ISSN: 2277-8713
Dhaval Patel, IJPRBS, 2012: Volume1 (2): 191-214 *IJPRBS*

RESEARCH ARTICLE

INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

A Path for Horizing Your Innovative Work

FORMULATION AND EVALUATION OF BILAYER FLOATING TABLET FOR GASTRIC RETENTION

***DHAVAL PATEL, AK MAHAJAN, ANAND PATEL, RITESH GASHADIYA, ANKIT PATEL, TANVI PANDYA.**

Department of Pharmaceutics, A.P.M.C. College of Pharmaceutical Education And Research, Motipura, Himatnagar-383001, Gujarat state, India

Corresponding Author Email: dhavalpatel_gurubhai@yahoo.in

Accepted Date: 21/04/2012 **Publish Date: 27/04/2012**

Abstract: The present investigation concerns the development and evaluation of floating tablets of Ciprofloxacin hydrochloride which, after oral administration, are designed to prolong the gastric residence time and increase drug bioavailability. Bilayer floating tablets comprised two layers, immediate release and controlled release layers. The immediate release layer comprised sodium starch glycolate as a super disintegrant and the controlled release layer comprised HPMC K15M and Carbopol 934P as release retarding polymers. Sodium bicarbonate was used as a gas generating agent. The controlled layer was compressed and powders of the immediate release layer were added to it then both layers were compressed using a single punch tablet machine. Direct compression method was used for formulation of the bilayer tablets. The tablets were evaluated for hardness, thickness, friability, Drug content, swelling index, floating lag time, floating duration and *in vitro* drug release. Final formulation released approximately 93% drug in 12 h in vitro, while the floating lag time was 10 sec, because of prompt disintegration of the fast releasing layer and the enhanced rate of dissolution of Ciprofloxacin hydrochloride from the system

Keywords: Bilayer floating tablet, Ciprofloxacin hydrochloride, direct compression method.

INTRODUCTION

Splendid achievements have been made in management of disease through invention of oral controlled release dosage forms have been developed for the past three decades due to their various benefit characteristics[1].

One of the novel approaches in the area of oral sustained release drug delivery is Gastro retentive drug delivery system (GRDDS). Drugs those are having a narrow absorption window and having more solubility in gastric region are suitable candidates for GRDDS[2]. GRDDS prolongs the retention time of dosage forms in the stomach or upper gastrointestinal tract, as to improve solubility, bioavailability and the therapeutic efficacy of the drugs[3].

Several techniques have been proposed to increases the gastric residence time of dosage forms such as buoyancy or floating system, hydrodynamically balanced system, expanding or swelling system, bio/mucoadhesive system, sedimentation or high density system, geometry or modified shape system may also use to increase gastric residence time.[4]

The bilayer system is used mostly when maximum relief needs to be achieved quickly followed by a sustained release phase. It also avoids repeated administration of drug. Coronary vasodilator, antihypertensive, antihistaminic, analgesic, antipyretics and antiallergenic agents are mainly used for this system. The bilayer system may contain one or two drugs for immediate release and sustained release layer[5].

The objective of designing a controlled release system is to deliver drug at a rate necessary to achieve and maintain a constant drug blood level. The bilayered tablet concept has been long utilized to develop sustained release formulations. Such a tablet has a fast releasing layer and may contain bi- or triple layers to sustain the drug release. The pharmacokinetic advantage relies on the fact that drug release from fast releasing granules leads to a sudden rise in the blood concentration. However, the blood level is maintained at steady state as the drug is released from the sustaining granules[6].

Ciprofloxacin hydrochloride (Cipro HCl) is a broad spectrum fluoroquinolone antibiotic. It is approved for use in the treatment of

bone and joint infections, infectious diarrohea, lower respiratory tract infections, urinary tract infections, hospital-acquired infections and meningococcal prophylaxis[7]. Since the drug is freely soluble in water (1 g in 25 mL), lower bioavailability of 60% and has a short elimination half-life of about 4 h, various sustained-release preparations were prepared aiming to enhance its antibacterial activity[8]. It has a narrow absorption window and is mainly absorbed in the proximal areas of GIT. Therefore, certain Cipro HCl floating systems were developed by some research groups[9,10].

MATERIALS AND METHODS

Materials

Ciprofloxacin hydrochloride was a gift from Cadila pharmaceuticals Pvt Ltd., ahmedabad. sodium starch glycholate, HPMC K15 M, HPMC K100 M was a gift from Themis pharmaceuticals Pvt. Ltd., Vapi. Carbopol 934P, Crosspovidone, Dicalcium phosphate, Na bicarbonate, Magnesium stearate and Talc was purchased from S.D.fine chemicals, Mumbai.

Methods

Drug-excipients compatibility studies

The compatibility of drug and polymer under the experimental conditions is an important pre-requisite to formulation. It is therefore necessary to confirm that the drug does not react with poly (vinyl alcohol) polymer under experimental conditions.[11]

Fourier Transform Infrared spectroscopy (FT-IR)

To investigate any possible interaction between the drug and the polymer under investigation. FT-IR spectrophotometer method was used. Samples of pure drug and drug with HPMC, Carbopol, SSG, other excipients were differntly crushed with KBr to make KBr pallets then The IR spectra of pure drug (Ciprofloxacin **hydrochloride**) and Sample were carried out by using FT-IR spectrophotometer on Shimadzu 8400S FTIR spectrometer (Shimadzu, Japan). The following range was selected for IR spectra 400cm^{-1} to 4000cm^{-1}.

Differential Scanning Calorimetry (DSC)

The DSC thermograms of pure drug (Ciprofloxacin **hydrochloride**) and drug with HPMC, Carbopol, SSG, other excipients were carried out to investigate

any possible interaction between the drug and the polymer and 50 °C to 300 °C heating rate was selected at an increase in 100 ºC per minute.

Optimization of immediate release layer

The immediate release layer contained uniform mixture of Ciprofloxacin Hcl and excipients. The tablets were prepared by using direct compression technique. Weighed quantities of drug and excipients as shown table1 in were mixed properly in a mortar. After the uniform mixing tablets are prepared by using single punch tablet machine with a die and punch of 14 mm diameter. Two different polymers (SSG and crosspovidone) were used in different batches. All these batches were evaluated for different evaluation parameters i.e. Disintegration time and friability.

Optimization of Bilayer Floating Tablet (BFT) using 3^2 full factorial designs:

A 3^2 full factorial design was used in this study and two factors were evaluated, each at three levels; experimental batches were performed at all nine possible combinations as shown in Table.A 2-factor 3-level factorial experimental design technique was employed to investigate the dependent variables like bioadhesion and percent cumulative drug release using the Design Expert Software (Version 7.1.4). The responses given by the software are expressed in terms of the quadratic polynomial equations which are given below:

$$Y = b0 + b1X1 + b2X2 + b12X1X2 + b11X1X1 + b22X2X2$$

Where, Y is the dependent variable, b_0 is the arithmetic mean response of the all trials, and bi (b_1, b_2, b_{12}, b_{11} and b_{22}) is the estimated coefficient for the corresponding factor Xi (X_1, X_2, X_{12}, X_{11} and X_{22}), which represents the average result of changing one factor at a time from its low to high value. The interaction term (X_1X_2) shows how the response changes when 2 factors are simultaneously changed. The polynomial terms (X_1X_1 and X_2X_2) are included to investigate the nonlinearity.

Table2: 3^2 Full Factorial Design Layout

Formulation Code	Variables	
	X1	X2
F1	+1	0
F2	0	0
F3	-1	0
F4	0	-1
F5	-1	-1
F6	+1	+1
F7	-1	+1
F8	+1	-1
F9	0	+1

	Actual values(mg)	
	X1	X2
-1	60	40
0	80	60
1	100	80

Formulation design

Preparation of immediate release layer

The immediate release layer contained uniform mixture of drug, and excipients. The tablets were prepared by using direct compression technique. Weighed quantities of drug and excipients as shown in (Table3) were mixed properly in a mortar. After the uniform mixing tablets are prepared by using a single punch tablet machine.

Preparation of sustained release layer

The sustained layer contains uniform mixture of drug, polymers and excipients. The tablets were prepared by using direct compression technique. Weighed quantities of drug was mixed properly in a mortar with weighed amount of polymer and excipients as shown in (Table 3) The well-mixed powder was compressed using a punch tablet machine with a die and punch of mm diameter .

Preparation of BFT

BFT is prepared as mentioned above in the procedure of preparation of sustained release layer. After the compression upper punch was lifted and the blend of powder for immediate release layer was poured in the die, containing initially compressed BFT and compressed using a single punch tablet machine with a die and punch of 12mm diameter. All these batches were evaluated for different evaluation parameters i.e. Thickness(mm), Diameter(mm), Hardness (Kg/Cm^2), Average Weight, Friability (%), % Drug Content, Floating Lag Time (Sec), Floating Duration (Hr), Swelling Index(%), % Cumulative Drug Release.

Evaluation of Bilayer Floating Tablet

Weight variation test[12]

Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation. A little variation is allowed in the weight of a tablet by USP. The following percentage deviation in weight variation is allowed.

In all formulations, the tablet weight was more than 324 mg, hence 5% maximum difference allowed.

Thickness[13]

The thickness of the tablets was determined by using micrometer meter screw gauze. Five tablets from each formulation were used, average values and standard deviation were calculated. The results are shown in Table 5.

Hardness test[14, 15]

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of (kg/cm²) tablet was determined by using Monsanto tester. In all the cases, mean of five replicate determinations were taken. The results are shown in Table 5.

Friability test[16, 17]

As per IP, this was determined by weighing 26 tablets after dusting, placing them in the Roche friabilator and rotating the plastic cylinder vertically at 25 rpm for 4 min. After dusting, the total remaining weight of the tablets was recorded and the percent friability was calculated according to following equation.

$$\% \text{ Friability} = \frac{\text{Initial weight of tablets} - \text{Final weight of tablets}}{\text{Initial weight of tablets}} \times 100$$

% Friability of tablets less than 1% are considered acceptable. The results are shown in Table 5.

In vitro buoyancy study[18, 19]

The time between introduction of dosage form and its buoyancy on the SGF 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 Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TET). Floating behaviour study were carried out in a USP XXIII dissolution apparatus type II (Paddle) at a speed 50 RPM in 900 ml SGF at 37±0.5^{0}C for 12 hr to mimic *in vivo* conditions. The results are shown in Table 5.

Content uniformity[20]

Ten tablets were finely powdered, quantities of the powder equivalent to 50 mg of ciprofloxacin hydrochloride were accurately weighed and transferred to a 100 ml of volumetric flask containing methanol and mixed thoroughly. The solution was made up to volume and filtered. Appropriate dilutions were done using methanol and absorbance of the resulting solution was measured at the maximum at 271 nm using a UV spectrophotometer. The results are shown in Table 5.

Swelling Index[21]

The individual tablets were weighted accurately and kept in 50 ml of 0.1 N HCl.

Tablets were taken out carefully after each hour upto 12 hours, blotted with filter paper to remove the water present on the surface and weighed accurately. Percentage swelling (swelling index) was calculated by using following formula. The results are shown in Table 8 and Graph 2.

$$\text{Swelling index} = \frac{\text{Wet weight of tablet} - \text{Dry weight of tablet}}{\text{Dry weight of tablet}} \times 100$$

In vitro dissolution study[22]

In vitro dissolution study was performed for the prepared tablet formulations. The following conditions were maintained for the dissolution process:

Instrument: TDT-06T Veego VDA-63 USP Standards

Apparatus: IP Type-I paddle apparatus

Temperature: 37 ± 0.5^{0}C

RPM: 50

Sample: BILAYER FLOATING TABLET

Dissolution medium: 0.1 N HCL

Volume of medium: 900 ml

Sampling interval : 15 min, 30 min, 45 min, 1 hr, 2 hr, 3 hr,……, 12 hr

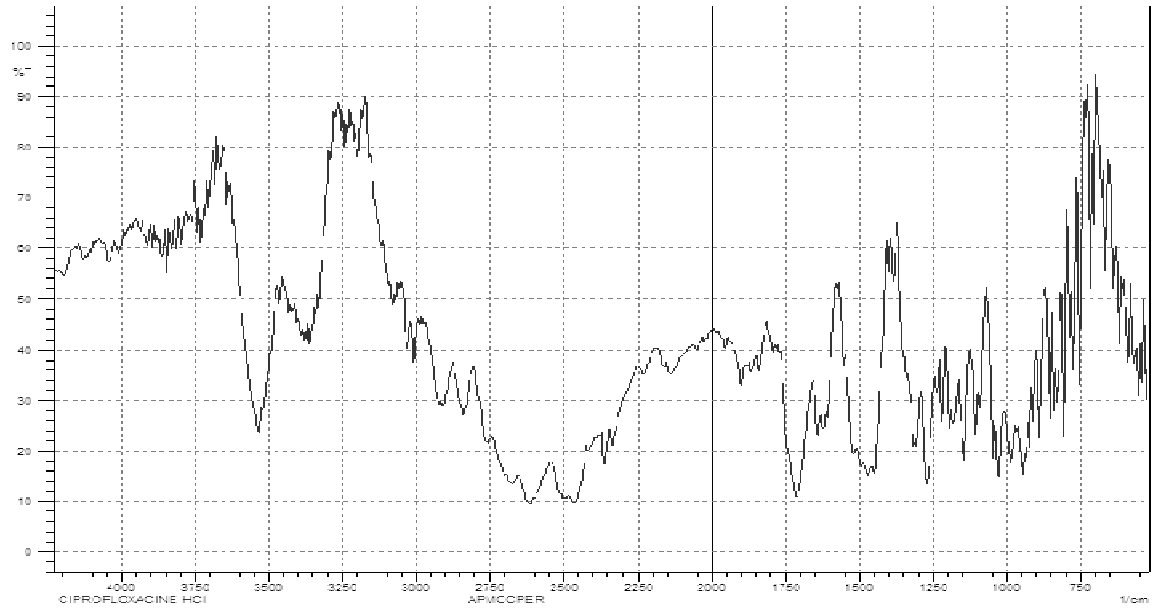
Sample volume: 10 ml withdrawn and replaced with 10 ml of fresh 0.1 N HCL

10 ml of the sample withdrawn was filtered through whatmann filter paper. Appropriate dilutions were made to get the absorbance in linearity range of medium. The absorbance of the samples was determined at wavelength of 271 nm by using UV spectrophotometer against 0.1 N HCL as a blank. The amount of drug present in the filtrate was calculated from the calibration curve equation and cumulative percent of drug release was calculated. The dissolution profiles of batch are shown in Table 6 and figure 1.

Results:

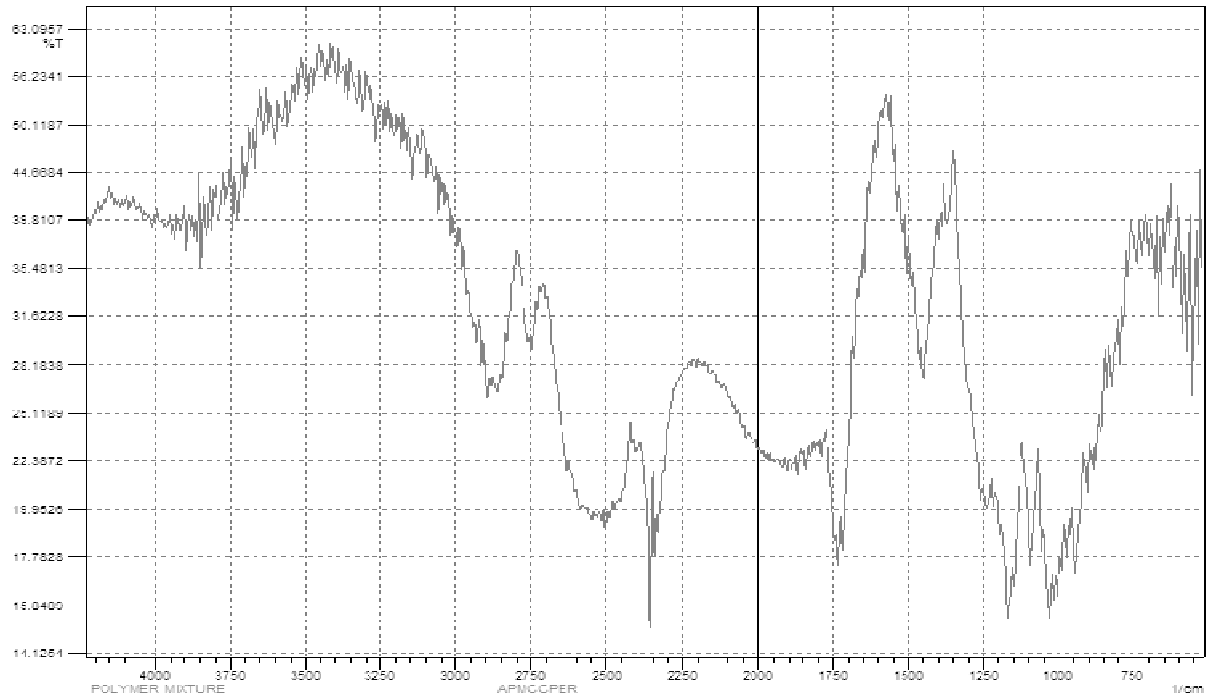
Drug-excipients compatibility studies:

FT-IR spectrum of Ciprofloxacin Hydrochloride

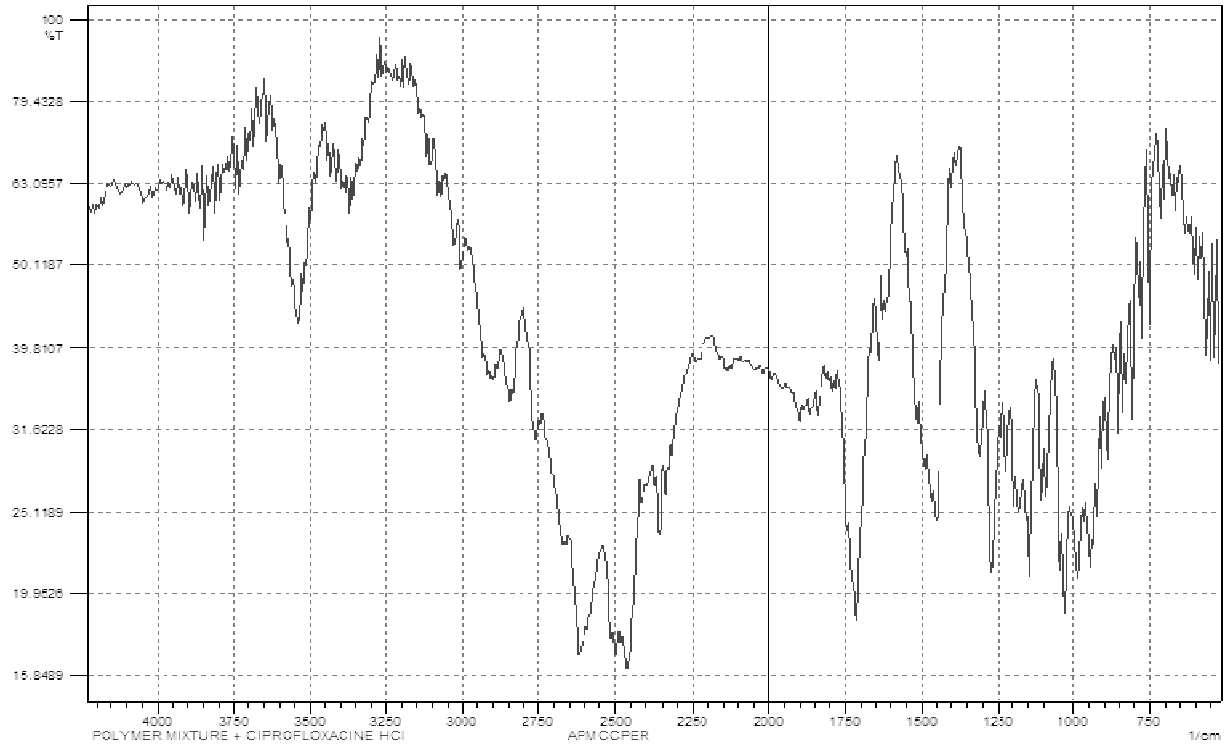


Sr. No.	Functional Group	Frequency (cm^{-1})
1	C=O of carbonyl group	1696
2	C-N stretch	1480
3	O-H stretch	3490
4	N-H stretch	3320
5	Aliphatic C-H stretch	2930
6	N-C stretch	2840
7	C=O stretch of quinoline	1605

FT-IR spectrum of HPMC, Carbopol, SSG and other excipients



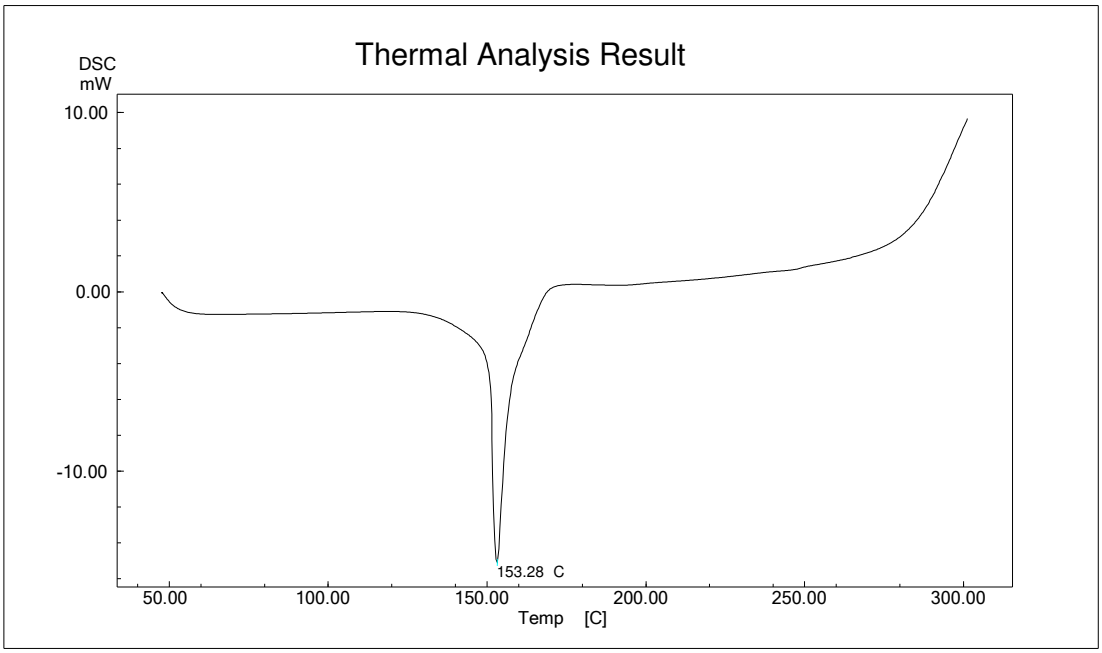
FT-IR spectrum of Ciprofloxacin Hydrochloride with HPMC, Carbopol, SSG and other excipients



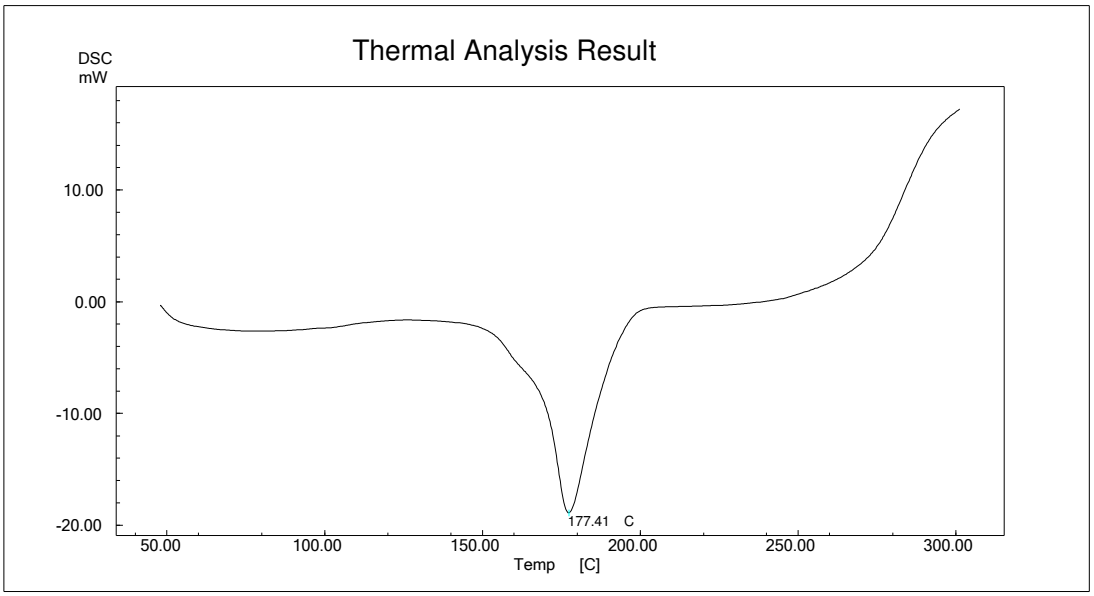
Physical mixture of drug and polymer was characterized by FTIR spectral analysis for any physical as well as chemical alteration of the drug characteristics. From results, it was concluded that there was no interference in the functional group as the principle peaks of the Ciprofloxacin Hydrochloride were found to be unaltered in the drug polymer physical mixture. The physical parameters of drug as well as excipients concluded that these were considerably good to formulate the tablet using direct compression technique.

Differential Scanning Calorimetry (DSC):

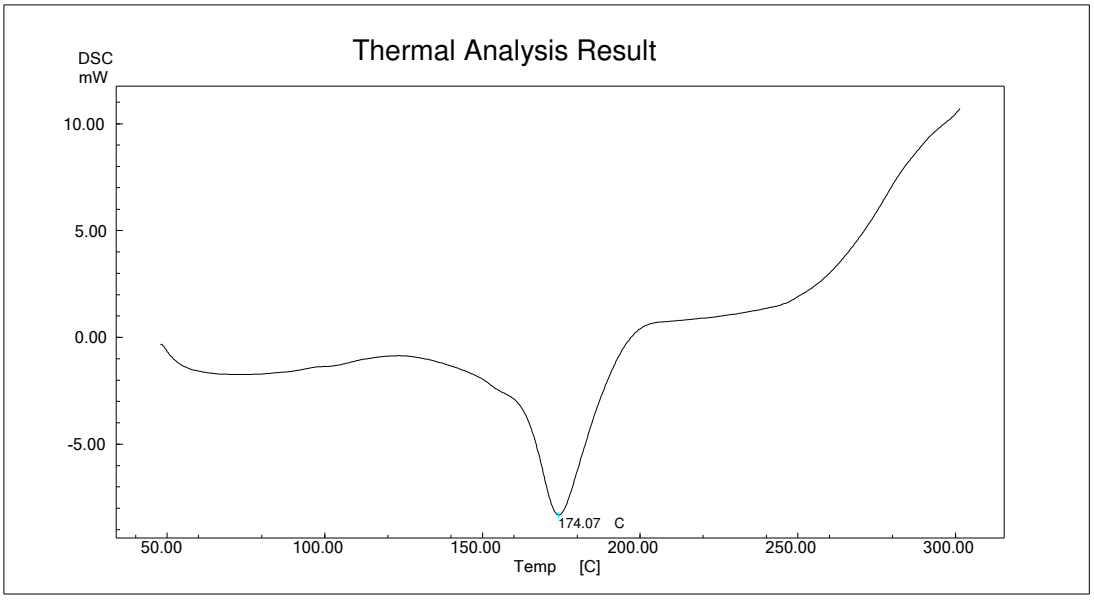
DSC of pure Ciprofloxacin Hydrochloride:



DSC of HPMC, Carbopol, SSG and other excipients:



DSC of Ciprofloxacin Hydrochloride with HPMC, Carbopol, SSG and other excipients:



The DSC thermograms for the pure Ciprofloxacin Hydrochloride and Ciprofloxacin Hydrochloride with HPMC, Carbopol, SSG and other excipients were determined to understand the drug polymer interaction. It was observed from the above thermogram that there was no appearance of new peaks, no change in peak shapes. The results indicated that there was no interaction with the drug. Hence the drug was compatible with polymers and other excipients.

Evaluation preliminary batches for the selection of polymer for immediate release layer

From the results of batch P1-P9 it was concluded that 6% SSG was best as minimum disintegration time and friability was seen in batch P5. From two polymer SSG and crosspovidone results shows that SSG SSG gives the maximum disintegration at the 6 %.

Bi-layer floating tablets were prepared by using optimized immediate release and floating sustained release formula. It was observed from *in vitro* drug release study that immediate release layer disintegrated rapidly in 0.1 N hydrochloric acid buffer pH 1.2 (simulated gastric fluid without enzymes) from bi-layered tablet. Subsequently, floating sustained release layer started floating in 0.1 N hydrochloric acid buffer pH 1.2 and sustained drug release. This showed biphasic drug release i.e. immediate drug release from immediate release layer and then sustained drug release from floating sustained layer.

For floating drug delivery system, the polymers used must be highly swellable in shortest time. Hence, HPMC was chosen as a main swellable polymeric material. In order to get the longer duration of floating time the high viscosity polymer selected, HPMC K15M was chosen and it was found that, increased viscosity of a polymer prolongs the drug delivery from the dosage form. In order to retain the dosage form in the stomach for a long period of time and to avoid gastric emptying of dosage form, carbopol 934-P was included. It was reported earlier that, carbopol belongs to the class of swellable and adhesive polymers and to utilize this property of carbopol, and also possibly to control the release of ciprofloxacin Hcl from the dosage form.

From the results of floating lag time it was concluded that as the concentration of gas generating agent increases the floating lag time get shortens. Hence, sodium bicarbonate ($NaHCO_3$) is added in the formulation which upon contact with HCl liberates carbon dioxide (CO_2) and expels from the dosage form creating pores through which the water can penetrate into the dosage form and the rate of wetting of polymer increases and the time required for drug release decreases. Another aspect of result of these studies clears that the level as well as viscosity of the polymer had a great impact over the floating lag time and total floating time, as the level and viscosity of the polymer was reduced the floating lag time get shorten.

The rate of swelling of polymer depends upon the amount of water taken up by the polymer. Hence, sodium bicarbonate ($NaHCO_3$) is added in the formulation which upon contact with HCl liberates carbon dioxide (CO_2) and expels from the dosage form creating pores through which the water can penetrate into the dosage form and the rate of wetting of polymer increases and the time required for drug release decreases.

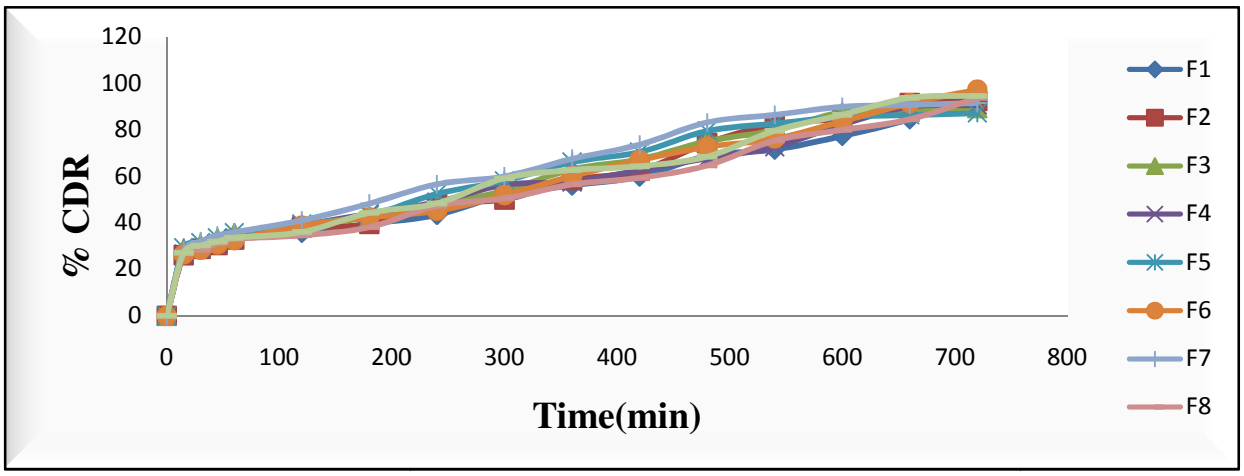


Figure 1. *In vitro* drug release profile of formulation F1-F9

From the results it can be concluded that as the concentration of polymer increases the drug release decreases. To overcome an initial burst effect, the high viscosity HPMC polymer used. HPMC-K100M gives prolonged floating and drug release as compare to the low viscosity polymers. According to free volume of theory of diffusion, the probability for a diffusing molecule to jump from one cavity into other decreases due to high viscosity and more concentration of polymer. This leads to decreased drug diffusion coefficient and decreased release rates with increasing polymer content or viscosity of the polymer.

Final Equations in Terms of Coded Factors (% CDR)

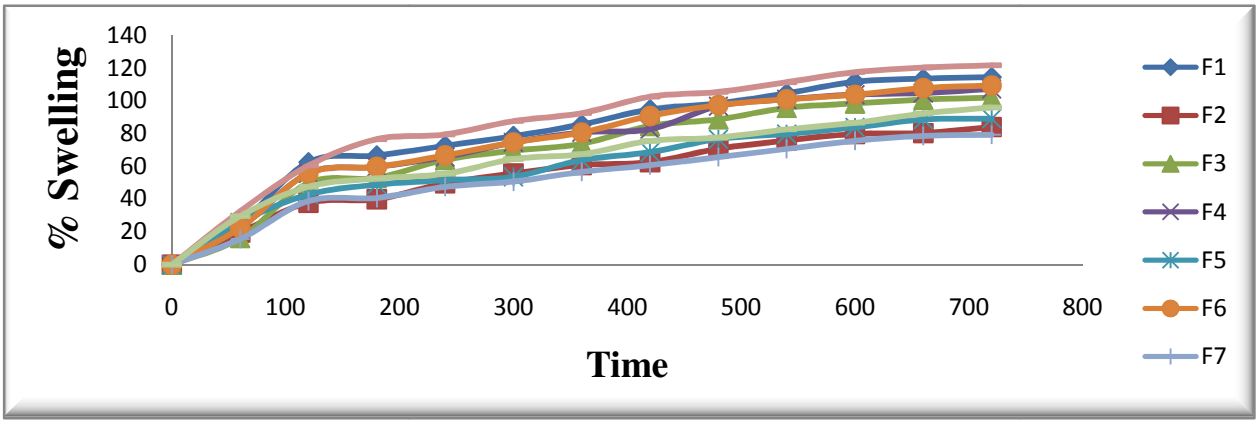
$$Y = 92.48 + 3.09X1 + 1.96X2 + 0.22X1X2 + 0.15X1X1 + 0.15X2X2$$

Final Equations in Terms of Coded Factors Floating duration)

$$Y = 9.50 + 0.75X1 - 1.33X2 - 0.25X1X2 + 0.25X1X1$$

The polynomial equations can also be used to draw conclusions considering the magnitude of co-efficient and the mathematical sign it carries; i.e. positive or negative. The positive coefficient of variable X1 i.e. HPMC K15M in case of response i.e. Floating duration indicates that, as the concentration of HPMC K15M was increased, the Floating duration was increased. The negative coefficient of

variable X2 i.e. Carbopol 934 P in case of response i.e. Floating duration indicates that, as the concentration of Carbopol 934 P was increased, the Floating duration was decreased.



Graph 2: Swelling study of formulation F1-F9

Results of water uptake (swelling) study cleared that order of swelling observed in these polymers (HPMC) could indicate the rates at which the preparations are able to absorb water and swell. Maximum liquid uptake and swelling of polymer was achieved after 6-8 hrs and then gradually decreased due to erosion. The percentage water uptake was found to be increased on increasing the concentration of HPMC K15M in the formulations and hence the water uptake capacity increases. Drug diffusion depends significantly on the water content of the tablet. This may be because the mobility of the polymer chains is very dependent on the water content of the system. In the case of high water content, polymer chain relaxation takes place with volume expansion resulting in marked swelling of the system.

CONCLUSION

Sodium bicarbonate has predominant effect on the buoyancy lag time, while HPMC K15M and has predominant effect on total floating time and drug release. Carbopol P934 has given extra adhesion property and helped to maintain the integrity of the tablet. Bilayered floating matrix tablet with

immediate release layer give good floating and a controlled release pattern .

Table1.

Various batches of Optimization of immediate release layer

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
Ciprofloxacin Hcl	135	135	135	135	135	135	135	135	135	135
SSG	4(2%)	-----	8(4%)	-----	12(6%)	-----	16(8%)	-----	20(10%)	-----
Crosspovidone	-----	4(2%)	-----	8(4%)	------	12(6%)	-----	16(8%)	-----	20(10%)
Dicalcium phosphate	45	45	45	55	55	55	55	65	65	65
Talc	8	8	8	8	8	8	8	8	8	8
Mg stearate	16	16	16	16	16	16	16	16	16	16

Table3.

3^2 Factorial Design for preparation of BFT of ciprofloxacin HCl.

	F1	F2	F3	F4	F5	F6	F7	F8	F9
IR layer									
Ciprofloxacin Hcl	135	135	135	135	135	135	135	135	135
SSG	12 (6%)	12 (6%)	12 (6%)	12 (6%)	12 (6%)	12 (6%)	12 (6%)	12 (6%)	12 (6%)
Dicalcium phosphate	55	55	55	55	55	55	55	55	55
Talc	8	8	8	8	8	8	8	8	8
Mg stearate	16	16	16	16	16	16	16	16	16
SR layer									
Ciprofloxacin Hcl	340	340	340	340	340	340	340	340	340
HPMC K15M	100	80	60	80	60	100	60	100	80
Carbopol 934P	60	60	60	40	40	80	80	40	80
Sodium bicarbonate	38 (7.5%)	36 (7.5%)	35 (7.5%)	35 (7.5%)	33 (7.5%)	38 (7.5%)	36 (7.5%)	36 (7.5%)	38 (7.5%)
Talc	5(1%)	5(1%)	5(1%)	5(1%)	5(1%)	5(1%)	5(1%)	5(1%)	5(1%)
Mg stearate	10(2%)	10(2%)	10(2%)	10(2%)	10(2%)	10(2%)	10(2%)	10(2%)	10(2%)
Total	779	757	736	736	714	800	757	757	779

Table 4.

Weight variation test

Average weight of tablet	Percent deviation
130 mg or less	10
>130 mg and < 324 mg	7.5
324 mg or more	5

Table 5.

Results of various batches of Optimization of immediate release layer

	Disintegration time (sec)	Friability (%)
P1	20	0.46
P2	22	0.49
P3	16	0.41
P4	17	0.48
P5	12	0.21
P6	14	0.35
P7	13	0.27
P8	15	0.39
P9	14	0.32
P10	17	0.43

Table 6.

Results of various batches of Optimization of BFT

	Hardness (kg/cm^2)	Thickness (mm)	Diameter (mm)	Friability (% w/w)	Average weight (mg)	% Drug content	Floating lag time (sec)	Floating duration (hr)	Swelling index (%)	%CDR
F1	4.1±0.2	9.5±0.1	11.1±0.1	0.38±0.02	780±3	101.98±0.12	13±2	10.5	114.48	95.4996
F2	3.8±0.1	9±0.2	11.1±0.2	0.35±0.03	757±5	100.05±0.64	15±3	9.5	84.01	92.3747
F3	4.2±0.1	8±0.2	11.0±0.1	0.46±0.02	735±1	98.84±0.36	17±1	9	101.90	89.2854
F4	3.9±0.2	8±0.1	10.9±0.0	0.37±0.01	735±3	99.08±0.54	12±3	11	107.21	90.7233
F5	4.1±0.1	7.5±0.1	11.1±0.3	0.47±0.03	715±1	98.14±0.53	14±2	10	89.09	87.2105
F6	4.0±0.2	10±0.2	11.0±0.1	0.33±0.02	800±4	102.34±0.74	17±1	9	109.37	97.2699
F7	3.8±0.2	9±0.1	11.2±0.2	0.39±0.01	757±1	99.45±0.28	20±3	8	79.26	91.5544
F8	4.1±0.1	9±0.2	10.9±0.0	0.41±0.03	757±2	100.73±0.84	10±2	12	121.79	93.7913
F9	3.9±0.2	9.5±0.1	11.1±0.1	0.43±0.02	780±3	101.12±0.17	20±1	8	96.02	94.6474

Table 7.

***In vitro* drug release profile of formulation F1-F9**

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
15	27.125	26.075	28.7	26.6	29.225	26.425	28	26.775	27.125
30	28.65139	28.81472	30.76889	28.82056	31.47472	28.29361	31.98611	28.2975	30.22639
45	31.20989	30.49997	33.34839	31.03081	33.53622	30.67361	34.57786	31.2025	31.92564
60	33.61614	32.72422	35.60064	33.26031	35.79022	32.54961	35.96736	33.08375	33.63889
120	35.69339	37.94272	38.92214	38.83406	39.46347	38.81636	41.04236	34.63075	36.06614
180	39.53814	39.53522	42.27339	43.93531	43.34497	42.34261	48.26461	38.115	44.28939
240	43.41789	48.31497	48.10439	48.90881	52.51147	45.20036	56.60511	47.40575	48.39139
300	52.05764	50.00372	53.81464	56.37781	58.09047	51.93261	59.94936	50.48575	59.18014
360	56.05464	58.35472	63.07739	57.61681	66.17022	60.12786	67.52161	56.567	62.72214
420	59.91164	62.40947	67.35264	62.71281	70.47522	67.00011	73.58886	59.37925	64.36889
480	68.70189	74.37422	75.16464	67.67931	79.54197	72.71036	83.21036	64.66425	68.47614
540	71.44939	82.25272	79.89839	72.68956	82.74272	76.19636	86.44611	75.4215	79.61839
600	77.36789	84.95297	87.64739	82.29356	85.61797	83.73536	89.88136	79.98025	86.49064
660	84.56389	91.52247	88.46639	89.88681	86.41422	91.51761	90.71786	84.5775	93.77414
720	95.49964	92.37472	89.28539	90.72331	87.21047	97.26986	91.55436	93.79125	94.64739

Table 8.

Results from statistical analysis

Response	b0	B1	b2	b12	b11	b22
%CDR	92.48	3.09	1.96	0.22	0.15	0.15
p Value	<0.0001	<0.0001	<0.0001	0.0213	0.1235	0.1243
Floating duration	9.50	0.75	-1.33	-0.25	0.25	0.00
p Value	0.0015	0.0016	0.0003	0.0577	0.1240	1.000

Table 9.

Results of swelling kinetics

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
60	25.152	19.546	16.23421	22.423	25.838	22.423	15.575	32.637	29.638
120	62.536	37.789	49.738	55.721	42.738	55.721	38.764	60.567	47.638
180	66.544	39.928	52.942	59.6712	48.783	59.6712	40.668	76.679	52.662
240	72.577	49.647	63.892	65.733	51.627	66.683	47.453	79.537	55.527
300	78.437	55.727	69.536	74.567	53.647	74.567	50.689	87.679	64.466
360	85.547	60.738	73.748	80.673	63.798	80.673	56.567	92.537	67.527
420	94.738	62.657	84.626	82.648	68.682	90.748	60.656	102.566	75.578
480	98.43	70.738	88.63	96.738	76.638	97.372	65.6576	105.536	77.682
540	104.578	75.838	95.637	100.893	79.783	100.893	70.575	111.425	82.637
600	111.627	79.738	98.321	103.784	83.783	103.784	75.568	117.567	86.683
660	113.575	80.354	100.652	104.683	88.568	107.748	78.5465	120.423	92.356
720	114.4872	84.01585	101.9048	107.21088	89.0909091	109.375	79.26024	121.7966	96.025

REFERNCES

1. Chien Y.W. "Novel Drug Delivery Systems", 2nd Edition, Drugs and Pharmaceutical Sciences, Volume-50, Marcel Dekker, Inc.

2. Hoffman, D. Stepensky, E. Lavy, S. Eyal E. Klausner and M. Friedman: Pharmacokinetics and pharmacodynamic aspects of gastroretentive dosages forms, Int J Pharm. 2004; 277: 141.

3. R. Talukder and R. Fassihi: Gastroretentive delivery systems: A mini review, Drug Dev Ind Pharm 2004; 30: 1019.

4. M. Lauretta, E. Machiste, M. Torre, U. Conte. Formulation of biphasic release tablets containing slightly soluble drugs, Eur J Pharm Biopharm.1999; 48: 37.

5. Makhija SN and Vavia PR: Once daily sustained release tablets of venlafaxine, a novel antidepressant. Eur. J. Pharm. Biopharm. 2002; 54: 9–15.

6. Remington: The Science and Practice of Pharmacy, 21st ed., Lippincott Williams & Wilkins, Philadelphia, **2005** (electronic version).

7. Y.I. Jeong, H.S. Na, J.W. Nah and H.C. Lee: Preparation of ciprofloxacin-encapsulated poly (DL-lactide-co-glycolide) microspheres and its antibacterial activity. J.Pharm. Sci. 2009; 98: 3659–3665.

8. RA Arza, CS Gonugunta, PR Veerareddy: Formulation and evaluation of swellable and floating gastro retentive ciprofloxacin hydrochloride tablets. AAPS PharmSciTech. 2009; 10: 220–226.

9. J. Varshosaz, N. Tavakoli and F. Roozbahani: Formulation and *in vitro* characterization of ciprofloxacin floating and bioadhesive extended-release tablets, Drug Deliv. 2006; 13: 277–285.

10. A. Srinatha, JK Pandit: Multi-unit floating alginate system: effect of additives on ciprofloxacin release, Drug Deliv. 2008; 15: 471–476.

11. Dhanasingh S, Shunmuga Kumar: Nallaperumal Chitosan/Casein Microparticles: Preparation, Characterization and Drug Release Studies. International Journal of Engineering and Applied Sciences 2010: 12

12. Gangadharappa HV, Balamuralidhara V and Pramod Kumar TM:Formulation and *in vitro* evaluation of gastric floating tablets of Atenolol. Journal of Pharmacy Research 2010; 3: 1450-1455.

13. Lachman L, Liberman HA and Kanig JL. The Theory and Practice of industrial Pharmacy, 3rd Edn, Varghese Publishing House, Bombay **1987**: 297-300.

14. Schwartz LM: Advances in acid-base gran plot technology. Journal of Chemistry Education 1987; 64: 947-950.

15. Miller MM, Wasik SP and Huang GL, Relationships between octanol water partition coefficient and aqueous solubility, Environmental Science Technology 1985; 19: 522–29.

16. Martin A, Micromeretics, In: Martin A, ed. Physical Pharmacy, Baltimores, MD: Lippincott Williams and Wilkins, **2001**: 423-454.

17. Indian Pharmacopoeia, Government of India, Ministry of Health and Family welfare, The Indian pharmacopoeia commission, Ghaziabad, 2007, 1, 182, 183.

18. Tadros M: Controlled-release effervescent floating matrix tablets of ciprofloxacin hydrochloride: Development, optimization and *in vitro – in vivo* evaluation in healthy human volunteers. European Journal of Pharmaceutics and Biopharmaceutics, 2010; 74: 332–339.

19. Maru AD, Lalla JK, "Intragastric floating tablets as novel oral drug delivery systems. Indian drugs 1987; 25: 57-69.

20. Costa P and Lobo JMS: Modeling and comparison of dissolution profiles. European Journal of Pharmaceutical Science 2001; 12: 123-133.

21. Klaus Florey, Analytical profiles of drug substances; 64th Edn. Elsevier Academic press **2005**; 5: 327-44.

22. Hokanson GC: A life cycle approach to the validation of analytical methods during pharmaceutical product development. Pharmaceutical technology 1994; 2: 118-130.