. Summary and Conclusion

The floating drug delivery based on effervescent was a hopeful approach to achieve invitro floating. In above formulations the addition of gel forming polymer (HPMC K4M), suspending polymer carbopol and gas generating agent is sodium bicarbonate, citric acid were essential to achieve the invitro buoyancy. The drug release from the tablets was sufficiently controlled due to the presence of polymer and Bees wax. Levofloxacin floating tablet drug delivery system showed improved in-vitro bioavailability and extended drug release which may favour the reduced dose frequency and increases patient compliance. Further clinical evaluation may prove the efficacy of this formulation.

9. Reference

1. Yie W. Chein " Novel Drug Delivery System " 2nd ed. Marcel jekker Inc., New York. **1992**, 1-3.
2. Lee, V.H. and Robinson, J.P. " Sustained and Controlled Release Drug Delivery System ". Marcel dekker, New York, **1978**, 7-11.
3. Sanjay Garg and Shringi Sharma , " Gastroretentive drug delivery systems", Pharmatech, **2003**, 160-166 volumes
4. Kim K. H., Sing B. N., "Encyclopedia of Pharmaceutical Technology ", 2nd ed., Vol. 1, ed. By Swarbrick J., Boylan J. C., Marcel Dekker, New York, **2002,** pp. 886-909.
5. Sanjay Garg and Shringi Sharma , " Gastroretentive drug delivery systems", Pharmatech, **2003**, 160-166 volumes
6. Deshpande A.A., Rhodes C.T., Shah N. H., Malick A. W., " Drug De. Ind. Pharm ", **1996**, 22, 531-539.
7. Sing B.N., Kim K.H., J. Control Release, **2000**, 63, 235-259.
8. Lee, V.H. and Robinson, J.P. " Sustained and Controlled Release Drug Delivery System ". Marcel dekker, New York, **1978**, 7-11.
9. Shweta Arora, Javed Ali , Alka Ahuja, Roop k. Khar, and Sanjula Baboota, "Floating drug delivery systems." AAPS PharmSci Tech., **2005**, 6(3) Article 47.
10. Ritschel W. A., Menon A., Sakr A., "Methods Exp. Clin. Pharmacol ", **1991**, **13**, 629-636.
11. Jain,N.K., "Controlled Novel Drug Delivery", 1st Eds., CBS Publishers and Distributors, New Delhi, **2002**, pp.236-55.
12. Gangadharappa H.V, Pramod Kumar T.M and Shiva Kumar H.G, "Gastric floating drug delivery systems." Indian J. Pharm. Educ. Res, 41(4), Oct-Dec **2007**, 295-306.
13. Joseph NJ, Laxmi S, Jayakrishnan A, "A floating type oral dosage form for Piroxicam based hallow microspheres : in vitro and in vivo evaluation in rabbits". J. Control . Release., **2002**, **79**: 71-79.
14. Gangadharappa H.V, Pramod Kumar T.M and Shiva Kumar H.G, "Gastric floating drug delivery systems." Indian J. Pharm. Educ.Res, 41(4), Oct-Dec, **2007,** 295-306.