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Research Article

FORMULATION AND IN-VITRO EVALUATION OF FLOATING MATRIX TABLETS OF CIPROFLOXACIN HCL

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Abstract: Floating matrix tablets of Ciprofloxacin HCl were prepared by using two different synthetic polymers. The floating properties and in-vitro drug release properties were optimized by changing the effervescent agent and total 4 formulations were developed. The synthetic polymers used were HPMC K15M and HPMC K100M. Each polymer was used differently in combination with two different effervescent agents like $CaCo_3$ and $NaHCO_3$. In this study it was confirmed that the formulations containing HPMC K100M, have shown better floating properties and finally the formulation containing a combination of HPMC K100M and $CaCO_3$, has shown better in-vitro release properties.

Key**words:** Floating matrix tablets, Ciprofloxacin HCl, HPMC K15M, HPMC K100M, Gastric retention

INTRODUCTION

Drug absorption from gastrointestinal tract (GIT) is a complex process influenced by many variables. It has been reported that the extent of drug absorption from the GIT is related to contact time with gastro intestinal mucosa [1]. Floating drug delivery systems are good promising options for drugs which show good absorption in the stomach and which are degraded, less efficient in the intestine. These drug delivery systems are beneficial to achieve the more local action in the gastric environment. Floating systems are one type of gastro retentive drug delivery systems (GRDDS) which are retained in the stomach for longer period of time and there by improve the bioavailability, local action of drugs that are preferentially absorbed from upper GIT [2]. These floating systems will improve the contact time of drug with gastric mucosa and there by provide the beneficial results.

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].

Ciprofloxacin HCl, chemically (1- Cyclopropyl 6-fluoro-4-oxo,7-piperzine-1-yl quinolone-3-carboxylic acid), is a second generation fluoroquinolone antibiotic. It inhibits the replication of DNA interfering with the action of DNA gyrase. It is a weak acidic drug with pKa of 3.6 and half life of 4 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 Ciprofloxacin HCl 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, Ciprofloxacin HCl 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 Ciprofloxacin HCl (Venkateswara scientific traders) and polymers like HPMC K15M, HPMC K100M, and other excipients like Micro crystalline cellulose (Venkateswara scientific traders), Magnesium stearate, Talc, Sodium bicarbonate and Calcium carbonate (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 analysed.

2. Preparation of floating matrix tablets

Ciprofloxacin HCl was mixed manually in polybags with gastro retentive polymers separately as per

formulae and MCC was added as diluent and sodium bicarbonate or calcium carbonate were added as effervescent agents (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 12.0 mm punches on a 12 station rotary tablet punching machine (Cemach machineries). Total four ormulations were developed.

Table 1: Formulation composition of Ciprofloxacin HCl floating tablets of F1 to F4

Formulation	F1	F2	F3	F4
Drug	291mg	291mg	291mg	291mg
HPMC K15M	200mg	-	200mg	-
HPMC K100M	-	200mg	-	200mg
NaHCo3	140mg	140mg	-	-
Calcium carbonate	-	-	140mg	140mg
Mcc	55mg	55mg	55mg	55mg
Mg. Sterate	14mg	14mg	14mg	14mg

3. Evaluation

a) Characterization of tablets for physicochemical parameters

The prepared Ciprofloxacin HCl 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 Ciprofloxacin HCl 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 278.10 nm for Ciprofloxacin HCl 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 (F2). 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 Ciprofloxacin HCl 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 Ciprofloxacin HCl, the presence of peaks at 3435.34, 3627.92 cm^{-1} (>N-H stretching), 1624.12, 1708.99 and 1844.01 cm^{-1} (>C=0 stretching), 3012.91 cm^{-1} (Aromatic >C-H 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.

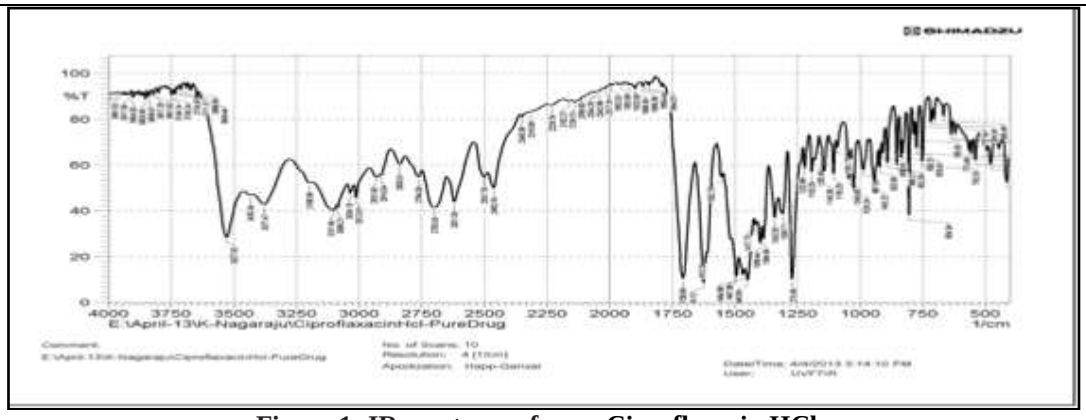

Figure 1: IR spectrum of pure Ciprofloxacin HCl.

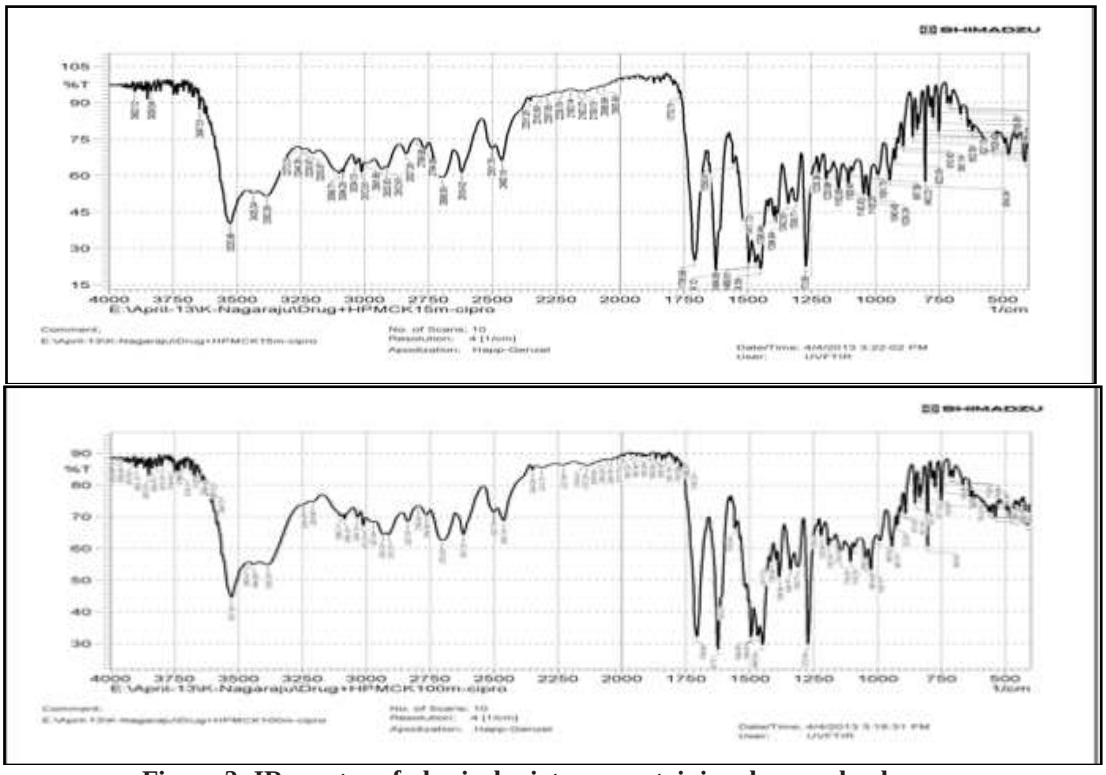

Figure 2: IR spectra of physical mixtures containing drug and polymers

2. Weight variation, hardness, friability and assay

The weight variation of the tablets (Table 6) was within the limits of uniformity. The mass ranged from 699.50 to 701.30 mg with SD values 0.69–1.30. The mass of all compressed tablets were within the limits as per USP. The drug content ranged from 99.50 ± 0.42 % in formulation F1 to 103.41 ± 0.26 % in formulation F4 and the friability was ranged from 0.56 to 0.83. 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.

Table 2: Weight variation, Friability and Assay

Formulation	Mass (mg) Mean ± SD	Friability (%)	Assay (%)
F1	699.5 ± 1.30	0.56	99.50 ± 0.42
F2	700.70 ± 0.76	0.67	101.25± 0.47
F3	701.3. ± 0.69	0.83	100.25± 0.59
F4	699.1 ± 0.75	0.79	103.41±0.26

3. In vitro floating lag time and floating duration

The formulations like F3, F4 and had floating lag times below 5 minutes, where as the formulations like F1, F2 has shown floating lag time of more than 1 hour and 15 minutes respectively (Table 7). From these results it was found that the formulations containing $CaCO_3$ as effervescent agent, have shown less floating lag time and formulations containing $NaHCO_3$ as effervescent agent, have taken more time to float on the surface of 0.1 N HCl.

All the formulations were allowed to float constantly on dissolution medium. The formulations F1and F2 containing $NaHCO_3$ as effervescent agent were floated up to 6 hours where as the formulations F3 and F4 containing $CaCO_3$ as effervescent agent, have shown their floating duration of more than 12 hours.

These results indicate that $CaCO_3$ has more capacity to decrease the density of tablets when compared to $NaHCO_3$. These results also reveal that the effervescent agent ($NaHCO_3$ or $CaCO_3$) brings about better buoyancy to the tablets in the presence of HPMC K100 M when compared to HPMC K15 M. This may be due to better hydro colloidal formation of HPMC K100 M around the tablet.

Table 3: Floating lag time and Floating duration

Formulation	Floating lag time (sec)	Floating duration time(hrs)
F1	1 hr 13 min	6 hrs
F2	18 min 52 sec	More than 12 hrs
F3	2 min 39 sec	6hrs
F4	13sec	More than 12 hrs

4. In vitro drug release

The release of Ciprofloxacin HCl from gastro retentive floating tablets (Table 8 and Figure 14) varied according to the type of matrix forming polymers. The drug release from the formulations F2 and F4 was controlled up to 10 hrs. The drug release in case of formulation F1 and F3 was not extended up to 10 hrs and immediate drug release pattern was observed The matrix forming ability was more in case of formulations F2 and F4 containing polymer like HPMC K100M, where as matrix forming ability was less in case of formulations F1 and F3 containing polymer like HPMC K15M. It may be due to high capacity of HPMC K100M to form the matrix in the tablet because of its high viscosity.

Table 4: In-vitro release profiles of formulations F1, F2 and F3, F4

Time (hrs)	F1	F2	F3	F4
0	0	0	0	0
1	56.01 ± 0.85	29.14 ± 1.24	47.69 ± 1.33	58.60 ± 0.84
2	104.12 ± 0.69	32.72 ± 1.04	78.13 ± 0.63	65.44 ± 0.96
4	-	43.46 ± 1.33	100.11 ± 1.49	70.32 ± 1.41
6	-	60.23 ± 0.66	-	83.34 ± 0.81
8	-	65.93 ±0.87	-	87.09 ±1.11
10	-	81.55 ±0.87	-	92.46 ± 1.41

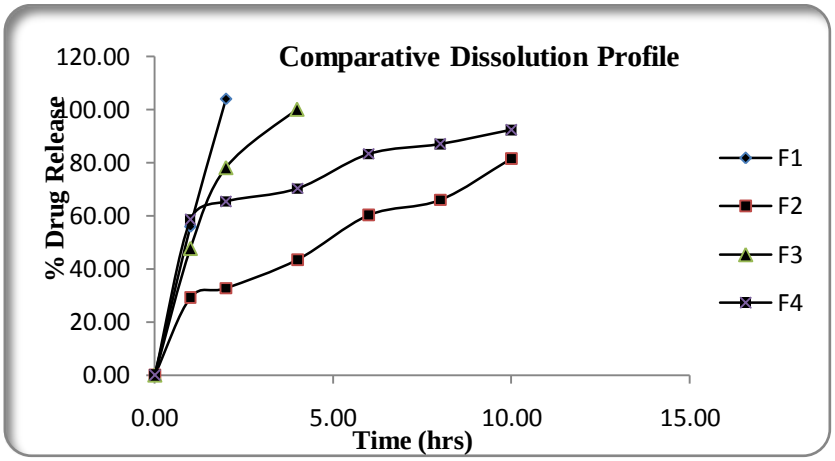

Figure 3: Dissolution Profile of F1, F2 and F3, F4

5. Characterization of drug in floating tablets

IR analysis (figure 4) revealed that there was no evidence to the presence of known chemical interaction of drug with polymers and other ingredients in selected best formulations.

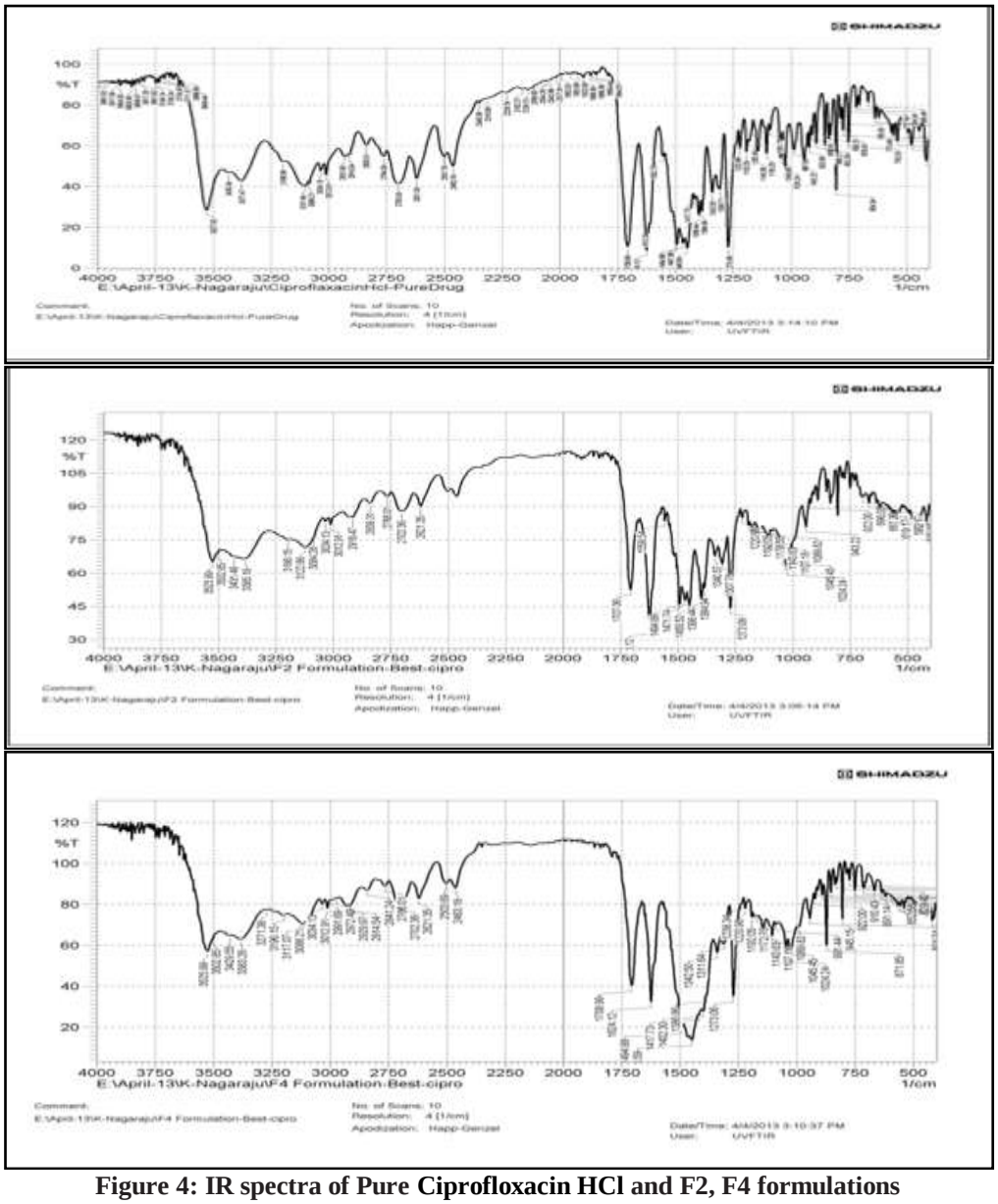

Figure 4: IR spectra of Pure Ciprofloxacin HCl and F2, F4 formulations

Conclusion:

New gastro retentive delivery systems for Ciprofloxacin HCl were developed and evaluated. The results propose that synthetic polymers HPMC K15M and HPMC K100M in combination with $CaCO_3$ can increase the retention time of formulation in stomach and also can control the drug release from formulation due to matrix formation thereby increasing drug absorption and reducing the dose frequency. It can be concluded that the antimicrobial action of Ciprofloxacin HCl may be increased in the stomach due to increased retention and absorption by using formulations F2 and F4. Further work is needed to claim the results in human beings by in-vivo studies.

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