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FORMULATION AND EVALUATION OF FLOATING RAFT FORMING FORMULATION OF CIPROFLOXACIN HYDROCHLORIDE

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ABSTRACT

Ciprofloxacin is a broad-spectrum antibiotic which belongs to fluoroquinolones. It is used to treat the patients with bacterial infections of urinary tract (UTIs), skin, bone, chest (pneumonia) and stomach. The absorption window of ciprofloxacin is in the stomach. In this study floating raft forming drug delivery system of ciprofloxacin was prepared by using different concentration of polymers like sodium alginate, pectin and aloevera gel powder. The compatibility of drug and the polymers was investigated by FTIR and it was found that there was no interaction between them. The prepared formulations were tested for various parameters like viscosity, pH, *in-vitro* gelling, *in-vitro* buoyancy and results were found to be satisfactory. The drug content was within the range of 98.57 ± 1.66 % to 99.28 ± 0.79 %. The *in-vitro* drug release was found to be between 65.66 ± 0.48 % to 93.32 ± 0.30 %. The formulations F5 and F8 showed 93.32 ± 0.30 % and 65.66 ± 0.48 % of drug release at 9 h respectively. The *in-vitro* drug release followed first order kinetics and non-fickian anomalous diffusion mechanism. The Formulation F8 was selected best as it sustained drug release and it was subjected to stability study. The result of stability study indicated that the formulation was stable during study period.

Keywords: Floating raft formulation, Ciprofloxacin, Sodium alginate, Aloevera gel powder, Pectin.

I. INTRODUCTION

Oral delivery of drugs is by far the most preferred route of drug delivery due to ease of administration, patient compliance and flexibility in formulation. (1) Conventional oral dosage forms provide a specific drug concentration in systemic circulation without offering any control over drug delivery. It is clear from the recent research and patent literature that there is an increased interest in novel dosage forms that are retained in the stomach for a prolonged and predictable period of time. (2, 3) A major constraint in oral controlled drug delivery is that not all drug candidates are absorbed uniformly throughout the gastrointestinal tract (GIT). Some drugs are absorbed only in a particular portion of GIT or are absorbed to a different extent in various segments of the GIT. An absorption window exists because of physiological, physicochemical or biochemical factors. The pH dependent solubility and stability level of a drug plays an important role in its absorption. Frequent dosing of these drugs is required to achieve suitable therapeutic activity. The developments of oral sustained-controlled release formulations are an attempt to release the drug slowly into the GIT and maintain an effective drug concentration in the systemic circulation for a long time. (4)

Gastroretentive drug delivery systems (GRDDS) are the novel approaches in this area. GRDDS is helps to improved absorption of drug in the absorption window in stomach by continuously releasing for a prolonged

period of time before it reaches its absorption site, thus ensuring its optimal bioavailability. (4,5) Drugs should be released in the region preceding and in close vicinity to the absorption window is only available for absorption. After crossing the absorption window, there is no or less absorption takes place. Raft forming systems are one of the GRDDS approaches to increase residence time of drug in stomach. Raft forming systems have received much attention for the delivery of the drug for gastrointestinal infections and disorders. (3, 6)

As compared to the solid oral dosage forms, liquid dosage forms are easy to administer to paediatric, geriatric and dysphasic patients who have difficulty in swallowing. Formulation of raft forming drug delivery systems is a useful approach to overcome this problem. The system involves the formation of a viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft. The layer of the gel floats on the gastric fluid because it has bulk density less than the gastric fluid, as low density is created by the formation of CO_2. So, the system remains buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. Thus, it results in retention of dosage form and increases gastric residence time leading to prolonged drug delivery in gastrointestinal tract. (6) After release of the drug, the residual system is emptied from the stomach.

Approaches of Raft Forming System (6)

Different approaches and mechanisms are utilized in the production of the raft formation are as follows:

- Based on producing a physical mechanism: swelling, diffusion
- Based on producing a chemical mechanism: ionic crosslinking, enzymatic crosslinking
- Based on physiological stimuli mechanism: pH dependent, temperature dependent

Ciprofloxacin is a member of the fluoroquinolone class of antibacterial agent. Ciprofloxacin is a faintly yellowish to light yellow crystalline substances with a molecular weight of 385.8 g/mol. The dose of Ciprofloxacin usually varies from 100-250 mg for pediatrics and 250-500 mg for adults. The absolute bioavailability of ciprofloxacin when given as an oral tablet is approximately 70 % with no substantial loss by first pass metabolism. The serum elimination half-life is subject with normal renal function is approximately 4 hours. (7, 8)

For this drug, which has complete absorption in the stomach, it is appropriate to increase resident time of the formulation in stomach by forming rafts. The drug should be released for effective local and systemic therapeutic action. Sodium alginate (9), Pectin (9) and aloevera gel powder (10) are used as gel forming polymers.

II. MATERIALS AND METHOD

Ciprofloxacin HCl was obtained as a gift sample from KAPL, Bangalore, Sodium alginate, Sodium citrate and calcium carbonate were procured from SD fine-chem limited, Mumbai. Pectin was purchased from Sigma Aldrich chemicals, India. Aloevera gel powder procured from Phoenix medicaments Pvt. Ltd, Ahmedabad. All other chemical were of analytical grade.

2.1 Calibration curve of Ciprofloxacin

Accurately weighed 50 mg of Ciprofloxacin was dissolved in 50 ml 0.1N HCl to get stock solution A. From the stock solution A 10 ml was taken and made up to 100 ml using 0.1N HCl to get stock solution B. Different concentrations were prepared by pipetting out stock solution B as per requirement. The absorbance was recorded at 277.5 nm using U V-spectrophotometer (Shimadzu UV-1601, Japan) against a suitable blank.

2.2 FTIR analysis

FTIR spectra were obtained to determine the interactions between drug and excipients. The samples of ciprofloxacin, polymers and prepared formulation were subjected to scanning from 4000 cm^{-1} to 400 cm^{-1} using FTIR spectrophotometer (BRUKER, ALPHA II).

2.3 Melting point determination

Melting point of the drugs was determined by taking a small amount of drug in a capillary tube closed at one end and placed in a Theil's melting point apparatus and the temperature at which the drug melts is noted. The averege of three readings were noted and reported as mean ± SD (n=3).

2.4 Determination of pH

A drug solution of concentration 5 % w/v in distilled water was prepared and pH of the solution was determined using a pH meter. Average of three readings was computed and the values are reported as mean ± SD (n=3).

2.5 Preparation of ciprofloxacin raft forming formulation

Accurate quantity of drug and the other ingredients were weighed as per the formulation table. Sodium alginate and pectin or aloevera gel powder were dissolved in a beaker with sufficient quantity of water and stirred for 10 – 20 min using stirrer (Remi industries, Mumbai)for uniform dispersion. Weighed drug was added to the beaker which contains water. This was added to the beaker containing polymer mixture and stirred for 10 min. Calcium carbonate and sodium citrate were dissolved in sufficient amount of water and this was added to the above mixture and made up to the volume using water and stirred for 10 min. Then preservatives were added and mixed well. Final formulation was obtained and evaluated.

Table 1: Ciprofloxacin raft forming formulation

Sodium 0.25 % to all saccharine w/v added formulations.

Ingredients (%)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ciprofloxacin HCl	1	1	1	1	1	1	1	1	1
Sodium alginate	3	2	1.5	3	2	1.5	3	2	1.5
Pectin	-	-	-	-	-	-	0.5	0.5	0.5
Aloevera gel powder	-	-	-	0.5	0.5	0.5	-	-	-
Sodium citrate	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Calcium carbonate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Propylparaben	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Methylparaben	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Water	100	100	100	100	100	100	100	100	100

III. EVALUATION OF CIPROFLOXACIN FLOATING RAFT FORMULATIONS

The prepared floating rafts were evaluated for the following parameters:

3.1 Measurement of viscosity

Viscosity determinations of the prepared formulations were carried out using Brookfield viscometer.

3.2 pH of raft forming formulation

The determination of Ph of prepared formulations was carried out on using Ph meter.

3.3 In-vitro gelling study (11-16)

Gelation capacity was determined by pouring the formulation in a beaker containing 200 ml of 0.1 N HCl (pH 1.2) as gelation medium. The gel formation was visually assessed and the time taken for the first detection of gelling (gelation lag time) were noted for each formulation and the study was performed in triplicate.

3.4 In-vitro buoyancy study (Floating lag time and floating duration) (11-16)

In-vitro buoyancy study was characterized by floating lag time and total floating duration. *In-vitro* buoyancy study of the floating raft was carried out by taking 10 ml of the formulation was poured to the beaker containing 200 ml of 0.1N HCl (pH 1.2). The time required for the raft to rise to the surface of the medium (Floating Lag time) and the duration of the time for which the raft constantly floated on the medium (Floating duration) were noted for each formulation and the study was performed in triplicate.

3.4 Drug content

Accurately, 5 ml of formulations (equivalent to 50 mg of Ciprofloxacin) from all the batches were taken and to this 50 ml of 0.1 N HCl was added and sonicated for 30 min containing the strength of 1000 µg/ml. The complete dispersion of contents was ensured, and the contents were filtered using Whatman filter paper. From this solution, 1 ml was withdrawn and diluted with 0.1N HCl up to 100 ml. Absorbance was determined at 277.5 nm using double beam UV-Visible spectrophotometer (Shimadzu UV-1601, Japan) against a suitable blank. The concentration of Ciprofloxacin was determined from a previously prepared calibration curve. This study was performed in triplicate.

In-vitro drug release study of Ciprofloxacin raft formulations (11-16)

The release rate of ciprofloxacin from the floating raft was determined. The USP Type II dissolution test apparatus was used with 50 RPM, temperature of 37±0.5 ℃. Raft forming formulation 10 ml was added into dissolution medium. The samples were withdrawn at different time intervals upto 9 h and replenished with an equal volume of dissolution media at each time interval. The absorbance of samples was measured at 277.5 nm using UV spectrophotometer (Shimadzu UV-1601, Japan) using suitable blank. The study was performed in triplicate.

3.5 Analysis of drug release kinetics (17)

The *in-vitro* release data of the formulations were analysed using various models to describe the kinetics and mechanism of drug release.

Zero order:

Zero order was calculated by following equation

$$Q_t = Q_0 - K_0 t$$

Where,

Q_t = Drug release at time 't'

Q_0 = Initial drug concentration

K_0 = Zero order rate constant (h^{-1})

First order kinetics:

First order was calculated by the following equation

$$\text{Log } C = \log C_0 - K*t / 2.303$$

Where,

C= Amount of drug remained at time 't'.

C_0 = Initial amount of drug.

K = First order rate constant (h^{-1})

Higuchi's model:

Drug release from the matrix devices by diffusion has been described by following Higuchi's classical diffusion equation.

$$Q = Kt^{1/2}$$

The graph was plotted between square root of time and cumulative % drug release.

Korsmeyer – Peppa's model:

Korsmeyer-Peppa's Model indicates the study mechanism of drug release from the matrix tablets which also describes the drug behaviour from polymeric systems.

$$M_t / M_\infty = Kt^n$$

Table 2: Mechanism of drug release as per Korsmeyer – Peppa's model

n-value	Mechanism of drug release
n = 0.45	Fickian release
0.45 < n < 0.89	Non- fickian release
n = 0.89	Case II transport
n > 0.89	Super case II transport

3.6 Stability studies

Stability of a pharmaceutical product may be defined as the capability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications throughout its shelf life.

Method

The optimized formulation was subjected for 8 weeks stability study. The selected formulation was kept in the bottle and it was stored at 40 ± 0.5 ℃ temperature and 75 ± 5 % relative humidity conditions for 8 weeks. After the period of 8 weeks, it was evaluated for % drug release.

IV. RESULTS

1. Standard curve for Ciprofloxacin

Calibration curve of the pure drug ciprofloxacin was prepared in the concentration range of 1 µg/ml to 10 µg/ml and absorbance was determined at the wavelength of 277.5 nm. It followed Beer's and Lambers law in the above concentration range. The calibration curve showed good linearity and regression coefficient was 0.9994 (R^2 value).

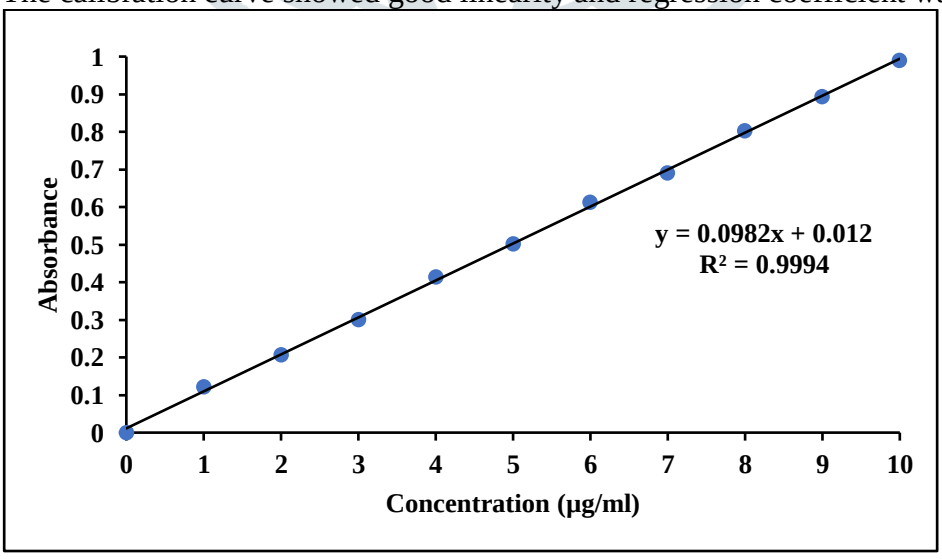


Figure 1: Calibration plot of Ciprofloxacin HCl

2. FTIR study

Pure drug Ciprofloxacin and polymers were subjected to FTIR analysis to ascertain any chemical interaction between the drug and the polymers used in formulations.

The FTIR study was performed for drug, polymers and selected formulations. For the pure drug Ciprofloxacin, the peaks were present at 3528.01 cm^{-1} N-H Stretching, 3379.77 cm^{-1} O-H Stretching of COOH, 2920.55 cm^{-1} C-H

Stretching, 1701.89 cm^{-1} C-O Stretching, 1451.58 cm^{-1} C-H deformation, 1312.81 cm^{-1} C-N Stretching and 1142.18 cm^{-1} C-O Stretching, the same peaks were observed in the spectra of formulation F2, F5 and F8. This indicated that there were no interactions between drug and excipients.

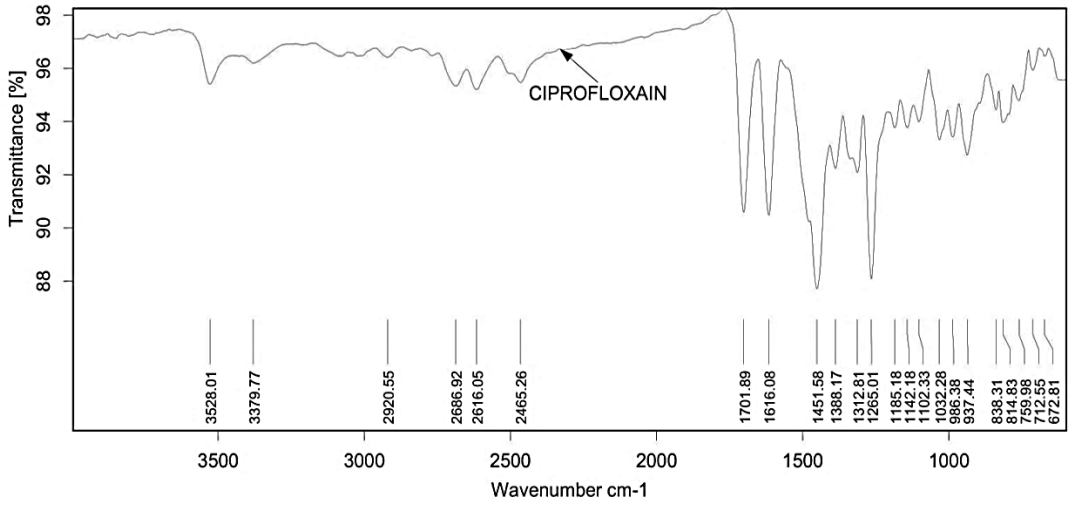


Figure 2: FTIR spectra of Ciprofloxacin HCl

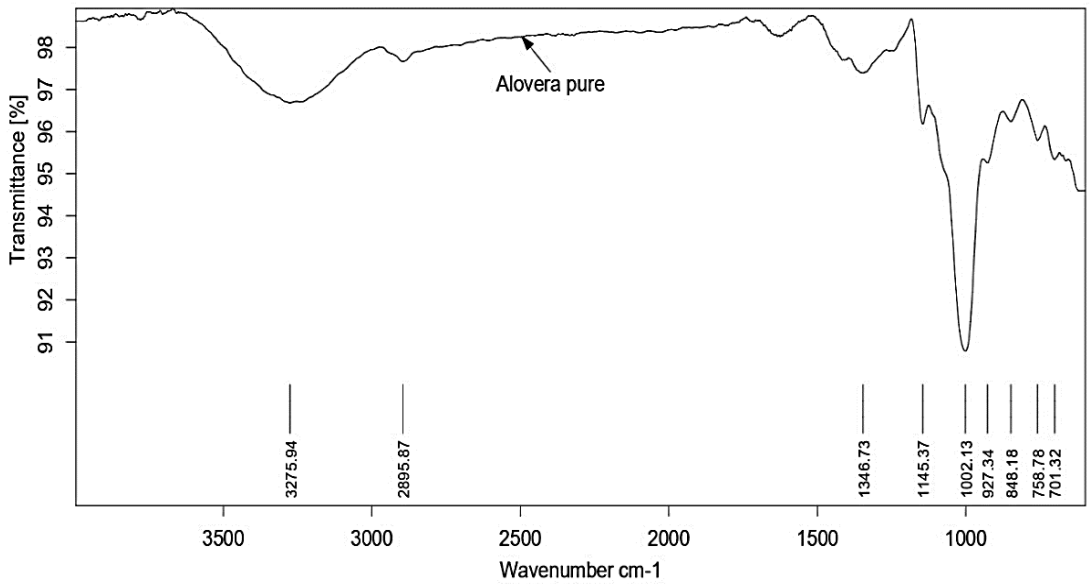


Figure 3: FTIR spectra of Aloevera gel powder

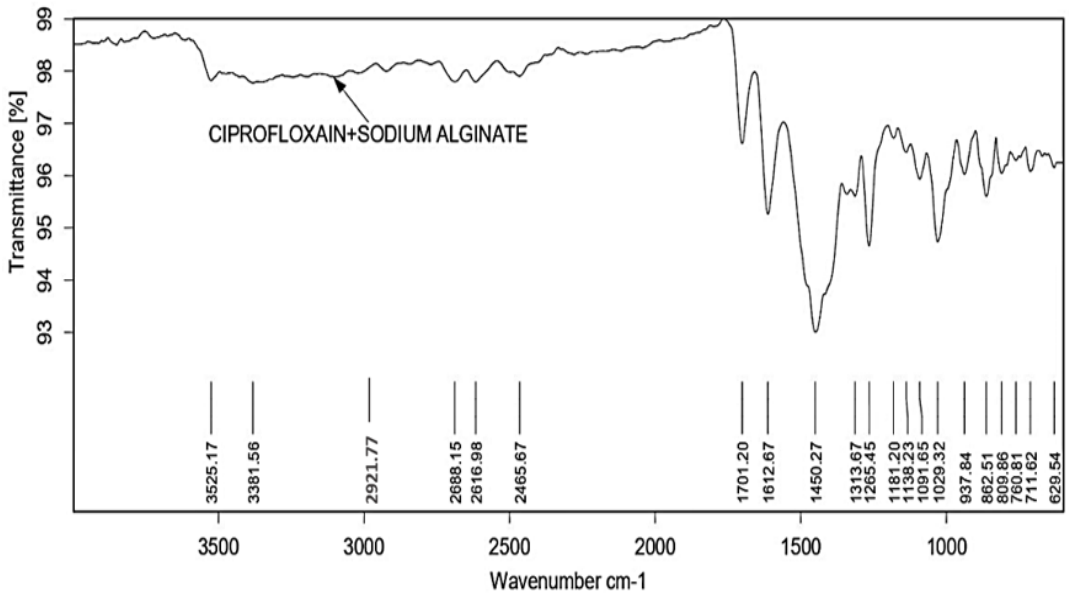


Figure 4 FTIR spectra of formulation F2

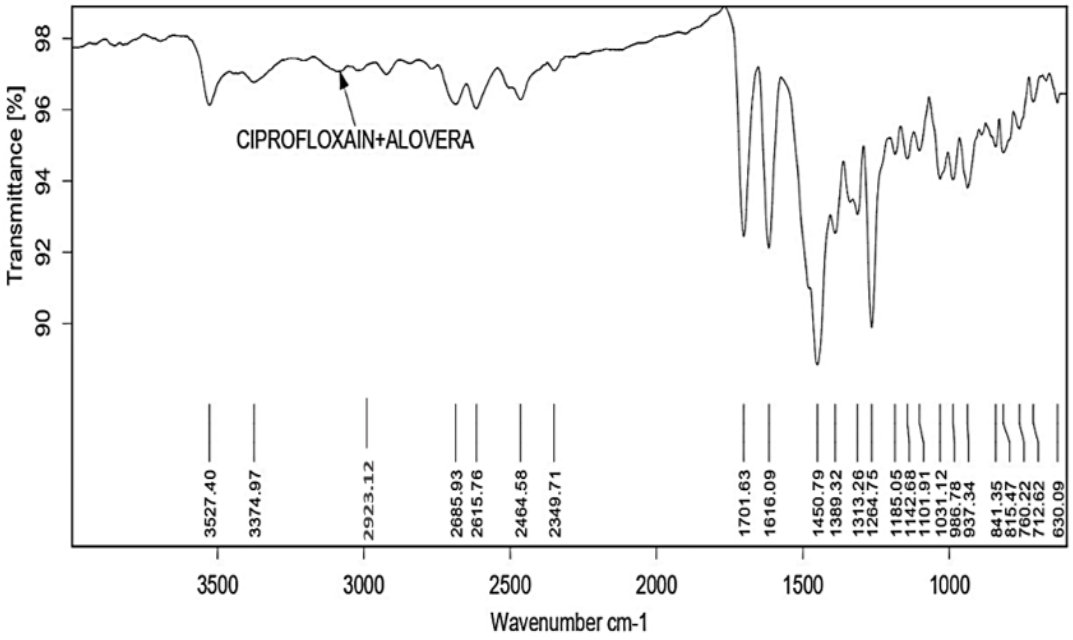


Figure 5: FTIR spectra of formulation F5

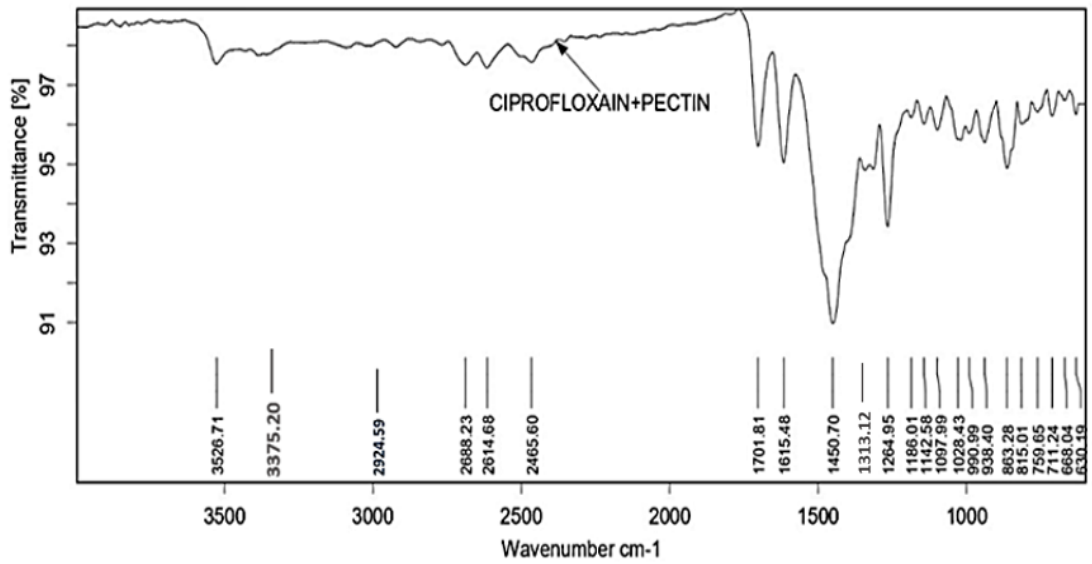


Figure 6: FTIR spectra of formulation F8

Table 3: FTIR peaks of Ciprofloxacin and the combination of drug and polymer.

Functional groups	Major peaks (wave number cm^{-1})			
	Pure ciprofloxacin	Formulation F2	Formulation F5	Formulation F8
N-H Str	3528.01	3525.17	3527.40	3526.71
O-H Str	3379.77	3381.56	3374.97	3375.20
C-H Str	2920.55	2921.77	2923.12	2924.59
C=O Str	1701.89	1701.20	1701.63	1701.81
C-H def	1451.58	1450.27	1450.79	1450.70
C-N Str	1312.81	1313.67	1313.26	1313.12
C-O Str	1142.18	1138.23	1142.68	1142.58

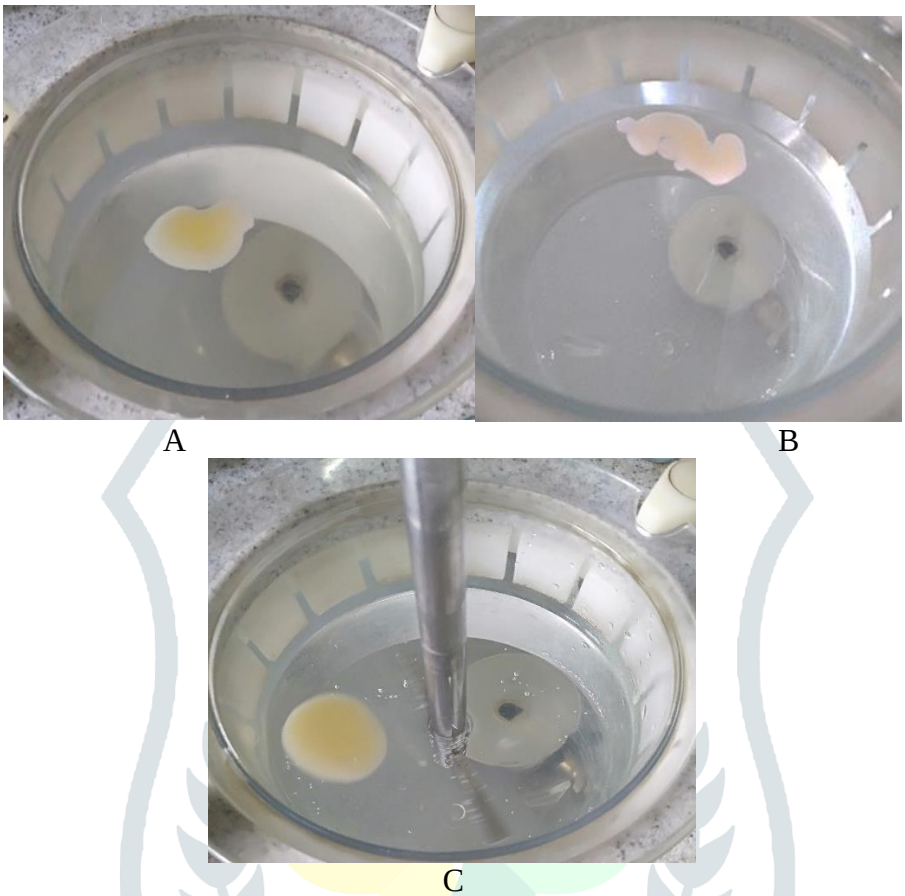
3. Pre-formulation studies

Determination of Melting point, pH and absorbance maxima

Table 4: Melting point, pH and absorbance maxima of Ciprofloxacin HCl

Parameters	Results
Melting point	291 ± 0.5 ℃
pH	5.7 ± 0.5
Absorbance maxima (λ_{max})	277.5 nm

4. Evaluation of raft forming formulations



A B C

Photo 1: Different floating raft formulations (A) Formulation F2, (B) Formulation F5 and C) Formulation F8

i. Evaluation of viscosity and pH

Table 5: Viscosity and pH of various ciprofloxacin formulations

Formulation Code	Viscosity (Cps)	pH of formulations
F1	1247.66 ± 8.17	7.66 ± 0.01
F2	1161.33 ± 2.49	7.55 ± 0.02
F3	1090.66 ± 5.24	7.88 ± 0.05
F4	1107 ± 5.09	7.45 ± 0.03
F5	1095.33 ± 2.05	7.33 ± 0.01
F6	1054.33 ± 4.10	7.29 ± 0.04
F7	1988.33 ± 5.31	7.56 ± 0.03
F8	1966.33 ± 6.59	7.81 ± 0.08
F9	1895.66 ± 2.86	7.52 ± 0.02

Values are in mean ± S.D (n=3)

ii. *In-vitro* gelling time

Table 6: *In-vitro* gelling study, *In-vitro* buoyancy study and Drug content of different raft formulations.

Formulation Code	*In-vitro* gelling study (Sec)	*In-vitro* buoyancy study (Sec)	Drug content (%)
F1	3.33 ± 1.15	11.33 ± 2.08	98.87 ± 0.72
F2	3.00 ± 1.00	14.00 ± 3.60	99.28 ± 0.79
F3	3.33 ± 1.52	11.33 ± 2.08	99.18 ± 0.58
F4	11.00 ± 1.73	19.66 ± 2.30	98.57 ± 1.66
F5	10.00 ± 1.00	20.00 ± 2.64	99.21 ± 0.58
F6	10.66 ± 1.52	19.33 ± 2.51	98.91 ± 0.29
F7	6.00 ± 1.73	13.33 ± 3.51	99.08 ± 0.68
F8	6.33 ± 1.52	13.00 ± 3.00	99.18 ± 0.50
F9	6.00 ± 1.00	11.00 ± 1.73	99.28 ± 0.41

Values are in mean ± S.D (n=3)

The *in-vitro* gelling time was determined for all the prepared formulations. The formulations were poured to the 0.1N HCl (pH 1.2) in a beaker and by visual inspection recorded the gelling lag time. The formulations showed *in-vitro* gelling time within 3 ± 1 to 11 ± 1.73 sec. The formulation F2 showed the minimum gelling lag time and formulation F4 showed maximum gelling lag time.

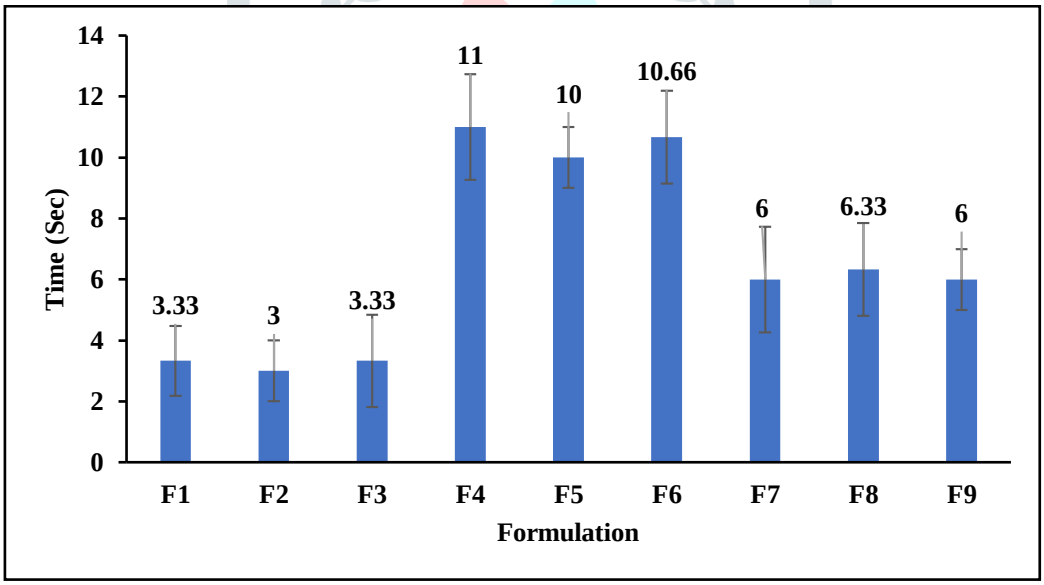


Figure 7: *In-vitro* gelling study of formulations F1 to F9

iii. *In-vitro* buoyancy study

The *in-vitro* buoyancy was determined for all the prepared formulations. The formulations were poured to the 0.1N HCl (pH 1.2) in a beaker and by visual inspection recorded the floating lag time of the rafts. The prepared formulations showed *in-vitro* buoyancy time within 11 ± 1.73 to 20 ± 2.64 sec. The formulation F9 showed the minimum floating lag time and formulation F5 showed maximum floating lag time.

iv. Drug content

The drug content was analysed spectrophotometrically at 277.5 nm. The formulations exhibited uniform drug content and minimum batch variability. All the formulations showed uniform drug content ranging 98.57 ± 1.66 % to 99.28 ± 0.79 %. The drug content for formulation F1 (98.87 ± 0.72 %), F2 (99.28 ± 0.79 %), F3 (99.18 ± 0.58 %), F4 (98.57 ± 1.66 %), F5 (99.21 ± 0.58 %), F6 (98.91 ± 0.29 %), F7 (99.08 ± 0.68 %), F8 (99.18 ± 0.50 %) and F9 (99.28 ± 0.41 %).

The drug content analysis of the formulations showed that the process employed to prepare the floating raft in this study could give raft with uniform drug content and minimum batch variability

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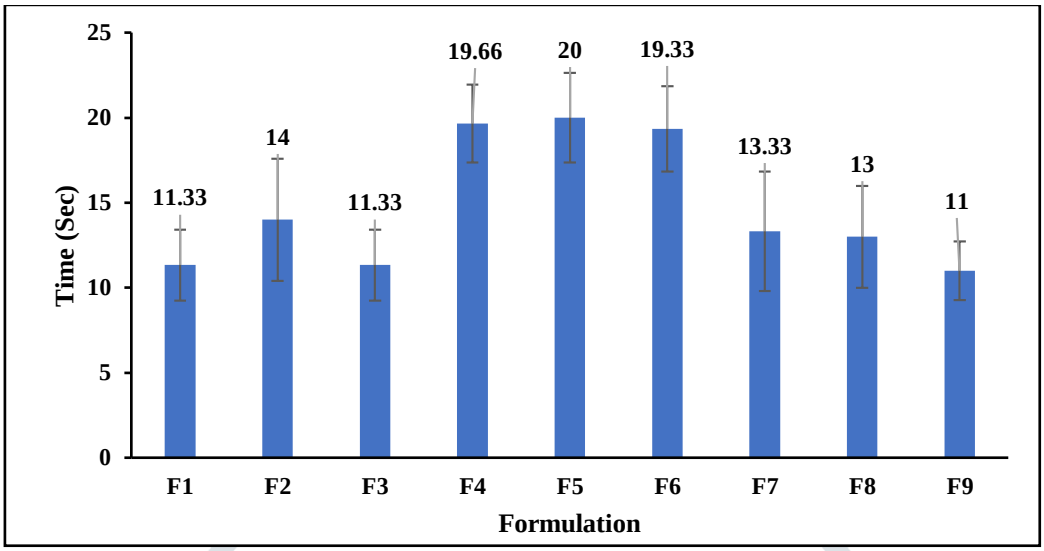

Figure 8: *In-vitro* buoyancy study of formulation F1 to F9

v. *In-vitro* drug release studies

The *in-vitro* drug release studies from floating raft formulations were performed for 9 h in 0.1N HCl (pH 1.2). From the dissolution studies, at the end of 9 h, it was observed that the release of drug from different formulations was in the range of 65.66 ± 0.48 % to 93.32 ± 0.30 %. Formulations F1-F3 prepared with only sodium alginate showed higher drug release of 92.47 ± 0.62 % to 93.04 ± 0.84 % in 7 hrs as compared to other formulations. The drug release was found to be higher than the reported values. (15) The formulations prepared using combinations of sodium alginate and aloevera gel powder showed drug release of 81.5020 % to 93.3218 % in 9 hrs. The formulations prepared using combination of sodium alginate and pectin showed drug release of 65.66 ± 0.48% to 74.08 ± 0.74% in 9 hrs. This indicated that the formulations showed sustained release of drug. The formulation F5 showed maximum drug release 93.32 ± 0.30 % and Formulation F8 showed lowest drug release 65.66 ± 0.48 % when compared to all other formulations.

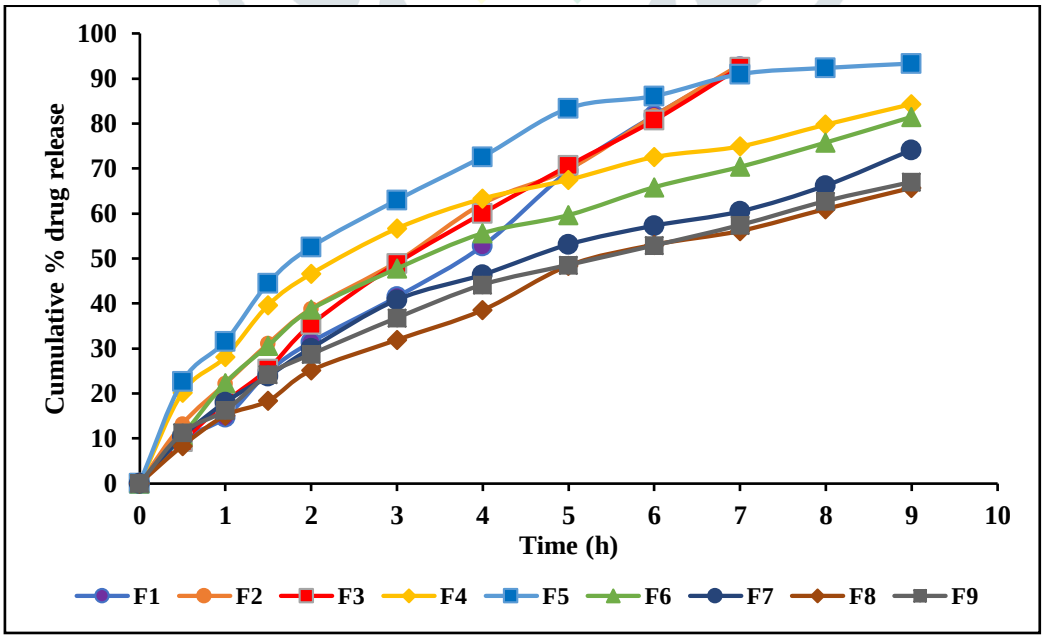

Figure 9: Cumulative % drug release from formulations F1 to F9.

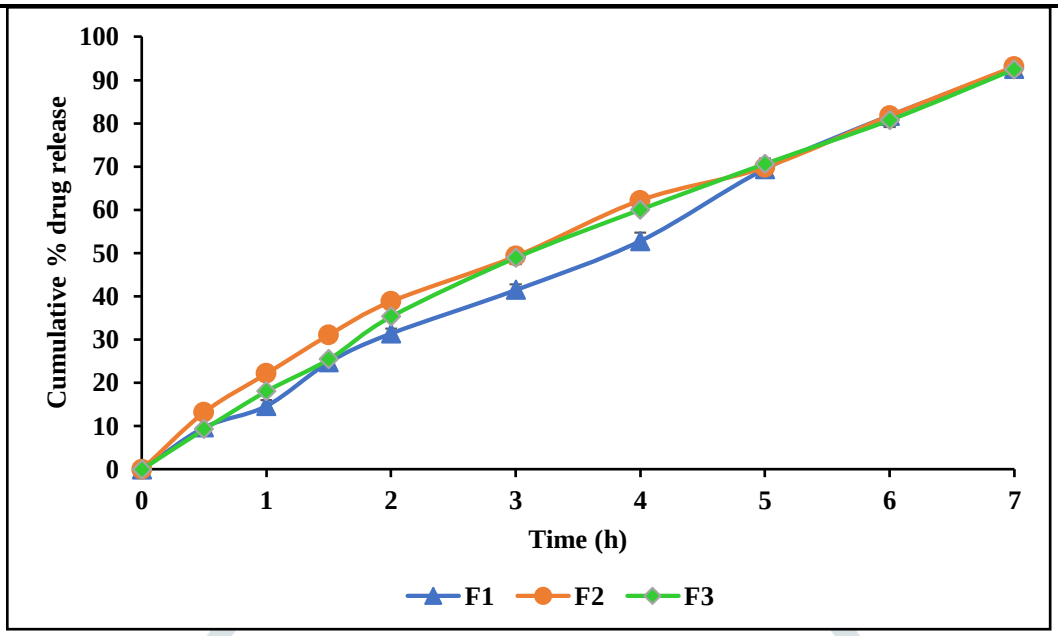

Figure 10: Cumulative % drug release from formulations F1, F2 and F3.

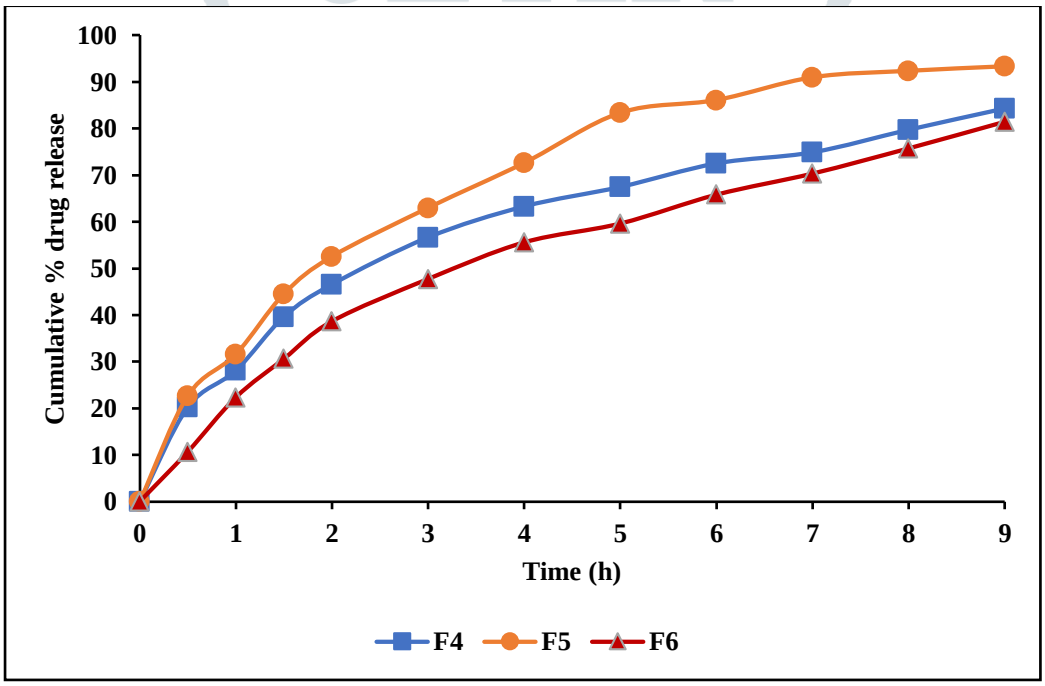

Figure 11: Cumulative % drug release from formulations F4, F5 and F6.

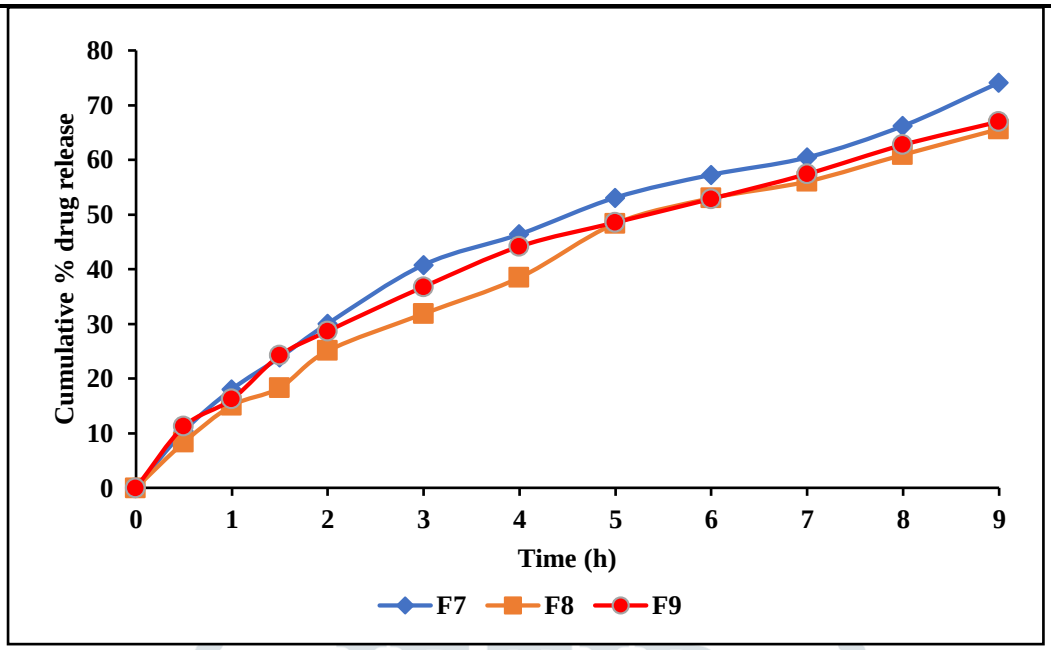

Figure 12: Cumulative % drug release from formulations F7, F8 and F9.

vi. Release kinetic studies

Table 7: Kinetics of drug release of Ciprofloxacin floating raft formulations

Formulation code	Regression co-efficient (R^2)			Korsmeyer' s -Peppas plot 'n' values
	Zero order (R^2)	First order (R^2)	Higuchi equation (R^2)	
F1	0.9965	0.9069	0.9358	0.9867
F2	0.9814	0.9270	0.9746	0.9467
F3	0.9887	0.9317	0.9601	0.9989
F4	0.8684	0.9800	0.9853	0.8463
F5	0.8214	0.9862	0.9653	0.8584
F6	0.9238	0.9902	0.9908	0.9699
F7	0.9484	0.9873	0.9901	0.9590
F8	0.9672	0.9957	0.9830	0.9912
F9	0.9466	0.9909	0.9939	0.9218

***In-vitro* drug release kinetics**

The kinetics of drug release was obtained by fitting *in-vitro* drug release data in various kinetic models. For all the formulations the *in-vitro* drug release data was best fit to Higuchi model of diffusion.

Formulations F8 followed first order and case II diffusion release mechanism. The formulation F8 contained sodium alginate and pectin 2 % and 0.5 % respectively. The formulation F8 showed sustained drug release of 65.66 ± 0.48 % in 9hrs as compared to all the other formulations. Formulation F8 was selected as best sustain release formulation.

vii. Stability study

The formulation F8 was subjected to stability study and the results of the *in-vitro* drug release study indicated that the formulation was stable during study period.

The *in-vitro* dissolution profiles of the formulation F8 after stability study was not significantly different ($p > 0.05$).

Table 8: Cumulative % drug release from formulation F8 after stability study.

Time (h)	Cumulative % drug release of formulation F8	Cumulative % drug release of formulation F8 at 40 ± 0.5 ℃ temperature and 75 ± 5 % RH after 8 weeks
0	0	0
0.5	8.32 ± 0.25	8.39 ± 0.28
1	15.07 ± 0.52	15.10 ± 0.89
1.5	18.33 ± 0.04	18.11 ± 0.46
2	25.09 ± 0.70	24.65 ± 0.19
3	31.88 ± 0.37	31.13 ± 0.68
4	38.49 ± 0.48	38.45 ± 0.43
5	48.37 ± 0.62	47.81 ± 0.80
6	53.01 ± 0.62	52.85 ± 0.43
7	56.07 ± 0.22	56.00 ± 0.27
8	60.97 ± 0.50	60.99 ± 0.39
9	65.66 ± 0.48	64.69 ± 0.03

Values are in mean ± S.D (n=3)

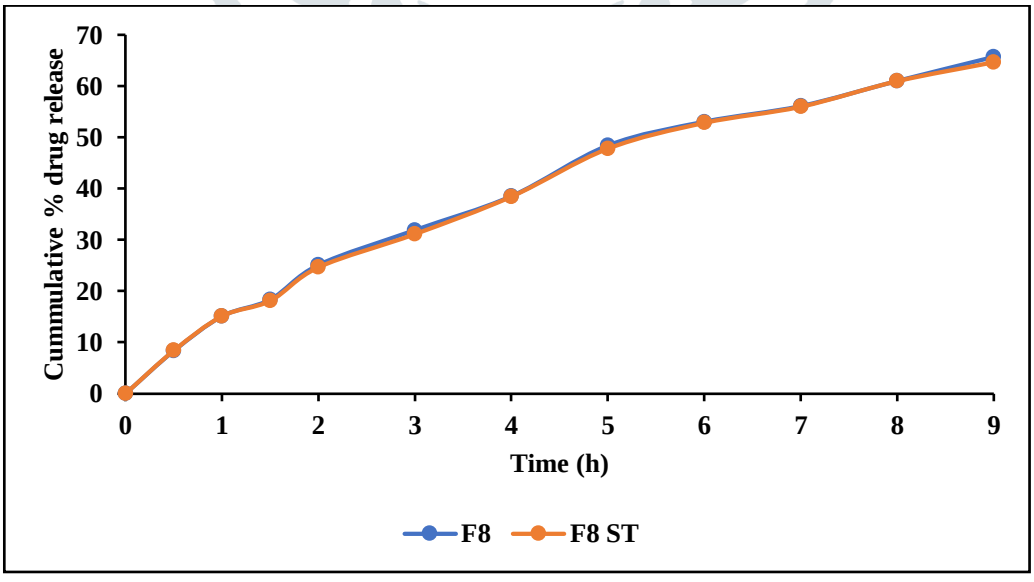

Figure 13: Comparison of cumulative % drug release from formulation F8 before and after stability (8 weeks).

V. CONCLUSION

Ciprofloxacin is a broad-spectrum antibiotic drug. The floating raft forming formulations of ciprofloxacin were formulated using sodium alginate, pectin and aloevera gel powder. The results of FTIR studies showed that there was no interaction between drug and excipients. The formulation F8 showed greater potential of sustaining drug release as the drug release was found to be lowest amongst prepared formulations.

VI. REFERENCES

1. Sharma S, Nanda A, Singh L. Gastroretentive drug delivery system: An overview. Int J Pharm Biomed Sci. 2011;2(3):954-958.
2. Chawla G, Gupta P, Koradia V, Bansal A K. Gastroretention: A means to address regional variability in intestinal drug absorption. Pharm Tech.2003: Jul:50-68.
3. Prajapati V D, Jani G K, Khutliwala T A, Zala B S. Raft forming system-An upcoming approach of gastroretentive drug delivery system. J Controlled Release. 2013; 168:151-165.
4. Sathish D et al., Floating drug delivery systems for prolonging gastric residence time: A review. Current Drug Deliv. 2011; 8:494-510.
5. Garg R, Gupta G D et al., Progress in controlled gastroretentive delivery systems. Trop J Pharm Res. 2008; 7(3):1055-1066.
6. Bineesha K B, Dharan S S, Jousha S A, Panicker J T, James J E et al., Gastricretentive raft forming drug delivery: A novel expansion. IJPPR. 2019; 15(4):200-212.
7. Available at: www.accessdata.fda.gov.2016:1-53 [Accessed July 24rd 2023]
8. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/Ciprofloxacin#section=Depositor-Provided-PubMed-Citations [Accessed August 23rd 2023]
9. Rowe RC, Sheskey PJ, Quinn M. Handbook of pharmaceutical excipients. 6th ed. Stuttgart, Germany: Deutscher Apotheker Verlag. 2009; 86-89, 478-479, 622-624, 640-642.
10. Adil P, Shah D, Desai TR, Noolvi MN. Development and evaluation of chitosan and aloevera gel mucilage interpolymer complex- based mucoadhesive buccal films of tramodolol hydrochloride. Asian J Pharm. 2016; 9(5): S43-49.
11. Abou Youssef NAH, Kassem AA, Magda Abd El Samea El Massik, Boraie NA. Development of gastroretentive metronidazole floating raft system for targeting *Helicobacter pylori*. Int J Pharma. 2015; 486(1-2):297-305.
12. Teaima MH, Abdel Hamid MM, Shoman NA, Jasti BR, Mohamed A. El-Nabarawi, Yasser M. Formulation, characterization and comparative pharmacokinetic study of bupropion floating raft system as a promising approach for treating depression. J Pharm Sci. 2020; 109:3451-3461.
13. Ahmad Bani-Jaber and Abdullah S. Development and characterization of novel Ambroxol sustained-release oral suspensions based on drug-polymeric complexation and polymeric raft formation. Pharm Dev and Tech. 2020; 1-10. https://doi.org/10.1080/10837450.2020.1729799.
14. Bunlung S, Nualnoi T, Issarachot O, wiwattanapatapee R. Development of raft-forming liquid and chewable tablet formulations incorporating quercetin solid dispersions for treatment of gastric ulcers. Saudi Pharm. J. 2021; 29 (10): 1143–1154.
15. Pashikanti SP, Jyothsna B. Formulation and evaluation of floating *in-situ* gel of ciprofloxacin. Int J Applied Pharma. 2019; 11(1):198-204.
16. Prajapati ST, Mehta AP, Modhia IP, Patel CN. Formulation and optimisation of raft-forming chewable tablets containing H_2 antagonist. Int J Pharma Investigation. 2012; 2(4):176.
17. Costa P, Sousa Lobo JM. Modeling and comparison of dissolution profiles. Eur J Pharm Sci 2001; 13:123-33.