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IMPROVING BIOAVAILABILITY OF CEFUROXIME AXETIL BY INCREASING RETENTION TIME IN STOMACH WITH THE HELP OF NATURAL POLYMER: FORMULATION AND EVALUATION

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ABSTRACT

In the present research, an attempt was made to develop gastric retentive tablets of Cefuroxime Axetil (CA) using PMG (Pomegranate) peel powder as release retarded material. Cefuroxime Axetil (CA) is 1-acetoxyethyl ester of a b-lactamase-stable cephalosporin, cefuroxime with a broad spectrum of activity against Gram-positive and Gram-negative microorganisms. After oral administration CA is absorbed and rapidly hydrolyzed by esterases to produce cefuroxime. The 1-acetoxyethylester group at 4th position of CA ensures lipophilicity and promotes the absorption of cefuroxime but at the same time compromises on solubility and hence, the prodrug shows poor and variable oral bioavailability. CA exists in crystalline as well as amorphous forms; of these, latter exhibits higher bioavailability owing to improved solubility. CA is known to have good absorption from upper parts of GIT. Thus, retaining CA in this region for longer time would be beneficial in improving its bioavailability, which makes CA suitable candidate for formulating it as a gastric retentive dosage form for improved bioavailability. The formulation of floating tablets of CA was prepared by direct compression technique. All ingredients except sodium bicarbonate and magnesium stearate were first sifted. These sifted ingredients were mixed well. Then separately sodium bicarbonate and Magnesium stearate are sifted, the drug was mixed well with sifted sodium bicarbonate and then subsequently mixed with sifted magnesium stearate. The above mixture was compressed on Karnavati mini tab eight-station tableting machine using 12 mm flat faced punch. Floating tablets of Cefuroxime Axetil containing PMG peel powder shows good retention. The sodium bicarbonate and citric acid were used as effervescent agents which shows good effervescence. The tablets prepared were evaluated and found to have acceptable physicochemical properties.

From the present study carried out on CA floating tablets using PMG peel powder as a sustained release polymer and sodium bicarbonate as gas generating agent, the in vitro release data of optimized formulation was treated with mathematical equations and was concluded that drug release followed zero-order kinetics with anomalous transport mechanism. Based on the results it can be concluded that floating tablets of Cefuroxime Axetil containing PMG peel powder provides a better option for sustained release action and improved bioavailability.

KEYWORDS: Floating tablets; Cefuroxime Axetil; Retentive material; GRDDS.

INTRODUCTION

Oral drug delivery is the most favored route among the diverse types of drug delivery systems for systemic effects due to ease of administration, patient compliance, economical and non-invasive methods. Sustained release dosage form releases the drug at a slow rate through the oral route. Hence, it is highly desirable to develop sustained drug

delivery systems, which releases the drug at a predetermined rate to achieve optimal drug levels at the site of action. These systems have disadvantages like non-suitability for the drugs having site-specific absorption in the upper part of the gastrointestinal tract (GIT), precipitation of drug, degradation of the drug in the distal part of GIT. This has resulted in the development of gastro retentive drug delivery systems (GRDDS) which overcomes the disadvantages associated with sustained-release formulations.

Gastric persisting systems swells and retained in the stomach for some hours, while it continuously releases the drug at a controlled rate leading to higher bioavailability, therapeutic efficacy, reduced time intervals for drug administration and thus improved patient compliance. [1] Hence these GRDDS are advantageous for the drugs absorbed mainly from the upper part of GIT having a narrow absorption window and are unstable in the medium of distal intestinal regions. [2] They are even beneficial in the local therapy of the stomach.

In the present study, CA floating drug delivery system was prepared with PMG peel powder as rate retarding material which contains Phenolic compounds like punicalagins, gallic acid, catechin, epigallocatechin gallate, quercetin, rutin, anthocyanidins, other flavonoids being thus neutral polymers. [3]

MATERIALS & EXPERIMENTAL WORK

Materials

Cefuroxime Axetil was received as a gift sample from Lupin Pharma, Aurangabad. Pomegranate peel powder was purchase from Heilen Biopharm. HPMC K4M, Acacia, Sodium bicarbonate, PVP K30, Lactose, magnesium stearate all excipients used are of analytical grades.

Experimental work

Cefuroxime Axetil has good stability, solubility in acidic pH. Tablets were prepared by the direct compression method using PMG peel powder as retardant material.

Preformulation studies

Preformulation studies involve investigation of the physical and chemical properties of a pure drug and with or without excipients. It is the first step in the rational development of dosage forms.

Precompression parameters of powder blends

The formulation of floating tablets of CA was prepared by direct compression technique. All ingredients except sodium bicarbonate and magnesium stearate were first sifted through sieve no. 30. These sifted ingredients were mixed well. Then separately sodium bicarbonate sifted through sieve no. 60. Magnesium stearate sifted through sieve no. 40. The drug was mixed well with sifted sodium bicarbonate and then subsequently mixed with sifted magnesium stearate. The above mixture was compressed on Karnavati mini tab eight-station tableting machine using a round-shaped 12 mm flat faced punch. [6]

Angle of repose

The angle of repose is the maximum angle possible between the surface pile of granules and horizontal plane. A fixed amount of blend was accurately taken and carefully poured through the funnel whose tip was secured at a height of 2.5 cm above the graph paper which is placed on a horizontal surface. The blend was poured until the apex of the conical pile just touches the tip of the funnel. The angle of repose is calculated by the following formula.

$\theta = \tan^{-1}(h/r)$ (1)

Where, θ = angle of repose, r = radius of the pile, h = height of the pile.

Bulk density

Bulk density is defined as the ratio mass of an untapped powder divided by the bulk volume including the inter particulate void space. Apparent bulk density (BD) was determined by pouring the blend into a graduated cylinder. The bulk volume (V) and the weight of the powder (M) were determined. The bulk density was calculated using the formula.

$BD = M/V$ (2)

Tapped density

The tapped density attained after mechanically tapping of graduated measuring cylinder containing the powder sample by raising the cylinder or vessel and allowing it to drop, under its mass. The measuring cylinder containing a known mass of blend was tapped for a fixed time (around 100). The minimum volume (V_t) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (TD) was calculated using the formula,

$TD=M/ (V_t)$ (3)

Compressibility index

The compressibility index is an indirect measure of bulk density, size, and shape, surface area, moisture content and cohesiveness of materials. The correlation between compressibility index and powder flow properties is given in the formula,

CI (%) = Tapped density (TD) – Bulk density (BD) / Tapped density (TD) × 100 (4)

Hausner's ratio

It is an indirect index of ease of powder flow and is measured by the ratio of the tapped density to bulk density.

Hausner's ratio = Tapped density/ Bulk density

(5)

DRUG-EXCIPIENTS COMPATIBILITY STUDIES

Fourier transform infrared (FTIR)

The spectrum analysis of pure drug and physical mixture of drug and different excipients that are used for the preparation of tablets was studied by FTIR. FTIR spectra were recorded by preparing potassium bromide (KBr) disks using a Shimadzu Corporation (Koyto, Japan). KBr disks were prepared by mixing a few mg of a sample with potassium bromide and compressed at 10 tons' pressure. The resultant disc was mounted in a suitable holder in the IR spectrophotometer and the spectrum was recorded from 4000 cm^{-1} to500cm^{-1}.

FORMULATION OF CEFUROXIME AXETILFLOATING TABLETS

Dose calculation [7]

All formulations contain 300 mg of Cefuroxime Axetil per tablet equivalent to 250 mg of Cefuroxime.

Preparation of tablets

The formulation of floating tablets of Cefuroxime Axetil was prepared by the direct compression technique. All ingredients except sodium bicarbonate and magnesium stearate were first sifted through sieve no. 30. These sifted ingredients were mixed well. Then separately sodium bicarbonate sifted through sieve no. 60. Magnesium stearate sifted through sieve no. 40. The drug was mixed well with sifted sodium bicarbonate and then subsequently mixed with sifted magnesium stearate. The above mixture was compressed on Karnavati mini tab eight-station tableting machine using a 12 mm flat faced punch.

Table 1: Formulation of Cefuroxime Axetil floating tablets.

Ingredients	Formulation codes								
(mg/tablet)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Cefuroxime Axetil	300	300	300	300	300	300	300	300	300
PMG Peel powder	70	90	110						
HPMC K4M				70	80	90			
Acacia							50	60	70
Sodium bicarbonate	60	60	60	60	60	60	60	60	60
PVP K30	10	10	10	10	10	10	10	10	10
Lactose	40	40	10	50	40	30	70	60	50
Magnesium stearate	10	10	10	10	10	10	10	10	10
Total	500	500	500	500	500	500	500	500	500

EVALUATION OF CEFUROXIME AXETIL FLOATING TABLETS

The prepared bilayer tablets are evaluated for varied parameters like weight variation, thickness, hardness, friability, [6] drug content, content uniformity and in vitro dissolution studies. [8]

Tablet thickness

The thickness in millimeters (mm) was measured individually for 20 pre-weighed tablets by using Vernier Calipers. The average thickness and standard deviation were reported.

Tablet hardness

Tablet hardness was measured using Monsanto hardness tester. The average crushing strength of the 10 tablets with known weight and thickness of each was reported.

Friability test

Ten tablets were accurately weighed and placed in the friability test apparatus (Roche friabilator), rotated at 25 rpm for 4 minutes. The tablets were taken, dedusted and reweighed. The friability was calculated as the percentage weight loss using Eq. 11. Friability values below 1 % are generally acceptable.

$$\% \text{ Friability} = (W1 - W2) / W1 \times 100 \quad (6)$$

Where, W1 = initial weight of the tablets, W2 = final weight of the tablets

Weight Variation Test

To study weight variation individual weights (W_I) of 20 tablets from each formulation were noted down using an electronic balance. Their average weight (W_A), percentage weight variation was calculated using Eq. 12.

$$\% \text{ Weight variation} = (W_A – W_I) / W_A \times 100 \quad (7)$$

Drug content [9]

Twenty tablets were weighed and taken into a mortar and crushed into a fine powder. An accurately weighed portion of the powder equivalent to 100 mg of Cefuroxime Axetil was transferred to a 100 ml volumetric flask containing methanol. It was shaken by mechanical means for 1hr. Then it was filtered through what man filter paper. From this resulted solution 1 ml was taken, diluted to 10 ml with 0.1N HCl and absorbance was measured against blank at 264 nm using UV-Spectrophotometer. The drug content of the floating tablets meets the requirements if the tablet amount lies within the range of 90% to 110%.

Buoyancy / floating test

The tablet is introduced into a 100 ml beaker containing 0.1N HCl and the time gap between the introduction and time for the tablet to emerge onto the surface of the medium is called “floating lag time”. The total duration of time by which the dosage form remain buoyant is called “Total floating time (TFT)”.

In vitro dissolution studies [9]

The tablet was placed in a dissolution test apparatus USP II, containing 900 ml of 0.1N HCl at a speed of 50 rpm. 5 ml of aliquot was withdrawn for every 1 hr up to 12 hrs and replaced with 5 ml of fresh dissolution medium. Each sample was analyzed at 264 nm using a double beam UV spectrophotometer against reagent blank.

Determination of gastric retention period by x-ray imaging studies

Evaluation of gastric retention of Cefuroxime Axetil sintered floating tablet was performed on the rabbit by the use of radio-opaque marker barium sulfate. X-Ray imaging studies are the non-invasive method, provides identification or monitoring of total GI residence time without affecting normal gastrointestinal motility.

Dose translation was based on Body Surface Area (BSA). The animal dose should not be extrapolated to a Human Equivalent Dose (HED) by a simple conversion based on body weight, as reported.

The rabbit dose was calculated according to the following equation:

$$\text{Animal dose (mg/ kg)} = \text{Human equivalent dose} \times \text{Human Km value} / \text{Animal Km value} \quad (13)$$

Conversion: dose in mg/ kg = dose in mg/ m^2×Km value.

Human (human adult of weight 60 kg) Km value is 37, animal (rabbit weighing 1.8 kg) Km value is 12.

Values-based on data from FDA Draft Guidelines.

Animal dose (mg/ kg) = 4.75 x 37/ 12 = 4.75 x 3.08 = 14.63 mg/ kg.

Rabbit under study was weighing 1.9 kg. So dose = 14.63 × 1.9 = 27.80(28) mg.

Hence the dose for in vivo studies taken was 28 mg. 25% of drug concentration was taken for barium sulfate i.e., so 7.0 mg per each tablet. The formula for in vivo gastro retentive tablet is given in Table 2.

Table 2: The formula for animal dose

S. No.	Ingredients	Quantity is taken (mg)
1	Cefuroxime Axetil	21
2	Barium sulfate	7
3	PMG Peel powder	10.26
4	Sodium bicarbonate	5.6
5	PVP K30	1.0
6	Lactose	1.0
7	Magnesium stearate	1.0
	Total	47

A healthy rabbit of 2.0 kg fasted overnight and on the next day morning, selected tablet (F 3) which was adjusted to rabbit dose and containing barium sulfate in place of cefuroxime Axetil was administered through plastic tubing followed by flushing of 25–30 ml of water. During the entire study, the rabbits had free access to water only. At different time intervals of 0, 1, 2, 4, 6 and 8 hours, rabbit G.I.T. was X-Ray photographed in the supine position and observed for the nature and position of the cefuroxime Axetil floating tablet.

Accelerated stability studies

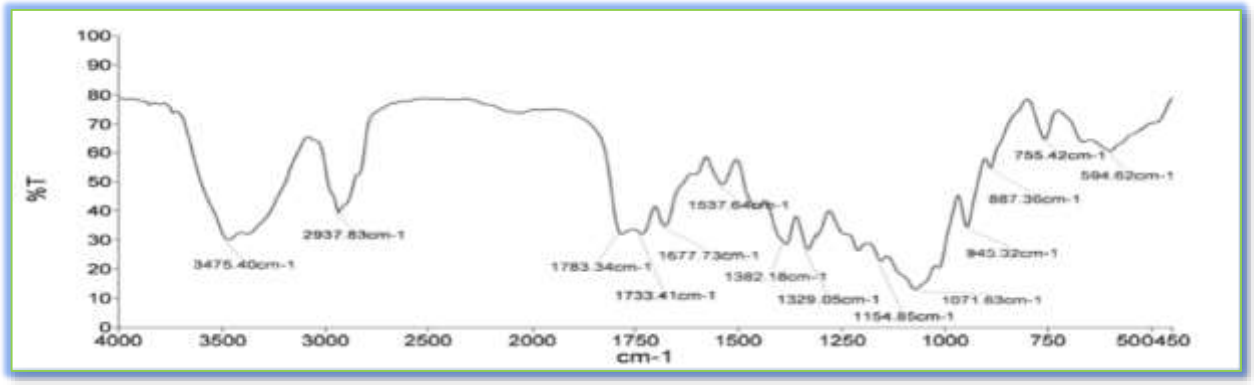
Optimized formulation F 3 was subjected to stability studies at 40 ºC ± 2 ºC/75% ± 5% RH and room temperature analyzed for its physical characteristics, drug content and dissolution every month for one month.

RESULTS AND DISCUSSION

Preformulation studies

Drug-excipients compatibility study by FTIR

(a)



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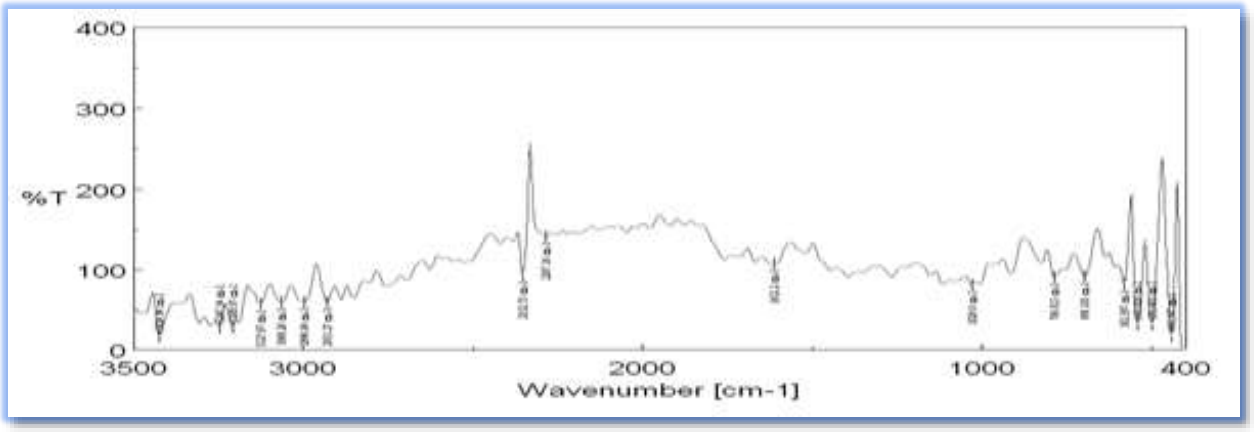

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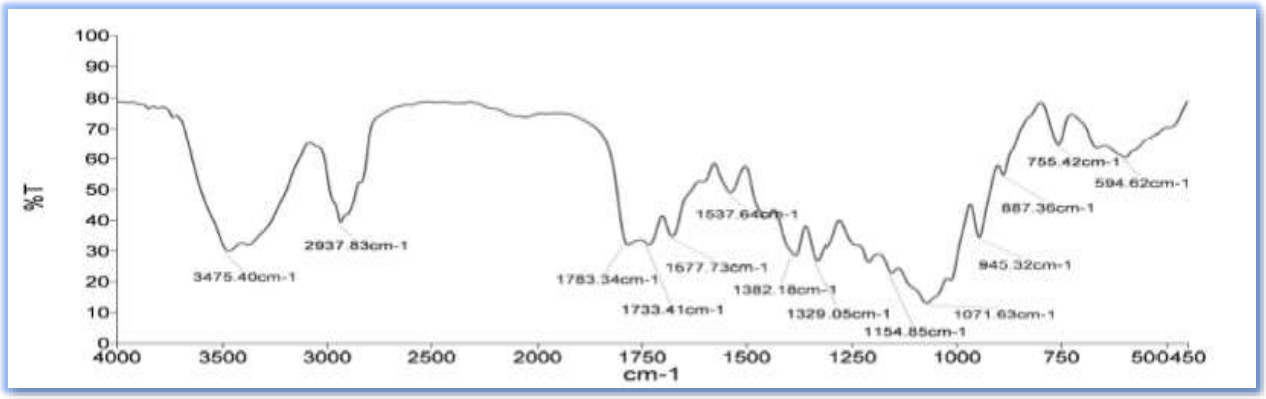


Figure 1: FTIR spectra of (a) Cefuroxime Axetil (b) PMG peel powder and (c) physical mixture of Cefuroxime Axetil and PMG peel powder.

Table 3: Interpretation of Cefuroxime Axetil FTIR scan

S.N.	Peak observed (cm^{-1})	Interpretation
1	2937	C-H stretching(aliphatic)
2	2984	C-H stretching(aromatic)
3	3330	N-H stretching
4	1618	N-H bending
5	1074, 1099	C-O stretching
6	1761	C=O stretching
7	674	C-S-C stretching
8	1274	C-N stretching

From the above IR graphs (Figure 1) the peaks representing the pure drug were similar in all the graphs suggesting that there is no interaction and the pure drug is unaltered when mixed with PMG peel powder.

Evaluation of flow properties

Table 4: Precompression parameters of the powder blends

Batches code	Bulk density	Tapped density	Hausner's ratio	Carr's index	Angle of repose
F1	0.38±0.36	0.43±0.34	1.1±0.32	10±0.34	25.36±0.45
F2	0.39±0.35	0.42±0.34	1.07±0.31	7.24±0.36	25.66±0.45
F3	0.40±0.34	0.44±0.39	1.11±0.33	10±0.35	23.65±0.43
F4	0.40±0.41	0.42±0.35	1.06±0.31	5.71±0.39	26.45±0.44
F5	0.37±0.42	0.40±0.39	1.09±0.35	8.33±0.40	27.88±0.49
F6	0.38±0.44	0.41±0.43	1.07±0.36	7.14±0.41	25.44±0.45
F7	0.40±0.36	0.44±0.36	1.09±0.39	8.45±0.45	25.65±0.44
F8	0.38±0.39	0.42±0.45	1.09±0.33	8.57±0.41	25.44±0.40
F9	0.38±0.41	0.43±0.40	1.1±0.39	10±0.39	28.44±0.39

Values are expressed as mean ±SD, *n = 3.

It was found that the drug and the other powder blends possess the required flow characteristics for direct compression as the values of angle of repose, Hausner's ratio, carr's compressibility index were found to be within flow property limits which are shown in Table 4.

Evaluation of Cefuroxime Axetil floating tablets

Prepared floating tablets were evaluated for hardness, thickness, weight variation, friability and drug content.

Table 5: Evaluations of Floating tablets.

Batches code	Thickness (mm)	Hardness (kg/cm^2)	Friability	Drug content	Average Weight (mg)
F1	4.1±0.36	5.4±0.47	0.44±0.51	96.33±0.54	505±0.56
F2	4.2±0.39	5.3±0.56	0.42±0.52	96.12±0.54	515±0.59
F3	4.1±0.32	7.4±0.54	0.42±0.59	98.12±0.53	501±0.54
F4	4.3±0.35	6.5±0.54	0.45±0.56	95.75±0.49	510±0.58
F5	4.3±0.34	7.3±0.53	0.43±0.59	95.63±0.52	505±0.57
F6	4.4±0.45	6.4±0.59	0.46±0.58	98.23±0.59	515±0.49
F7	4.4±0.48	5.3±0.45	0.48±0.54	99.53±0.56	510±0.41
F8	4.3±0.49	6.3±0.55	0.47±0.51	99.06±0.59	505±0.49
F9	4.2±0.47	4.9±0.59	0.45±0.53	97.31±0.51	505±0.47

Values are expressed as mean ±SD, *n = 3.

The results of hardness, thickness, weight variation, friability and drug content shown in Table 5**.** The hardness of Cefuroxime Axetil floating tablets was found to be in the range of 4.3 – 4.5 $kg/cm^{2.}$ The thickness of the tablets was found to be in the range of 4.10 – 4.40 mm. In the weight variation test, the pharmacopeia limit for the % deviation for the tablets of 324mg and more (USP) is ±5 %. The average % deviation of all the tablet formulations was found to be within the limits. The percentage friability of all the formulations was below 1% indicating that the friability was within the prescribed limits. The drug content values varied between 95.63 – 99.53%. Thus all the parameters of the floating tablets were within compendial standards which are shown in Table 5.

Buoyancy / Floating test

From the results given in Table 7, it is evident that sodium bicarbonate has a significant effect on lag time. Total floating times were increased and floating lag times decreased with the increase in $NaHCO_3$ concentrations. The minimum lag time was found to be 49 Sec. [10] [11]

Table 6: Floating lag time and total floating time of formulations.

Formulation code	Floating lag time (sec)	Total floating time (hrs)
F1	57±0.5	>24
F2	50±0.3	>24
F3	49±0.5	>24
F4	57±0.4	>24
F5	50±0.6	>24
F6	50±0.3	>24
F7	56±0.3	>24
F8	51±0.6	>24
F9	51±0.4	>24

Values are expressed as mean ±SD, *n = 3.

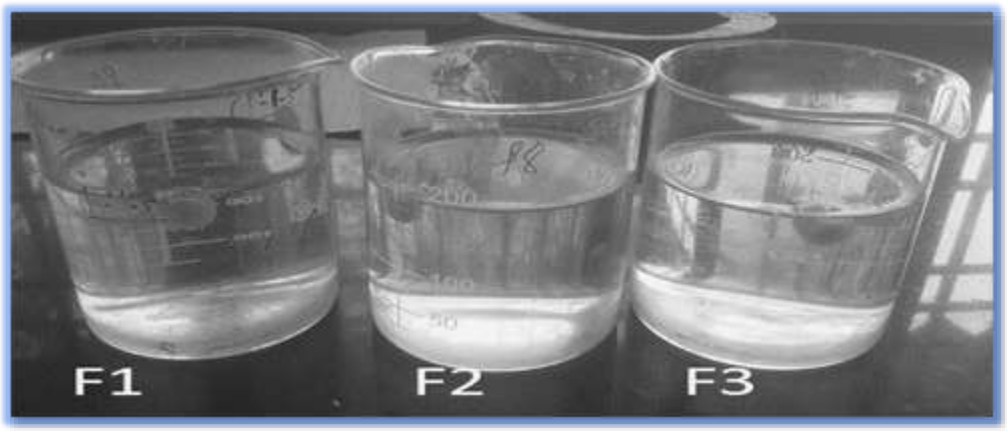


Figure 2: Floating of Cefuroxime Axetil tablets batch F1 optimized batch.

The formulations showing the lag time of less than 49 sec and total floating time of greater 12 hours were selected and subjected to dissolution studies for optimization of floating tablets.

In vitro drug dissolution testing of floating tablets

From the results given in Table 8, the in-vitro drug dissolution of the formulations F1 to F9 is subjected to dissolution studies for further optimization. Fig. 3 shows dissolution profiles.

Table 7: The in-vitro drug release profile for batches F1 to F9:

Time (Hrs)	Cumulative % drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	13.55±0.32	17.24±0.34	18.36±0.32	09.11±0.23	09.55±0.52	12.21±0.65	9.16±0.32	10.32±0.22	20.13±0.53
2	19.33±0.12	23.76±0.42	25.73±0.14	14.41±0.36	12.36±0.65	18.88±0.55	14.45±0.55	15.36±0.12	30.12±0.63
4	23.96±0.63	28.43±0.63	38.63±0.36	20.83±0.35	22.42±0.55	23.44±0.33	18.10±0.54	20.66±0.35	36.88±0.42
6	33.78±0.32	35.33±0.35	49.75±0.52	34.85±0.42	34.08±0.44	37.20±0.36	29.22±0.52	28.66±0.22	47.42±0.36
8	41.55±0.12	45.11±0.31	56.22±0.33	40.26±0.12	38.33±0.45	43.60±0.53	36.22±0.15	29.47±0.47	56.44±0.15
10	57.56±0.32	53.41±0.45	67.43±0.46	49.23±0.63	45.55±0.35	60.33±0.43	45.65±0.15	36.88±0.54	61.44±0.25
12	69.45±0.65	69.21±0.12	78.24±0.11	57.11±0.52	56.33±0.63	69.55±0.26	55.88±0.22	47.33±0.59	74.22±0.55
16	76.66±0.32	75.80±0.25	89.63±0.21	65.64±0.56	70.15±0.32	78.35±0.24	62.66±0.36	58.95±0.56	77.65±0.61
20	84.45±0.25	88.71±0.32	93.82±0.69	76.33±0.64	85.63±0.11	83.66±0.15	70.55±0.44	64.32±0.58	79.55±0.43
24	88.61±0.14	92.45±0.14	98.67±0.44	88.65±0.45	92.66±0.65	94.76±0.59	76.58±0.45	79.55±0.41	83.45±0.25

Values are expressed as mean ±SD, *n = 3.

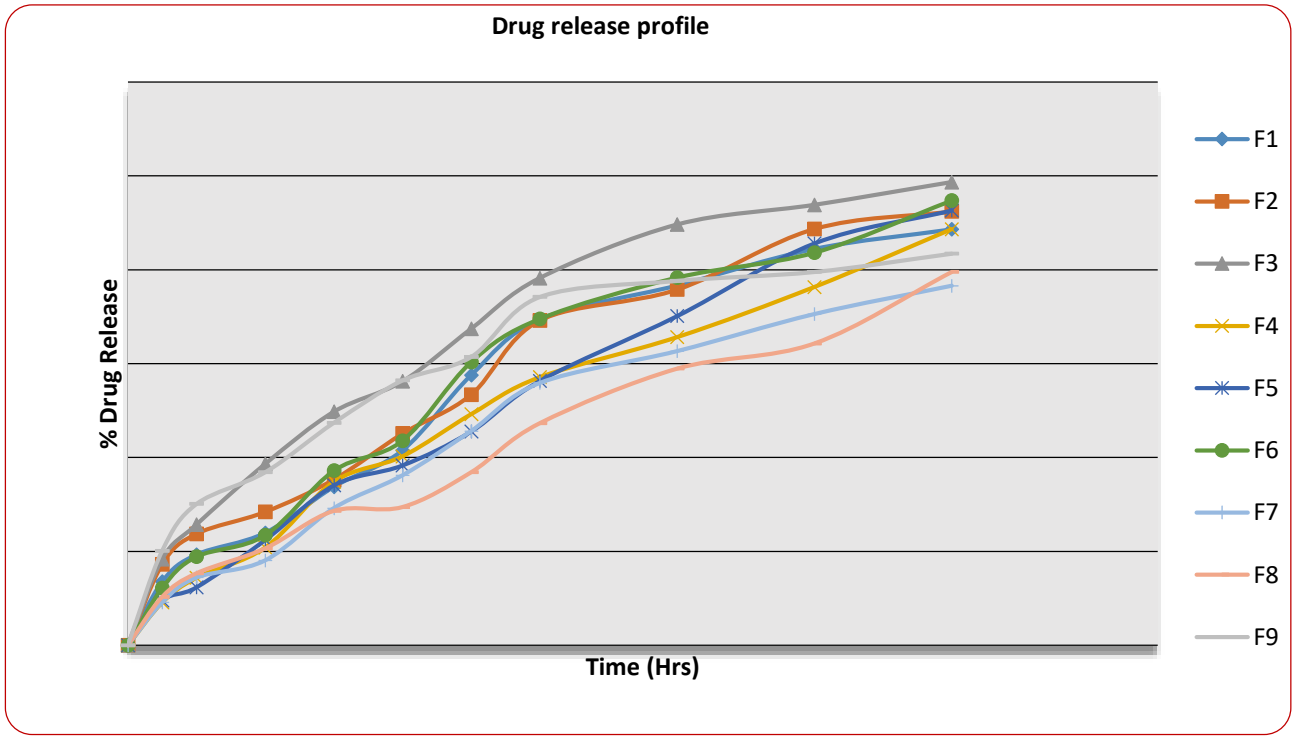


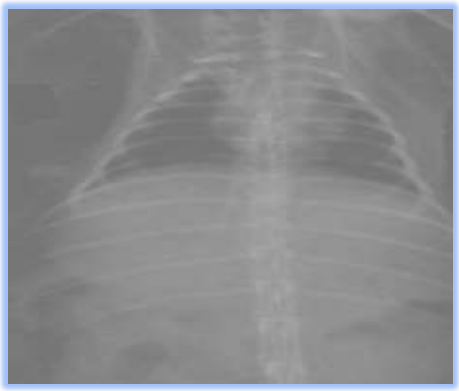
Figure 3: Dissolution profiles of different formulations.

Formulation F3 containing PMG peel powder of 30mg and sodium bicarbonate 55mg has shown sustained release for 24 hrs [12-14]. It was observed that as the concentration of $NaHCO_3$ increases the effervescence or liberation of CO_2 increases thereby reduces the floating lag time and increases floating buoyancy due to increased porosity by the gas-forming agent.

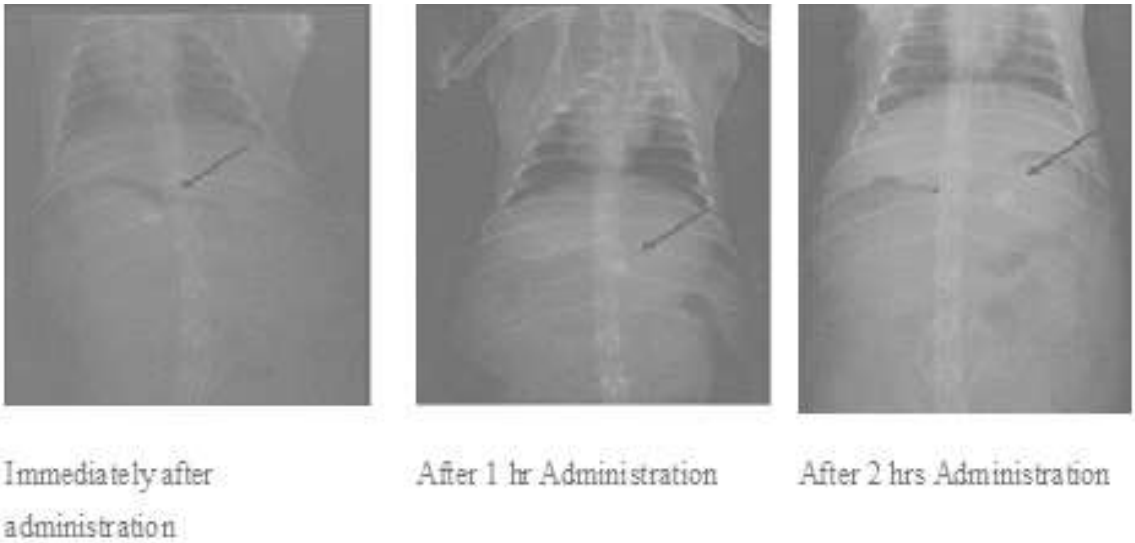
In vivo buoyancy study

In vivo buoyancy was determined by X-ray imaging studies on healthy rabbits. The animal dose was calculated using dose translation based on Body Surface Area (BSA). Fig. 4 depicts the position and nature of the tablets at different time intervals after oral administration.

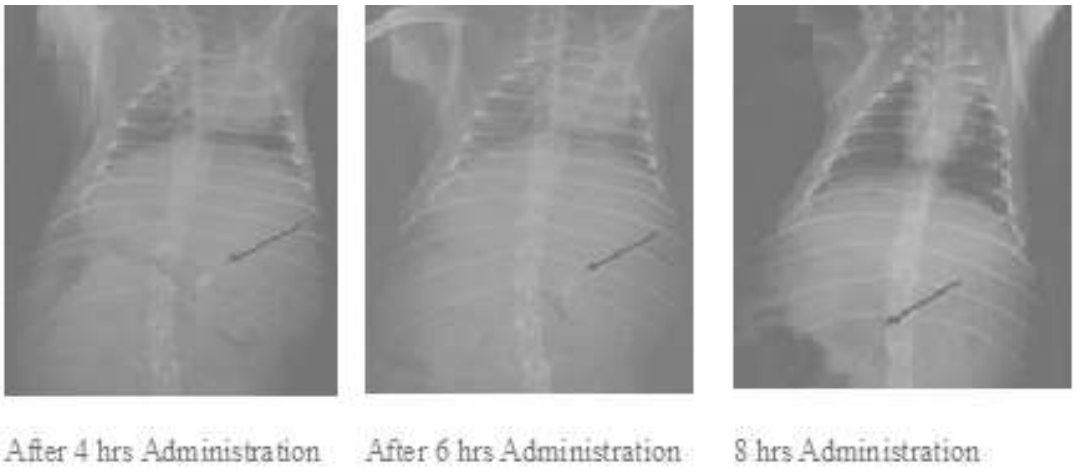
From the obtained results it was observed that the floating tablets formulated with Cefuroxime Axetil and locust bean gum remained in the gastric region even after 8 hours of administration indicating good retention of the tablets in the stomach region.



(A) Before administration



(B) Immediately after administration, After 1 hr, After 2 hrs Administration



(C) After 4 hrs, After 6 hrs and 8 hrs Administration

Figure 4: X-ray photographs of GIT of rabbit at different time intervals after administration of floating tablets.

Drug release kinetic- model dependent method [15] [16] [17]

From the results given in Table 9, Release kinetics for different formulations was calculated using Microsoft Office Excel 2007 version. The release data were analyzed by fitting the drug release profiles of all the formulations into zero, first, Higuchi and Korsmeyer-Peppas model. Regression coefficients (R^2) were calculated for all the formulations.

Table 8: Model dependent kinetic analysis for the dissolution profile of the different formulation

Formulation code	Regression coefficient (R^2)				
	Zero-order	First-order	Higuchi	Korsmeyer-Peppas	Release exponent 'n'
F1	0.6483	0.9135	0.9586	0.9701	0.5866
F2	0.6945	0.9788	0.9756	0.9961	0.5720
F3	0.9980	0.9520	0.9980	0.9810	0.5758
F4	0.7962	0.9490	0.9915	0.9860	0.5580
F5	0.9055	0.9830	0.9955	0.9747	0.5565
F6	0.8640	0.9770	0.9840	0.9865	0.5454
F7	0.2262	0.7940	0.8960	0.9820	0.5260
F8	0.7120	0.9362	0.9680	0.9675	0.5225
F9	0.7140	0.9410	0.9620	0.9230	0.5150

It is found that the passage of the drug through the matrix is dependent on the square root of time. When the release profile was plotted versus square root of time a linear relationship was observed with the regression coefficient close

to one. Batches show 'n' higher than 0.5 and lower than 1, which concludes that the formulation exhibit anomalous transport mechanism. To analyze the release of a CP release mechanism in vitro drug release data is fitted in the various release equation and kinetic model (Zero order, First order, Higuchi and Korsmeyer-Peppas) For all formulated batches.

For matrix treatment the R^2 value for F3, F4 and F5 shows close to one which exhibit matrix release kinetics. Whereas, F2 exhibit Korsmeyer-Peppas kinetics of drug release.

Accelerated stability studies

Optimized formulation F3 was subjected to stability studies and results are given in Table 9.

Table 9: Evaluation of optimized formulation during stability

Parameters	Initial readings	After one-month readings
Floating lag time	49±0.4 sec.	48 sec.
Total floating time	24 hours	24 hours
Hardness	4.4±0.54 kg/cm^2	4.4 kg/cm^2
Drug content	98.12±0.53 %	98.01 %
% drug release up to 12 hours	98.62±0.44 %	97.45 %
Thickness	4.1±0.32 mm	4.1 mm
Friability	0.42±0.59 %	0.43 %
Weight of tablet	248±0.54 mg	249.5 mg
Swelling index	99.41±1.4 %	101.1 %

Based on the results it can be concluded that, optimized tablets were stable during accelerated stability studies, with an insignificant change in the floating lag time, floating time, drug content and in vitro drug release characteristics.

CONCLUSION

In conclusion, F3 formulation which has been prepared using PMG peel powder as rate control polymer at the ratio of 0.3:1.0 (PMG peel powder: drug), shows better-floating properties such as <49 sec. and 99.63% drug release in 24 hrs dissolution as required. Hence, F3 can be concluded as a final optimized formulation for the floating matrix tablet of Cefuroxime Axetil as an approach to increase gastric residence time and thereby improving its bioavailability.

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REFERENCES

1. Arora, S., Ali, J., Ahuja, A., Khar, R.K., Baboota, S., 2005. Floating drug delivery system: a review. AAPS Pharm. Sci. Tech. 6, 372–390.
2. Baumgartner, S., Kristl, J., Vrecer, F., Vodopivec, P., Zorko, B., 2000. Optimization of floating matrix tablets and evaluation of their gastric residence time. Int. J. Pharm. 195, 125–135.
3. Arzu Akpinar-Bayizit, Tulay Ozcan and Lutfiye Yilmaz-Ersan, "The Therapeutic Potential of Pomegranate and Its Products for Prevention of Cancer", Uludag University Turkey. Publisher InTech, Published online 20, 2012, Pages 331 to 372.
4. Ankur Raj Sharma, Afroz Khan. Gastro retentive drug delivery system: an approach to enhance gastric retention for prolonged drug release, International journal of pharmaceutical science and research,5 (4), 2014;1095-1106.
5. Arorra s., Javed Ali, floating drug delivery system: A Review, American Association of Pharm Sci. 2005: 5(2): 372-390.
6. Mohammad Al-Pokhiti, Khaled Al-Tahami. Development and evaluation of sustained release matrix tablets of ketoprofen employing natural polymers (pomegranate peel and acacia powders). Journal of Chemical and Pharmaceutical Research, 8(4), 2016;822-827.
7. Indian Pharmacopeia, vol. II (2010), (Published by Indian Pharmacopeia Commission, Ghaziabad, 2010) pp. 751- 754.
8. VD Havaldar, AS Kulkarni, Floating matrix tablets of atenolol: Formulation and in vitro evaluation, Asian Journal of Pharmaceutics, 2009:286-291.
9. United States Pharmacopeia 24 and National Formulary 19, 2000 by United States Pharmacopeial Convention, INC, pp. 1941-43.
10. Uttam Kumar Mandal, Bappaditya Chatterjee, Gastroretentive drug delivery system and their in-vivo success: A recent updates, Asian journal of pharmaceutical sciences, 2016;11;575-584.
11. L Whitehead, J T Fell, et al, Development of a gastroretentive dosage form, European Journal of Pharmaceutical Sciences.1996 4: S182.
12. S.U. Zeta, P.I Kothawade, Gastroretentive bioadhesive drug delivery system: A review, international journal of pharm tech and research,2;2010;1227-1235.
13. Raghavendra Kumar Gunda, J. N. Suresh Kumar1, Design, Formulation and Evaluation of Atenolol Gastro Retentive Floating Tablets, Asian Journal of Pharmaceutics, vol. 9;2015: S34-S41.
14. Deshpande, A., Shah, N.H., Rhodes, C.T., Malick, W., 1997. Development of a novel controlled release system for gastric retention. Pharm. Res. 14, 815–819.

15. Patel G.M. Floating drug delivery system: An innovative approach to prolong gastric retention, Research journal of pharmaceutical dosage forms and technology, 4.2012:93-103.
16. Rocca J. G., Omidian H, and shah K. Progress in gastro retentive drug delivery system, Business Briefing: Pharmatech. 2003: 152-156.
17. V Kamalakkannan, C Kannan, gastro retentive drug delivery system for cefpodoxime proxetil-development and optimization, Research journal of pharmaceutical, biological, and chemical science, vol.4:2013:1150-1167.
18. L Kukati, K Chittimalli, Formulation, and evaluation of floating tablets of cefpodoxime proxetil, Journal of scientific research, vol.6. 2014;563-579.
19. Pankaj H Prajapati, Vijay V Nakum et al. Formulation and evaluation of floating matrix tablet of stavudine, international journal of pharmaceutical investigation vol.2;2012:83-89.
20. Dhumal, R.S., Rajmane, S.T., Dhumal, S.T., Pawar, A.P., 2006. Design and evaluation of bi-layered floating tablets of Cefuroxime Axetil for bimodal release. J. Sci. Ind. Res. 65, 812–816.