ISSN 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

Available online at: http://www.iajps.com *Research Article*

FORMULATION AND EVALUATION OF CEFADROXIL GASTRO RETENTIVE DRUG DELIVERY SYSTEMS

E. Sathish Reddy[*1], Dr. MD. Ibrahim[2], Akhila Alladi[1], M. Sharath Chandra[1]

1. Department of Pharmaceutics, PNR College of pharmacy, Peddashapur (Vi) Shamshabad (Md), R.R.Dist , Telangana, India.
2. Nizam Institute of Pharmacy, Deshmukhi, Pochampally(M, Nalgonda, Telangana.

ABSTRACT

The aim of the Present study is to formulate and evaluate Antibiotic Cefadroxil as gastro retentive drug delivery system in raft formulation using sodium alginate as the polymer. Formulations were designed using different grades of Eudragit polymers. Cefadroxil is a broad-spectrum antibiotic of the cephalosporin type, effective in gram-positive and gram-negative bacterial infections. It is a bactericidal antibiotic, cefadroxil is a first-generation cephalosporin antibacterial drug that is the para-hydroxy derivative of cefalexin, and is used similarly in the treatment of mild to moderate susceptible infections such as the bacterium Streptococcus pyogenes, causing the disease popularly called strep throat or streptococcal tonsillitis, urinary tract infection, reproductive tract infection, and skin infections. Considering the wide range of activity of Cefadroxil, the objective of this study was to decrease the dose frequency and increase the speed of recovery from the indications by increasing the rate of bacterial killing and thereby increasing patient compliance. The formulations were designed using eudragits of different grades in different concentration ratios individually and in combination. All the formulations were evaluated for their Preformulation and Post formulation studies. The formulations were optimized and the best formulation was selected by the invitro drug release studies. The optimized formulation was found to sustain the drug for maximum time and is found to be stable.

Keywords: *Cefadroxil, Gastro retentive, Sodium alginate, Eudragits.*

Corresponding Author:
E.Sathish Reddy.
Department of Pharmaceutics,
PNR college of pharmacy,
Peddashapur (Vi),Shamshabad(Md)
R.R.Dist,Telangana,
India.

QR code

Please cite this article in press as Sathish Reddy et al. **Formulation and Evaluation of Cefadroxil Gastro Retentive Drug Delivery Systems,** *Indo American J of Pharm Sci 2015:2(2):573-580.*

INTRODUCTION

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance and cost-effective manufacturing process [1-4].

These difficulties of controlled release targeted action of drug delivery systems have prompted researchers to design a drug delivery system which can stay in the stomach for prolonged and predictable period. Attempts are being made to develop a controlled drug delivery system, which can provide therapeutically effective plasma drug concentration for a longer period, thereby reducing the dosing frequency and minimizing fluctuations in plasma drug concentration at steady-state by delivering the drug in a controlled and reproducible manner [5, 6, 7].

Different methodologies have been reported in the literature to increase the gastric retention of drugs, like intra-gastric floating systems, hydrodynamic ally balanced systems, extendable or expandable and super porous biodegradable hydrogel systems. The floating drug delivery systems result in long lasting intra-gastric buoyancy which may not only provide a sustained site specific therapeutic action but also may lead to a reduction in side effects and better patient compliance [8].

Oral delivery of drug is most preferable route of drug delivery due to ease of administration, patient compliance and flexibility of formulation, etc. From immediate release to site specific delivery, oral dosage forms have really progressed. Several difficulties have been faced in designing controlled release systems for better absorption and enhanced bioavailability [9-11]. The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric residence time for dosage form and controlled drug release. Preparation remains buoyant in stomach content due to its lower density than that of gastric fluid. It is well accepted fact that it is difficult to predict the real *in vivo* time of release with solid, oral controlled release dosage forms. Thus drug absorption in gastrointestinal tract may be very short and high variable in certain circumstances. Gastric emptying of floating system would occur in consistent manner with reduce intersubject variability in absorption. On each subsequent gastric emptying, sunken particles will spread out over large area of absorption site, increasing the opportunity for drug release and absorption[1].

Cefadroxil, an antibiotic used in treatment of bacterial infection, has short biological half life (1.5 hrs). It is a semi synthetic cephalosporin intended for oral administration. It is used for urinary and respiratory tract infection. Due to its rapid elimination from the body, frequent dosing is essential [12, 13].

Hence in the present work an attempt is being made to develop and characterize floating microspheres, which after oral administration could prolong gastric residence time and increase drug bioavailability. Other advantages of floating microspheres are[3,4]: Bioavailability enhanced despite first pass effect because fluctuations in plasma drug concentration is avoided, a desirable plasma drug concentration is maintained by continuous drug release. Site specific drug delivery to stomach can be achieved. Superior to single unit floating dosage forms as such microspheres releases drug uniformly and there is no risk of dose dumping.

MATERIALS AND METHODS

Chemicals:

Cefadroxil was obtained as a gift sample from Covalent Pharmaceuticals Pvt. LtD., All the other chemicals were purchased from S.D chemicals.

Compatibility studies:

The compatibility of Cefadroxil with different excipients was tested using FT-IR Spectrophotometer.

Preparation of Gastro retentive Cefadroxil Tablets by Direct Compression Method

Floating tablets are prepared by direct compression. The various Polymers like, Eudragit RLPO and Eudragit RSPO were used. All the ingredients are passed through sieve no. 40. Required quantity of each ingredient is taken for each specified formulation and all ingredients were mixed. Aerosil and magnesium stearate were then passed through mesh no.60 mixed and blended with initial mixture. The resulting mixture is compressed into tablet using 16 station rotary press.

Table 1: Formulation Design of Gastro Retentive Tablets of Cefadroxil using Eudragit RSPO

Formulation code/Chemicals	FC1 (mg)	FC2 (mg)	FC3 (mg)	FC4 (mg)	FC5 (mg)	FC6 (mg)	FC7 (mg)	FC8 (mg)	FC9 (mg)	FC10 (mg)
Cefadroxil	500	500	500	500	500	500	500	500	500	500
Eudragit RSPO	50	75	100	125	150	175	200	225	250	300
Sodium CMC	20	20	20	20	20	20	20	20	20	20
Sodium alginate	50	50	50	50	50	50	50	50	50	50
Magnesium stearate	10	10	10	10	10	10	10	10	10	10
PVP K 30	25	25	25	25	25	25	25	25	25	25
Aerosil	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Sodium bicarbonate	100	100	100	100	100	100	100	100	100	100
Citric acid	100	100	100	100	100	100	100	100	100	100
Microcrystalline cellulose	287.5	262.5	237.5	212.5	187.5	162.5	137.5	112.5	87.5	37.5
Total	1200	1200	1200	1200	1200	1200	1200	1200	1200	1200

Table 2: Formulation Design of Gastro Retentive Tablets of Cefadroxil using Eudragit RLPO

Formulation code/Chemicals	FC11 (mg)	FC12 (mg)	FC13 (mg)	FC14 (mg)	FC15 (mg)	FC16 (mg)	FC17 (mg)	FC18 (mg)	FC19 (mg)	FC20 (mg)
Cefadroxil	500	500	500	500	500	500	500	500	500	500
Eudragit RLPO	50	75	100	125	150	175	200	225	250	50
Sodium CMC	20	20	20	20	20	20	20	20	20	20
Sodium alginate	50	50	50	50	50	50	50	50	50	50
Magnesium stearate	10	10	10	10	10	10	10	10	10	10
PVP K 30	25	25	25	25	25	25	25	25	25	25
Aerosil	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Sodium bicarbonate	100	100	100	100	100	100	100	100	100	100
Citric acid	100	100	100	100	100	100	100	100	100	100
Microcrystalline cellulose	287.5	262.5	237.5	212.5	187.5	162.5	137.5	112.5	87.5	287.5
Total	1200	1200	1200	1200	1200	1200	1200	1200	1200	1200

Evaluation of Cefadroxil Gastro Retentive Tablets:

The Formulated Tablets were evaluated for weight variation, Hardness, Frability, Content uniformity, and in-vitro drug release.

Weight Variation:

20 tablets were selected randomly from the lot and weighted individually to checked for weight variation. The weight variation test was performed and the weights of the tablets were between 1148 to 1153 mg , As the weight of the tablet is 1200 mg.

Hardness and Friability (F)

Hardness or tablet crushing strength is the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester and the friability was tested using a roche friabilator.

Content Uniformity:

Ten tablets were randomly selected and tested for their drug content. Each tablet was powdered and to it 10 ml of 0.1 N Hcl was added and the resulting solution was measured for its absorbace at 233 nm using a UV-Visible spectrophotometer.

Raft strength measurement by Texture Analyzer

The raft strength of the most satisfactory formulation (batch F_5) was determined by a sophisticated instrument called Texture Analyzer (Brookfield QTS).

Powder of tablets equivalent to unit dose was transferred to 150 ml of 0.1 N HCl and maintained

at 37°C in a 250 ml glass beaker. The raft was allowed to form around an L-shaped wire probe (diameter: 1 mm) held upright in the beaker throughout the whole period (30 min) of raft development. After 30 min of raft development, the probe was pulled vertically up through the raft at a rate of 30 mm/min. The force required to pull the wire probe up through the raft was recorded by the Texture Analyzer.

***In-vitro* Release Studies**

The invitro drug release studies were carried out in an USP Type II (Paddle) dissolution apparatus to stimulate the physiological conditions of the GIT. The medium used for dissolution is 0.1N Hcl with a pH of 1.2.The volume of the medium in the dissolution apparatus was maintained at 900ml.The stirring rate was 50 rpm and the temperature was maintained at 37± 0.5^0C.Aliquots of dissolution medium were withdrawn at predetermined time intervals and the same volume of medium was replaced to maintain the constant volume.

RESULTS AND DISCUSSIONS

Compatibility Study: From the FT-IR study the drug was found to be compatible with all the excipients.

Micromeritics Properties: Cefadroxil powder blends were free flowing as indicated by the values of bulk density(0.39 to 0.59 gm/cc),Tapped density(0.44 to 0.68 gm/cc), Hausners ratio(1.049 to 1.22), Compressibility index (11.36 to 31.6 %) and the Angle of repose ranged from 24.28 ^{0} to 30.42^0 . The values are given in **table 3.**

Table 3: Micromeritics Properties of the Powder of Blend

Formulation code/Parameter	Bulk density	Tapped density	Angle of repose	Hausners Ratio	Compressibility index
F1	0.446±0.10	0.56±0.01	25.74	20.35±0.02	1.25±0.01
F2	0.48±0.11	0.637±0.20	24.28	24.6±0.02	1.32±0.01
F3	0.478±0.21	0.586±0.06	26.06	18.43±0.01	1.22±0.01
F4	0.469±0.11	0.561±0.08	27.4	16.39±0.02	1.19±0.021
F5	0.462±0.09	0.539±0.02	26.72	14.46±0.03	1.16±0.01
F6	0.451±0.02	0.565±0.06	25.65	20.17±0.01	1.25±0.01
F7	0.50±0.01	0.625±0.04	28.17	20±0.021	1.25±0.02
F8	0.52±0.005	0.55±0.03	29.24	15.45±0.02	1.057±0.01
F9	0.45±0.002	0.55±0.02	30.42	18.18±0.01	1.22±0.01
F10	0.53±0.002	0.62±0.05	28.24	16.120±0.02	1.19±0.01
F11	0.41v0.004	0.47±0.02	28.94	12.76±0.01	1.14±0.01
F12	0.39±0.001	0.44±0.06	29.48	11.36±0.025	1.12±0.02
F13	0.43±0.004	0.49±0.05	26.72	12.24±0.01	1.14±0.01
F14	0.52±0.01	0.55±0.01	29.24	15.45±0.036	1.057±0.01
F15	0.45±0.05	0.55±0.05	30.42	18.18±0.021	1.22±0.02
F16	0.52±0.04	0.57±0.06	29.24	16.45±0.018	1.049±0.02
F17	0.45±0.02	0.55±0.05	28.42	18.18±0.026	1.22±0.01
F18	0.52±0.01	0.62±0.05	28.24	16.120±0.014	1.19±0.01
F19	0.446±0.02	0.560±0.06	26.35	36.5±0.017	1.25±0.01
F20	0.480±0.03	0.560±0.04	28.28	31.1±0.062	1.16±0.01

Post Compression Evaluation parameters of formulated GRT's:

Cefadroxil gastro retentive tablets were uniform in weight (1197 to 1202 mg),The hardness of all the tablets was found to be between 5.0 to 5.3 kg/cm^2 ,While the friability of the tablets ranged from 0 .09 to 0.72% the tablets had enough hardness and friability to withstand stress and were mechanically stable during handling and transportation. The content uniformity of all the formulations were ranged form 97% to 100% w/w .

The buoyancy floating lag time ranged from 24 to 10 mins and Floating log time showed 24 hrs, concluding the tablets to float efficiently, the raft forming capacity of sodium alginate was analysed and the values were forung between 4.0 to 4.5 thus showing efficient raft formation with the values were tabulated in Table no :4.

Table 4: Post Compressional Parameters of Formulated GRT's

Formulation code/Parameter	Avg. Weight (Mean± S.D) (n=20)	Hardness (kg/cm^2) (n=3)	Friability (Mean±S.D) (n=20)	Raft strength formation	%Drug content (mg)	Buoyancy Lag time (min)	Total floating Time(hrs)
F1	1202±0.1	5.2±0.1	0.21±0.01	4.2±0.2	99.98±0.22	6	24
F2	1200±0.1	5.1±0.2	0.26±0.02	4.2±0.1	99.54±0.11	7	24
F3	1203±0.1	5.0±0.1	0.24±0.01	4.3±0.2	99.62±0.13	8	24
F4	1200±0.2	5.2±0.1	0.12±0.13	4.2±0.2	99.74±0.21	6	24
F5	1198±0.1	5.2±0.1	0.11±0.02	4.3±0.2	99.68±0.15	6	24
F6	1200±0.2	5.2±0.2	0.37±0.015	4.2±0.2	100.02±0.11	6	24
F7	1200±0.1	5.2±0.1	0.32±0.06	4.0±0.3	98.98±0.13	9	24
F8	1196±0.1	5.3±0.2	0.34±0.21	4.0±0.1	99.47±0.12	8	24
F9	1200±0.1	5.2±0.3	0.42±0.19	4.4±0.2	99.23±0.22	6	24
F10	1198±0.1	5.3±0.1	0.10±0.18	4.0±0.3	99.68±0.13	5	24
F11	1200±0.2	5.2±0.2	0.18±0.16	4.1±0.2	99.37±0.16	6	24
F12	1196±0.1	5.0±0.2	0.09±0.01	4.2±0.5	99.76±0.12	7	24
F13	1200±0.1	5.0±0.1	0.12±0.02	4.3±0.2	99.32±0.24	7	24
F14	1204±0.1	5.1±0.1	0.23±0.01	4.2±0.4	99.65±0.21	8	24
F15	1202±0.2	5.0±0.1	0.54±0.02	4.1±0.1	99.34±0.23	7	24
F16	1203±0.1	5.1±0.2	0.72±0.01	4.2±0.2	98.98±0.34	8	24
F17	1197±0.1	5.1±0.1	0.18±0.01	4.2±0.3	98.82±0.01	7	24
F18	1198±0.1	5.2±0.2	0.113±0.02	4.0±0.5	99.12±0.01	6	24
F19	1199±0.1	5.2±0.2	0.18±0.01	4.±0.1	100.02±0.24	6	24
F20	1203±0.1	5.1±0.1	0.31±0.01	4.3±0.2	99.89	6	24

Table 5: *In-vitro* dissolution study of formulations using eudragit RSPO

Formulation code/Parameter	FC1 (%)	FC2 (%)	FC3 (%)	FC4 (%)	FC5 (%)	FC6 (%)	FC7 (%)	FC8 (%)	FC9 (%)	FC10 (%)
1 hr	49.28	45.62	37.55	33.28	30.28	32.54	30.63	28.42	27.66	27.61
2 hr	63.15	67.34	53.17	54.64	44.25	47.37	55.55	36.55	34.37	32.95
4 hr	94.78	77.38	67.52	63.25	57.64	56.18	67.53	47.45	41.22	38.63
6 hr		96.19	78.37	77.37	68.27	79.67	74.61	53.69	49.13	46.18
8 hr			93.16	83.28	74.38	83.14	79.66	74.34	58.15	51.34
10 hr				97.24	88.47	89.96	86.73	82.28	63.67	55.69
12 hr					96.98	94.56	92.77	86.51	69.24	60.24
14 hr						96.62	96.95	91.60	77.69	65.21
16 hr							98.24	96.53	89.34	68.35
18 hr								98.18	92.25	76.85
20 hr									98.55	85.96
22 hr										96.11
24 hr										

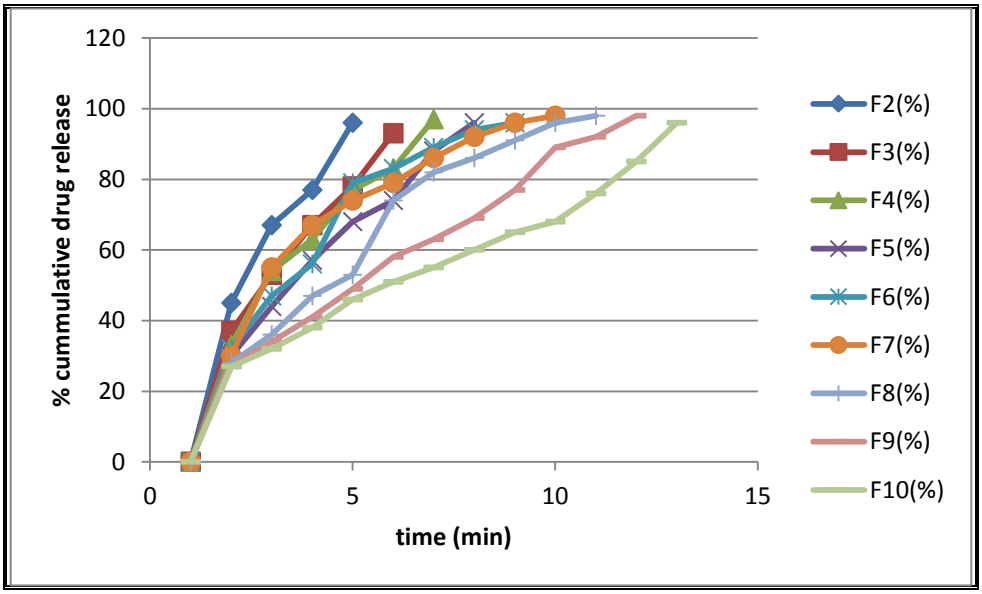

Fig 1: *In-vitro* drug release of formulations using Eudragit RSPO as release rate controlling polymer

Formulations FC1 to FC10 are Formulated with Eudragit RSPO as polymers. Sodium alginate was used as the raft polymer and all the formulation showed raft appearance in the dissolution apparatus. the maximum sustainability of the formulations were observed with FC 10showing 96.11% drug release within 22 hrs. The in-vitro drug release plots were plotted and was shown in table 5 and Fig no 1

Formulations F11 to F20 are Formualated with Eudragit RLPO and combination of eudragit S100,Eudragit RSPO and Euragit RLPO in combination as polymers.Sodium alginate was used as the raft polymer and all the formulation showed raft appearance in the dissolution apparatus. The formulations F11 to F20 were formulated using Eudragit RLPO as the rate controlling polymer, the maximum sustainability of the formulations were observed with F18 showing 98% drug release within 24 hrs. The in-vitro drug release plots were plotted and shown in table 6 and Fig no 2. The formulations F19 was formulated with Eudragit S100 and Eudragit RLPO in combination and it showed a drug release of 96.36 % for 20 hrs. Formulation F20 was formulated with eudragit RLPO it showed a drug release 99.17 % in 24 hrs. It was observed that of all the formulation formulation F18 was observed to be the best polymer with maximum sustainability of the drug release for 20 hrs.

Table 6: *In-vitro* Dissolution Studies of Formulations Eudragit RLPO

Formulation code/Parameter	FC11 (%)	FC12 (%)	FC13 (%)	FC14 (%)	FC15 (%)	FC16 (%)	FC17 (%)	FC18 (%)	FC19 (%)	FC20 (%)
1 hr	**58.17**	**55.24**	**47.22**	**43.56**	**44.18**	**42.15**	**36.54**	**33.21**	**32.63**	**24.84**
2 hr	65.38	68.62	56.54	55.24	58.16	56.78	43.62	38.50	38.54	32.62
4 hr	73.14	77.37	63.29	66.87	66.21	61.36	57.18	46.43	46.76	44.36
6 hr	96.36	93.25	74.55	73.55	72.20	68.54	65.34	52.39	52.54	53.17
8 hr		98.56	85.26	87.25	86.39	75.12	72.66	64.67	58.15	61.52
10 hr			92.65	93.21	95.54	86.39	83.34	76.26	66.65	68.98
12 hr				97.36	98.23	93.65	89.62	83.81	72.23	74.45
14 hr					98.36	96.21	94.87	88.54	83.69	79.87
16 hr						98.78	96.96	92.33	88.45	84.63
18 hr							98.27	95.86	92.16	89.18
20 hr								98.20	96.36	94.63
22 hr										98.54
24 hr										99.17

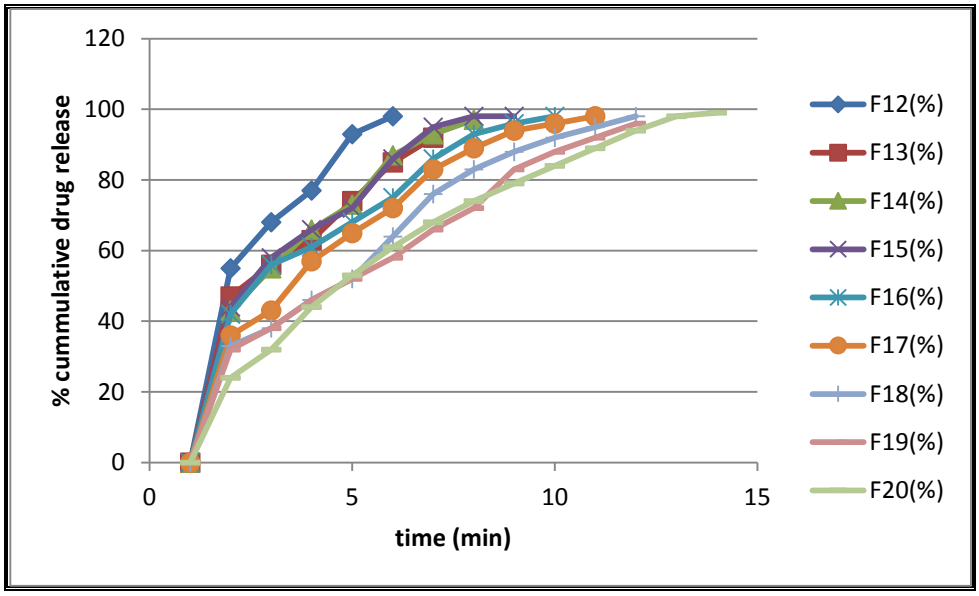

Fig 2: *In-vitro* drug release of formulations using Eudragit RLPO as release rate controlling polymer

CONCLUSION

The present study was aimed to formulate and evaluate control release gastro retentive drug delivery systems of Cefadroxil. Sodium alginate was used as the raft forming polymer, and it showed the good raft formation for all the formulations. The formulations were formulated with, Eudragit RSPO and Eudragit RLPO as rate controlling polymers individually as well as in combination. It was observed that FC20 was found to be the best formulation with 99.17 % drug release for 24 hrs when compared to all formulations. The results were tabulated. It was observed that as the concentration of rate controlling polymer increased there was a gradient decrease in the release of the drug showing good sustainability.

.

REFERENCES

1.Aulton M.E: Pharmaceutics-The sciences of dosage form design, third ed. International student edition., Churchill Living Stone 2007.
2.Benette P.N,Brown M.J: Clinicla pharmacology,2003.
3.Brahmankar D.M, Jaiswal S.B: Biopharmaceutics and Pharmacokinetics. New Delhi ,2003.
4.Chien Y.W and Lin S: Drug Delivery-Controlled Release In Encyclopedia of

Pharmaceutical technology, 2nd edition, Vol- I.
5.Sastry S.V,Nyshadham J.r,Fix J.A.,2002: Recent technological advances in oral drug delivery. Pharmacy science technology today;3:138-45.
6.Shargel L, Andrew BC: Applied Biopharmaceutics and Pharmacokinetics. IV edition. Prentice-Hall International: 139-143.
7.Chein Y.W :Novel Drug Delivery Systems. 2nd edition.
8.Gupta SK, Gupta U, Omray LK,Yadav R, Soni VK. Preparation and characterization of floating drug delivery system of Acyclovir. International Journal of Applied Pharmaceutics. 2010; 2(3): 7-10.
9.Ramesh B, Rongala ASN, Madhusudan RY, Kishan V. Development and evaluation of gastroretentive norfloxacin floating tablets. Acta Pharm 2009;59:211–21.
10. Raghavendra RNG, Pentewar R, Thube k, Suryakar VB**.** Formulation and in vitro evaluation of gastric oral floating tablets of Cefadroxil for controlled release. Res J Pharm Biol Chem Sci 2010;1(3):141-54
11.Jaimini M, Rana A.C, Tanwar Y.S. Formulation and Evaluation of Famotidine floating tablets. *Current Drug delivery*, 2007; 4:51-55.
12.Rahman Z, Ali M, Khar RK. Design and evaluation of bilayer floating tablets ofcaptopril. Acta Pharm.2006; 56:49-57.
13.Raghavendra RNG, Pentewar R, Thube k, Suryakar VB**.** Formulation and in vitro evaluation of gastric oral floating tablets of Cefadroxil for controlled release. Res J Pharm Biol Chem Sci 2010;1(3):141-54.