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Research Article

## FORMULATION DESIGN AND OPTIMIZATION OF ORAL FLOATING MATRIX TABLETS OF CIPROFLOXACIN HCL BY USING HPMC AND XANTHAN GUM WITH EXPERIMENTAL DESIGN

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### ABSTRACT

The oral floating matrix tablets of Ciprofloxacin Hydrochloride were formulated by Experimental design by using HPMC K<sub>100</sub>M and Xanthan gum as the retardant polymers each with three different levels with an approach to increase gastric residence and thereby improve drug bioavailability. From FTIR results confirm the absence of chemical interaction between the drug with the excipients used in tablet formulations. Also, there was no shift in the endotherm of in the drug- excipients mixtures indicating compatibility of drug with all the excipients. All the tablets were prepared by effervescent approach in which Sodium bicarbonate was added as a gas generating agent. Floating Matrix tablets were prepared by direct compression method and prepared tablets were evaluated for weight variation, percentage friability, hardness and drug content studies. All the formulations showed compliance with pharmacopeia standards. Floating lag times of all the formulations were within 1 minute and Total floating time of all the formulations were more than 12 hours. In vitro release studies revealed that the release rate decreased with increase polymer proportion of retarding polymers. The formulation CHX<sub>8</sub> sustained release of drug for 12 hrs with 20% release of drug after 1hr and more than 97% at the end of 12 hrs. From the Kinetic model it was found that the optimized formulation CHX<sub>8</sub> showed linearity in case of Zero order (R<sup>2</sup>: 0.952) and Higuchi model (R<sup>2</sup>: 0.948). By fitting data to Korsmeyer-Peppas model and 'n' value lying above 0.5 indicating non Fickian release.

**Keywords:** Oral floating matrix tablets; Experimental design; HPMC K<sub>100</sub>M; Xanthan gum; Ciprofloxacin Hydrochloride.

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### INTRODUCTION

Gastro Retentive Drug Delivery System gets retained for longer period of time in stomach, thus helping in absorption of drug for the intended duration of time, which in turn improves bioavailability by reducing drug wastage, and improving solubility of drugs that are less soluble at high pH environment. It also helps in achieving local delivery of drug in the stomach and proximal small

intestine. Floating systems are one of the important categories of drug delivery systems with gastric retentive behavior.<sup>[1]</sup> Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is

emptied from the stomach.<sup>[2]</sup> Ciprofloxacin belonging to the family of quinolones (term refers to potent chemotherapeutic antibacterial agents). CPF is a broad-spectrum antibiotic active against both Gram-positive and Gram-negative bacteria. It functions by inhibiting DNA gyrase, a Type II topoisomerase and topoisomerase IV, enzymes necessary to separate bacterial DNA, thereby inhibiting cell division and also affects mammalian cell replication. It is used in the treatment of infections such as lower respiratory tract, urinary tract, bone and joint infections, hospital acquired infections, and diarrheal infections. Ciprofloxacin is a broad-spectrum antibiotic active against both Gram-positive and Gram-negative bacteria. It is absorbed completely (70%) after oral administration and having a biological half-life of 3.5 to 4.5 hrs. The drug should be administered twice a day. A rationale for developing Ciprofloxacin HCl as a gastro retentive dosage form, which is retained in the stomach for prolonged period of time and produces a constant input of drug to the absorption site. This improves bioavailability of the drug, reduces frequency of dosing, thus minimizing side effects.<sup>[3]</sup> The aim of the present study is formulation design and optimization of oral floating matrix tablets of Ciprofloxacin HCl by using Experimental Design. The objective of the present study is to formulate the Ciprofloxacin HCl floating tablets using HPMC K<sub>100</sub>M and Xanthan gum as the retardant polymers by direct compression techniques.

## MATERIALS AND METHODS

### MATERIALS

Ciprofloxacin Hydrochloride was obtained as a gift sample from Dr Reddy's Lab (Hyderabad, India), HPMC K<sub>100</sub> and Xanthan gum were obtained from Aurobindo Pharma Ltd, (Hyderabad, India), Micro Crystalline Cellulose and Mg. Stearate from Loba Chem (Mumbai, India). All other chemicals and ingredients were used for study are of commercial grade.

### METHODS

#### Identification of drug

The drug was identified by Infrared spectroscopy (IR) and Ultraviolet spectroscopy (UV).

#### Infrared Spectroscopy

Infrared (IR) spectra of received gift sample of drugs was performed in the range of 4000cm<sup>-1</sup> to 400cm<sup>-1</sup> by using FT-IR (DRS) technique (FT IR-Affinity-1 spectrophotometer (DRS-8000) SHIMADZU, Japan) and studied for the presence of characteristic peaks.

#### Ultraviolet Spectroscopy

The samples were subjected to UV Spectrophotometric analysis and were scanned for absorption maxima ( $\lambda_{max}$ ) in the range of 200 to 400nm using UV-Visible Spectrophotometer in an appropriate medium and the same was compared with that of reference values in literature.

### Drug-polymer compatibility study

It is well known that prior to the development of any dosage form with a new or old drug candidate, it is essential that certain fundamental physical and chemical properties of the drug molecule and other derived properties of the drug powder are determined. This information will dictate many of the subsequent events and possible approaches in formulation development. Hydrophilic polymers, as well as other excipients, contain reactive functional groups that may give rise to chemical and physical transformations. Thus, when studying new pharmaceutical formulations, it is important to verify the possibility of occurrence of incompatibilities between the components of the formulation.

#### Fourier-Transform Infrared Spectroscopy (DRS)

Fourier-transform infrared (DRS) spectra were obtained by using an FT IR-Affinity-1 spectrophotometer (DRS-8000) SHIMADZU, Japan. The pure drug samples (Ciprofloxacin) were previously ground and mixed thoroughly with potassium bromide, an infrared transparent matrix, at 1:1 (Sample: KBr) ratio, respectively. The KBr powder was used as blank for background correction in FT-IR (DRS) studies. Forty five scans were obtained at a resolution of 4 cm<sup>-1</sup>, from 4000 to 400 cm<sup>-1</sup>.

#### Differential scanning calorimetry

The DSC measurements were performed on a DSC-4000 (Seiko Instruments, Japan) differential scanning calorimeter with a thermal analyzer. All accurately weighed samples (about 2 mg of sample or its equivalent) were placed in sealed aluminum pans, before heating under nitrogen flow (20 ml/min) at a scanning rate of 10°C min<sup>-1</sup> from 50°C to 350°C. An empty aluminum pan was used as reference.

#### Experimental design<sup>[4]</sup>

Some possible experimental trials, generated by application of 3<sup>2</sup> factorial designs, were conducted to evaluate each independent factor at 3 levels. Formulation combinations (CHX<sub>1</sub> – CHX<sub>9</sub>) using factorial design were shown in **Table 3 & 4**. The percentages of HPMC K<sub>100</sub>M (X<sub>1</sub>) and Xanthan gum (X<sub>2</sub>) were chosen as control variables while, Y<sub>1</sub> (Cumulative % of drug released at 1 hr), Y<sub>6</sub> (Cumulative % of drug released at 6 hr), Y<sub>12</sub> (Cumulative % of drug released at 12 hr) were selected as response variables by using Design Expert Software.

#### Pharmacokinetic model<sup>[5, 6, 7]</sup>

##### Zero order kinetics

Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly (assuming that area does not change and no equilibrium conditions are obtained) can be represented by the following equation:

$$W_0 - W_t = K_0t$$

Where  $W_0$  is the initial amount of drug in the pharmaceutical dosage form,  $W_t$  is the amount of drug in the pharmaceutical dosage form at time  $t$  and  $k$  is proportionality constant. Dividing this equation by  $W_0$  and simplifying:  $f_t = k_0t$  Where  $f_t = 1 - (W_t/W_0)$  and  $f_t$  represents the fraction of drug dissolved in time  $t$  and  $k_0$  the apparent dissolution rate constant or zero order release constant.

#### First order kinetics

This type of model to analyze drug dissolution study was first proposed by Gibaldi and Feldman and later by Wagner. The relation expressing this model:

$$\text{Log } Q_t = \text{Log } Q_0 + K_1 t / 2.303.$$

Where  $Q_t$  is the amount of drug released in time  $t$ ,  $Q_0$  is initial amount of drug in the solution and  $K_1$  is the first order release rate constant.

#### Korsmeyer -Peppas model

Korsmeyer developed a simple semi empirical model, relating exponentially the drug release to the elapsed time ( $t$ ).  $Q_t/Q_\infty = K_k t^n$

Where  $K_k$  is a constant incorporating structural and geometric characteristic of the drug dosage form and  $n$  is the release exponent, indicative of the drug release mechanism.

#### Higuchi model

$Q_t = K_H t^{1/2}$  Where  $Q_t$  = the amount of drug released at time  $t$  and  $K_H$  = the Higuchi release rate.

**Table: 3.**  $3^2$  full factorial design for the preparations of batches of HPMC K<sub>100</sub> M and Xanthan gum

Formulation No	Factors in Coded form	
	HPMC K <sub>100</sub> M	Xanthan gum
CHX <sub>1</sub>	0	-1
CHX <sub>2</sub>	1	-1
CHX <sub>3</sub>	-1	0
CHX <sub>4</sub>	1	0
CHX <sub>5</sub>	-1	-1
CHX <sub>6</sub>	1	1
CHX <sub>7</sub>	0	1
CHX <sub>8</sub>	0	0
CHX <sub>9</sub>	-1	1

**Table: 4.** Factors used and coded level for  $3^2$  full factorial designs

Factors used	Coded Level		
	-1	0	+1
HPMC K100M (mg)	40	60	80
Xanthan gum (mg)	20	40	60

**Table 1.** Release exponent and drug transport mechanism

Release exponent (n)	Drug transport mechanism
0.5	Fickian diffusion
$0.5 < n < 1.0$	Anomalous transport
1.0	Case-II transport
Higher than 1.0	Super Case-II transport

#### Formulation development of matrix floating tablets of Ciprofloxacin Hydrochloride

**Table 2.** Batch Codes for drugs and polymers

Drug and polymers	Batch Code
Ciprofloxacin Hydrochloride	C
HPMC K100M	H
Xanthan Gum	X
HPMC K <sub>100</sub> M and Xanthan Gum combination	HX

**Table: 5.** Composition of various floating matrix tablets of Ciprofloxacin HCl

SI. No.	Ingredients (mg)	CHX <sub>1</sub>	CHX <sub>2</sub>	CHX <sub>3</sub>	CHX <sub>4</sub>	CHX <sub>5</sub>	CHX <sub>6</sub>	CHX <sub>7</sub>	CHX <sub>8</sub>	CHX <sub>9</sub>
1	Ciprofloxacin HCl	250	250	250	250	250	250	250	250	250
2	HPMC K <sub>100</sub> M	60	80	40	80	40	80	60	60	40
3	Xanthan gum	20	20	40	40	20	60	60	40	60
4	Sod. bicarbonate	100	100	100	100	100	100	100	100	100
5	MCC	60	40	60	20	80	0	20	40	40
6	Talc	5	5	5	5	5	5	5	5	5
7	Mg.stearate	5	5	5	5	5	5	5	5	5
Total Tablet Weight (mg)		500	500	500	500	500	500	500	500	500

### Brief manufacturing procedure for Preparation of Ciprofloxacin floating matrix tablet

Matrix embedded controlled release tablets of Ciprofloxacin were prepared by direct compression technique using various concentrations of Xanthan Gum and HPC<sub>K100</sub>M. All the ingredients were sieved through the 40 mesh screen and mixed. All ingredients except Magnesium stearate and talc were blended in glass mortar uniformly. After the sufficient mixing of drug as well as other components, Magnesium stearate and Talc were added and mixed for additional 2-3 minutes. Microcrystalline cellulose was used as directly compressible vehicle. Magnesium stearate was used as lubricant and Talc was used as glidant. Finally after proper mixing, the powder mixture was compressed on a 10 station tablet compression machine (rotary tableting machine, Rimek Minipress-I, India) using 12-mm punches.

### Evaluation of pre compression parameters <sup>[8]</sup>

#### Bulk Density

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. The loose bulk density is accurately weighted amount of sample (5 gm) was transferred into a 25 ml measuring cylinder carefully to read the unsettled apparent volume to the nearest graduated unit. The tapped bulk density is accurately weighted amount of sample (5 gm) was transferred into a 25 ml measuring cylinder. The measuring cylinder was then tapped 100 times on a plane hard wooden surface and measure the tapped volume to the nearest graduated unit. Calculate the loose bulk density and tapped bulk density in

gm / ml by the following formula:

Loose bulk density (LBD) = Weight of granules / Apparent Volume

Tapped bulk density (TBD) = Weight of granules / Tapped volume

#### Compressibility Index

Percent compressibility of granules as determined by Carr's compressibility index is tapped bulk density

minus loose bulk density divided by tapped bulk density.

#### Hausner Ratio

Hausner ratio is tapped bulk density divided by loose bulk density.

#### Angle of Repose ( $\theta$ )

The frictional forces in a loose powder or granules can be measured by angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane. A funnel was kept vertically in a stand at a specified height above a paper placed on a horizontal surface. The funnel bottom is closed and 10 gm of sample powder is filled in funnel. Then funnel was opened to release the powder on the paper to form a smooth conical heap, is found by measuring in different direction. The height of the heap was measured by using scale. The value of angle of repose are calculated by using the following formula,  $\tan \theta = h/r$

$$\theta = \tan^{-1} (h/r)$$

Where

$\theta$  = Angle of repose,

h = Height of the heap and

r = Radius of the heap

### Post Compression Parameters <sup>[9, 10]</sup>

#### Tablet Dimension

Thickness and diameter were measured using a calibrated screw gauge. Three tablets of each formulation were picked randomly and thickness was measured individually.

#### Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling the hardness of the tablets was determined using Monsanto hardness tester. It is expressed in Kg/cm<sup>2</sup>. Three tablets were randomly selected and hardness of the tablets was determined.

#### Friability Test

The friability of tablets was determined using Roche friabilator. It is expressed in percentage (%). Ten tablets were initially weighed ( $W_{\text{initial}}$ ) and transferred into

friabilator. The friabilator was operated 25rpm for 4minutes or run up to 100 revolutions. The tablets were weighed again ( $W_{final}$ ). The percentage friability was then calculated.

### Uniformity in Weight

Twenty tablets were selected randomly from each batch and weighed. Weight of each tablet was recorded with the help of digital balance. The readings were recorded and tabulated.

### In vitro Buoyancy Studies

The time between introduction of dosage forms and its buoyancy in the simulated gastric fluid and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called total lag time (TLT) or buoyancy lag time (BLT) and the total duration of time by which dosage form remain buoyant is called total floating time.

### In-vitro Drug Release Studies

Three tablets of each formulation were used in the release experiment. In-vitro drug release of tablets was studied using USP type II apparatus at  $37 \pm 0.5^\circ\text{C}$  in 900ml 0.1N HCl solution (pH; 1.2) with a speed of 50 rpm. At appropriate time intervals 5ml of sample was withdrawn and an equal volume of medium was added to maintain the volume constant. Samples were analyzed by using UV- Visible Spectrophotometer at 276nm. The dissolution data obtained were plotted as percent cumulative drug release versus time.

## RESULTS AND DISCUSSION

### Identification of drugs

The received gift samples of Ciprofloxacin were characterized by Infrared (IR) Spectroscopy, melting point determination and ultraviolet (UV) spectroscopy.

### Infrared (IR) spectra

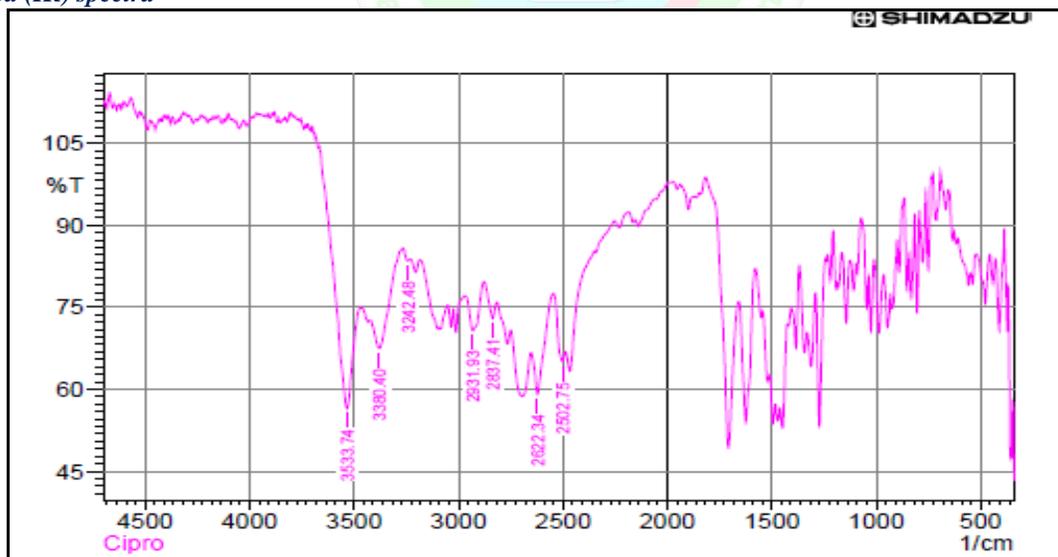


Figure 1: FTIR Spectra of Ciprofloxacin

The IR spectra of the drugs were recorded by using FT-IR (DRS) technique. The spectrum showed peaks corresponding to the functional groups present in the drug structure.

### Melting point

The melting point of the drug sample Ciprofloxacin was found to be  $147^\circ\text{C}$  and  $190^\circ\text{C}$  respectively that comply with the reference data.

### Ultraviolet (UV) spectroscopy

In UV scanning from standard solutions of Ciprofloxacin, the wavelength of maximum absorption ( $\lambda_{max}$ ) was determined at 0.1N HCl. It was found to be 276nm in 0.1N HCl for Ciprofloxacin which are similar to the values given in literature.

### Drug-polymer compatibility study

Interaction between the drug and added excipients plays a vital role in establishing stability of the formulation. Hence, the drug-excipient compatibility study is highly desirable before developing any formulation. Interaction between drug and excipient can occur by means of several mechanisms like adsorption, complexation, chemical interaction, pH effect, eutectic formation resulting in drug products with desired or undesired properties.

### Fourier-Transform Infrared Spectroscopy

Fourier-transform infrared (DRS) spectra were obtained by using an FT IR-Affinity-1 spectrophotometer (DRS-8000) SHIMADZU, Japan. The drug sample (Ciprofloxacin) was previously ground and mixed thoroughly with potassium bromide, an infrared transparent matrix, at 1:1 (Sample: KBr) ratio, respectively. The KBr powder was used as blank for background correction in FT-IR studies. Forty five scans were obtained at a resolution of  $4\text{ cm}^{-1}$  from  $4000$  to  $400\text{ cm}^{-1}$ .

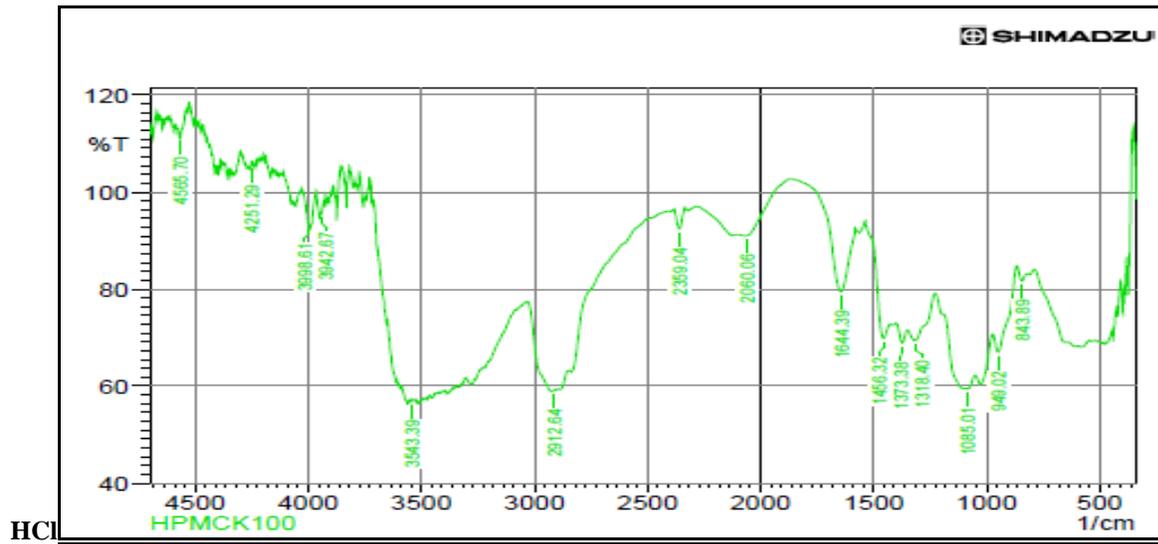


Figure 2: FTIR Spectra of HPMC K<sub>100</sub>

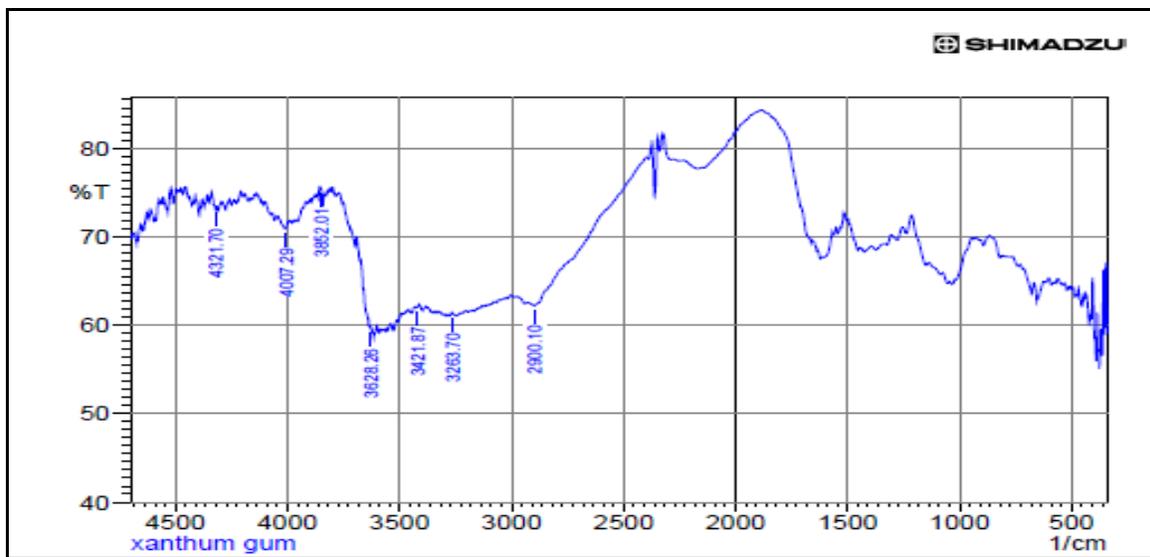


Figure 3: FTIR Spectra of Xanthan gum

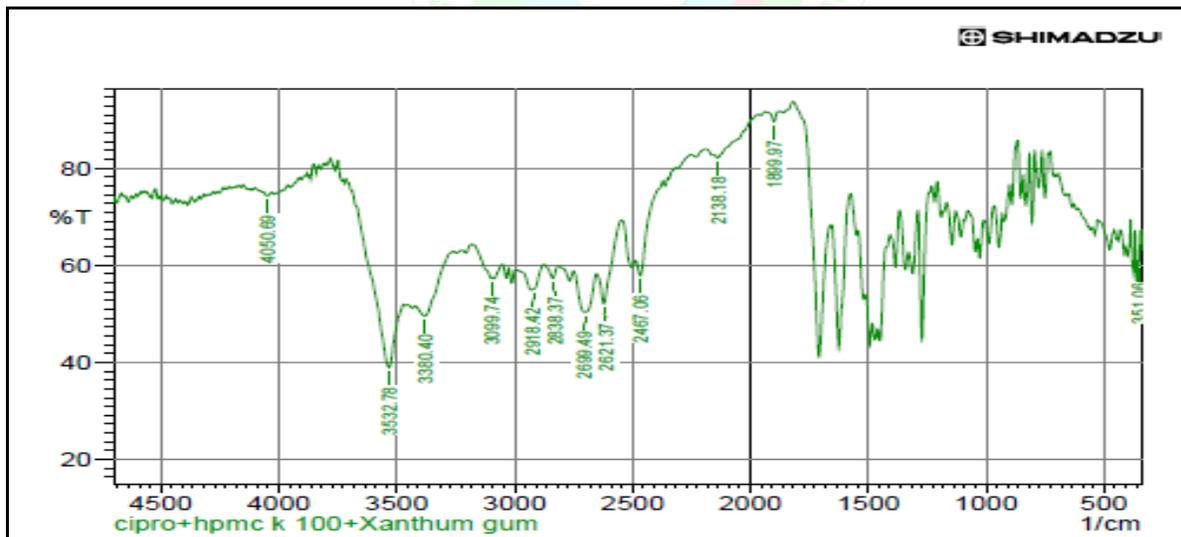


Figure 4: FTIR Spectra of Ciprofloxacin with Xanthan gum and HPMC K<sub>100</sub>M

### Differential Scanning Calorimetry

The interactions between drugs and a distinct mixture [1:1] were then investigated by DSC. Interactions in the sample are derived or deduced from DSC by changes in the thermal events, such as elimination of an

endothermic or exothermic peak, or appearance of a new peak. However, some broadening of peaks leading to changes in the area, onset of peak, and changes in peak temperature occur simply due to mixing of the components without indicating any significant interaction.

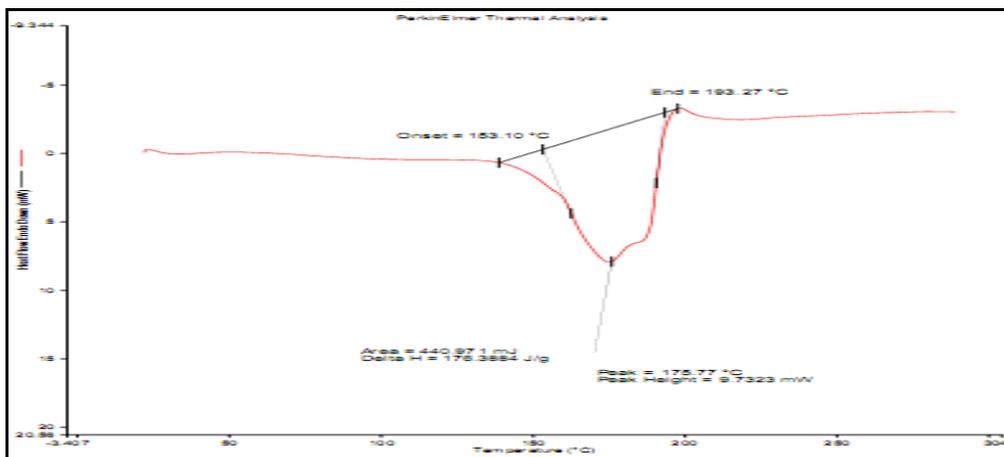


Figure 5: DSC thermogram of Ciprofloxacin HCl

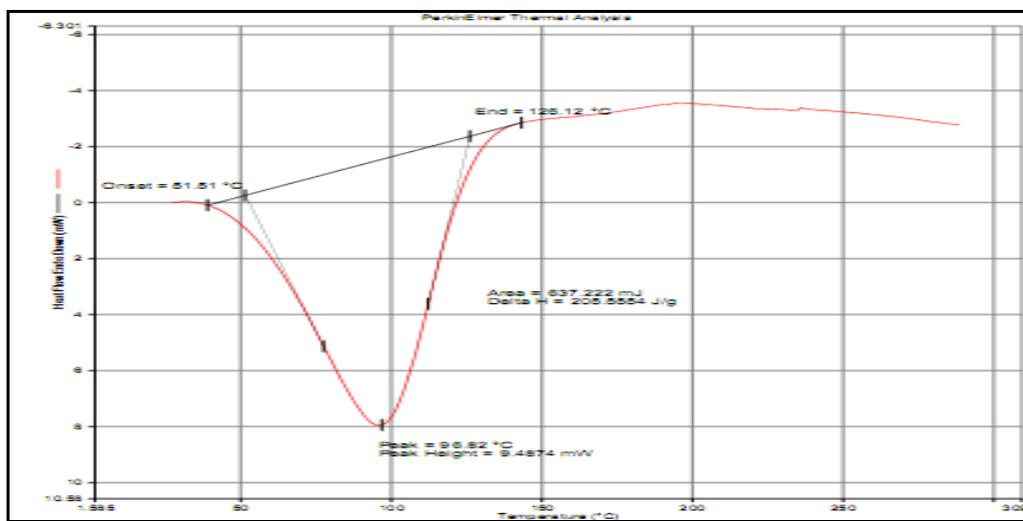


Figure 6: DSC thermogram of HPMC K<sub>100</sub> M

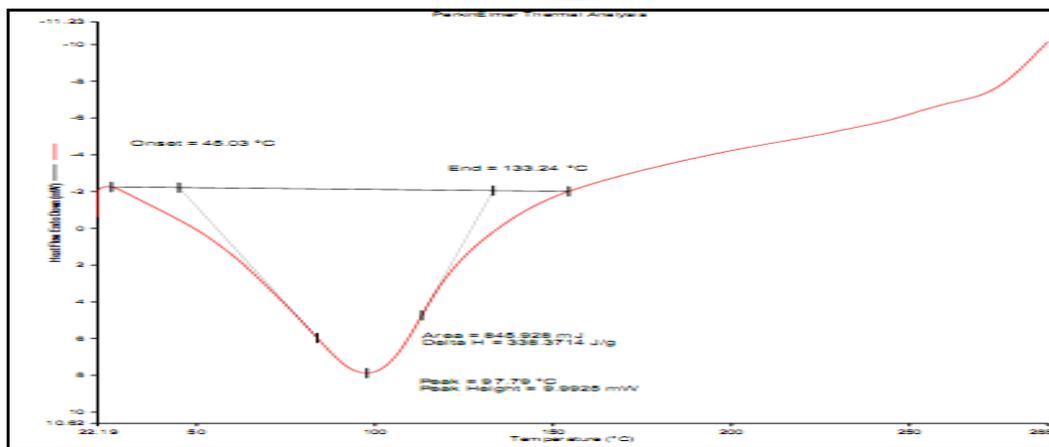


Figure 7: DSC thermogram of Xanthan gum

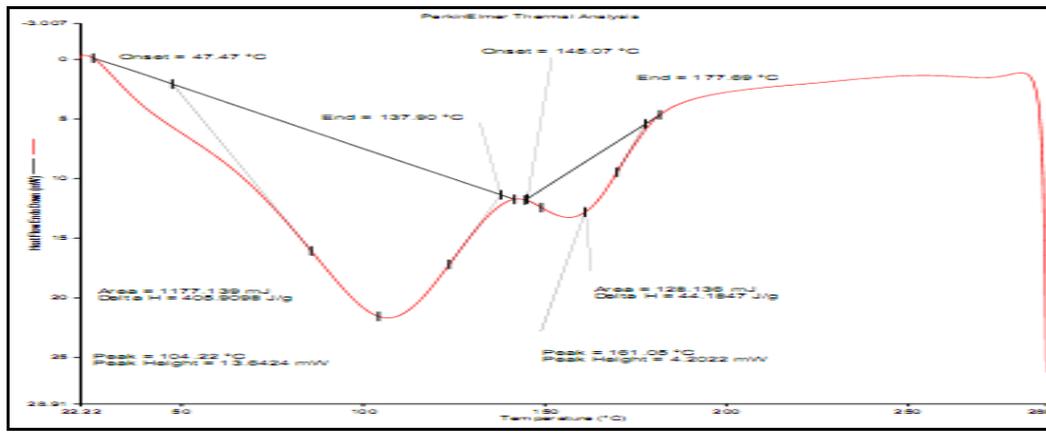


Figure 8: DSC thermogram of Ciprofloxacin with HPMC K<sub>100</sub> M and Xanthan gum

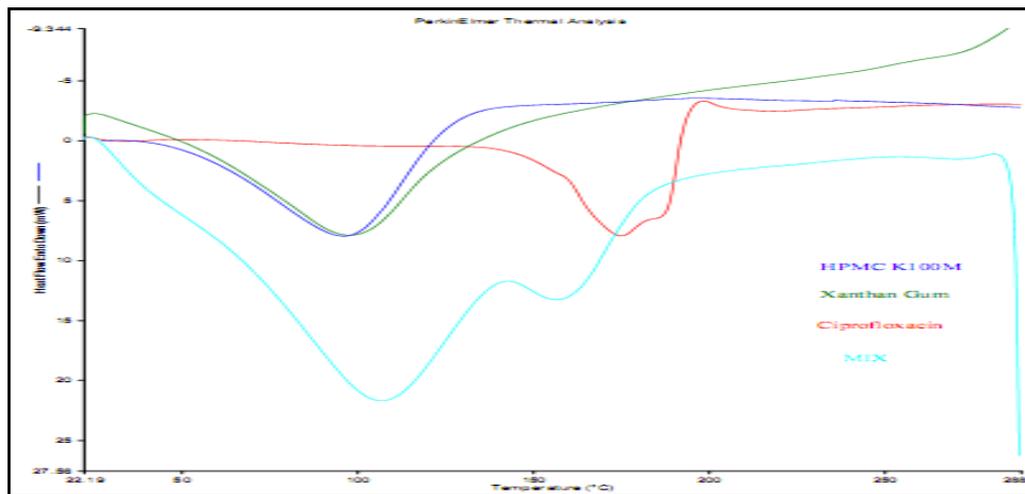


Figure 9: DSC thermogram of Overlay spectra of HPMC K<sub>100</sub>, Ciprofloxacin, Xanthan gum and Mixture

**Analytical method development**

**UV-Vis Spectrophotometric Method Development for Ciprofloxacin HCl**

Serial dilution of Ciprofloxacin was prepared in 0.1 N HCl from 2µg/mL to 10µg/mL and scanned for absorption maxima ( $\lambda_{max}$ ) in the range of 200 to 400nm

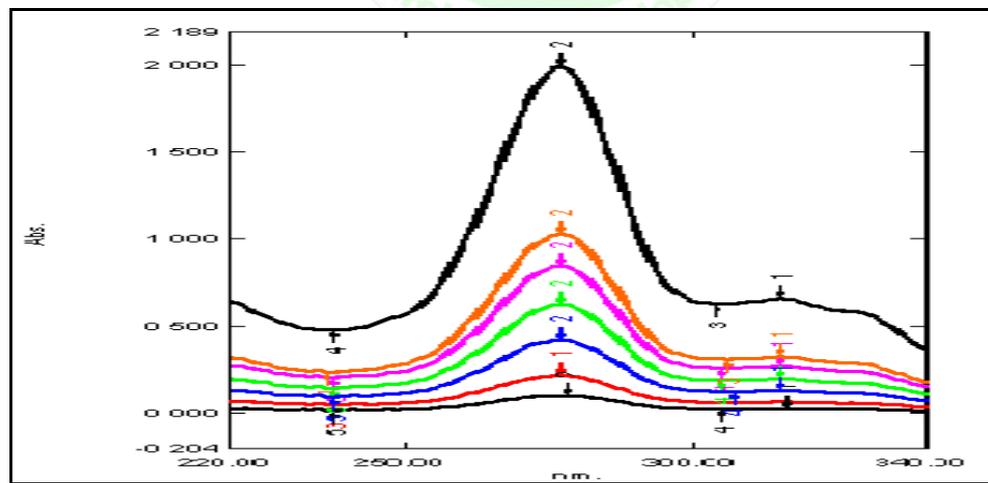


Figure 10: Overlay Spectra of Ciprofloxacin in 0.1N HCl

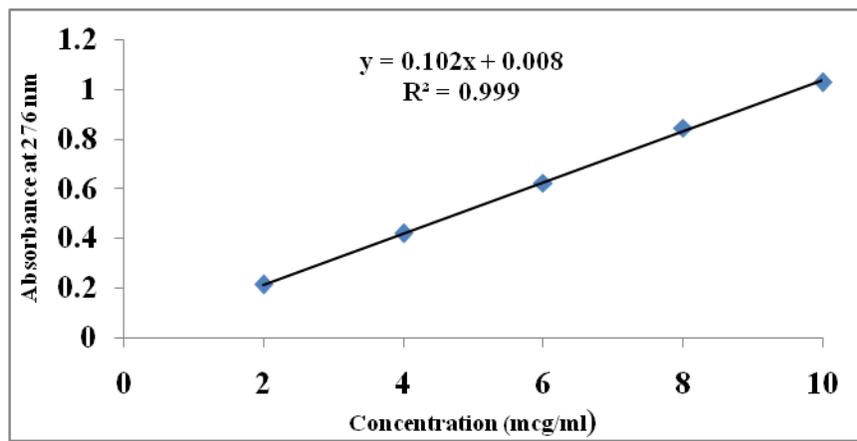


Figure 11: Calibration Curve of Ciprofloxacin HCl in 0.1N HCl

Formulation development and evaluation of Ciprofloxacin floating tablets

Table 6. Physical Parameters of Ciprofloxacin Tablet formulations CHX1 to CHX9

Blend Parameters	Batches								
	CHX <sub>1</sub>	CHX <sub>2</sub>	CHX <sub>3</sub>	CHX <sub>4</sub>	CHX <sub>5</sub>	CHX <sub>6</sub>	CHX <sub>7</sub>	CHX <sub>8</sub>	CHX <sub>9</sub>
Bulk Density (gm/ml)	0.482	0.572	0.616	0.581	0.502	0.534	0.513	0.452	0.481
Tapped Density (gm/ml)	0.594	1.14	1.153	1.133	0.572	0.616	0.581	0.604	0.621
Carr's Compressibility (%)	18.9	0.502	0.534	0.513	12.23	13.31	11.8	25.65	22.54
Hausner's Ratio	1.23	0.616	0.581	0.604	1.14	1.153	1.133	1.336	1.291
Tablet Parameters									
Weight Variation (mg)	503 ± 5.3	503 ± 5.27	510 ± 5.22	513 ± 5.23	498 ± 5.27	506 ± 5.22	501 ± 5.23	503 ± 5.32	503 ± 5.26
Hardness (kg/cm <sup>2</sup> )	5.8 ± 0.53	5.7 ± 0.52	5.2 ± 0.54	6.1 ± 0.54	6.4 ± 0.6	6.1 ± 0.71	5.7 ± 0.52	5.5 ± 0.54	6.3 ± 0.54
Friability (%)	0.6	0.68	0.71	0.52	0.58	0.46	0.63	0.65	0.62
Drug Content	98.72	98.2	96.43	99.53	93.12	99.56	98.2	100.43	99.53

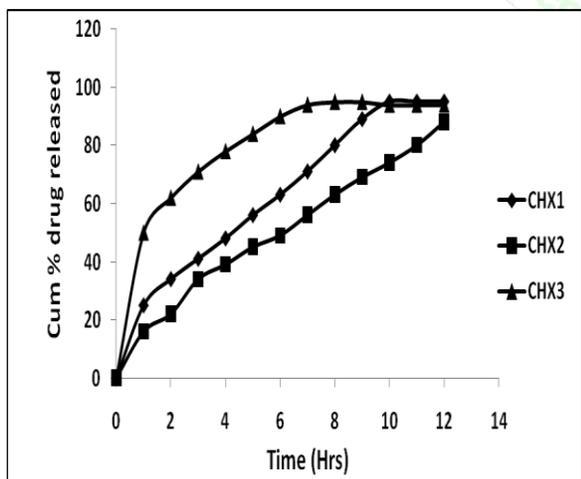


Figure 12: Dissolution curve of formulations CHX1, CHX2 and CHX3

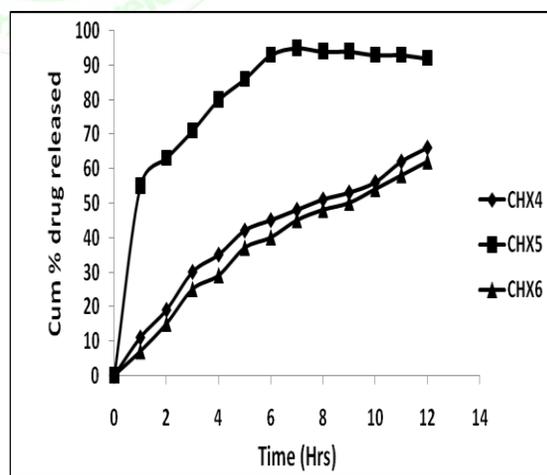


Figure 13: Dissolution curve of formulations CHX4, CHX5 and CHX6

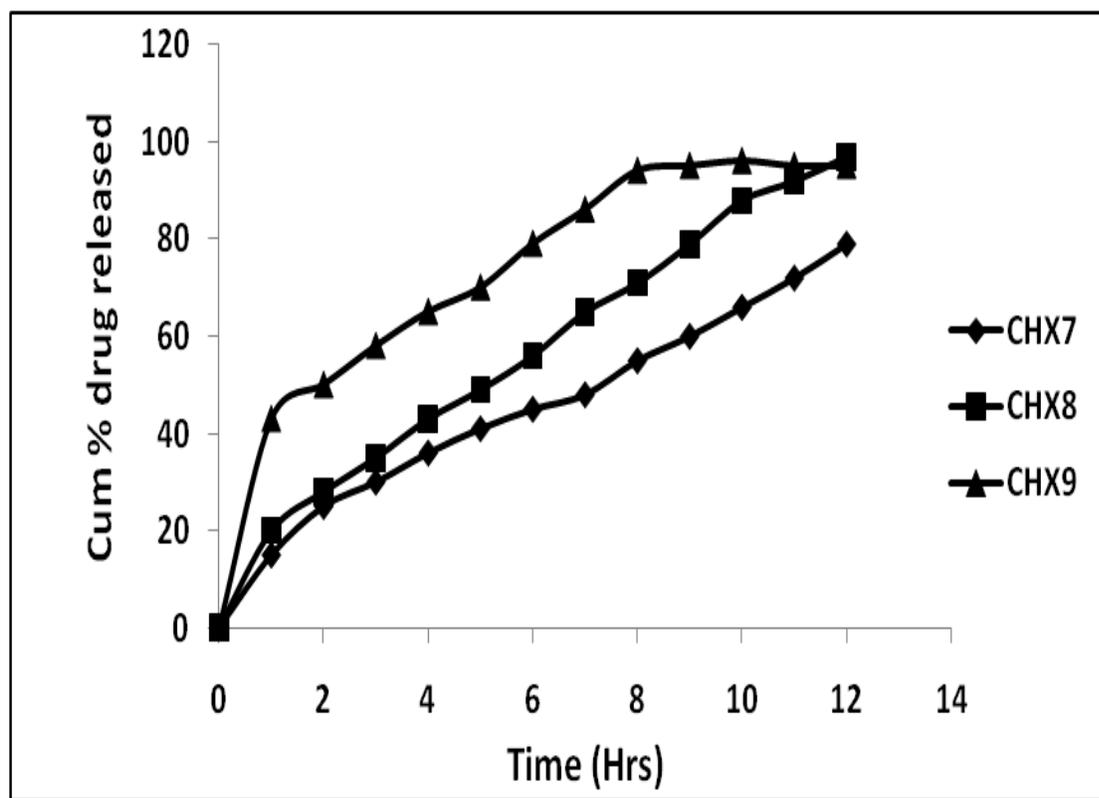


Figure 14: Dissolution curve of formulations CHX7, CHX8 and CHX9

Table: 7. Kinetic Analysis of Dissolution profile of Ciprofloxacin from CHX<sub>1</sub> to CHX<sub>9</sub>

Models		CHX <sub>1</sub>	CHX <sub>2</sub>	CHX <sub>3</sub>	CHX <sub>4</sub>	CHX <sub>5</sub>	CHX <sub>6</sub>	CHX <sub>7</sub>	CHX <sub>8</sub>	CHX <sub>9</sub>
Peppas Model	n	0.585	0.691	0.267	0.689	0.232	0.838	0.636	0.662	0.365
	R <sup>2</sup>	0.984	0.992	0.946	0.977	0.914	0.975	0.991	0.988	0.970
	K <sub>p</sub>	22.9	14.99	52.48	12.35	56.23	8.39	14.99	18.03	11.69
Higuchi Model	R <sup>2</sup>	0.972	0.949	0.791	0.975	0.719	0.950	0.958	0.948	0.948
	K <sub>h</sub>	27.5	22.33	32.84	18.02	32.91	16.57	19.99	25.41	31.03
Zero- Order	R <sup>2</sup>	0.879	0.951	-0.10	0.863	-0.28	0.930	0.929	0.952	0.439
	K <sub>0</sub>	9.44	7.738	10.82	6.175	10.80	5.729	6.907	8.806	10.39
First- Order	R <sup>2</sup>	0.924	0.934	0.842	0.980	0.714	0.991	0.949	0.871	0.921
	K <sub>1</sub>	0.282	0.157	0.218	0.079	0.184	0.077	0.113	0.261	0.275

**Table: 8.** Factorial design of various polymer concentrations of HPMC K<sub>100</sub> and Xanthan gum

Std	Run	Block	Factor 1 A:X1 HPMC K100 mg	Factor 2 B:X2 Xanthan gum mg	Response 1 Y1%	Response 2 Y6 %	Response 3 Y12 %
7	1	Block1	60.00	20.00	25	63	95
2	2	Block1	80.00	20.00	16	49	88
5	3	Block1	40.00	40.00	50	90	94
6	4	Block1	80.00	40.00	11	45	66
1	5	Block1	40.00	20.00	55	93	92
4	6	Block1	80.00	60.00	7	40	62
8	7	Block1	60.00	60.00	15	45	79
9	8	Block1	60.00	40.00	20	56	97
3	9	Block1	40.00	60.00	43	79	95

**Anova for Response surface cubic model of HPMC K<sub>100</sub> and Xanthan gum**

Response: Y1						
ANOVA for Response Surface Reduced Cubic Model						
Analysis of variance table [Partial sum of squares]						
Source	Sum of Squares	DF	Mean Square	F Value	Prob > F	
Model	2542.86	7	363.27	13077.57	0.0067	
A	760.50	1	760.50	27378.00	0.0038	
B	50.00	1	50.00	1800.00	0.0150	
A <sup>2</sup>	213.56	1	213.56	7688.00	0.0073	
B <sup>2</sup>	0.056	1	0.056	2.00	0.3918	
AB	2.25	1	2.25	81.00	0.0704	
A <sup>2</sup> B	0.083	1	0.083	3.00	0.3333	
AB <sup>2</sup>	0.75	1	0.75	27.00	0.1210	
Residual	0.028	1	0.028			
Cor Total	2542.89	8				
Std. Dev.	0.17		R-Squared	1.0000		
Mean	26.89		Adj R-Squared	0.9999		
C.V.	0.62		Pred R-Square	0.9980		
PRESS	5.06		Adeq Precisor	305.470		
Factor	Coefficient Estimate	DF	Standard Error	95% CI Low	95% CI High	VIF
Intercept	20.11	1	0.12	18.53	21.69	
A-X1 HPMC K100	-19.50	1	0.12	-21.00	-18.00	3.00
B-X2 Xanthan gum	-5.00	1	0.12	-6.50	-3.50	3.00
A <sup>2</sup>	10.33	1	0.12	8.84	11.83	1.00
B <sup>2</sup>	-0.17	1	0.12	-1.66	1.33	1.00
AB	0.75	1	0.083	-0.31	1.81	1.00
A <sup>2</sup> B	-0.25	1	0.14	-2.08	1.58	3.00
AB <sup>2</sup>	0.75	1	0.14	-1.08	2.58	3.00
<b>Final Equation in Terms of Coded Factors:</b>						
Y1 =						
+20.11						
-19.50 * A						
-5.00 * B						
+10.33 * A <sup>2</sup>						
-0.17 * B <sup>2</sup>						
+0.75 * A * B						
-0.25 * A <sup>2</sup> * B						

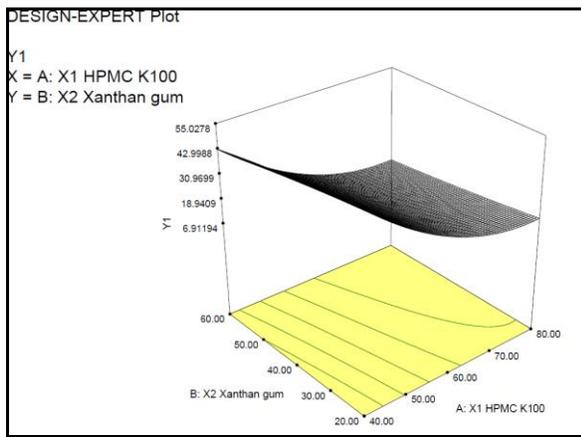


Figure 15: Surface design of response Y1% by varying quantities of HPMC K<sub>100</sub>M and Xanthan gum.

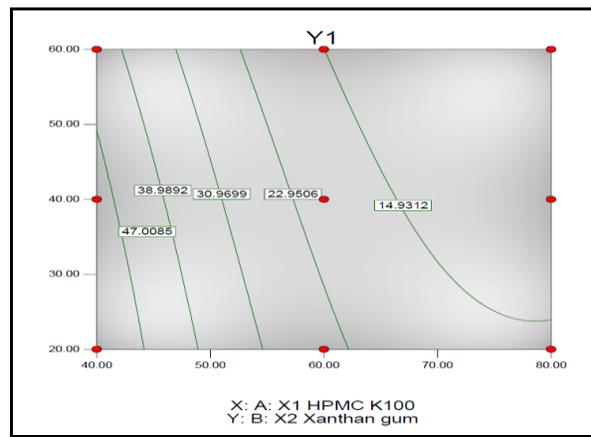


Figure 16: Related contour plot indicating various levels of HPMC K<sub>100</sub>M and Xanthan gum

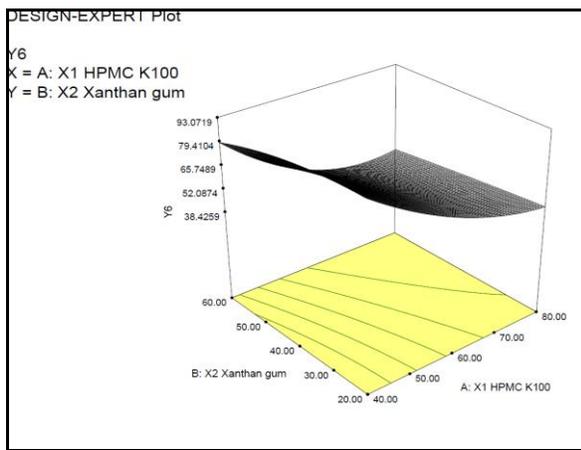


Figure 17: Surface design of response Y6% by varying quantities of HPMC K<sub>100</sub>M and Xanthan gum.

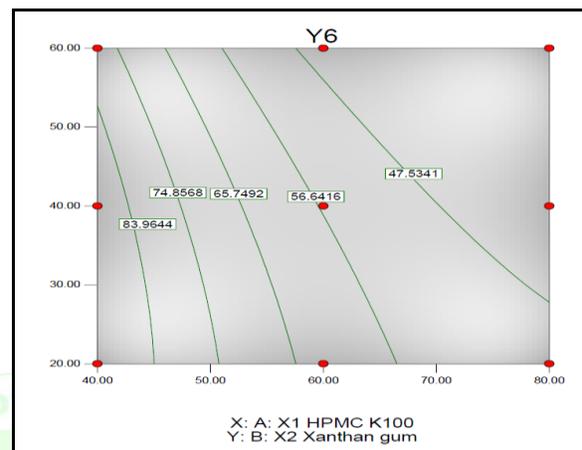


Figure 18: Related contour plot indicating various levels of HPMC K<sub>100</sub>M and Xanthan gum

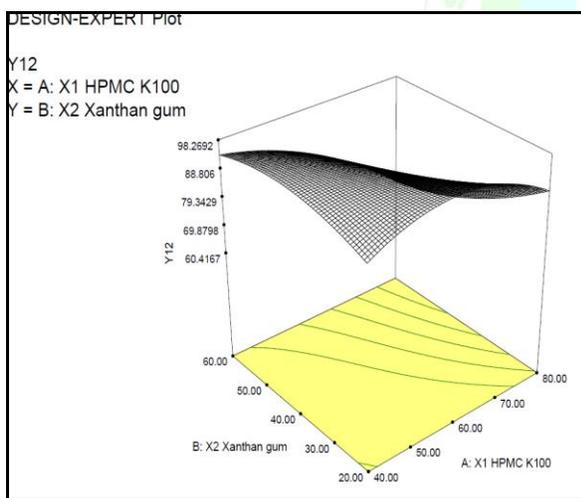


Figure 19: Surface design of response Y12% by varying quantities of HPMC K<sub>100</sub>M and Xanthan gum

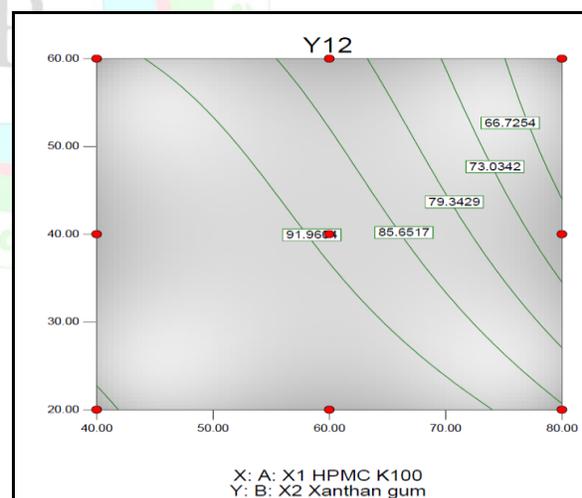


Figure 20: Related contour plot indicating various levels of HPMC K<sub>100</sub>M and Xanthan gum

The oral floating matrix tablets of Ciprofloxacin Hydrochloride were formulated by Experimental design by using HPMC K<sub>100</sub>M and Xanthan gum as the retardant polymers each with three different levels with an approach to increase gastric residence and thereby improve drug bioavailability. Floating Matrix tablets

were prepared by direct compression method and prepared tablets were evaluated for weight variation, percentage friability, hardness and drug content studies. All the formulations showed compliance with pharmacopeia standards. Floating lag times of all the formulations were within 1 minute and Total floating

time of all the formulations were more than 12 hours. In vitro release studies revealed that the release rate decreased with increase polymer proportion of retarding polymers. The formulations CHX<sub>8</sub> sustained release of drug for 12 hrs with 20% release of drug after 1hr and more than 97% at the end of 12 hrs. From the Kinetic model it was found that the optimized formulation CHX<sub>8</sub> showed linearity in case of Zero order ( $R^2$ : 0.952) and Higuchi model ( $R^2$ : 0.948). By fitting data to Korsmeyer-Peppas model and 'n' value lying above 0.5 indicating non Fickian release. It can be concluded that

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stable formulation could be developed by incorporating in a definite proportion of HPMC and Xanthan gum, along with definite amount of gas generating agent (Sodium bicarbonate) , So that oral floating matrix profile is maintained for an extended periods of time.

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