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Full Length Original Research Paper

Development and Optimization of Cefaclor Gastroretentive Osmotic control release Tablets

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Abstract:
The purpose of this present research work was to development and optimization of different formulations of osmotic control gastroretentive tablets containing Cefaclor. The cefaclor osmotic control gastroretentive tablets was formulated by 3 step process involve core tablet, coating and pore forming. Core tablets were formulated by using different polymers HPMC, polyox and sodium CMC alone and in combination. Initially drug excipients interactions were carried by using FTIR spectra; results showed that there was no interaction. Twelve different formulations of cefaclor osmotic control gastroretentive were prepared and characterized for flow properties and physical properties. Results of these parameters were within the Pharmacopoeial limits. Floating behaviour of all formulations was reported to be less than 100sec of floating lag time and greater than 12hr of duration of floating. F 7 formulation was selected as a optimised based on in vitro drug release studies. It showed the drug release patters similar to that of theoretical release. In vitro dissolution data of all formulation were fit into different kinetic models to know the mechanism of drug release; results revealed that the optimised F 7 formulation gave perfect zero order type of drug transport. Finally, stability studies were performed for optimised formulation and result revealed no significant difference between before and after storage for selected formula.

Keywords: Cefaclor, Osmotic control, gastroretentive, floating behaviour, In vitro drug release, tablets.

Introduction

The oral ingestion is the predominant and most preferable route for drug delivery. Effective oral drug delivery may depend upon the factors such as gastric emptying process, gastrointestinal transit time of dosage form, drug release from the dosage form and site of absorption of drug. Time controlled oral drug delivery systems offer several advantages over immediate-release dosage forms, including the minimization of fluctuations in drug concentrations in the plasma and at the site of action over prolonged periods of time, resulting in optimized therapeutic concentrations and reduced side effects; a reduction of the total dose administered (while providing similar therapeutic effects); and a reduction of the administration frequency leading to improved patient compliance[1-5]. The real issue in the development of oral controlled release dosage form is to extend the duration of action of drug from the small intestine. For the successful performance of oral CRDDS the drug should have good absorption throughout the GIT, preferably by passive diffusion[6].

The real challenge in the development of a controlled drug delivery system is not just to sustain he drug release but also to prolong the presence of the dosage form in the stomach or the upper small intestine until all the drug is completely

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released in the desired period of time (1–2). The residence of a drug delivery system in the upper part of the gastrointestinal tract (GIT) can be accomplished by several drug delivery systems, such as 1. Intragastric floating systems with low density providing sufficient buoyancy to float over the gastric contents which are two types a) Non effervescent systems (Hydrodynamically balanced systems (HBS), intragastric floating drug delivery device, floating tablets and floating Microballoons), b) Effervescent systems or Gas generating systems (Tablets, Beads, volatile liquid containing systems, Intragastric osmotically controlled systems, raft-forming systems or *in situ* gels, low-density systems). 2. Bioadhesive systems having the adhesion dosage form to gastric mucosa enabling the localized retention of the system in the stomach. 3. High-density systems, which remaining in the stomach for longer period of time, by sedimenting to the folds of stomach. 4. Super porous hydrogels. 5. Modified shaped systems and 6. Magnetic systems[7-12].

Among all the above approaches gastroretentive osmotically driven system hold a prominent place because of their reliability and ability to delivery the contents at predetermined zero order rates for prolonged periods. The osmotic pressure generated in the core induces release of the drug in solution at a slow but constant rate. To gain the advantages of pH and agitation independent release performance leading to similar in vitro/in vivo delivery, these systems effectiveness in the treatment of chronic conditions, reduced side effects, and greater patient convenience due to simplified dosing schedule[13-15].

Cefaclor is a broad spectrum semi-synthetic, β-lactamase-stable antibiotic in the second generation of the cephalosporin class. It has an oral bioavailability of 75% and short biological half life (1-2 hr). Cefaclor shows incidence of antibiotic-associated colitis, which might have been caused by the high concentration of antibiotic entering the colon. To avoid the drug absorption in the colon gastro-retentive dosage form would be required to ensure drug delivery within drug-absorbable intestinal regions. Cefaclor had higher absorption in the proximal region of the GI tract and poor absorption, as well as antibiotic-associated colitis, when a large amount of drug entered the colon suggest it is an ideal candidate for a gastroretentive drug-delivery system that will prolong the gastric residence time of the dosage form, giving prolonged drug release in the upper GI tract, where absorption of Cefaclor is well confined. Cefaclor is an antibiotic, in order to get the constant rates of plasma concentration (zero order rates) it need to administer in the osmotically controlled systems. The purpose of present research work was to development and evaluation of new gastroretentive osmotic controlled release delivery system using floating and osmotic tablet technology for cefaclor[16].

MATERIALS AND METHODS

Materials: Cefaclor was obtained as a gift sample from Aurobindo Pharma Ltd., Hyderabad, HPMC K100M, HPMC K15M and HPMC K4M were kindly gifted by Dr.Reddy's Laboratories, Hyderabad. Polyox WSR and polyox coagulant were obtained from MSN Laboratories Pvt. Ltd., Hyderabad. HPMC E50 and HPMC E15 were collected from Mylan Pharmaceuticals Private Limited, Mumbai. All other materials and solvents used were of analytical grade or pharmaceutical grade.

Experimental Methods:

Drug-excipients interactions

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Fourier Transform Infrared Spectroscopy (FTIR): FTIR spectra of drug, placebo tablet (with all excipient except drug) and optimized tablet were obtained on a JASCO FTIR 5300, Japan. Samples were prepared by mixing with KBr and placing in the sample holder. The samples were scanned from 4000 to 500 cm^{-1} [17-19].

Formulation of Cefaclor gastroretentive osmotic control release tablets:

Formulations of cefaclor gastroretentive osmotic control release tablets entail 3 steps process. First core tablets was prepared by passing all the ingredients through the 60 sieve, mix the cefaclor, polymers, osmotic agent (dextrose/sodium chloride/sucrose) uniformly as shown Table 1. Wet granules were prepared with PVP in IPA as a binding agent and using 14 meshes, and then dried at room temperature to get dried granules. Dried granules were passed through the 12 mesh and blended with gliadent and lubricant. The blend was then compressed into tablets using a 16 station rotary tablet punching machine fitted with 10 mm round standard concave punches.

These core tablets were coated by compression coating with a gelling agent (HPMC-K4M) and gas generating agent (Sodium bicarbonate). About one third quantity of coating formulation is placed in die cavity (10 mm diameter), core tablet was carefully positioned in the centre of the die cavity, then filled with the remainder of the coat formulation. It was compressed around the core tablet using 12 mm round concave punches. Finally an appropriate size orifice (500 µm) was made on coated tablets using microdrill[19-21].

Table 1: Composition of cefaclor osmotic control gastroretentive tablets

Formulations	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
CORE TABLET COMPOSITION (mg)												
Cefaclor	375	375	375	375	375	375	**375**	375	375	375	375	375
Dextrose	50	100	150	200	150	150	**150**	150	150	150	150	150
SCMC	40	50	60	70	40	40	**40**	40	40	40	40	40
HPMC K100M	-	-	-	-	20	-	**-**	-	-	-	-	-
HPMC K15M	-	-	-	-	-	20	**-**	-	-	-	-	-
HPMC K4M	-	-	-	-	-	-	**20**	-	-	-	-	-
Poly ox wsr-08	-	-	-	-	-	-	**-**	20	-	-	-	-
Poly ox coagulant	-	-	-	-	-	-	**-**	-	20	-	-	-
HPMC E50	-	-	-	-	-	-	**-**	-	-	20	-	-
HPMC E15	-	-	-	-	-	-	**-**	-	-	-	20	-
HPC	-	-	-	-	-	-	**-**	-	-	-	-	20
PVP	25	25	25	25	25	25	**25**	25	25	25	25	25
Talc	6	6	6	6	6	6	**6**	6	6	6	6	6
Mg. stearate	12	12	12	12	12	12	**12**	12	12	12	12	12
MCC	92	32	32	2	32	32	**32**	32	32	32	32	32
TOTAL	**600**	**600**	**660**	**690**	**660**	**660**	**660**	**660**	**660**	**660**	**660**	**660**
COATING MATERIAL (mg)												
HPMC K4M	140	140	140	140	140	140	**140**	140	140	140	140	140
Sodium bicarbonate	60	60	60	60	60	60	**60**	60	60	60	60	60
Talc	2	2	2	2	2	2	**2**	2	2	2	2	2
TOTAL	**202**	**202**	**202**	**202**	**202**	**202**	**202**	**202**	**202**	**202**	**202**	**202**

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Evaluation

Flow properties of core tablet granules

Angle of repose: The angle of repose of granules was determined by fixed funnel method, where accurately weighed granules were carefully poured through the funnel with its tip at 2-cm height, h, until the apex of the conical heap so formed just reached the tip of the funnel. The mean diameter of the base for the powder cone was measured and the angle of repose (θ) was calculated using the equation, Tan θ = h/r Where, h, r and θ are the height, radius and angle of repose of the powder pile[22].

Bulk density and tapped density: Accurately weighed 3 g of the core tablet granules were transferred in to the measuring cylinder of bulk density apparatus.

Carr's index: The carr's index of the powder was determined by using formula:

$$\text{Carr's index (\%)} = ((TD - BD) \times 100)/TD$$

Where, BD is the bulk density and TD is the tapped density.

Hausner's Ratio: Hausner found that the ratio Tapped density/ Bulk density was related to interparticle friction and, as such, could be used to predict powder flow properties[23-25].

Physical characters of cefaclor osmotic control gastroretentive tablets

Thickness: Thickness of the cefaclor osmotic control gastroretentive tablets were measured by using screw gauge. Ten tablets from each formulation were randomly selected and used. Thickness is expressed in millimeters.

Hardness: The hardness of the tables was measured using the Pfizer hardness tester. Six tablets from each formulation were randomly selected and used. The average hardness and the standard deviation were calculated. It is expressed in Kg/cm2.

Friability: Friability of formulated tablets were determined by taking 10 tablets randomly, weighed and placed in the Roche Friabilator. The apparatus was rotated at 25 rpm for 4 min. After revolutions the tablets were dedusted and weighed again. The percentage friability was measured using the formula,

$$\% \text{ Friability} = \frac{\text{Initial wt. of tablets} - \text{Final wt. of tablets}}{\text{Initial wt. of tablets}} \times 100$$

Weight uniformity: Ten tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated.

Determination of drug content: Ten tablets were accurately weighed and powdered. A quantity of the powder equivalent to 375 mg of cefaclor was weighed accurately and extracted in 100 ml methanol by shaking for 20 min. After filtration through whatmann filter paper no.1 and sufficient dilution with 0.1 N HCl, samples were analyzed spectrophotometrically. Amount of drug present was determined from the calibration curve of cefaclor in 0.1 N HCl[26-30].

In vitro floating behavior

The in vitro buoyancy behavior was characterized by buoyancy time and duration of buoyancy (n = 6). The test was performed using USP 23 dissolution apparatus II was 900 ml of 0.1N HCl at paddle speed 100 rpm at 37°C ± 0.5°C. The time required for the tablet to rise to the surface of the dissolution medium and the duration of time the tablet constantly floated on the dissolution medium were noted as buoyancy time and duration of buoyancy respectively.

Dimensional Stability and *In Vitro* Dissolution Studies

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The dimensional stability and in vitro dissolution of the formulations was studied using USP 23 dissolution Apparatus II for the period of 12hr. The dissolution medium was 900ml of 0.1N HCL (1.2 pH). The temperature was maintained at 37 ± 0.5°C at 50 rpm. The dimensional stability of cefaclor formulations were observed visually and in dissolution studies10ml of aliquot were withdrawn at predetermined time intervals of every one hour. The medium was replaced with 10ml of fresh 0.1N HCl each time. Sample was analyzed by using UV spectrophotometry.

Mechanisms of *In Vitro* Drug Release studies

The dissolution profile of all the batches was fitted to zero-order, first-order, Higuchi, Hixon-Crowell and Korsmeyer and Peppas using R-analysis.

First data was fitted in to zero-order equation

$$Q = k0t$$

Where Q is the amount of drug released at time t, and k0 is the release rate constant, fitted to the first order equation

$$\ln (100–Q) = \ln 100 – k1t$$

Where k1 is the release rate constant. The dissolution data was fitted to the Higuchi's equation.

$$Q = k2\ t1/2$$

Where k2 is the diffusion rate constant.

The dissolution data was also fitted to the well known equation (Korsmeyer equation), which is often used to describe the drug release behavior from polymeric systems.

$$\log (Mt/M\infty) = \log k + n \log t$$

Where Mt is the amount of drug released at time t, M∞ is the amount of drug release after infinite time, k is a release rate constant incorporating structural and geometric characteristics of the tablet and n is the diffusional exponent indicative of the mechanism of drug release[30-35].

Stability

Stability studies were performed according to ICH and WHO guidelines. Optimized formulations were strip packed in laboratory in aluminum foil with polyethylene lamination and various replicates were kept in the humidity chamber maintained at 45°C and 75% RH and 37°C for 3 months. At the end of studies, samples were analyzed for the drug content, in vitro dissolution, floating behavior and dimensional stability[36.37].

Results and Discussion

Cefaclor is a broad spectrum antibiotic with less oral bioavailability of 75%, short biological half life (1-2 hr) and better absorption form upper part of GIT. Plasma concentrations of antibiotic with zero order were needed to maintain for prolonged period in order to control the disease. So cefaclor was formulated in the osmotic control gastroretentive tablets.

First drug- selected excipient interactions were determined by using FTIR spectra. The FTIR spectra of plain drug, physical drug excipient mixture and Placebo were depicted in figure 1. The characteristic peaks of pattern followed the same trajectory as that of the drug alone with minor difference due to dilution effect indicated that there is no drug excipient interaction.

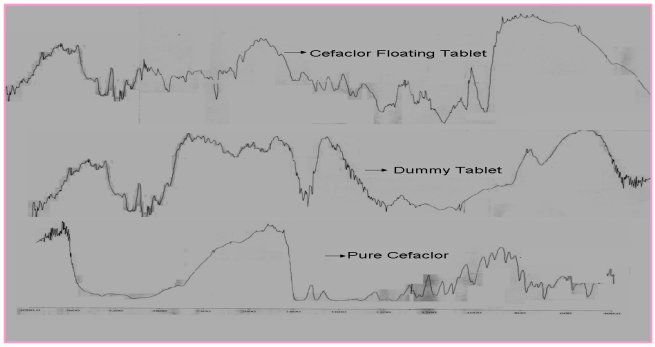

Figure 1: FTIR spectra of (A) Plain Cefaclor Drug (B) Placebo tablet (tablet with only excipients) (C) F 7 formulation

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Flow properties of core tablet granules: Granules flow is a complicated matter and is influenced by so many interrelated factors. Therefore, the granules of different formulations were evaluated for angle of repose, bulk density and tapped density, compressibility index and hausner's ratio and their values were shown in Table 2. The bulk density and tapped bulk density values ranged from 0.32 ± 0.35 & 0.38 ± 0.42 to 0.42 ± 0.03 & 0.48 ± 0.04 respectively. The results of angle of repose and compressibility index (%) ranged from 16.70 ± 0.89 to 22.29 ± 1.21 and 8.68 to 17.66 respectively. The results of angle of repose (<30) and compressibility index (<22) indicates fair to passable flow properties of the powder mixture. Finally, optimized formulation F 7 that were proven to be acceptably flowing according to either the angle of repose, carr's index and hausner's ratio were compressed into tablets and subjected for further evaluation.

Table 2: Flow properties of cefaclor osmotic control gastroretentive core tablet granules

Formulations	Angle of repose (Θ)	Bulk density (gm/cc^3)	Tapped density	Carr's index (%)	Hausner's ratio
F1	16.70 ± 0.89	0.32 ± 0.35	0.39 ± 0.40	17.66	1.21
F2	21.57±1.20	0.42±0.02	0.48±0.04	11.04	1.12
F3	19.42±0.72	0.40±0.04	0.46±0.02	13.75	1.15
F4	18.37±0.42	0.40±0.02	0.47±0.02	14.52	1.16
F5	22.29±1.21	0.42±0.03	0.46±0.03	8.68	1.09
F6	19.19±0.75	0.39±0.03	0.46±0.02	14.23	1.16
F7	18.21±0.69	0.41±0.02	0.48±0.01	15.46	1.18
F8	20.00±0.96	0.40±0.05	0.46±0.04	13.31	1.15
F9	22.28±1.34	0.39±0.01	0.46±0.05	15.44	1.18
F10	19.20 ± 0.34	0.36 ± 0.39	0.42 ± 0.39	14.55	1.17
F11	18.10 ± 0.91	0.32 ± 0.38	0.38 ± 0.42	15.31	1.18
F12	20.18±0.91	0.41±0.01	0.48±0.01	13.92	1.16

Physical characters of cefaclor osmotic control gastro retentive tablets: Formulated cefaclor osmotic control gastroretentive tablets were subjected for their post compression parameters. In weight variation test, the Pharmacopoeial limit for the tablets of not more than 10% of the average weight. The mean hardness of every formulation was determined and results were kept in Table 3 and proving that all the osmotic tablet formulations had acceptable hardness.

The entire the cefaclor osmotic control gastroretentive tablets had acceptable friability as none of the tested formulae had percentage loss in tablets weights that exceed 1% also, no tablet was cracked, split or broken in either formula. Since all the prepared formulae met the standard friability criteria, they are expected to show acceptable durability and withstand abrasion in handling, packaging and shipment. The drug content uniformity for all the osmotic formulations was found to be in the limits too.

Osmotic control gastroretentive tablets of 12 batches had floating lag time below 100 seconds as shown in table 4 regardless of viscosity and content of polymers because of evolution of CO_2 resulting from the interaction between sodium bicarbonate and dissolution medium (0.1N HCl); entrapment of gas inside the hydrated polymeric matrices enables the dosage form to float by lowering the density of the matrices. It was

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reasoned that as for HPMC content of 10% or more, the particles of HPMC are close enough to permit a faster establishment of the gel layer inside which the CO_2 gas gets entrapped leading to decreased density ultimately leading to floating of the tablet. Duration of floating for the HPMC and other polymers based formulations were above 12 hrs.

Table 3: Physical characters of cefaclor osmotic control gastroretentive tablets

Formulations	Weight Variation (mg)	Hardness (Kg/cm2)	Thickness (mm)	Friability (%)	Drug Content (%)
F1	802 ± 3.23	4.3 ± 0.38	5.01 ± 0.02	0.35 ± 0.02	98.33 ± 1.11
F2	812 ± 4.61	4.6 ± 0.43	4.82 ± 0.01	0.44 ± 0.04	98.34 ± 1.92
F3	862 ± 2.66	5.5 ± 0.84	4.91 ± 0.05	0.41 ± 0.03	96.26 ± 1.49
F4	885 ± 3..84	4.8 ± 0.47	5.22 ± 0.03	0.48 ± 0.02	98.89 ± 1.08
F5	612 ± 3.63	5.6 ± 0.63	4.59 ± 0.02	0.36 ± 0.02	99.89 ± 1.37
F6	792 ± 2.67	4.7 ± 0.42	4.80 ± 0.07	0.29 ± 0.05	99.63 ± 1.67
F7	811 ± 3.02	5.3 ± 0.38	4.81 ± 0.06	0.63 ± 0.07	99.35 ± 2.53
F8	795 ± 3.32	5.0 ± 0.33	4.75 ± 0.04	0.71 ± 0.09	97.52 ± 1.75
F9	804 ± 2.59	5.3 ± 0.27	4.69 ± 0.03	0.52 ± 0.02	98.99 ± 1.52
F10	815 ± 2.38	5.0 ± 0.55	4.91 ± 0.02	0.77 ± 0.03	95.76 ± 1.91
F11	809 ± 2.95	6.3 ± 0.51	4.89 ± 0.04	0.59 ± 0.04	98.77 ± 1.76
F12	807 ± 2.55	4.7 ± 0.57	5.09 ± 0.06	0.49 ± 0.07	96.83 ± 1.09

Table 4: Floating behavior of cefaclor osmotic control gastroretentive tablets

Formulations	Floating Lag Time (sec)	Duration of Floating (hr)
F1	72 ± 2	> 12
F2	81 ± 4	> 12
F3	80 ± 3	> 12
F4	78 ± 2	> 12
F5	73 ± 5	> 12
F6	84 ± 3	> 12
F7	78 ± 2	> 12
F8	80 ± 4	> 12
F9	77 ± 5	> 12
F10	82 ± 2	> 12
F11	80 ± 3	> 12
F12	81 ± 2	> 12

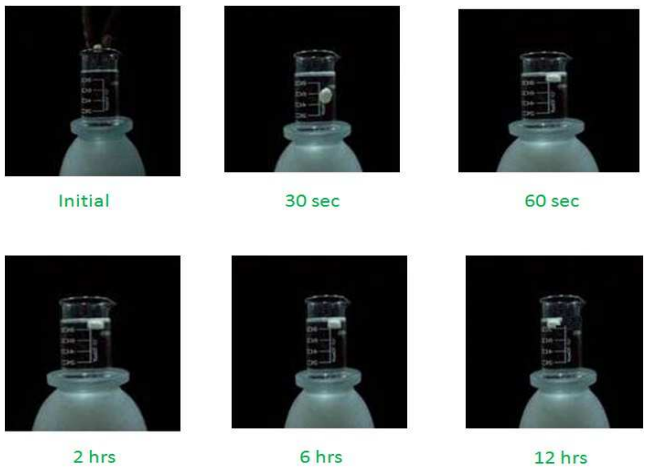

Figure 2: Floating behavior of optimized formulation F 7

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Dimensional stability and In vitro dissolution studies:

First coating composition was optimized by using different trial and error batches and selected composition was used for further studies. Initial cefaclor osmotic control gastroretentive tablets F 1 to F 4 were tried with the different concentration of dextrose as osmotic agent and sodium CMC as polymer in which as a concentration of osmotic agent and polymer increases with decrease in cumulative amount of drug release as shown in the figure 3 & 4. F 3 formulation showed near theoretical drug release but not accurate. So that partial amount of sodium CMC was replaced with gel forming polymer like different grades of HPMC and polyox polymer from formulations F 5 to F 12. Formulation F 7 gave the best results in terms of floating behavior (buoyancy lag time 78 ± 2 seconds, duration >12 hours), and release the drug same as the theoretical value calculated in accordance with dose calculation. The amount dissolved at 1, 4, 8 and 12 hours should be 8.12 ± 0.37%, 34.58 ± 0.69%, 66.26 ± 0.88%, and more than 99% as show in the figure 4 respectively.

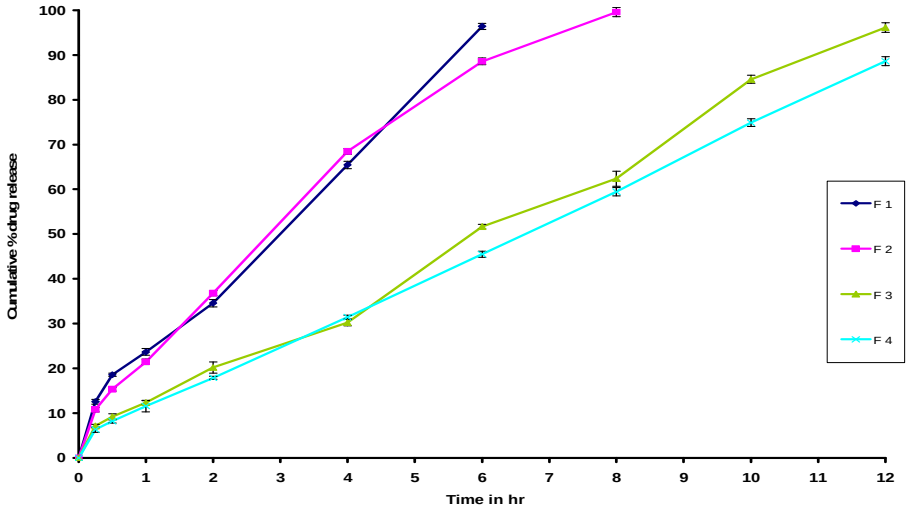

Figure 3: Dissolution data of cefaclor osmotic control gastroretentive tablets from F 1 to F 4

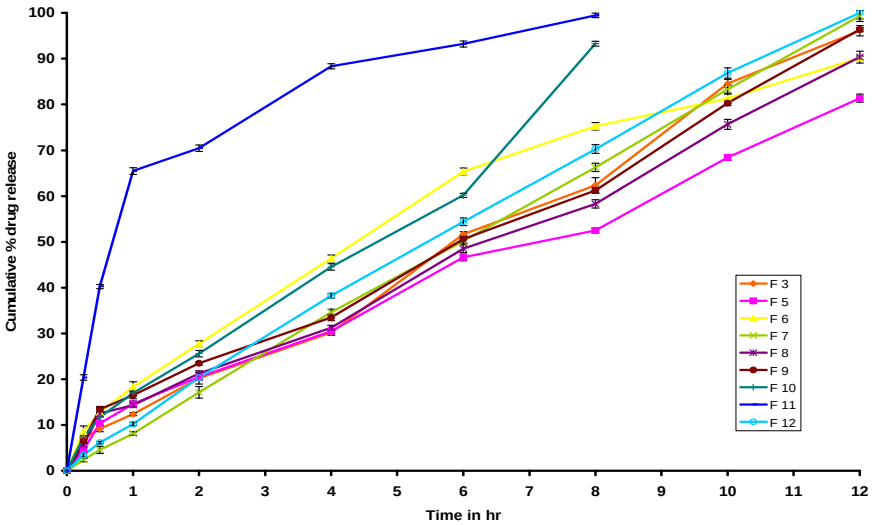

Figure 4: Dissolution data of cefaclor osmotic control gastroretentive tablets from F 3, F 5 to F 12.

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Mechanisms of *in vitro* drug release studies: To analyze the cefaclor osmotic control gastroretentive tablets release mechanism from all formulations, in vitro release data were fitted into various kinetic models like first order, zero order, higuchi and korsmeyer and peppas. The results are shown in Table 5 and graphs in figure 3 to 6 of optimized formulation F 7. For optimized formulation F 7 showed zero order release with fairly linear as indicated by their high regression values (r2 = 0.9998) shown in Figure 5-8. To confirm the exact mechanism of drug release from optimized formulation, the data were presented in higuchi's and peppas equation. Results revealed that F 7 formulation follows the zero order transport mechanism based on the slope value in peppas model and regression coefficient value in higuchi's model.

Table 5: Mechanisms of *in vitro* drug release studies from all batches

MODEL		Formulations											
(R^2)		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Zero order		0.9886	0.9714	0.9939	0.9981	0.9894	0.9595	0.9998	0.9922	0.9906	0.9850	0.7226	0.9978
First order		0.8721	0.8608	0.8567	0.9247	0.9518	0.9898	0.7291	0.9027	0.8220	0.8284	0.9415	0.5942
Korsmeyer and peppas	r	0.9701	0.9899	0.9711	0.9795	0.9857	0.9962	0.9994	0.97774	0.9784	0.9860	0.8863	0.9991
	n	0.623	0.676	0.692	0.700	0.683	0.627	0.972	0.661	0.642	0.699	0.412	0.881
Higuchi's		0.9463	0.9644	0.9373	0.9281	0.9219	0.9304	0.9401	0.9204	0.9177	0.9066	0.9257	0.9389

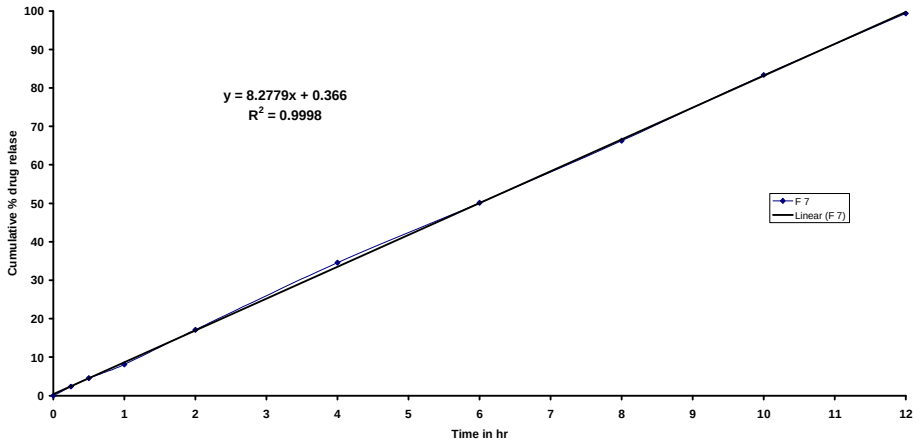

Figure 5: zero order release kinetics of optimized formulation F 7

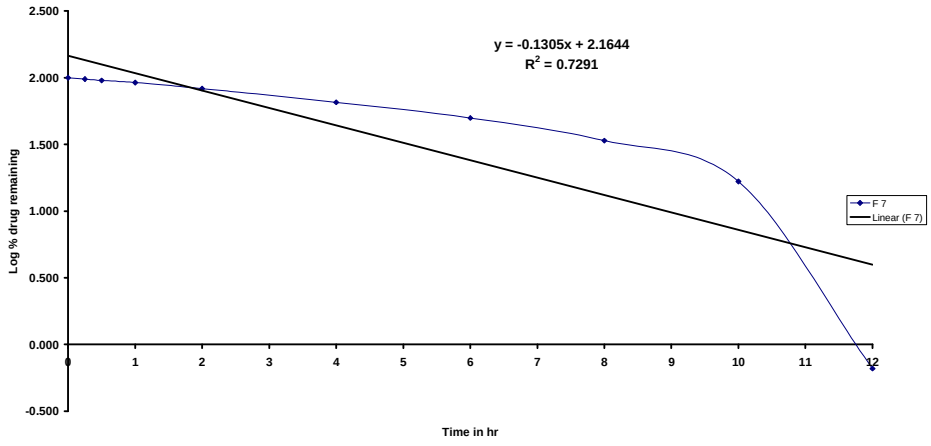

Figure 6: First order release kinetics of optimized formulation F 7

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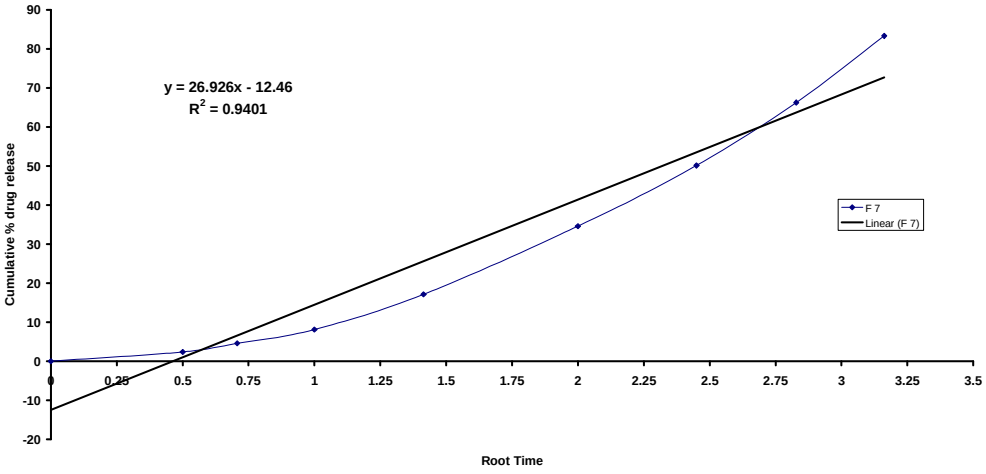

Figure 7: Higuch model release kinetics of optimized formulation F 7

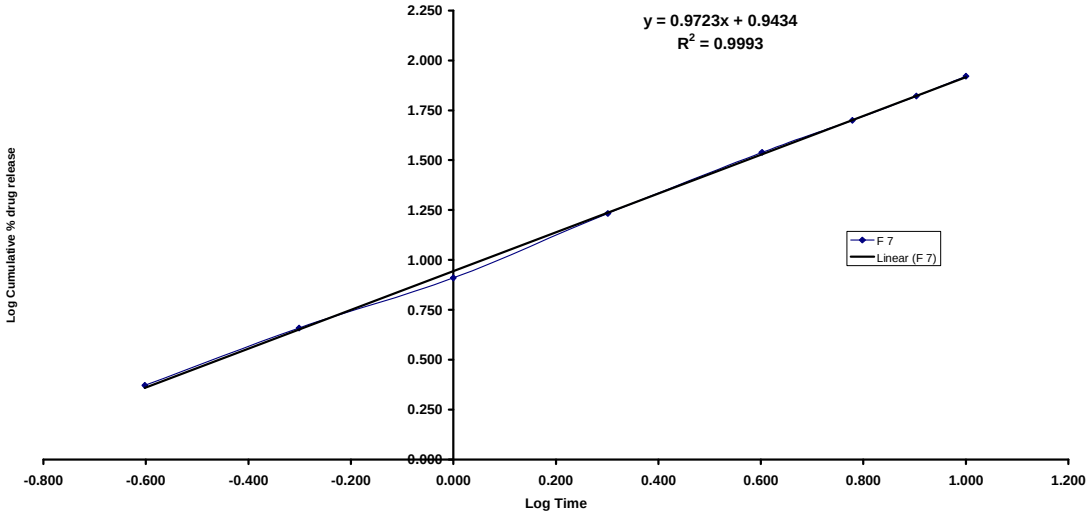

Figure 8: Peppas model release kinetics of optimized formulation F 7

Stability studies: Optimized F 7 formulations were packed in aluminum foil and stored at 45°C and 75% RH for three months to assess their long-term (2 years) stability of cefaclor osmotic control gastroretentive tablets. Drug content, physical and dissolution parameters were estimated before and after storage. The statistical analysis of the parameter of dissolution data (*f*2 = 79.45), buoyancy behavior and drug content before and after storage in the Table 6 and Figure 9 showed no significant change.

Table 6: Stability studies of optimized F 7 cefaclor osmotic control gastroretentive tablets

Parameters		Before storage [a,b]	After storage [a,b]
	Drug content (%)	99.35 ± 2.53	98.58 ± 2.12
	Hardness (kg/cm^2)	5.3 ± 0.38	5.3 ± 0.68
Floating Behavior	Floating lag time (Sec)	78 ± 2	80 ± 3
	Duration of floating (hr)	12	12
Dissolution	Matrix integrity	Very good	Very good
	Similarity factor	89.97 %	

[a] Storage at 45°C/75% RH for three months.
[b] Mean ± SD, *n* = 6

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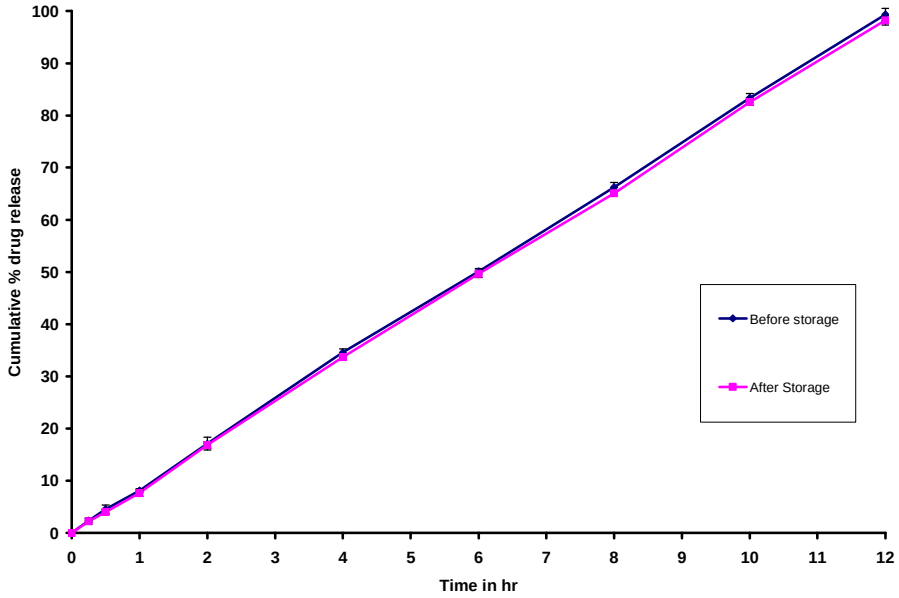

Figure 9: Dissolution data of optimized F 7 cefaclor osmotic control gastroretentive tablets before and after stability studies

Conclusion

Osmotic control gastroretentive tablets containing cefaclor can be formulated successfully by using both osmotic and gastroretentive techniques. The Tablets were subjected to various evaluation parameters such as pre and post compression parameters, floating behavior and in vitro drug release. It was revealed that tablets of all batches had acceptable pharmacopoeial limits. FTIR studies showed that there was no interaction between cefaclor and other excipients used in the formulation. It was found that combination of polymers like HPMC K4M and sodium CMC needed to get the better drug release as that of theoretical value. For F 7 optimized formulation drug release mechanism was found to be zero order transportation. Finally, stability studies were carried out according to ICH guideline which indicates that the selected formulation was stable.

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