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FORMULATION AND EVALUATION OF FLOATING MATRIX TABLET OF CIPROFLOXACIN

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ABSTRACT: Objectives: The objective of the present study is formulate and evaluate of floating matrix tablet of ciprofloxacin, which would remain in stomach and/or upper part of GIT for prolonged period of time. Experimental Work: The floating matrix tablets of ciprofloxacin were prepared by direct compression using HPMC K15M, HPMC K100M polymers as a swelling agent. Sodium bicarbonate was used as a floating effervescent agent. The tablets were formulated by taking various concentrations of polymers as a release retarding agents. The formulations were evaluated for various physical parameters, floating lag time and In-vitro drug release etc. Result and Discussion: From the results obtained, Batch S3 gives desirable sustained effect for 12 hours having 99.69% drug release at the end of the 12 hours. Batch S3 contain HPMC K15M and HPMC K100M on response parameters. From the formulated 32 factorial batches, S3 batch containing HPMC K15M and HPMC K100M showed the lowest lag time of 25.22±0.88 and the highest % CDR at 12th hr of 99.69 %.

KEYWORDS: Gastro-retentive, Ciprofloxacin, HPMC K15M, HPMC K100M.

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1. INTRODUCTION

Floating dosage forms have a bulk density lower than that of gastric fluid and therefore remain bouyant on the stomach contents to prolong the gastric retention time. Ciprofloxacin, 1-cyclopropyl-6-fluoro-4-oxo-7-piperazin-1-ylquinoline-3-carboxylic acid. Ciprofloxacin is a broad-spectrum

antibiotic that belongs to the family of fluoro quinolones. It is used for the treatment of gram-negative infections of the skin, sinuses, bone, lung, ear, abdomen, and bladder. Gastro-retentive delivery is one of the site specific delivery for the delivery of drugs either at stomach or at intestine. Gastric retention may increase solubility for the drugs which are poorly soluble in intestine due to alkaline pH before they get emptied from the stomach. These systems are also advantageous in improving GIT absorption of drug having narrow absorption windows and site-specific absorption limitations. A systematic approach for design and development of gastroretentive drug delivery system of Ciprofloxacin using polymers which increases the gastric residence time, decreases the diffusion distance and allow more of the antibiotic to penetrate through the gastric mucus layer and act locally at the infectious site to enhance the bioavailability and therapeutic efficacy of the drug [1-10].

2. MATERIALS AND METHODS

Ciprofloxacin was received as a gift sample from Galen Pharmaceuticals, Waghodia, Vadodara, Gujarat, India. All other excipients and solvents were used of analytical grade.

FORMULATION

A 3^2 full factorial design was used in the present study to obtain optimized formulation. In this design, 2 factors were evaluated, each at 3 levels and experimental trials were performed at all 9 possible combinations. The amount of HPMC K15M (X1) and amount of HPMC K100M (X2) were selected as independent variables response. The lag time (Y1) and % drug release (Y2) at12th hr were selected as dependent variables responses. [11]

3. RESULTS AND DISCUSSION

Independent Variables (Factors)	Coded Value			Actual Value		
	LOW	MEDIUM	HIGH	LOW	MEDIUM	HIGH
HPMC K15M	-1	0	+1	75	80	85
HPMC K100M (mg) (X2)	-1	0	+1	75	80	85

Table No. 1: Coded values and Actual values of the Independent Variables

Run	Coded Values		Actual Values	
Batch Code	X1	X2	HPMC K15M (mg) (X1)	HPMC K100M (mg) (X2)
S1	-1	-1	75	75
S2	-1	0	75	80
S3	-1	+1	75	85
S4	0	-1	80	75
S5	0	0	80	80
S6	0	+1	80	85
S7	+1	-1	85	75
S8	+1	0	85	80
S9	+1	+1	85	85

Table No. 2: Composition of the Floating matrix tablets

EVALUATION PARAMETERS

The floating matrix tablets of ciprofloxacin were evaluated for their pre compression parameters like Angle of Repose, Bulk density, Tapped density, Hausner's ratio, Carr's Index and their post compression parameters like hardness, friability, weight variation and drug content [12-22] **Floating Lag Time**

The in vitro buoyancy was determined by the lag time. The tablets were placed in a 100 ml beaker containing 0.1 N HCl. The time required for a tablet to rise to the surface for floating was determined as the lag time. [23- 24]

Floating Time

The tablet was placed in a 100 ml glass beaker containing 0.1 N HCl. The time for which the tablet remained floating on the surface of medium was determined as floating time. [25- 26]

In-Vitro Dissolution Studies

The release rate of ciprofloxacin from floating tablets was determined using The United States Pharmacopoeia (USP) dissolution testing apparatus II (Paddle Type). The dissolution was performed using 900 ml of 0.1 N HCl solutions at 37ºC ± 0.5 º C temperatures and at 50 rpm. At every 1 hour interval upto 12 hrs, samples of 5 ml was withdrawn from the dissolution medium and

that amount was replaced with fresh medium to maintain the volume constant. The absorbance of the solutions was measured at 260 nm for Ciprofloxacin using UV- Visible double beam spectrophotometer. [27-30]

Formulation Code	Angle of Repose(θ) (n=3)	Bulk Density (g/cm^3) (n=3)	Tapped Density (g/cm^3) (n=3)	Carr's Index (%) (n=3)	Hausner's Ratio (n=3)
S1	25.83±0.13	0.426±0.032	0.519±0.040	17.92±0.55	1.22±0.022
S2	26.69±0.56	0.473±0.025	0.525±0.014	9.90±0.76	1.11±0.023
S3	25.78±0.26	0.452±0.033	0.514±0.090	12.06±0.45	1.14±0.056
S4	28.24±0.46	0.467±0.052	0.536±0.012	12.87±0.88	1.15±0.067
S5	27.48±0.67	0.436±0.067	0.539±0.09	19.10±0.12	1.23±0.088
S6	25.36±0.73	0.445±0.018	0.528±0.012	15.72±0.75	1.19±0.035
S7	26.16±0.72	0.418±0.021	0.533±0.026	21.58±0.84	1.28±0.073
S8	26.78±0.84	0.423±0.035	0.538±0.028	21.38±0.66	1.27±0.034
S9	26.52±0.03	0.431±0.089	0.518±0.057	16.80±0.58	1.20±0.063

Table No. 3: Pre-Compression Parameters of Formulations (S1-S9)

Formulation Code	Hardness (Kg/Cm^2) (n=3)	Friability (%)	Weight Variation (mg) (n=20)	Drug Content (%) (n=10)	Lag time (sec) (n=3)	Floating time (hrs)
S1	4.44±0.12	0.28	699.01±0.12	98.57±0.63	30.12±1.01	>12
S2	4.63±0.16	0.24	698.45±2.35	99.82± 0.52	28.74±0.78	>12
S3	4.20±0.20	0.21	698.17±1.60	99.32± 1.12	25.22±0.88	>12
S4	4.34±0.18	0.16	696.42±2.77	98.94 ±1.31	48.18±1.32	>12
S5	4.01±0.18	0.13	697.87±1.58	99.89±0.10	38.15±2.92	>12
S6	4.40± 0.10	0.14	696.12±2.15	99.74± 0.58	36.36±2.03	>12
S7	4.43±0.19	0.10	698.01±0.12	99.65±1.02	59.48±1.11	>12
S8	4.39±0.26	0.11	699.12±2.15	98.56±1.14	50.48±1.25	>12
S9	4.48±0.78	0.10	697.01±1.61	99.57±0.87	39.40±1.79	>12

Table No. 4: Post-Compression Parameters of Formulations (S1-S9)

IN-VITRO DISSOLUTION STUDY

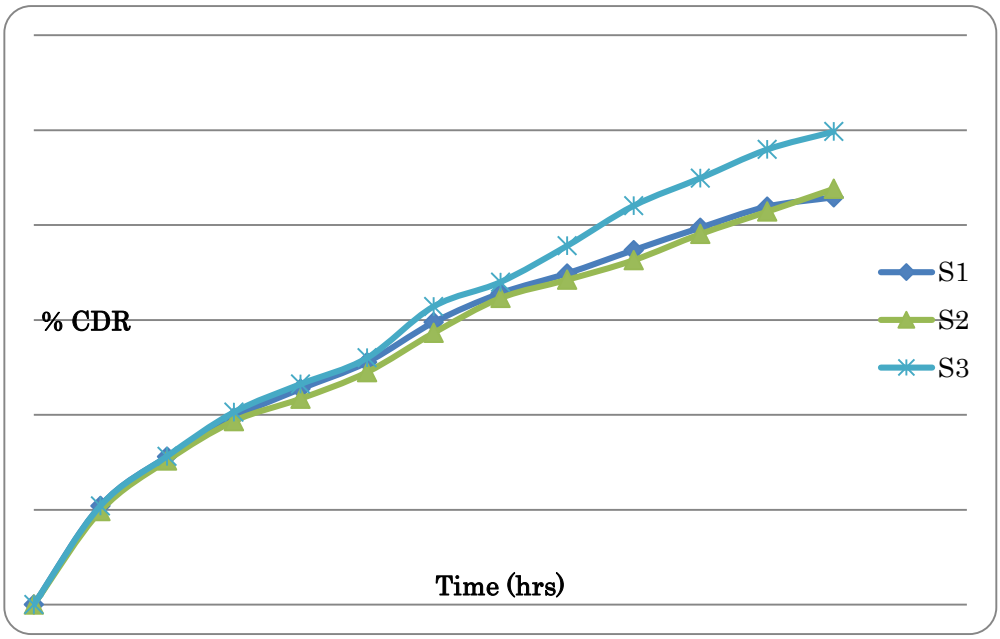

Figure 1: % Drug release of floating matrix tablet (S1-S3).

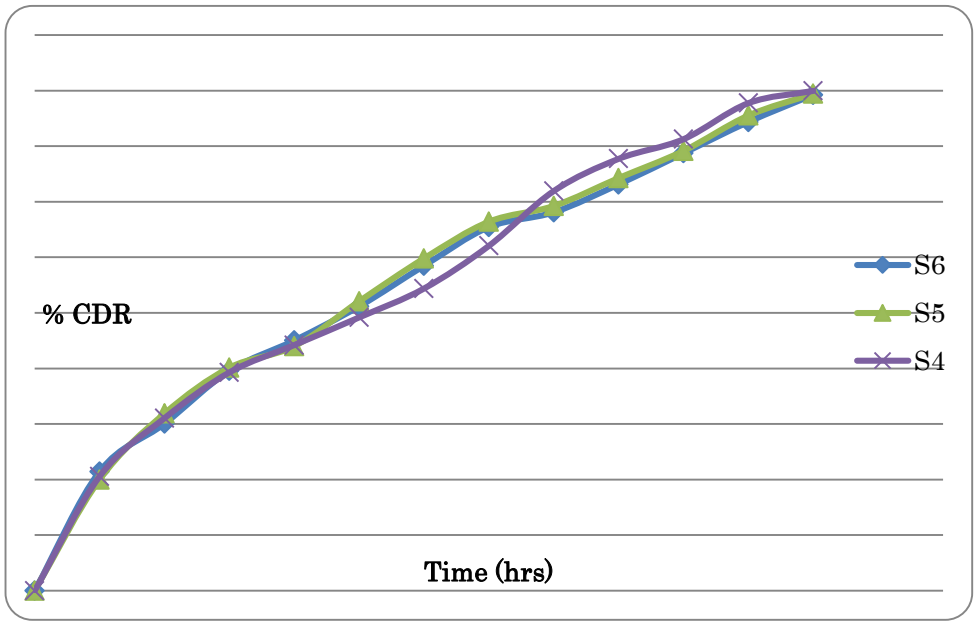

Figure 2: % Drug release of floating matrix tablet (S4-S6).

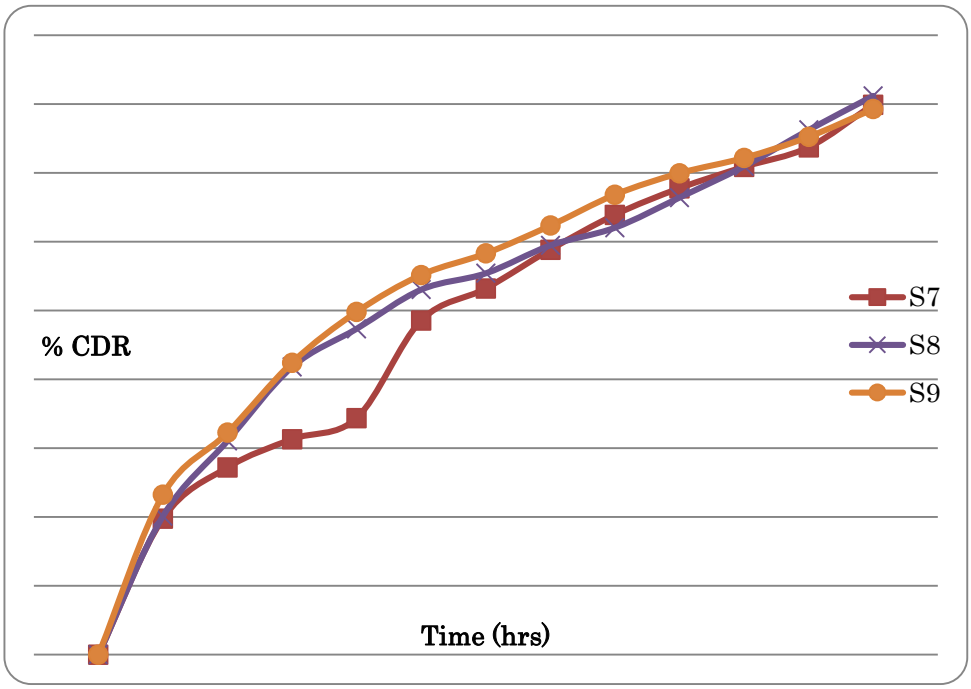

Figure 3: % Drug release of floating matrix tablet (S7-S9).

As seen from the, contour plot of the lag time revealed that there was corresponding increase in lag time with increase in the concentration of HPMC K15M (A). Moreover it was revealed that increase in concentration of HPMC K100M (B) also led to decrease in lag time. Thus combination of both in suitable concentration might decrease the lag time of the floating tablets.

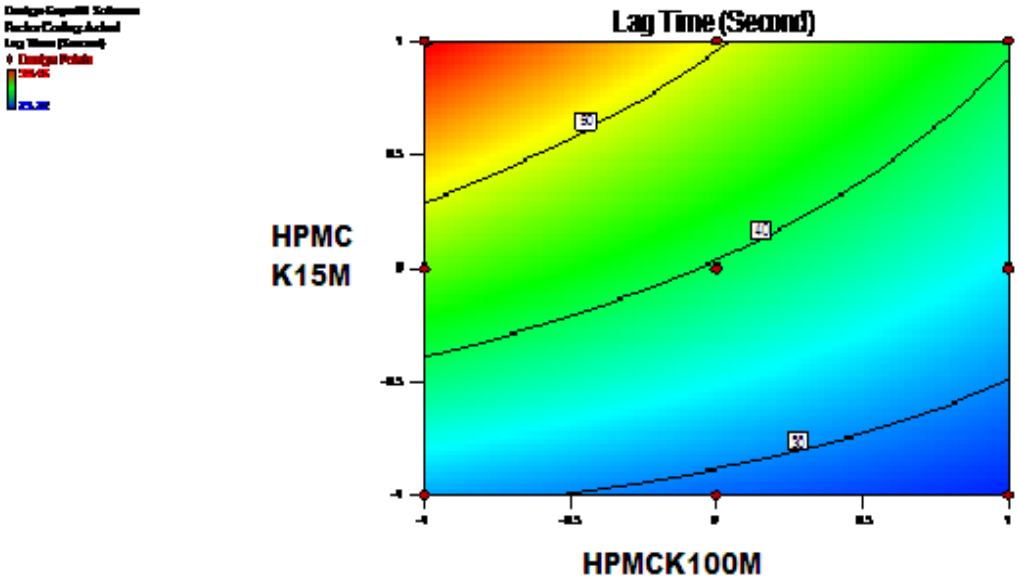

Figure 4: Contour plot showing the effect of HPMC K15M and HPMC K100M on lag time

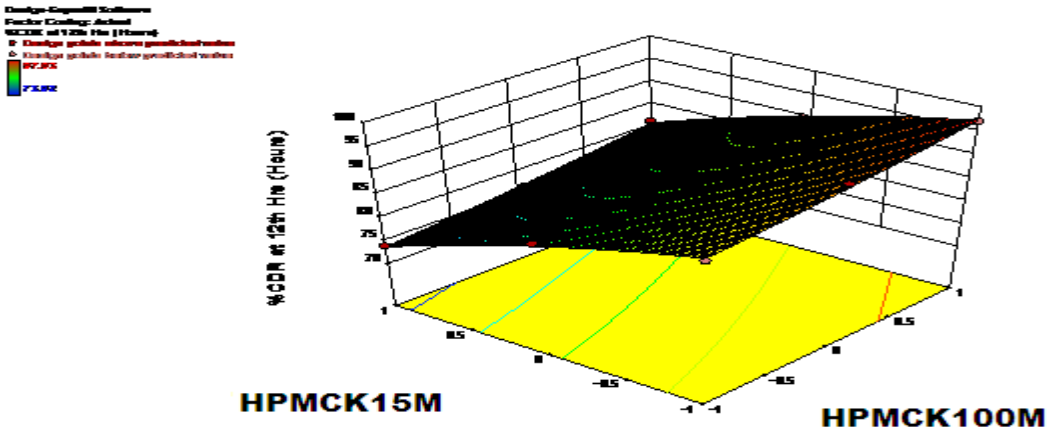

Figure 5: Response surface plot (3D) showing the effect of HPMC K15M & HPMC K100M on Lag Time

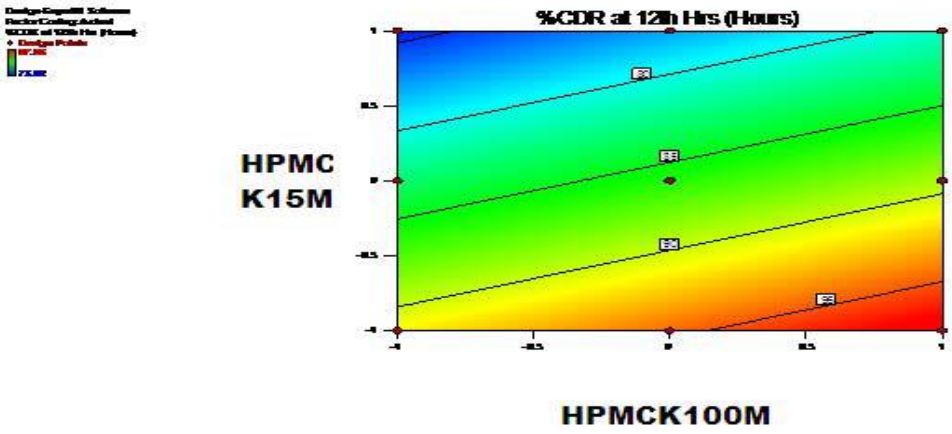

Figure 6: Contour plot showing the effect of standard error by %CDR of HPMC K15M and HPMC K100M at 12 hrs.

As seen from the fig, contour plot of the % CDR at 12th hr revealed that there was corresponding decrease in % CDR at 12th hr with increase in the concentration of HPMC K15M and HPMC K100M. Thus combination of both in suitable concentration might increase the% CDR at 12th hrs of the floating tablet.

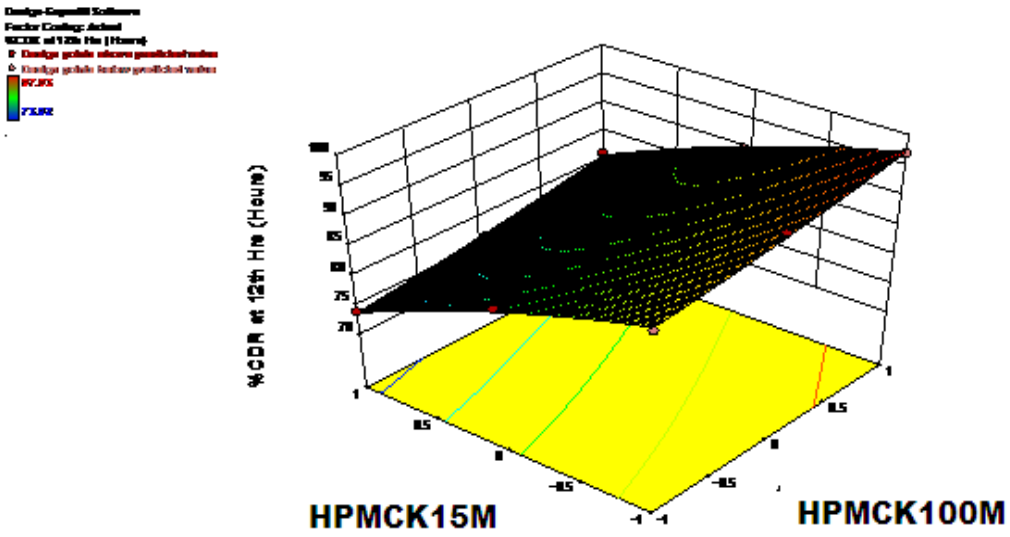

Figure 7: Response surface plot (3D) showing the effect of HPMC K15M &HPMC K100M on %CDR at 12 hrs.

Table No. 5: Evaluation of tablets by check point batch

Formulations	Parameters	Predicted Values	Obtained Values	% Error
CP1	Lag Time (Sec)	34.47	36.20	-1.73
	% CDR at 12 hrs	90.21	91.52	-1.31
CP2	Lag Time (Sec)	30.86	29.05	1.81
	% CDR at 12 hrs	92.12	89.10	3.02

Observed values were found to be closer to predicted values obtained from the check point batch. It was observed that there was no significant difference between observed and predicted values.

Data Analysis

Formulations	Factor 1 (X1): HPMC K15M (mg)	Factor 2 (X2): HPMC K100M (mg)	Response 1 Lag Time (Seconds)	Response 2 % CDR at 12th hr (Hours)
S1	75	75	30.12	85.84
S2	75	80	28.74	87.63
S3	75	85	25.22	99.69
S4	80	75	48.18	89.27
S5	80	80	38.15	89.46
S6	80	85	36.38	89.99
S7	85	75	59.48	79.92
S8	85	80	50.48	81.21
S9	85	85	39.40	79.29

Table No. 6: Data analysis of factorial formulations

4. CONCLUSION

The floating tablets of Ciprofloxacin were formulated by direct compression using two polymers like HPMC K15M and HPMC K100M as a release retardant agent. The formulations were evaluated for various parameters like Hardness, Friability, Weight variation, Floating lag time, Floating time, etc. From the results obtained, it was concluded that the optimized formulation containing HPMC K15M and HPMC K100M shows desired drug release properties and floating behavior. Hence HPMC K15M and HPMC K100M is a potential polymer candidate for formulation of effervescent floating tablets. It was found that batch S3 gives desirable sustained effect for 12 hrs having 99.69% releases at the end of 12 hrs.

CONFLICT OF INTEREST

The authors declare that no competing financial interests exist.

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