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Research Article

FORMULATION AND EVALUATION OF FLOATING TABLETS OF CEFUROXIME AXETIL

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ABSTRACT

The objective of research work was to formulate and evaluate the floating drug delivery system containing cefuroxime axetil using polymer HPMC K4M, Guar Gum. Effervescent floating tablets containing Cefuroxime axetil were prepared by direct compression technique using varying concentrations of different grades of polymer. Physical parameters like hardness, weight variation, thickness and friability were within pharmacopoeial limit. Percentage drug content in all floating tablet formulations was found to be 90% to 110%. The floating time was found to be more than 12 H. floating lag time was found to be 10±2.99 second. Formulation batch F8 was selected as an optimum formulation, as possessing less disintegration time, higher water absorption ratio and good content uniformity i.e. within acceptable limit.% drug release of formulation batch F8 was found to be 96.66% in 0.1 N HCL. The FT-IR studies of batch F8 was carried out which showed the peak values within the spectrum corresponding to the peak values of pure drug.

KEYWORDS: *Cefuroxime axetil, Guar Gum, Floating lag time, Effervescent floating tablets.*

INTRODUCTION

Oral sustained release dosage forms deliver the drug for a longer period and help in producing the therapeutic effect for 24 hr. for those drugs which are having low plasma half-life. Drugs that have narrow absorption window in the Gastro-intestinal tract (GIT) will have poor absorption. For these drugs, gastro retentive drug delivery systems (GRDDS) have been developed [1-3]. Oral sustained release dosage form with a prolonged residence time in the stomach helps in absorption of the drugs which are less soluble or unstable in the alkaline pH and those which are absorbed from the upper gastrointestinal tract. Gastro retentive dosage systems (GRDDS's) help in the maintenance of constant therapeutic levels for prolonged periods, increase therapeutic efficacy and thereby reduce the total dose of administration.

Cefuroxime is a broad-spectrum/ beta lactamase stable, second generation antibiotic with proven record of efficacy and safety in the parenteral management of various infection including urinary tract infections. Since cefuroxime is not absorbed orally, cefuroxime axetil (CA) (1-acetoxyethyl ester of a β-lactamase-stable cephalosporin), an orally absorbed pro-drug of cefuroxime is used in the treatment of common community acquired infections because of its in-vitro antibacterial activity against several gram-positive and gram-negative organisms. Cefuroxime is a β-lactam type of antibiotic. More specifically, it is a second-generation cephalosporin. Cephalosporin's work the same way as penicillin's: they interfere with the peptidoglycan synthesis of the bacterial wall by inhibiting the final transpeptidation needed for the cross-links. This effect is bactericidal. Cefuroxime is effective against the following organisms: Aerobic gram-positive microorganisms: Staphylococcus aureus, Streptococcus pneumonia, and Streptococcus pyogenes. Aerobic gram-negative microorganisms: Escherichia coli, Haemophilus influenza, Haemophilus parainfluenzae, Klebsiella pneumonia, Moraxella c, Neisseria gonorrhoeae, Spirochetes: Borreliaburgdorferi.

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METHODS AND MATERIALS

Materials Cefuroxime axetil was obtained as a kind gift sample Cipla Ltd, Bangalore. HPMC K4M has been purchased from Centre drug Lab, Delhi, Guar Gum are obtained from Lupin Pharma, Pune. Sodium bicarbonate and Magnesium stearate are purchased from SD fine chemicals, Mumbai. All other chemicals, reagents and solvents used are of analytical grade.

Formulation of effervescent floating tablet of cefpodoxime proxetil:

Effervescent floating tablets containing Cefuroxime axetil were prepared by direct compression technique using varying concentrations of different grades of polymers with sodium bicarbonate and citric acid. All the ingredients were accurately weighed. Different formulations were made in order to achieve desired friability, thickness, hardness and drug release. The tablets were formulated using drug, diluents, release rate retarding polymer, gas generating agent, binder,

lubricant and glidant. The direct compression method involves sifting of the drug along with the polymer through sieve # 40 and uniform mixing was carried out for 5 min in a mortal pestle. Afterwards, one by one all the ingredients were sifted and mixed in it except the magnesium stearate. The blend was mixed thoroughly for 15 min. Finally, magnesium stearate was added and mixed for a further 2-3 min.

Evaluation of pre-compression parameters:

Excipients, polymers and drug were characterized by their physical properties such as angle of repose, density, compressibility, Hausner's ratio

Table No. 1: Composition of tablet with using polymer and gum

Sr.No.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
1	Cefuroxime axetil	150	150	150	150	150	150	150	150
2	HPMC K4M	100	90	80	70	60	110	120	130
3	Guar Gum	100	110	120	130	140	90	80	70
4	Mag. Stearate	5.4	6.4	7.4	8.4	5.4	6.4	7.4	8.4
5	Sod. Bicarbonate	60	60	60	60	60	60	60	60
6	Citric acid	20	20	20	20	20	20	20	20

Evaluation of Cefuroxime axetil floating tablets:

Thickness: The thickness of the tablets was determined using a Vernier calliper. Five tablets from each type of formulation were used and average values were calculated. It is expressed in mm [8].

Hardness: The resistance of tablets to shipping, breakage, under conditions of storage, transportation and handling before usage depends on its hardness. For each formulation, the hardness of 6 tablets was determined using the Monsanto hardness tester. The tablet was held along its oblong axis in between the two jaws of the tester. At this point, reading should be zero kg/cm2

Friability: Then constant force was applied by rotating the knob until the tablet fractured. The value at this point was noted. Friability is the measure of tablet strength. Roche Friabilator was used for testing the friability using the following procedure. This test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. A sample of preweighed 6 tablets was placed in Roche friabilator which was then operated for 100 revolutions i.e. 4 min. The tablets were then dusted and reweighed. A loss of less than 1 % in weight in generally considered acceptable. Percent friability (% F) was calculated as follows.

$$\% F = \frac{\text{Initial weight - Final weight}}{\text{Initial weight}} \times 100$$

Weight variation test: To find out weight variation, 20 tablets of each type of formulation were weighed individually using an electronic balance, the average weight was calculated and individual tablet weight was then compared with average value to find the deviation in weight.

Floating behavior: The in vitro buoyancy was determined by floating lag time and floating time. The tablets were placed in dissolution vessel containing 900 ml of 0.1N HCl. The time required for the tablet to rise to the surface and afloat was determined as floating lag time. The duration for which the tablet remains afloat on the surface of the solution is known as floating time [9-10].

Swelling behaviour of tablets: The swelling of the polymers can be measured by their ability to absorb water and swell. Water uptake studies of the formulation were performed using USP dissolution apparatus II. The medium used was 0.1 N HCl (900 ml) rotated at 50 rpm, and maintained at 37±0.5 °C throughout the study. After a selected time interval, the formulation is withdrawn, blotted to remove excess water and weighed. Swelling characteristics of the tablets expressed in terms of water uptake (WU) are calculated as follow [11].

$$WU\ \% = \frac{\text{Swollen weight} - \text{Initial weight} \times 100}{\text{Initial weight}}$$

Uniformity of drug content: Five tablets of each type of formulation were weighed and crushed in mortar and powder equivalent to 50 mg of Cefuroxime axetil was weighed and dissolved in 100 ml of 0.1N HCl (pH 1.2). This was the stock solution from which 0.2 ml sample was withdrawn and diluted to 10 ml with 0.1N HCl. The absorbance was measured at wavelength 263.2 nm using double beam UV-Visible spectrophotometer. Content uniformity was calculated using formula–

$$\% \text{ Purity} = 10\ C\ (Au/As)$$

Where, C-Concentration, Au and As-Absorbance are obtained from unknown preparation and standard.

In vitro drug release In vitro dissolution tests were conducted in triplicate for all formulations in a USPXXII tablet dissolution apparatus (Electrolab, TDT-08L) for 12 h under sink conditions. The dissolution medium was 900 ml 0.1N HCl at 37±0.5 °C. The speed of rotation was maintained to 50 r. p. m. At a predetermined time intervals, 5 ml sample was withdrawn and diluted and absorbance was recorded. The samples were analyzed for drug release by measuring the absorbance at 263 nm using spectrophotometric method (Schimadzu UV).

Infrared spectroscopy: The FTIR of pure drug and physical mixture of formulation ingredients of the optimized batch was measured using Fourier transform infrared spectrophotometer (Model FTIR-8400S, Shimadzu, Japan). The amount of each formulation ingredient in the physical mixture was same as that in the optimized batch. The pure drug and physical mixture were then separately mixed with IR grade KBr. This mixture

was then scanned over a wave number range of 4000 to 400 cm-1 [12-15].

Accelerated stability testing: Stability testing of formulation batch was carried out to determine the stability of drug and carrier and also to determine the physical stability of formulation under accelerated storage condition at 45 °C/70% RH. The prepared tablets were placed in borosilicate screw-capped glass containers. The samples were kept at the condition of 45 °C/70% RH and were analyzed at 7th, 14th, 21st and 28th days for drug content, hardness and in vitro dissolution study [16].

RESULTS AND DISCUSSION

Evaluation of powder blend: Powder blends were evaluated for the angle of repose value which was found to be in the range of 25.45±0.49–30.97±0.85 indicating powder flow for all the eight formulations were good. Bulk density for all eight formulations was found to be in the range of 0.492±0.20–0.750±0.29 while tapped density was in the range of 0.699±0.22–0.775±0.26. The percent compressibility index for all eight formulations was found to be 14.69±0.48-21.28±0.24.

Evaluation of floating tablets:

The thickness of tablet indicates that die fill was uniform. The thickness depends on the size of the punches (9 mm). The thickness of formula from F1 to F8 was found to be 3.22±0.43-3.40±0.29 mm and hardness was found to be 3.2±0.26-4.9±0.24 Kg/cm2. The thickness of tablet of optimized formulation (F4) was found to be 3.27±0.54 mm and the hardness was found to be 3.8±0.35 kg/cm2. It has good mechanical strength. Percentage weight loss of the 10 tablets of each formulation (F1-F8) was measured and found to be a range of 0.56±0.25-0.98±0.22 % which was under the acceptable limit. Tablets from each batch showed the uniformity of content in the range 98.81±4.06to 103.96±1.82which is within pharmacopoeial specifications. All the formulations complies the test for uniformity of content as it found to be within the limit of 90-110%. The floating lag time for all formulations was tested in dissolution vessel and founds that is between 09±2.08 to 22±1.52 H.

Table No. 2: Physical parameters of powder blend (n=3)

Formulations	Bulk density	Tapped density	Angle of repose (°)	Carr's index	Hausner's ratio
F1	0.493±0.20	0.696±0.22	25.44±0.49	18.77±0.22	1.38±0.72
F2	0.588±0.38	0.678±0.38	26.99±0.39	20.49±0.46	1.26±0.51
F3	0.629±0.26	0.726±0.29	27.18±0.85	15.58±0.23	1.34±0.49
F4	0.678±0.15	0.738±0.19	29.39±0.45	16.96±0.61	1.26±0.68
F5	0.695±0.29	0.741±0.28	26.58±0.81	21.28±0.24	1.33±0.72
F6	0.718±0.36	0.765±0.28	25.97±0.39	19.85±0.47	1.28±0.67
F7	0.756±0.29	0.788±0.39	24.53±0.56	14.68±0.48	1.38±0.56
F8	0.649±0.35	0.777±0.26	30.95±0.85	16.25±0.63	1.29±0.79

Table No. 3: Physical parameters of tablets (n=3)

Batch	Hardness	Thickness	%Friability	Wt.Variation	Uniformity content	Flag (sec)	Float time (h)
F1	3.8±0.28	3.28±0.43	0.56±0.004	402.8±0.21	98.88±3.04	22±1.52	12.50±0.48
F2	3.6±0.26	3.40±0.24	0.75±0.004	398.8±0.27	99.85±3.79	09±2.08	11.19±0.57
F3	4.8±0.26	3.42±0.27	0.56±0.004	400.6±0.55	99.81±4.06	20±3.05	10.98.±0.4
F4	3.8±0.35	3.27±0.54	0.75±0.004	400.8±0.34	100.38±4.06	18±2.08	11.98±0.52
F5	3.8±0.31	3.46±0.29	0.63±0.004	400.3±0.28	102.96±1.82	20±3.51	10.68±0.55
F6	4.4±0.50	3.39±0.31	0.68±0.51	382.8±0.34	102.15±4.67	10±1.05	11.71±0.33
F7	3.8±0.57	3.35±0.53	0.95±0.22	368.9±0.29	100.50±3.46	10±1.05	10.59±0.45
F8	4.5±0.24	3.30±0.11	0.59±0.019	465.4±0.45	99.99±2.34	15±2.99	11.90±0.65

Swelling studies:

The formulation batch containing higher HPMC and Guar Gum showed higher swelling index. From the results obtained, it was observed that the increased concentration of polymers increases the swelling indices (Fig. 1).

In vitro drug release study:

Besides the satisfactory buoyancy, the Floating tablets are required to release Cefuroxime axetil gradually over a prolonged period. Hence, they were tested for release kinetics by conducting in vitro dissolution test. Floating tablet showed sustained release of the drug in acidic condition (pH 1.2) and the drug release was found to be approximately linear. Approximately 12-15% of the drug was released initially. Furthermore, drug release from the floating tablet was controlled by the polymer. As the polymer content was increased and the drug loading was decreased, the release of drug was decreased significantly. In order to increase the release rate of the drug, the ratio of the polymer was decreased and plasticizer was increased (Fig. 2).

Infrared absorption spectrum:

The FT-IR spectra of the pure Cefuroxime axetil and physical mixture of drug and polymers were analyzed to check for any interaction between drug and polymers. The characteristic peaks of Cefuroxime axetil appeared in the spectra without any significant change. The IR spectrum did not show the presence of any additional peaks for new functional groups indicating no chemical interaction between Cefuroxime axetil and the used polymers. IR spectrum showed all prominent peaks of Cefuroxime axetil which was comparable with standard IR graph. The major IR peaks observed in Cefuroxime axetil were (1504, 1494 and 1447) C-H stretching of the benzene ring, (2866, 2872) C-H Stretching of alkane, (786) Di-Substituted Ar-ring, (1614) C=C Stretching of an alkene, (2240) C=N stretching, (3192) Alcoholic–OH (Fig. 3-5).

Stability studies:

Accelerated stability studies (AST) was carried for optimized formulation F8 by exposing it to 40 °C/75% RH for one month and analyzed the sample at the interval of 7,14,21,28 d. The sample was analyzed for drug content, hardness and cumulative percentage drug release (Table 4).

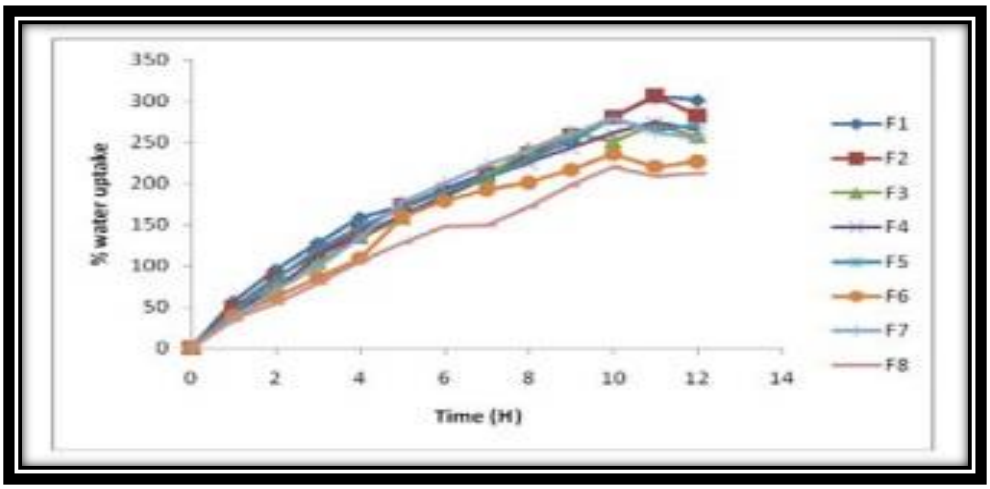

Fig. 1: % swelling index of the formulation

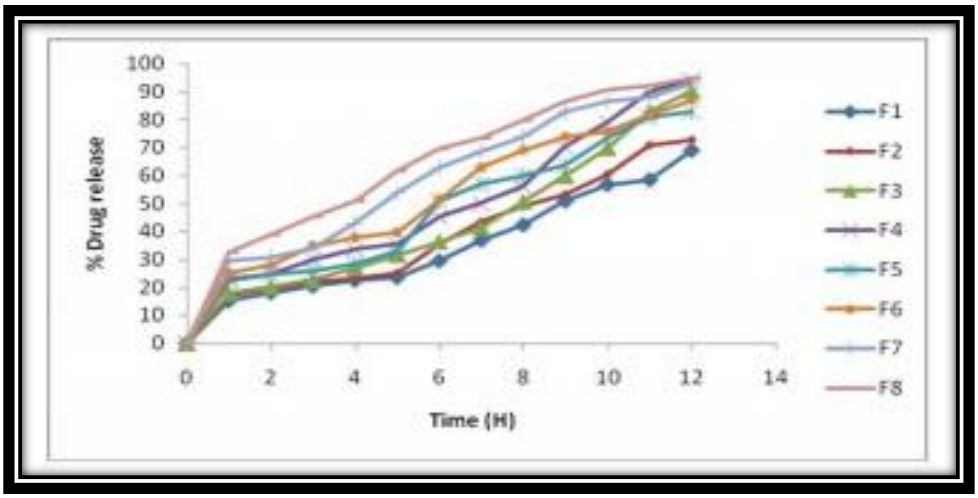

Fig. 2: % drug release of batches F1-F8

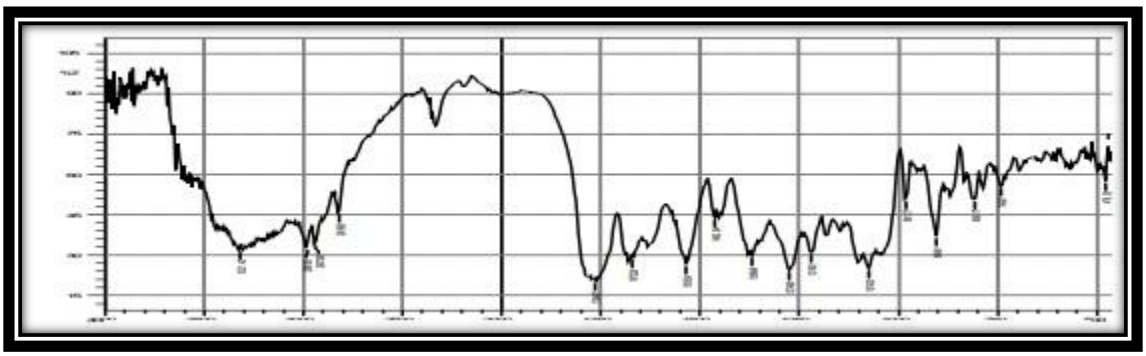

Fig. 3: FT-IR spectra of Cefuroxime axetil

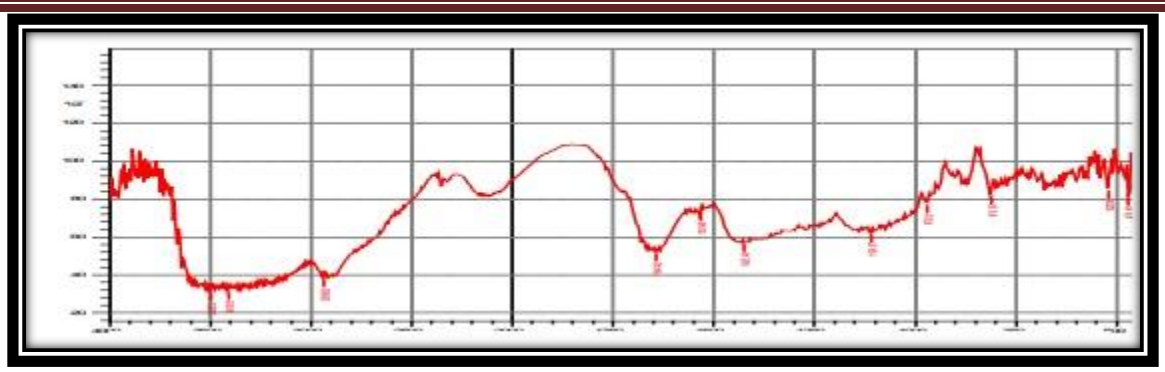

Fig. 4: FT-IR spectra of guar gum

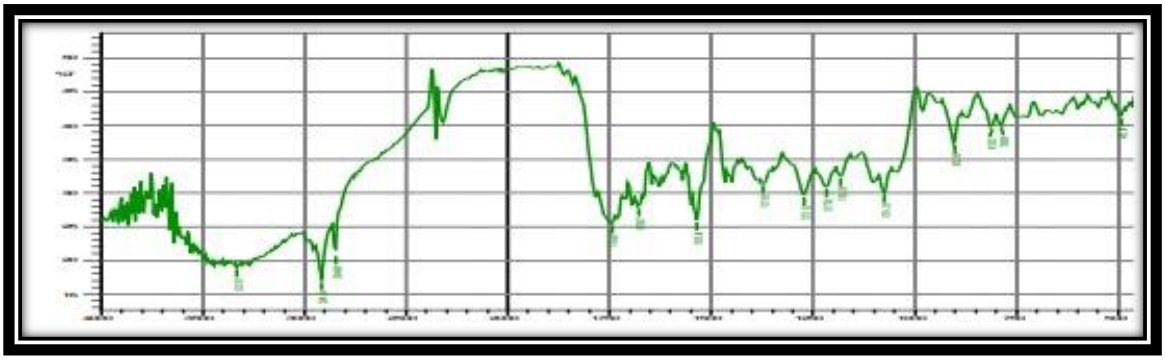

Fig. 5: FT-IR spectra of a physical mixture

Table No. 4: Stability studies

Parameters	0 Day	7 Day	14 Day	21 Day	28 Day
Hardness	3.08±0.35	3.06±0.13	2.10±0.1	2.06±0.13	2.00±0.10
Drug content (%)	100.38±0.96	99.90±0.90	99.65±0.50	99.50±0.20	98.98±0.84
In vitro disso	94.28±1.49	94.10±3.79	93.5±2.34	92.54±1.89	90.69±2.41

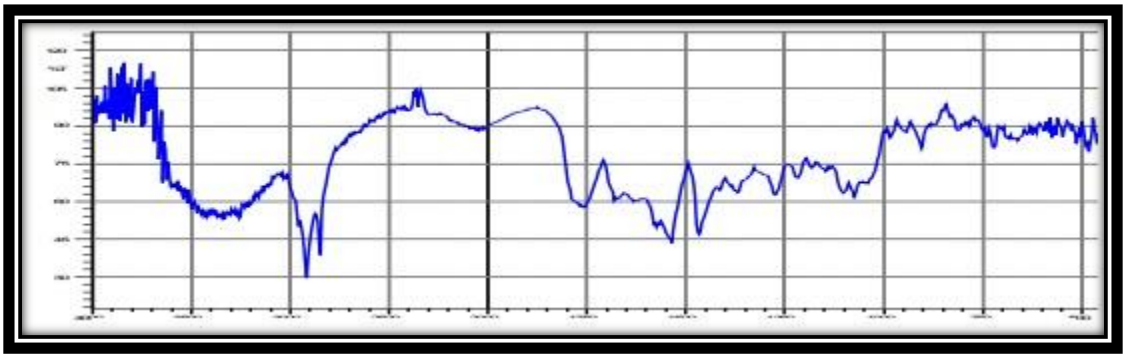

Fig. 6: IR spectrum of formulation F12 after stability study

CONCLUSION

The present study was carried out to develop the floating drug delivery with sustained release of Cefuroxime axetil using HPMC K4M, Guar gum polymers from the findings of various physical, chemical, in vitro tests it can be concluded that the developed formulations F4 achieved the objective of investigation as The floating lag time for all formulations was tested in dissolution vessel and founds that is between 09±2.08 to 22±1.52. Tablets from each batch showed the uniformity of content in the range of 98.88±3.04 to 102.96±1.82 which is within Pharmacopoeial specification. The % drug release of all formulations was found to be about 90 to 94%.

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