Research Article

Formulation and In-vitro Evaluation of Floating Matrix Tablets of Cephalexin

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ABSTRACT

Floating matrix tablets of Cephalexin were prepared by using synthetic and natural polymers each in two different concentrations. The floating properties and in-vitro drug release properties were optimized and total 10 formulations were developed. The synthetic and natural polymers used were HPMC K4M, HPMC K15M and Guar Gum, Xanthan gum respectively. Each formulation consists of polymer in any one ratio of 1:0.6 or 1:0.8. In this study it was confirmed that the formulations containing Xanthan gum in 1: 0.6 ratio, have shown better floating properties and better in-vitro release properties.

Keywords: Floating matrix tablets, Cephalexin, HPMC K4M, Xanthan Gum, Gastric retention.

INTRODUCTION

Gastro retentive drug delivery systems are the systems which are retained in the stomach for a longer period of time and thereby improve the bioavailability of drugs that are preferentially absorbed from upper GIT. Floating drug delivery systems (FDDS) offer a number of applications for drugs having poor bioavailability because of narrow absorption window in the upper part of gastrointestinal tract [1].

The ideal drug candidate for FDDS are drugs that are acting locally in upper gastro intestinal tract (GIT) or drugs that are degrading in lower GIT or drugs that show poor intestinal absorption or drugs that are absorbed only in the initial part of the small intestine and stomach. Acid labile drugs and other drugs that are causing gastric lesions are unsuitable for such formulations. The gastric retention of the dosage form in the stomach depends upon various factors like pH, size of the dosage form, food intake, and biological factors which include age, body mass index, gender, posture, and diseased states. Out of all available gastro retentive systems floating tablets, floating beads, floating granules, and floating microspheres have gained major importance in the formulation development more recently [2].

Cephalexin, chemically (6*R*, 7R)-7-{[(2*R*)-2-amino-2-phenylacetyl] amino} - 3-methyl-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene- 2-carboxylic acid, is a first generation cephalosporin antibiotic. It inhibits synthesis of bacterial cell wall, causing cell death. Cephalexin is a weak acidic drug with pKa of 3.6 and half life of 0.5-1.2 hours. According to Handerson-Hesselbach equation, the weak acidic drugs with pKa in the range of 2.5-7.5 show poor absorption in the intestine because of more ionization and show more absorption in stomach because of predominant unionization at gastric pH. Thus the Cephalexin is suitable to formulate as floating tablets in order to increase the bioavailability. As the half life of the drug is less, it can be formulated as matrix tablets to decrease the dose frequency.

In the present study, Cephalexin floating matrix tablets were prepared to increase the absorption of drug through gastric mucosa and to decrease the dose frequency. The prepared tablets were evaluated for their floating properties and in-vitro drug release.

MATERIALS AND METHODS

The chemicals used in this study were pure drug like Cephalexin (Venkateswara scientific traders) and polymers like HPMC K4M, HPMC K15M, Xanthan gum (Venkateswara scientific traders), Guar gum (Accord labs) and other excipients like Micro crystalline cellulose (Venkateswara scientific traders), Magnesium stearate, Talc, Sodium bicarbonate (Accord labs).

1. Preformulation study

Preformulation studies were conducted to identify the compatibility of drug with polymers. These studies were conducted by using FTIR method. In this method, the sample along with KBr was used to get the IR spectrum. The IR spectra of pure drug and physical mixtures

containing drug and polymers were produced and analyzed.

2. Preparation of floating matrix tablets

Cephalexin was mixed manually in polybags with gastro retentive polymers separately as per formulae and MCC was added as diluent and sodium bicarbonate was added as effervescent agent (Table 1) and mixed for 10 mins. The blend was lubricated with magnesium stearate for 3-5mins and talc was added as glidant. The mixed blend was then compressed into tablets by direct compression method using 12 mm punches on a twelve station rotary tablet punching machine (Cemach machineries). Total ten formulations were developed.

3. Evaluation

a) Characterization of tablets for physicochemical parameters

The prepared Cephalexin floating tablets were evaluated for their physicochemical parameters like weight variation, hardness, friability and drug content.

b) In vitro floating lag time

The in vitro buoyancy was determined by floating lag time. The tablets were placed in a 100 ml beaker containing 0.1N HCl. The media was kept in stagnant condition and the temperature was maintained at 37^{o} C. The time required for the tablet to rise to the surface and float was determined as floating lag time.

c) In vitro floating duration time

The floating capacity of the tablets was determined using USP Dissolution apparatus II containing 900ml of simulated gastric fluid. The time interval between introduction of the tablet in to the dissolution medium and its buoyancy to the dissolution medium was taken as buoyancy lag time and for which time the tablet constantly floats on the surface of the medium was observed visually and taken as floating duration.

d) In vitro drug release

The release of Cephalexin from floating tablets was determined by using Dissolution type II test apparatus. The dissolution test was performed using 900 ml 0.1N HCl solution at 37 ± 0.5^{o}C temperature and at 50 rpm. At specified time intervals, samples of 5 ml were withdrawn from the dissolution medium and that amount was replaced with fresh medium to maintain the volume constant. The samples were filtered and diluted to a suitable concentration with 0.1 N HCl. The absorbances of the diluted samples were measured at 257nm for Cephalexin by using UV-Visible double beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from standard curve.

e) Characterization of drug in Floating tablets

FTIR studies were conducted for characterization of drug in tablets of selected optimized formulation (F7). The floating tablets were compressed and powdered. The pelletized powder along with KBr was used for FTIR studies. The IR spectra were recorded using Fourier Transform Infrared spectrophotometer. The IR spectra of pure Cephalexin and pelletized powder of tablets were taken, interpreted and compared with each other.

RESULTS AND DISCUSSION

1. Preformulation study

In IR spectrum (figure 1) of pure Cephalexin, the presence of peaks at 3447.82, 3616.29 cm^{-1} (>N-H stretching), 1690.25, 1752.75 and 1835.12 cm^{-1} (>C=0 stretching), 3038.97 cm^{-1} (Aromatic >C-H stretching), 1645.79 (Aromatic -C=C- stretching) were characteristic to that of the pure drug and all of them remained unaltered in the IR spectra (figure 2) of physical mixtures containing drug and polymers. IR analysis revealed that there was no evidence to the presence of known chemical interaction of drug with polymers and other ingredients.

2. Weight variation, hardness, friability and assay

The weight variation of the tablets (Table 2) was within the limits of uniformity. The mass ranged from 547.50 to 552.40 mg with SD values 0.59–1.28. The mass of all compressed tablets were within the limits as per USP. The drug content ranged from 98.46 ± 0.26 % in formulation F1 to 95.58 ± 0.66 % in formulation F10 and the friability was ranged from 0.29 to 0.78. Friability and assay of all compressed tablets were within the limits as per USP. The hardness of all prepared tablets was in the range of 3.8 to 4 kgs.

3. In vitro floating lag time and floating duration

All formulations had floating lag times below 5 minutes (Table 3). The formulations containing HPMC K15M (F3 and F4) and Xanthan gum (F7 and F8) have shown less floating lag times among all other formulations. Formulation F9 containing a combination of HPMC K4M and HPMC K15M, has also shown less floating lag

time. From the results it was evident that the formulations with drug: polymer ratio of 1: 0.6 have shown less lag times compared to the formulations with drug: polymer ratio of 1: 0.8. This may be due to high capacity of effervescent agent to decrease the tablet density in the presence of less amount of polymer.

All the formulations were allowed to float constantly on dissolution medium. All the formulations were floated up to more than 8 hours.

4. In vitro drug release

The release of Cephalexin from gastro retentive floating tablets (Table 4, 5 and Figure 3, 4) varied according to the type of matrix forming polymers. The drug release from all the formulations was controlled up to 8hrs. In case of formulations containing single synthetic polymer, formulations F3 and F4 with HPMC K15M as rate controlling polymer have given more drug release compared to the formulations like F1 and F2 with HPMC K4M as polymer. In case of formulations containing single natural polymer, formulations F7 and F8 with Xanthan gum as rate controlling polymer have given more drug release compared to the formulations like F5 and F6 with guar gum as polymer. This may be due to more capacity of HPMC K4M and guar gum over HPMC K15M and Xanthan gum to retard the drug release by gel formation around the tablet.

In case of the formulations containing a combination of polymers, the formulation F9 with a combination of two synthetic polymers like HPMC K4M and HPMC K15M has shown more drug release compared to the formulation F10 with a combination of two natural polymers like guar gum and Xanthan gum. This may be due to more matrix formation by a combination of natural polymers compared to that by a combination of synthetic polymers.

The release data of all formulations except F10 seem to fit better with the first order kinetics and Higuchi model i.e. the release rate in these formulations, is dependent of its concentration or amount of drug in tablet at given time and the release mechanism is diffusion. Among all formulations more drug release (98.55%) was observed in formulation F7 containing Xanthan gum as polymer in drug: polymer ratio of 1: 0.6.

5. Characterization of drug in floating tablets

IR analysis (figure 5) revealed that there was no evidence to the presence of known chemical interaction of drug with polymers and other ingredients in selected best formulation.

CONCLUSION

New gastro retentive delivery systems for Cephalexin were developed and evaluated. The results propose that a natural polymer like Xanthan gum in drug to polymer ratio of 1:0.6 can increase the retention time of formulation in stomach and also can control the drug release

from formulation up to 8 hours due to matrix formation thereby increasing drug absorption and reducing the dose frequency. It can be concluded that the antimicrobial action of

Cephalexin may be increased in the stomach due to increased retention and absorption by using formulation F7 containing Xanthan gum in drug to polymer ratio of 1:0.6. The results obtained for used combination and ratio of polymers in the present work, were not reported earlier in any work. Further work is needed to claim the results in human beings by in-vivo studies.

Table 1: Formulation composition of Cephalexin floating tablets of F1 to F10

Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Drug	250 mg	250 mg	250 mg	250 mg	250 mg	250 mg	250 mg	250 mg	250 mg	250 mg
HPMC K4M	150 mg	200 mg	-	-	-	-	-	-	100 mg	-
HPMC K15M	-	-	150 mg	200 mg	-	-	-	-	100 mg	-
Guar gum	-	-	-	-	150 mg	200 mg	-	-	-	100 mg
Xanthan gum	-	-	-	-	-	-	150 mg	200 mg	-	100 mg
MCC	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg
$NaHCO_3$	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
Mg. Stearate	6 mg	6 mg	6 mg	6 mg	6 mg	6 mg	6 mg	6 mg	6 mg	6 mg
Talc	6 mg	6 mg	6 mg	6 mg	6 mg	6 mg	6 mg	6 mg	6 mg	6 mg

Table 2: Weight variation, Friability and Assay

Formulation	Mass (mg) Mean ± SD	Friability (%)	Assay (%)
F1	549.80 ± 1.00	0.50	98.46 ± 0.26
F2	548.70 ± 0.76	0.29	101.25± 0.47
F3	551.10 ± 0.69	0.32	109.25± 0.59
F4	550.40 ± 0.75	0.78	110.88±1.01
F5	552.40 ± 1.28	0.66	91.38±0.75
F6	549.00 ± 0.89	0.51	102.00±0.36
F7	548.20 ± 1.10	0.45	104.38± 0.48
F8	547.50 ± 0.99	0.30	95.38±0.36
F9	549.20 ± 1.18	0.46	97.58±0.96
F10	548.54 ± 0.59	0.53	95.58±0.66

Table 3: Floating lag time and Floating duration

Formulation	Floating lag time	Floating duration time(hrs)
F1	25 sec	More than 8 hrs
F2	100 sec	More than 8 hrs
F3	5 sec	More than 8 hrs
F4	15 sec	More than 8 hrs
F5	2 min	More than 8 hrs
F6	4 min	More than 8 hrs
F7	5 sec	More than 8 hrs
F8	20 sec	More than 8 hrs
F9	10 sec	More than 8 hrs
F10	4 min	More than 8 hrs

Table 4: In-vitro release profiles of formulations F1 to F5

Time (hrs)	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	26.10 ± 0.85	21.60 ± 1.24	28.80 ± 0.24	25.65 ± 0.91	23.40 ± 0.44
2	40.95 ± 0.69	36.90 ± 1.04	57.15 ± 1.34	55.80 ± 0.76	31.50 ± 0.87
4	54.00 ± 0.64	46.80 ± 1.33	74.25 ± 0.33	69.75 ± 1.13	45.90 ± 0.54
6	75.60 ± 0.86	73.35 ± 0.66	83.25 ± 0.36	80.55 ± 0.64	57.15 ± 1.24
8	78.75 ± 0.99	75.15 ± 0.87	96.30 ± 0.67	89.10 ± 0.47	68.85 ± 1.15

Table 5: In-vitro release profiles of formulations F6 to F10

Time (hrs)	F6	F7	F8	F9	F10
0	0	0	0	0	0
1	19.80 ± 0.95	30.15 ± 1.14	27.45 ± 0.74	24.30 ± 0.71	16.65 ± 1.06
2	24.75 ± 0.89	58.05 ± 0.64	56.25 ± 0.34	50.85 ± 1.26	24.75 ± 0.36
4	33.30 ± 0.54	75.60 ± 0.33	73.80 ± 1.33	62.55 ± 1.23	31.05 ± 0.97
6	45.00 ± 1.16	85.95 ± 0.56	84.15 ± 0.86	78.30 ± 0.57	49.50 ± 1.01
8	55.80 ± 0.39	98.55 ± 0.87	93.15 ± 0.47	88.65 ± 0.97	65.25 ± 0.59

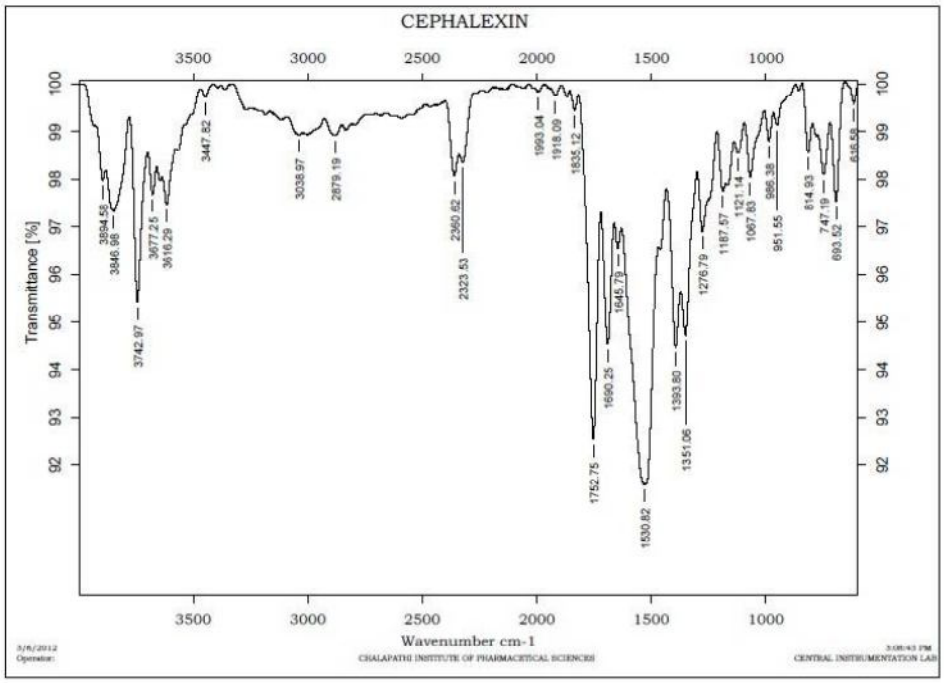
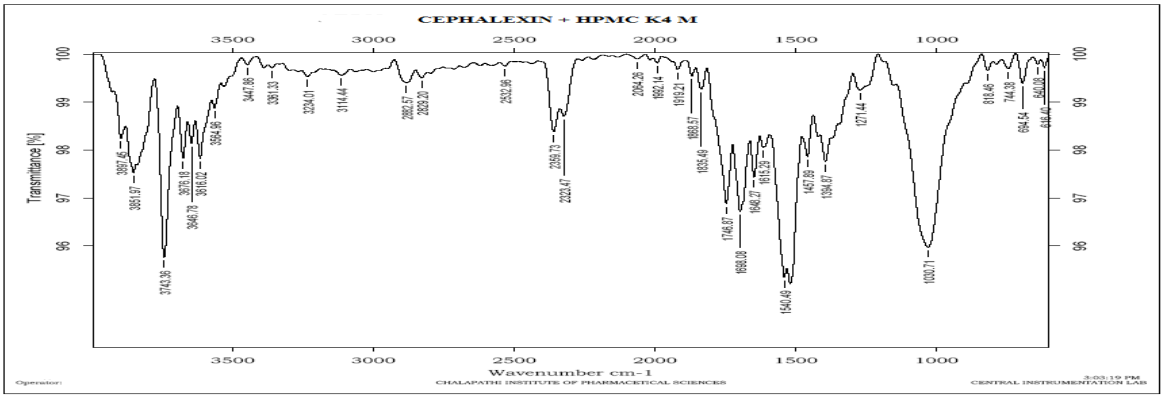
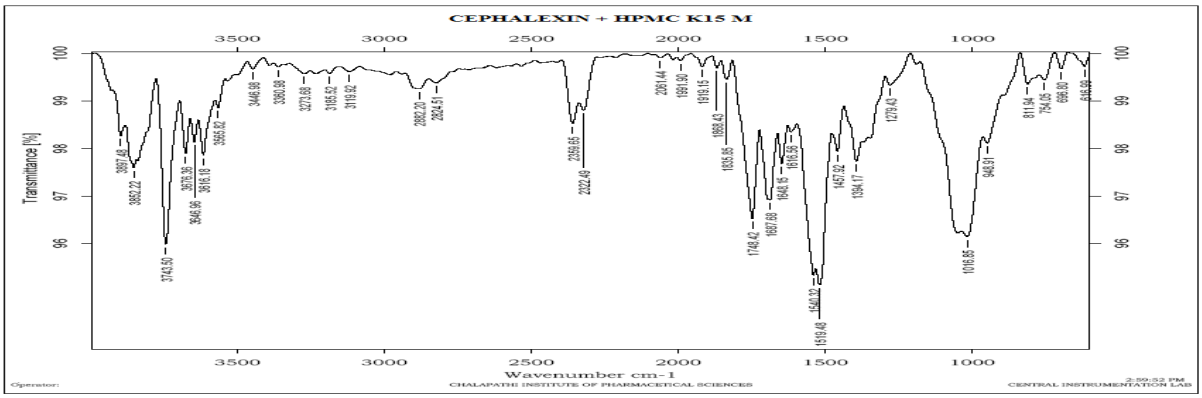
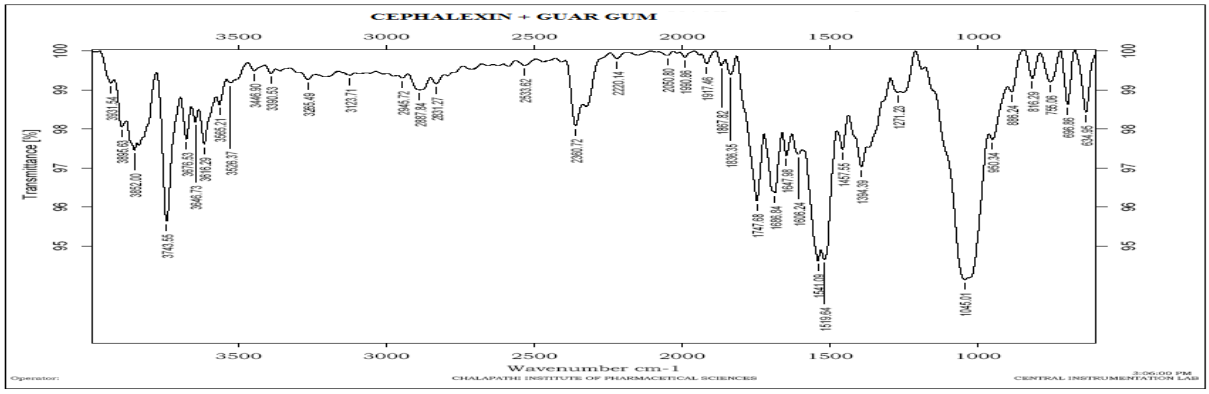


Fig. 1: IR spectrum of pure Cephalexin







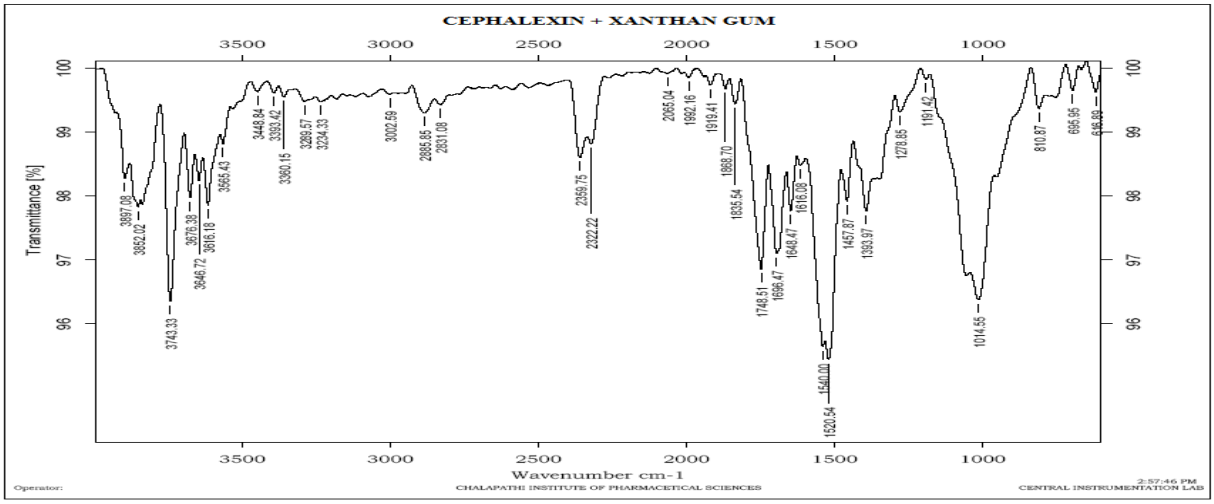


Fig. 2: IR spectra of physical mixtures containing drug and polymers *Figure 3:*

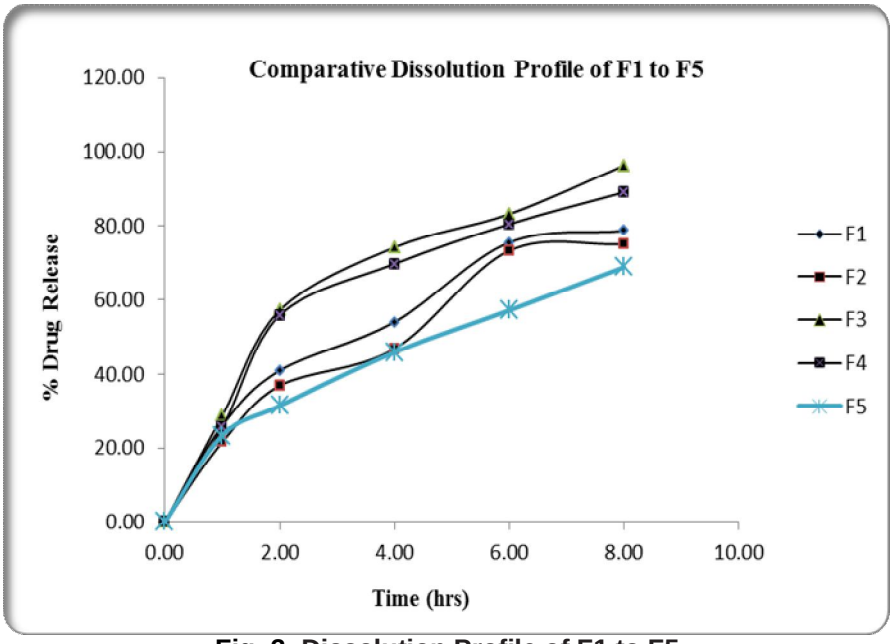


Fig. 3: Dissolution Profile of F1 to F5

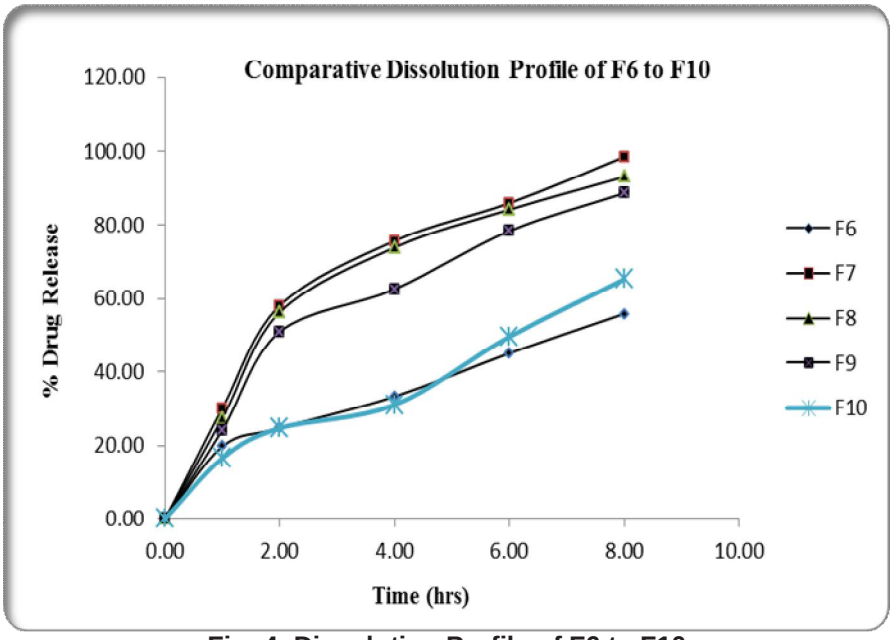
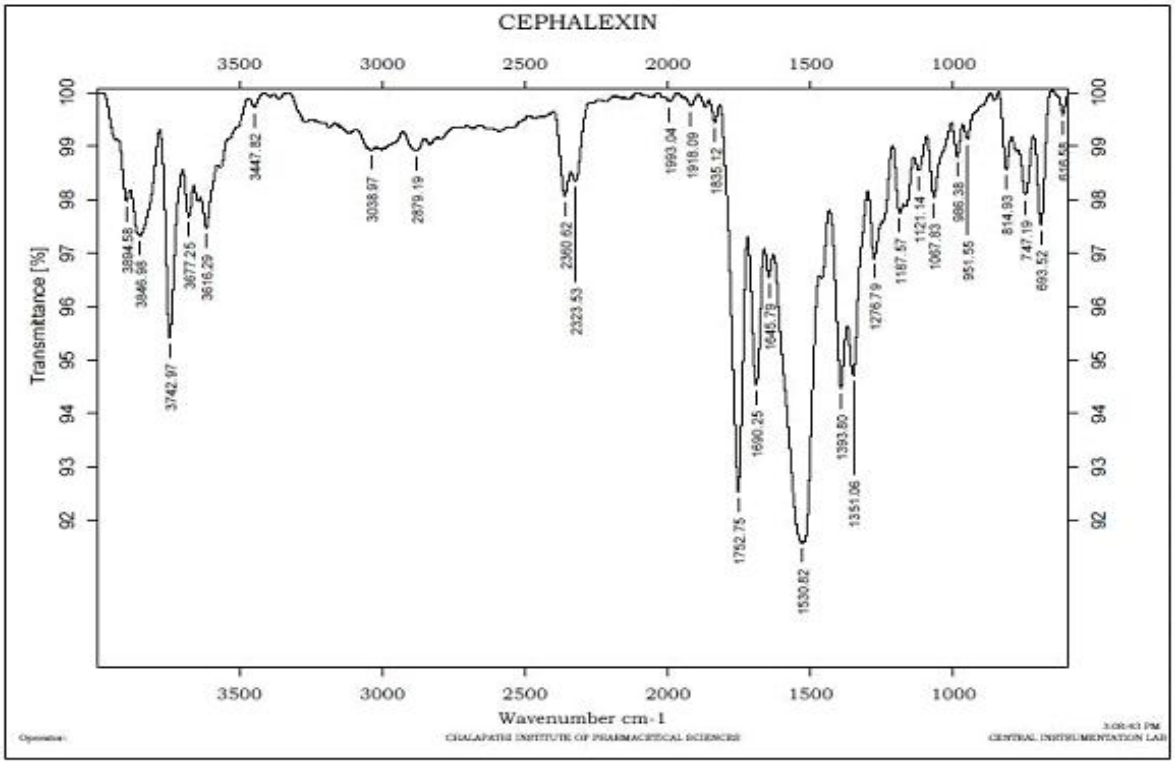


Fig. 4: Dissolution Profile of F6 to F10



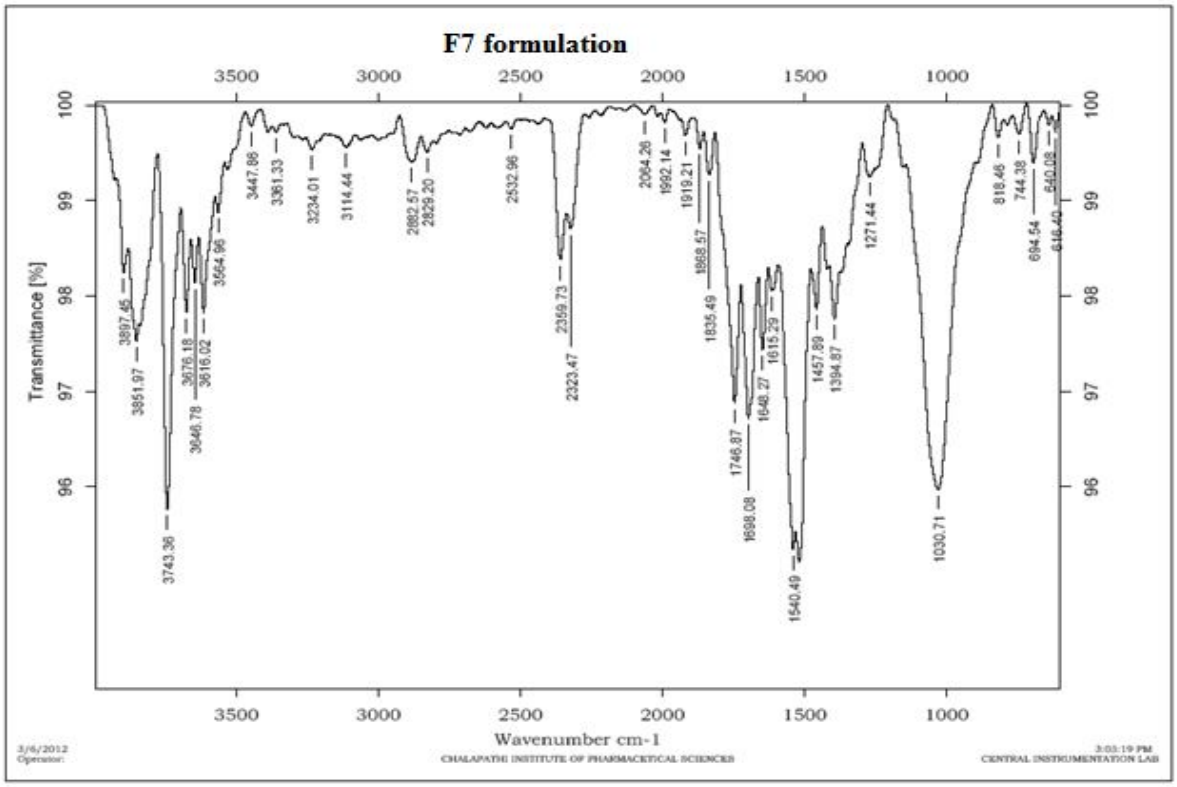


Fig. 5: IR spectra of Pure Cephalexin and F7 formulation

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