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FORMULATION AND EVALUATION OF GASTRORETENTIVE ORAL DOSAGE FORM OF CEFUROXIME AXETIL TABLETS

S.Ravichandran [1] and S.Selvakumar[2*]

[1]P.S.V. College of Pharmaceutical Science and Research, Orappam Village, Bargur (Tk), Krishnagiri (Dt), Tamilnadu –635108, India.
[2]Sri Ram Nallamani Yadava College of Pharmacy, Kodikurichi, Tirunelveli (Dt) Tenkasi. Tamilnadu -627804, India.

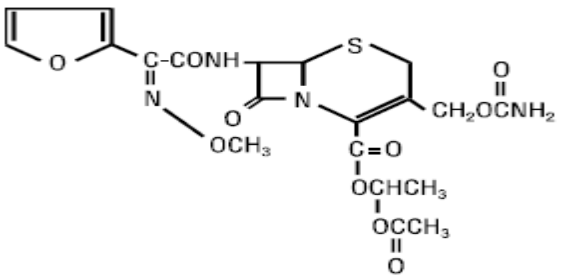
ABSTRACT

The purpose of this investigation was to prepare gastroretentive drug delivery systems of cefuroxime axetil floating tablets by HPMC K4M, K15M and K100M, sodium alginate. Cefuroxime axetil is a second generation cephalosporin with broad spectrum of activity with low bioavailability (32-50%), shorter biological half life (80min). It's better absorption from upper part of gastrointestinal tract. In the preparation of cefuroxime axetil floating tablets sodium bicarbonate was incorporated as a gas generating agent. The prepared tablets exhibited satisfactory physical parameters and good *in vitro* buoyancy. The *in-vitro* drug release of floating tablets followed non fickian diffusion controlled release and are best explained by Korsmeyer Peppas equation. The radiographic pictures in the healthy human volunteers confirm the *in vivo* buoyancy in the stomach for 6h (n=3). Fourier Transformed Infrared Spectroscopy studies of optimized cefuroxime axetil floating tablets showed no drug-excipient interaction.

Key words: Cefuroxime**,** Polymers, Controlled release, Floating tablets.

INTRODUCTION

The oral ingestion is the predominant and most preferable route for drug delivery [1-3]. Effective oral drug delivery may depend upon the factors such as gastric emptying process, gastrointestinal transit time of dosage form [4,5] drug release from the dosage form and site of absorption of drug. Time controlled oral drug delivery systems [6-8]) 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 [9,10] 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 [11]. 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 [12,13]. For the successful performance of oral CRDDS the drug should have good absorption throughout the GIT, preferably by passive diffusion [14,15]. Cefuroxime is a broad-spectrum antibiotic, cefuroxime axetil has saturation kinetics that could be overcome by slow release of drug from the formulation, by incorporating cefuroxime axetil in sustained drug-delivery system. Cefuroxime axetil has 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 cefuroxime is well confined.



Corresponding Author :- Dr.**S.Selvakumar** Email:- drselvakumar59@gmail.com

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The present work is aimed at preparing gastric retentive floating matrix tablet formulations of cefuroxime axetil using various low-density polymers. The composition of these formulations will be selected by using trial and error methods. To study the effect of various factors like drug polymer ratio, drug sodium bicarbonate ratio and polymer grade on the parameters like duration of buoyancy and release rate. To study the effect of different diluents on drug release. Release rate pattern of drug from the designed formulations will be determined and from the obtained data mechanism of drug release will be proposed.

METHODOLOGY

Standard graph of cefuroxime axetil

The calibration curve is based on the spectrophotometry. The maximum absorption was observed at 278nm. It obeyed Beer's law in the concentration range of 4 -24 µg/mL.

Method

Standard stock solution: The stock solution was freshly prepared by dissolving 100 mg of cefuroxime axetil in few ml of methanol (5ml) in a 100ml volumetric flask and then make up the solution upto the mark using 0.1N HCl for obtaining the solution of strength 1000 µg/mL (stock I). 10ml of this solution is diluted to 100ml with 0.1N HCl to obtain a solution of strength 100 µg/mL (stock II). From this secondary stock 0.4, 0.8, 1.2, 1.6, 2.0, and 2.4 mL, was taken separately and made up to 10ml with 0.1N HCl, to produce 4, 8, 12, 16, 20 and 24 µg/ mL respectively. The absorbance was measured at 278 nm using a UV spectrophotometer Systronic, . Standard calibration curve values were shown in Table 2. The standard calibration curve of cefuroxime axetil in 0.1N HCl was shown in Figure 1.

Preparation method of cefuroxime axetil floating tablets

Cefuroxime Axetil (300 mg equivalent to 250 mg of cefuroxime base) was mixed with the required quantities of polymers (HPMC K4M, HPMC K15M, and K100M and sodium alginate), sodium bicarbonate (12%), and lactose by geometric mixing. The powder blend was then lubricated with magnesium stearate (2%) and talc (1%) mixed for about 3 minutes. Finally this mixture was compressed on a 16-station rotary tablet machine Cadmach using a 12-mm standard flat-face punches.

All the formulations contain 1% of talc, 2% of magnesium stearate. Lactose was used as filler in formulations F1 to F16.MCC was used as filler in formulations F17 to F25.All the numerical values were expressed in mg.

Evaluation of tablets

Evaluation was performed to assess the physicochemical properties and release characteristics of the developed formulations. Following parameters were evaluated

Tablet thickness

The thickness in millimeters (mm) was measured individually for 10 pre weighed tablets by using vernier calipers. The average thickness and standard deviation were reported

Weight variation

Twenty (20) tablets from each batch were individually weighed in grams (gm) on an analytical balance. The average weight and standard deviation were calculated and the results were expressed as compliance or non-compliance of set limits.

Tablet hardness

Tablet hardness was measured using a Monsanto hardness tester. The crushing strength of the 10 tablets with known weight and thickness of each was recorded in kg/cm^2 and the average hardness and standard deviation was reported.

Friability

Twenty (20) tablets were selected from each batch and weighed. Each group of tablets was rotated at 25 rpm for 4 minutes (100 rotations) in the Roche friabilator. The tablets were then dusted and re-weighed to determine the loss in weight. Friability was then calculated as percent weight loss from the original tablets.

Content uniformity

The formulated cefuroxime axetil floating tablets were assayed for drug content.

From each batch of prepared tablets, ten tablets were collected randomly and powdered. A quantity of powder equivalent to weight of one tablet was transferred in to a 100 ml volumetric flask, to this 100 ml of methanol was added and then the solution was subjected to sonication for about 2 hours. The solution was made up to the mark with methanol. The solution was filtered and suitable dilutions were prepared with methanol. Same concentration of the standard solution was also prepared. The drug content was estimated by recording the absorbance at 278 nm by using UV-Visible spectrophotometer.

Buoyancy / Floating Test

The *in vitro* buoyancy was determined by floating lag time, as per the method. Here, the tablets were placed in a 100-mL beaker containing 0.1N HCl. The time required or the tablet to rise to the surface and float was determined as floating lag time and total duration of

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time by which dosage form remain buoyant is called Total Floating Time (TFT).

Water uptake studies

The swelling behavior of dosage unit can be measured either by studying its dimensional changes, weight gain or water uptake. The water uptake study of the dosage form was conducted by using USP dissolution apparatus-II in a 900ml of distilled water which was maintained at 37° ± 0.5°c, rotated at 50 rpm. At selected regular intervals the tablet was withdrawn and weighed. Percentage swelling of the tablet was expressed as percentage water uptake (%WU).

%WU = (Wt - Wo) * 100 / Wo

Where Wt is the weight of the swollen tablet and Wo is the initial weight of the tablet.

Dissolution Study of tablets

Apparatus : Dissolution test apparatus (USP XXIII)

Method :USP type 2 apparatus (paddle method)

Dissolution medium	:	0.1N HCl
Volume	:	900 ml
Temperature	:	37 ± 0.5 °C
Speed	:	50 rpm

Procedure

The tablet was placed inside the dissolution vessel. 5ml of sample were withdrawn at time intervals of 60, 120 and 180, 240, 300, 360, 420, 480, 540,600, 660, and 720minutes. The volume of dissolution fluid adjusted to 900 ml by replacing 5ml of dissolution medium after each sampling. The release studies were conducted with 3 tablets, & the mean values were plotted versus time. Each sample was analyzed at 278nm using double beam UV and Visible Spectrophotometer against reagent blank. The drug concentration was calculated using standard calibration curve.

Mechanism of drug release

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics

To study the zero–order release kinetics the release rate data are fitted to the following equation. **$F = K_o.t$**

Where 'F' is the drug release, 'K' is the release rate constant and't' is the release time.

The plot of % drug release versus time is linear.

First order release rate kinetics The release rate data are fitted to the following equation

$Log (100-F) = kt$

A plot of log % drug release versus time is linear.

Higuchi release model

To study the Higuchi release kinetics, the release rate data were fitted to the following equation, **$F = k\, t^{1/2}$**

Where 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model

The release rate data were fitted to the following equation,

$$M_t / M_\infty = K.t^n$$

Where, M_t / M_∞ is the fraction of drug released,'K' is the release constant,'t' is the release time.

'n' is diffusion exponent, if n is equal to 0.89, the release is zero order. If n is equal to 0.45 the release is best explained by Fickian diffusion, and if $0.45 < n < 0.89$ then the release is through anomalous diffusion or nonfickian diffusion (Swellable & Cylindrical Matrix). In this model, a plot of log (M_t/M_∞) versus log (time) is linear. .

***In vivo* confirmation of buoyancy by using radiographic studies**

For this study the tablets were prepared by replacing half of the amount of drug with barium sulfate. After overnight fasting of three healthy volunteers they were fed with low calorie food and allowed to take water after these tablets were administered orally. Radiographs were obtained at 30min, 1h 30min, 4h and 6 h. Over these periods volunteers were allowed to take water.

Fourier transform infrared spectroscopy

The infrared spectra of cefuroxime axetil pure drug, physical mixture of drug and excipients and placebo were recorded between 400 to 4000 cm^{-1}on FTIR. The IR spectra for the test samples were obtained using KBr disk method using an FTIR spectrometer.

RESULTS AND DISCUSSION

The study started with the construction of standard calibration curve of cefuroxime axetil. The λ_{max} of cefuroxime axetil in 0.1N HCl was scanned and found to have the maximum absorbance at 278 nm. Standard graph of cefuroxime axetil in 0.1N HCl was plotted by taking concentration ranging from 4 to 24 µg/mL and a good correlation was obtained with R^2 value of 0.9991. The physical evaluation parameters were also tested. The total weight of each formulation was maintained constant; the weight variation of the tablets were with in the permissible limits of 5%, as specified for tablet weighing more than 325 mg . Weight of the tablet was fixed at 500 mg and the weight variation for every batch was tested and found with in the acceptance limits (Table 3).Hardness of the tablet was fixed 6 kg/cm^2 and was maintained for all the batches in order to minimize the effect of hardness on the drug release

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because, the effect of polymer concentration is the only area of interest.

Tablet thickness was also used to assess the quality of tablets. Under uniform conditions of manufacture, the total weight of tablet and thickness were linearly related. The thickness of floating tablets ranged from 4.01 to 4.84 mm and linearly correlated with the weight of the tablets . Friability test of all the formulations was found satisfactory showing enough resistance to the mechanical shock and abrasion. Drug content uniformity in all formulations was calculated and the percent of active ingredient ranged from 95-98% (Table 3).

Further, the formulated tablets on immersion in 0.1N Hydrochloric acid media they remain buoyant for 12 h with lag time of 120 to 180 seconds. Sodium bicarbonate was added as a gas-generating agent. The optimized concentration of effervescent mixture utilized aided in the buoyancy of all tablets. This may be due to the fact that effervescent mixture in tablets produced CO_2 that was trapped in swollen matrix, thus decreasing the density of the tablet below 1 making the tablets buoyant.. All the batches showed good *in vitro* buoyancy. The results of the *in vitro* buoyancy study of cefuroxime axetil tablets are shown in Figure 2. The figure clearly indicates the floating lag time (2 min) of the cefuroxime axetil tablet and swelling tendency of the formulation. Hydroxypropyl methylcellulose (HPMC) K4M, K15M, K100M and sodium alginate was evaluated varying the sodium bicarbonate portion from 16% to 10%. Finally, lag time was observed less than 3 min for all the formulations and then optimizing the sodium bicarbonate portion at 12% w/w to the total tablet weight. Also the tablet integrity, swelling characteristics were found satisfactory. Floating characteristics like lag time, total floating time for all the formulations were studied and reported .

The *in vitro* dissolution testing was performed and the results of the formulations were expressed (Tables 4 to 10).

The release of cefuroxime axetil was studied using USP dissolution apparatus II. The dissolution media were 900 ml 0.1 N HCl maintained at 37 ± 0.5^0C with rotation speed of 50 rpm. Aliquots of 5 ml was collected at predetermined time intervals and replenished with equivalent volume of fresh medium. The samples were diluted to a suitable concentration with 0.1N HCl and were analyzed by using UV/VIS double beam spectrophotometer at 278 nm. The results are expressed as mean±S.D (n=3).

In vitro dissolution study of formulations F1, F2, F3 and F4 were done in 0.1 N HCl and the percent of drug release from formulations F2, F3 and F4 was 97.97, 80.05, 74.40 in 12 h respectively, formulation F1 unable to sustain the drug release desired period of time but in case of formulation F2, 97.97% of the drug was released in 12 h, this was considered due to different polymer concentrations in all the four formulations. All these four formulations floated for 12 h. Formulations F3 and F4 failed to drug release profile. Formulation F2 obtained the desired drug release profile and floated with a lag time of 120 sec, for these reasons, it was considered as best formulation among all the four formulations.

In vitro dissolution study of formulations F5, F6, F7 and F8, prepared with HPMC K15M were done in 0.1N HCl and the percent of drug release from formulations F6, F7 and F8 was 97.93, 90.91 and 86.25 in 12 h respectively. Formulation F5 unable to sustain the drug release desired period of time. This is because of change in polymer concentrations used in these formulations compared to K4M. Formulations F5, F7 and F8 failed to meet the desired drug release profile. Formulation F6 obtained the desired drug release profile and floated with a lag time of 139 sec, for these reasons it was considered as the best formulation among all the four formulations.

In vitro dissolution study of formulations F9 to F12 were also done in 0.1N HCl and the percent drug released was calculated. These four formulations prepared with K100M. The results indicated that higher viscosity grade of polymer concentrations drug release was retarded greatly. Comparing the three different grades of methocel (K4M, K15M and K100M), it was found that low-viscosity grade methocel K4M provided better-sustained release characteristics with excellent drug release and *in vitro* buoyancy.

The formulations containing sodium alginate F12 to F16 did not show promising results, however least lag time was optimized, but the drug release was poor, this is due to the conversion of sodium alginate to alginic acid in the acidic medium (pH 1.2) producing a tough and rubbery texture to the tablet. The drug release was further inhibited by sodium bicarbonate in the alginate matrices. The results obtained with the alginate matrices were also supported by the literature (16).

The variation in the change of filler on the drug release was minimized by keeping the different filler in the formulations. Formulation F1 to F16 was made with lactose as filler. After incorporation of lactose, the drug release pattern was good and was considered due to the capillary action of lactose, as this facilitated higher drug release without affecting the matrix. In formulations F17 to F25 was made with MCC as filler. The results showed that there is decrease in the drug release when the MCC was used as filler. (Table 8, 9 and 10).

The mechanism of release for the optimized formulations was determined by finding the R^2 value for each kinetic model viz. Zero-order, First-order, Higuchi, and Korsmeyer-Peppas corresponding to the release data of formulations. For most of the formulations the R^2 value of Korsmeyer-Peppas and zero-order model is very near to 1 than the R^2 values of other kinetic models. Thus it can be said that the drug release follows Korsmeyer-Peppas and zero-order model mechanism.

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The n values of Korsmeyer-Peppas model of the best formulations are in between 0.55-0.85. Therefore the most probable mechanism that the release patterns of the formulations followed was non-fickian diffusion or anomalous diffusion.

From this, best formulation from the each polymer (HPMC K4M, K15M) was found to be F2, F6 respectively (Table 11).

The IR spectra of pure drug (Cefuroxime axetil) showed the characteristic absorption peaks at 1661, 1787, 1733 cm^{-1} indicates the presence of C=O. Strong absorption band at 3484cm^{-1} belonging to the 1º amine group (N-H), characteristic band at 1212 cm^{-1}(C=H) (Figure 10). The IR spectra of physical mixture of optimized formulation also showed the above mentioned bands of cefuroxime axetil. So it is concluded that there is no interaction.

SUMMARY

Systematic studies were conducted using four different polymers in different concentrations to prepare cefuroxime axetil floating tablets. All the prepared systems were evaluated for the different properties. Formulated tablets gave satisfactory results for various evaluation parameters like tablet dimensions, hardness and weight variation, floating lag time, floating time, content uniformity and *in vitro* drug release. Comparing the three different grades of methocel (K4M, K15M and K100M), it was found that low-viscosity grades of methocel K4M and K15 provided better-sustained release characteristics with excellent drug release and in-vitro buoyancy. From the above results also indicated that at higher viscosity grades of polymer concentrations drug release was retarded greatly.The formulations containing sodium alginate did not show promising results, however least lag time was optimized, but the drug release was poor, this is due to the conversion of sodium alginate to alginic acid in the acidic medium (pH 1.2) producing a tough and rubbery texture to the tablet. The drug release was further inhibited by sodium .bicarbonate in the alginate matrices.

Table 1. Formulation composition of gastroretentive tablets of cefuroxime axetil

CODE	CA	SBC	HPMC K4M	HPMC K15M	HPMC K100M	S.A	LACTOSE	MCC
F1	300	60	70	-	-	-	55	-
F2	300	60	80	-	-	-	45	-
F3	300	60	90	-	-	-	35	-
F4	300	60	100	-	-	-	25	-
F5	300	60	-	40	-	-	85	-
F6	300	60	-	50	-	-	75	-
F7	300	60	-	60	-	-	65	-
F8	300	60	-	70	-	-	55	-
F9	300	60	-	-	40	-	85	-
F10	300	60		-	50	-	75	-
F11	300	60	-	-	60	-	65	-
F12	300	60	-	-	70	-	55	-
F13	300	60	-	-	-	40	85	-
F14	300	60	-	-	-	50	75	-
F15	300	60	-	-	-	60	65	-
F16	300	60	-	-	-	70	55	-
F17	300	60	40	-	-	-	-	85
F18	300	60	50	-	-	-	-	75
F19	300	60	60	-	-	-	-	65
F20	300	60	-	40	-	-	-	85
F21	300	60	-	50	-	-	-	75
F22	300	60	-	60	-	-	-	65
F23	300	60	-	-	40	-	-	85
F24	300	60	-	-	50	-	-	75
F25	300	60	-	-	60	-	-	65

CA=Cefuroxime axetil; SBC= Sodium bicarbonate; S.A= Sodium alginate; HPMC=Hydroxypropylmethyl cellulose; MCC= Microcrystalline cellulose.

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Table 2. Standard curve for cefuroxime axetil

Concentration	Absorbance
0	0
4	0.182
8	0.326
12	0.466
16	0.622
20	0.793
24	0.940

Table 3. Physical evaluation parameters

Formula code	Weight variation(mg)	Hardness kg/cm2	diameter (mm)	Thickness (mm)	Friability (%)	Drug Content (%)
F1	505±8.3	6±0.5	12±0.02	4.38±0.08	0.26	97.32±2.3
F2	515±3.8	6±0.5	12±0.02	4.02±0.06	0.23	98.56±2.0
F3	501±4.5	6±0.3	12±0.02	4.03±0.06	0.48	98.21±1.8
F4	504±8.3	6±0.5	12±0.02	4.01±0.09	0.51	95.91±1.5
F5	510±5.3	6±0.2	12±0.02	4.26±0.08	0.22	97.75±2.3
F6	505±2.3	6±0.5	12±0.02	4.20±0.05	0.41	96.25±1.8
F7	503±5.5	6±0.5	12±0.02	4.31±0.05	0.35	97.48±2.8
F8	505±5.6	6±0.2	12±0.02	4.14±0.02	0.38	97.69±2.4
F9	502±3.3	6±0.5	12±0.02	4.26±0.02	0.41	97.35±1.7
F10	508±6.2	6±0.3	12±0.02	4.84±0.16	0.29	96.55±2.4
F11	507±4.3	6±0.5	12±0.02	4.40±0.05	0.38	94.48±1.8
F12	505±2.3	6±0.4	12±0.02	4.20±0.09	0.41	95.42±.09
F13	501±2.9	6±0.5	12±0.02	4.32±0.05	0.52	95.99±1.3
F14	505±8.3	6±0.5	12±0.02	4.54±0.02	0.34	98.91±2.8
F15	515±3.8	6±0.4	12±0.02	4.61±0.02	0.45	98.46±3.2
F16	501±4.9	6±0.3	12±0.02	4.36±0.02	0.25	97.41±2.1
F17	504±8.3	6±0.1	12±0.02	4.42±0.02	0.28	97.97±2.6
F18	510±5.3	6±0.2	12±0.02	4.61±0.02	0.39	96.54±2.6
F19	505±2.3	6±0.5	12±0.02	4.64±0.02	0.48	96.33±2.5
F20	503±5.4	6±0.4	12±0.02	4.52±0.02	0.45	96.54±1.8
F21	505±5.6	6±0.3	12±0.02	4.69±0.02	0.31	98.77±2.6
F22	502±3.2	6±0.5	12±0.02	4.72±0.02	0.27	96.33±2.3
F23	508±8.2	6±0.4	12±0.02	4.21±0.02	0.55	97.41±2.1
F24	507±4.3	6±0.2	12±0.02	4.44±0.02	0.38	95.41±1.8
F25	505±2.3	6±0.1	12±0.02	4.54±0.02	0.36	96.54±2.6

Data represents mean ± SD (n=3)

Table 4. Cumulative percent drug release of formulations with HPMC K4M

Sampling time (h)	F1	F2	F3	F4
1	14.49±1.5	31.46±2.1	32.48±1.8	16.45±1.2
2	27.06±1.4	35.70±1.9	36.18±1.6	24.63±1.1
3	33.03±1.2	39.24±1.8	43.25±1.5	33.11±1.5
4	43.25 ±1.3	45.92±2.2	49.53±1.9	37.20±1.4
5	47.17±1.5	49.53±2.4	54.25±1..8	41.60±1.3
6	53.70±1.2	53.22±1.9	59.75±1.9	48.04±1.1
7	56.05±1.4	55.03±1.8	62.89±1.7	53.70±1.3
8	62.10±1.2	66.34±2.1	65.24±1.6	57.39±1.2
9	75.03±1.6	69.64±2.2	68.86±1.9	61.63±1.1

10	89.64±1.3	75.97±2.1	69.06±1.4	64.97±1.4
11	99.07±1.6	90.27±2.2	75.03±1.5	69.68±1.1
12	-	97.97±2.3	80.05±1.7	74.40±1.5

Data represents mean ± SD (n=3).

Table 5. Cumulative percentage drug release of formulations with HPMC K15M

Sampling time (h)	F5	F6	F7	F8
1	30.94±3.2	12.75±1.7	11.19±2.3.	15.51±1.2
2	38.98±3.1	19.08±1.5	17.44±2.1	24.38±1.4
3	52.6±2.9	28.05±1.6	26.02±2.4	33.56±1.6
4	55.68±2.7	35.46±1.8	32.11±2.6	38.92±1.1
5	63.01±3.1	37.65±1.8	37.65±2.3	42.81±1.3
6	72.85±2.8	44.67±1.7	39.91±2.4	52.15±1.4
7	75.93±3.2	51.70±1.4	45.84±2.1	60.62±1.7
8	88.41±3.1	60.12±1.5	58.56±2.5	69.02±1.3
9	93.72±3.4	65.59±1.6	64.81±2.3	71.05±1.2
10	99.96±2.8	71.52±1.8	70.27±2.4	73.65±1.3
11	-	87.48±1.7	73.39±2.3	79.87±1.4
12	-	97.93±1.6	90.91±2.1	86.25±1.3

Data represents mean ± SD (n=3)

Table 6. Cumulative percentage drug release of formulations with HPMC K100 M

Sampling time (h)	F9	F10	F11	F12
1	14.46±2.1	13.99±1.3	12.65±2.1	12.10±1.6
2	21.24±2.6	19.51±1.2	14.38±2.3	13.99±1.4
3	23.68±2.4	29.68±1.4	19.27±2.1	17.69±1.6
4	29.68±2.1	31.4±1.2	23.61±2.2	22.34±1.4
5	31.17±2.3	32.59±1.1	27.86±2.3	24.71±1.3
6	35.75±2.1	34.96±1.3	30.23±2.1	28.65±1.5
7	45.99±2.3	39.29±1.1	32.36±2.3	31.02±1.4
8	53.96±2.2	52.38±1.2	37.24±2.2	34.88±1.5
9	59.40±2.3	55.22±1.4	42.92±2.3	41.66±1.2
10	61.76±1.9	58.61±1.5	47.33±2.4	45.99±1.5
11	66.25±2.1	63.10±1.3	53.01±2.1	50.49±1.7
12	70.98±2.3	66.65±1.2	58.53±2.3	55.25±1.5

Data represents mean ± SD (n=3)

Table 7. Cumulative percent drug release of formulations with sodium alginate

Sampling time (h)	F13	F14	F15	F16
1	12.10 ±1.1	8.94 ±1.1	10.28 ±2.1	8.1 ±1.4
2	18.4 1±1.3	11.86 ±1.0	13.41 ±2.3	9.73 ±1.2
3	25.52 ±1.2	13.14.4±1.2	19.27 ±2.1	11.39 ±1.3
4	31.80 ±1.6	25.18 ±1.2	22.11 ±2.4	17.61 ±1.4
5	38.11 ±1.4	29.36 ±1.4	27.86 ±2.2	26.29 ±1.1
6	40.48 ±1.3	36.30 ±1.2	32.51 ±2.1	31.80 ±1.2
7	46.23 ±1.1	46.23 ±1.4	43.55 ±2.3	41.82 ±1.4
8	50.49 ±1.3	52.85 ±1.1	48.28 ±2.1	46.42 ±1.1
9	59.63 ±1.4	61.45 ±1.05	57.58 ±2.4	55.93 ±1.2
10	61.76 ±1.4	65.47 ±1.09	61.52 ±2.3	59.40 ±1.2
11	69.61 ±1.3	68.78 ±1.1	63.81 ±2.1	60.97 ±1.3
12	76.74 ±1.1	71.69 ±1.2	65.70 ±2.3	63.02 ±1.4

Data represents mean ± SD (n=3)

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Table 8. Cumulative percentage drug release of formulations HPMC K4M with MCC

Sampling time (h)	F17	F18	F19
1	8.60±1.2	8.44 ±1.4	7.11 ±1.1
2	11.51 ±1.4	10.25 ±1.2	9.70 ±1.2
3	20.30 ±1.1	19.91 ±1.3	18.42 ±1.1
4	22.82 ±1.3	22.58 ±1.4	21.17 ±1.2
5	31.70 ±1.1	29.34 ±1.1	27.69 ±1.3
6	39.32 ±1.2	38.22 ±1.4	36.73 ±1.4
7	45.92 ±1.4	44.35 ±1.2	43.48 ±1.1
8	49.45 ±1.2	47.10 ±1.3	45.13 ±1.3
9	57.94 ±1.1	55.82 ±1.5	54.17 ±1.2
10	67.05 ±1.0	65.40 ±1.1	61.55 ±1.2
11	80.05 ±1.3	71.77 ±1.3	63.12 ±1.3
12	84.35 ±1.2	80.05 ±1.4	74.9 ± 1.3

Data represents mean ± SD (n=3)

Table 9. Cumulative percentage drug release of formulations HPMC K15M with MCC

Sampling time (h)	F20	F21	F22
1	8.43±1.2	7.97 ±1.1	7.19 ±1.4
2	10.85 ±1.1	9.68 ±1.2	8.82 ±1.2
3	20.02 ±1.3	16.45 ±1.3	14.27 ±1.3
4	22.51 ±1.2	21.35 ±1.1	18.86 ±1.1
5	31.69 ±1.3	25.86 ±1.0	22.90 ±1.3
6	37.91 ±1.2	35.27 ±1.2	32.93 ±1.1
7	44.13 ±1.3	42.35 ±1.2	39.70 ±1.3
8	47.63 ±1.2	45.85 ±1.3	44.91 ±1.2
9	57.05 ±1.2	54.71 ±1.4	49.27 ±1.1
10	64.90 ±1.1	61.71 ±1.3	55.49 ± 1.2
11	70.03 ±1.0	67.47 ±1.2	62.26 ±1.1
12	77.70 ±1.1	73.81 ± 1.1	70.07 ±1.3

Data represents mean ± SD (n=3)

Table 10. Cumulative percentage drug release of formulations HPMC K100M with MCC

Sampling time (h)	F23	F24	F25
1	8.51±1.5	8.12±1.8	7.5±2.1
2	9.60±1.2	9.91±1.6	8.905±1.9
3	14.42±1.3	13.18±1.7	12.63±1.8
4	16.68±1.4	18.16±1.5	15.75±2.2
5	20.02±1.1	19.25±1.6	19.63±2.1
6	24.30±1.3	22.20±1.5	23.37±2.3
7	31.85±1.2	31.07±1.4	29.05±2.4
8	39.08±1.2	37.99±1.3	35.27±1.9
9	49.19±1.3	48.02±1.4	45.46±1.8
10	54.79±1.4	54.48±1.6	45.85±1.7
11	61.48±1.3	55.80±1.7	49.27±1.8
12	62.30±1.4	60.58±1.7	57.05±1.9

Data represents mean ± SD (n=3)

Table 11. Release kinetics of optimized formulations

S. No.	Formulation	Zero order	First order	Higuchi	Korsmeyer & Peppas	Peppas (n)
1	F2	0.974	0.684	0.898	0.994	0.57
2	F6	0.962	0.503	0.933	0.915	0.75

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Figure 1. Standard graph of cefuroxime axetil.

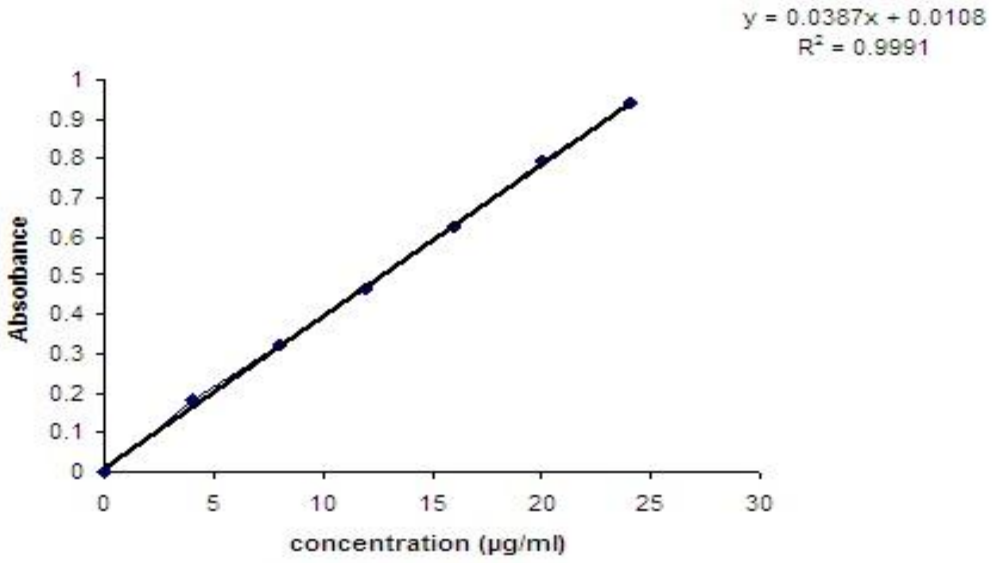
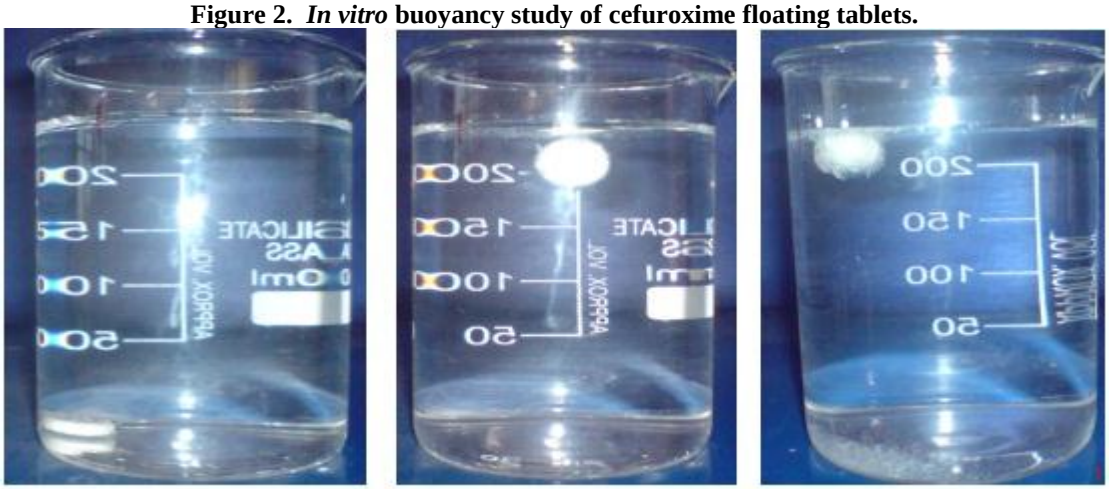
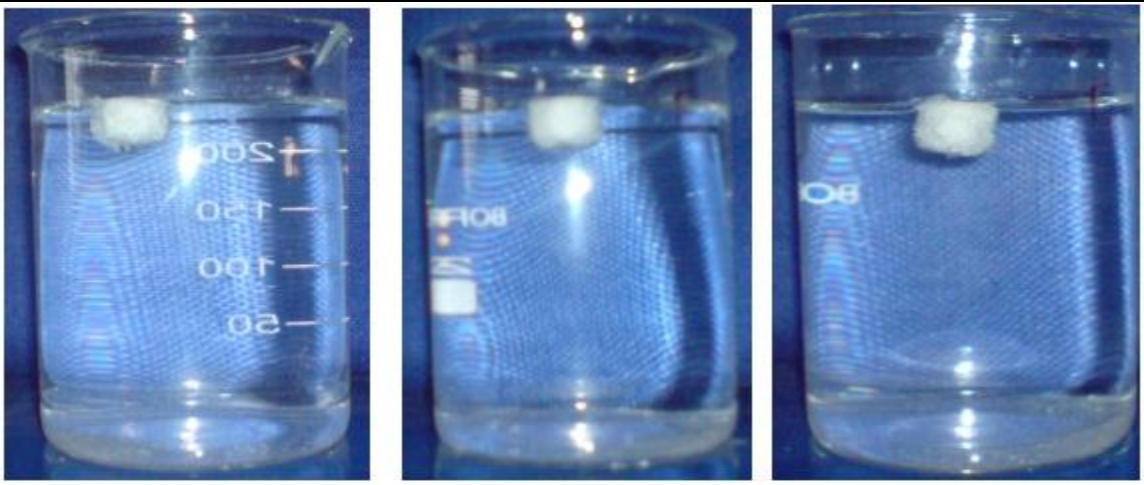


Figure 2. *In vitro* buoyancy study of cefuroxime floating tablets.



0 min **2min** **2h**



4h **8h** **12h**

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Figure 3. Cumulative % drug release of HPMC K4M with Lactose Vs Time.

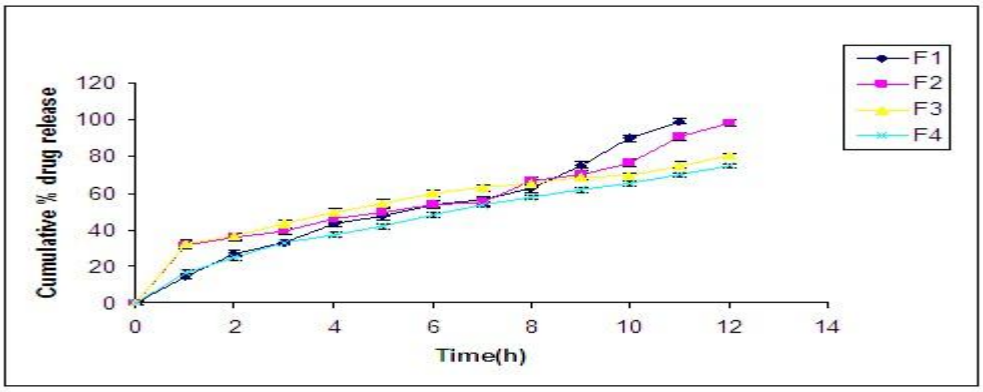

Figure 4. Cumulative % drug release of HPMC K15M with Lactose Vs Time.

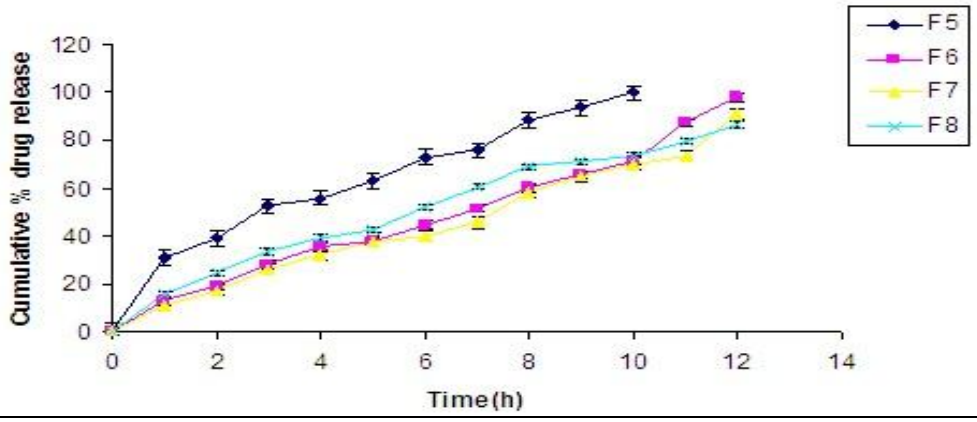

Figure 5. Cumulative % drug release of HPMC K100M with Lactose Vs Time.

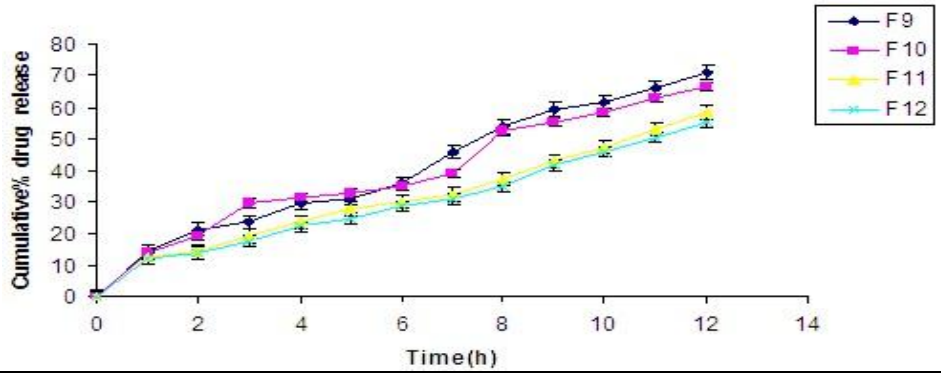

Figure 6. Cumulative % drug release of sodium alginate with Lactose Vs Time.

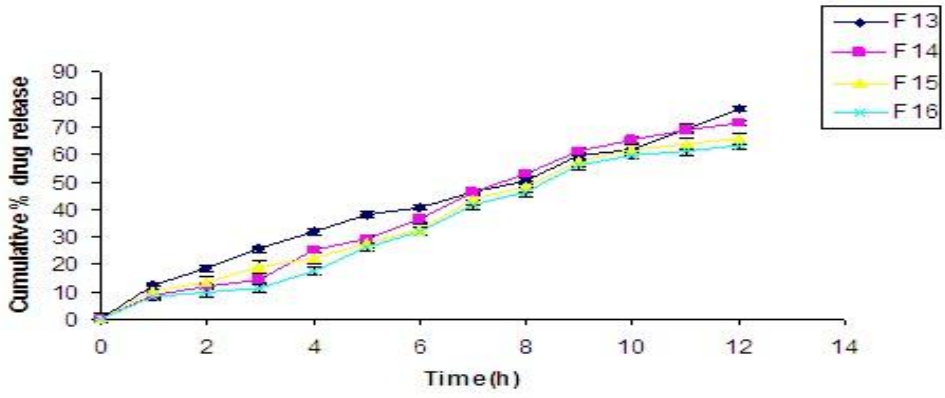

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Figure 7. Cumulative % drug release of HPMC K4M with MCC Vs Time.

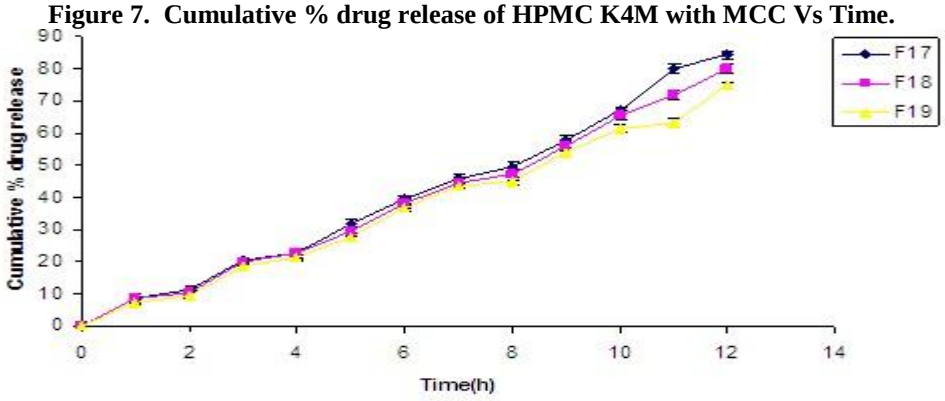


Figure 8. Cumulative % drug release of HPMC K15M with MCC Vs Time.

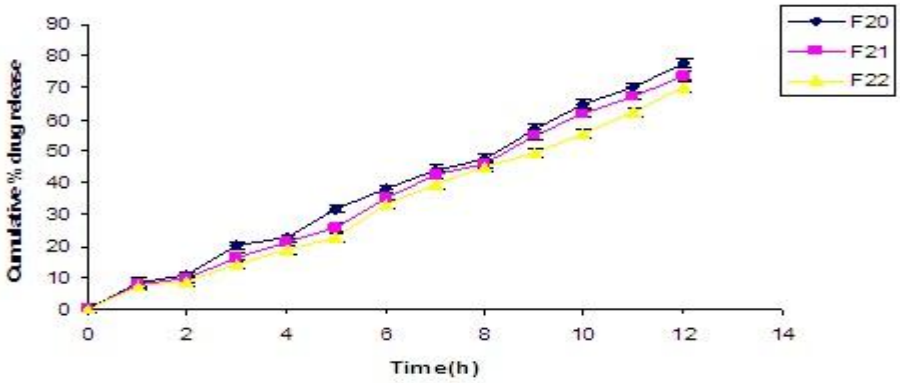


Figure 9. Cumulative% drug release of HPMC K100M with MCC Vs Time.

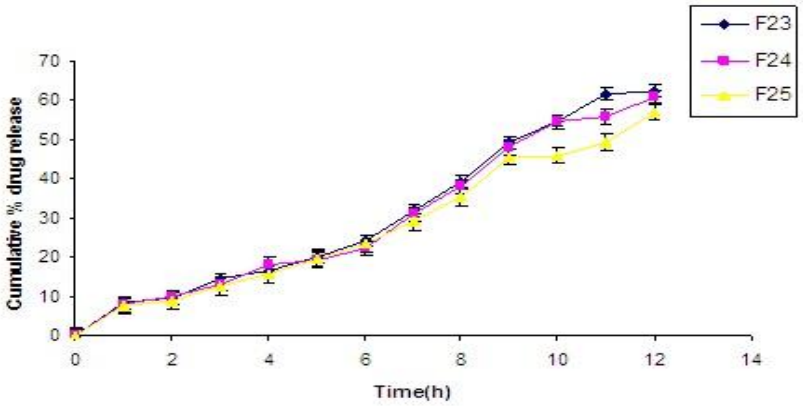
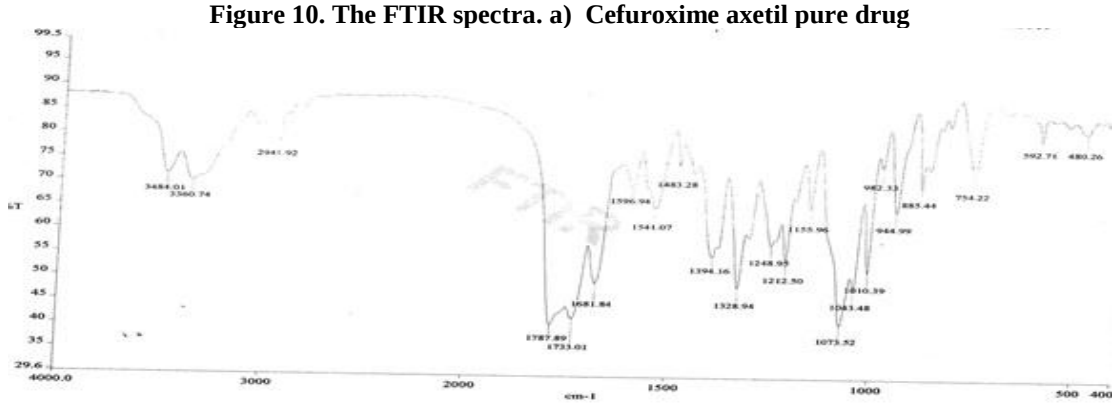


Figure 10. The FTIR spectra. a) Cefuroxime axetil pure drug



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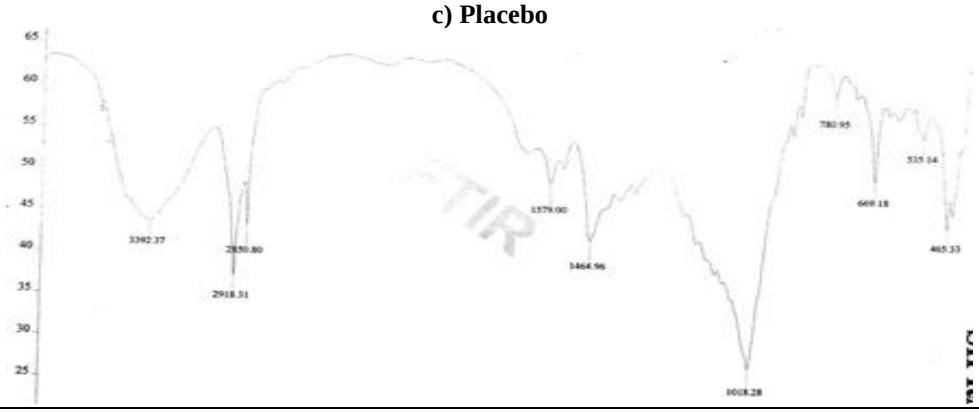
b) Physical mixture of optimized formulation

c) Placebo



CONCLUSION

Floating matrix tablet of cephalosporin antibacterial drug cefuroxime axetil can be formulated as an approach to increase gastric residence time and thereby improve its bioavailability. Formulation F2, F6 gave better-controlled drug release in comparison to the other formulations. Among the polymers used to improve the gastric residence, cellulose polymers HPMC K4M, HPMC K15M showed better control over drug release. The drug release pattern from the optimized formulations was best fitted to Korsmeyer-Peppas model and zero order kinetics.*In vivo* radiographic studies indicated that tablets remained in the stomach for 6h, which indicates the increase in the GRT is due to floating and swelling principle.Drug – excipients interaction of optimized formulations was carried out by using FTIR studies. In this analysis drug – excipients compatibility interactions were not observed.

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