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Investigation and Optimization of the Effect of Polymers on Drug Release of Norfloxacin from Floating Tablets

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of the article

Abstract

Background. Norfloxacin is fluoroquinolone anti-infective used in the treatment of urinary tract infections, prostatitis, gonorrhea and genital tract infections. It has plasma half life of 3 to 4 h requiring multiple dosing in the treatment. Release-retarding polymers can be used to modulate the drug release of norfloxacin.
Objectives. The objective of this study was to investigate the effect of release-retarding polymers on the drug release of norfloxacin from floating tablets.
Material and Methods. Norfloxacin was procured as a gift sample from Concept Pharma Ltd. Aurangabad (India) and HPMC K100M was procured as a gift sample from Colorcon Asia Pvt. Ltd., Goa (India). The tablets were prepared by direct compression method and various pharmaceutical parameters were evaluated.
Results. It was observed that all tablet formulations F1–F9 retained the drug release up to 12 h with good floating property but only Batch-F4 complies with the USP dissolution limits with a minimum floating lag time. The drug release kinetics were evaluated by the model-dependent (curve fitting) method using PCP Disso v3 software shows Batch-F4 shows to best fit with Peppas model for which R2 value was 0.9921 and the release exponent value was 0.6892.
Conclusions. The drug release kinetics study indicates that the floating tablets release the drug by diffusion followed by erosion mechanism. Obtained in-vitro drug release data was analyzed by design expert software for drug release at first hour and at 12th h values and found that release the selected independent variables like HPMC K100M and sodium alginate concentration has a significant effect on drug release **(Polim. Med. 2016, 46, 2, 117–127).**

Key words: floating drug delivery systems, gastroretentive drug delivery systems, norfloxacin, drug dissolution.

Oral delivery of drugs is by far the preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulation, etc [1]. The majority of formulations available on the market are oral drug delivery systems. Oral drug delivery systems have developed from immediate release to targeted or site specific delivery over a predefined period. An ideal drug delivery system possess two important characteristics that are with single dose frequency and ability to release the active drug directly at the site of action [2]. Thus, the objective of the pharmacist is to develop systems that release an optimal quantity of drug to a desired site of action. Attempts to develop a single-dose therapy for the whole duration of treatment has lead to the development of controlled or sustained release drug delivery systems.

Oral controlled release systems have been developed to achieve optimal drug delivery to the systemic circulation. Although such systems can precisely control the drug release for a prolonged period of time, even over a number of days, some drugs have a narrow absorption window due to them not being absorbed through the gastrointestinal tract, as the dosage formulation will pass through the absorption window. Thus, there was the need to develop a formulation which will prolong the gastric residence time of the system to achieve complete drug release in the gastrointestinal tract (stomach and small intestine) and which will modulate the drug release rate as predicted by the system.

Norfloxacin is amongst the most prescribed fluoroquinolone antiinfective for urinary tract infections, prostatitis, gonorrhea and genital tract infection [3].

The plasma half-life of norfloxacin is 3–4 h [4]. It is the Biopharmaceutical Classification Sytem Class-II drug with low solubility and high permeability. The bioavailability of norfloxacin is only 30–40%. Norfloxacin requires multiple dosing schedules in order to maintain adequate plasma concentration. Norfloxacin is poorly absorbed from the lower part of the gastrointestinal tract and it is well absorbed from the stomach [5, 6]. Floating drug delivery is advantageous over conventional sustained release approach in the case where drugs are absorbed in a narrow absorption window. The effervescent floating drug delivery system provides drug release for a longer period of time to the site of absorption by retaining buoyancy of formulation [7, 8]. Therefore, norfloxacin is a suitable drug candidate for the gastro-retentive drug delivery system. The formulation of floating tablets of norfloxacin will help to release drug continuously over a longer period of time in the upper part of the gastrointestinal tract and may improve patient compliance.

Material and Methods

Norfloxacin was procured as a gift sample from Concept Pharma Ltd. Aurangabad (India) and HPMC K100M was procured as a gift sample from Colorcon Asia Pvt. Ltd., Goa (India). The tablet compression machine (Minipress, Karnavati Engineering) was used for direct compression of tablets. The Roche friability test apparatus (VFT-2D, Veego Instruments Corp.), digital melting apparatus (Chief Scientific), dissolution test apparatus (VDA6DR, Veego Instruments Corp.) ultraviolet spectrophotometer (UV-1800, Shimadzu), fourier transform spectrophotometer (Thermo Fischer Scientific), differential scanning calorimeter (DSC-60, Schimadzu) were utilized for characterization raw materials and evaluation of tablet formulations under study.

Prefomulation Study and Compatibility Testing

The identification of norfloxacin was performed by organoleptic characteristics, melting point, ultraviolet spectroscopy, infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC).

The preformulation characteristics including bulk density, tapped density, Carr's index, an angle of repose [9] of norfloxacin and its blend with excipients in tablet formula were studied.

The drug excipient compatibility testing of norfloxacin with the polymers was studied using their physical their mixture in equal ratio. The mixtures were prepared by triturating the drug with HPMC K100M and sodium alginate. Mixtures were stored for a week at a temperature of 40°C. The mixtures were then analyzed by DSC at the heating rate of 20°C/min over a range of 0–300°C.

Formulation of Floating Tablets

The composition of tablets is given in Table 1 as 3^2 experimental design. A 3^2 full factorial design was constructed where the polymer ratio (HPMC K100M, sodium alginate) was selected as independent variables. The levels of the two factors were selected on the basis of the preliminary studies carried out before implementing the experimental design [10]. All other formulations and processing variables were kept constant throughout the study. All ingredients were sieved through sieve no. 100 and weighed according to formula weights in Table 1. To prepare floating tablets HPMC K100M and sodium alginate polymers were triturated together with norfloxacin for about 10 min. Then, sodium bicarbonate and citric acid were added to above polymeric blend as gas generating agent while polyvinyl pyrrolidone-K30 was added as a binder. Further, the required quantity of bulking agent MCC PH102 was added to the above blend and all the ingredients were passed

Table 1. Composition of final factorial design

Ingredients (mgs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drug	400	400	400	400	400	400	400	400	400
HPMC K100M	80	100	120	80	100	120	80	100	120
Sodium alginate	64	64	64	80	80	80	96	96	96
MCC PH102	130	110	90	114	94	74	98	78	58
Citric acid	10	10	10	10	10	10	10	10	10
Sodium bicarbonate	50	50	50	50	50	50	50	50	50
PVP K30	50	50	50	50	50	50	50	50	50
Magnesium stearate	8	8	8	8	8	8	8	8	8
Talc	8	8	8	8	8	8	8	8	8
Total weight (mgs)	800	800	800	800	800	800	800	800	800

through sieve no. 60, mixed uniformly. Immediately before tablet compression lubricants magnesium stearate and talc were mixed uniformly with a blend for tablets. The direct compression method was used to prepare the tablets which were compressed with a rotary tablet compression machine using 13 mm double concave punches, and the hardness was adjusted to 6–8 kg/cm^2.

Evaluation of Tablets

The prepared floating sustained release tablets of Norfloxacin were subjected to various evaluation parameters as given below:

Organoleptic Properties

These include the evaluation of color, surface texture, i.e. smooth vs rough, and appearance.

Thickness

The thickness of the unit tablet was measured using a digital vernier caliper, which permits accurate measurement and provides information about the dimension of tablets.

Weight Variation

The weight variation test was carried out as per USP/NF. The test was carried out by electronically weighing 20 tablets individually and calculating the average weight, and the individual tablet weight was compared with the average weight of 20 tablets [11].

Hardness

Monsanto hardness tester was used to check the hardness of the tablet. The tablet was placed diametrically between the jaws of the tester. The two jaws were put under tension by a spring and screw gauge. By revolving the screw, the load was increased, and at collapse, the applied pressure from the spring was measured in kg/cm^2 [12, 13].

Friability

Tablet friability was determined using the Roche friability test apparatus. Usually, it should be below 1%, an indication of the good mechanical resistance of tablets. A preweighed sample of 20 tablets was placed in the friability test apparatus and subjected to 100 revolutions for 4 min. The tablets were dedusted and reweighed. The friability was calculated by the formula as given below [14]:

$$\%F = (1 - Wo)/W \times 100,$$

where, F is friability, W_O is the weight of tablets before the test, W is the weight of tablets after the test.

Drug Content

Twenty tablets were weighed accurately, finely powdered and mixed. The tablet powder equivalent to 25 mg of norfloxacin was accurately weighed and dissolved in 25 mL of 0.1N HCl. The solution was sonicated for 10 min and then filtered through a Whatman filter paper no. 41 to separate the insoluble additives in the formulation. One mL of filtrate was diluted to 100 mL with 0.1N HCl. The absorbance of the resulting solution was determined using an ultraviolet spectrophotometer at 278 nm and drug content was calculated.

In-Vitro Dissolution Studies

The *in-vitro* release of drug from all formulations was determined using USP apparatus type II (Paddle method) [15]. The following conditions were followed to study the *in-vitro* dissolution study of norfloxacin floating tablet as given in Table 2.

At each time interval, 5 mL of aliquots were withdrawn from the dissolution medium for 12 h. The volume withdrawn was replaced by a fresh volume of dissolution medium. The filtered samples were analyzed spectrophotometrically at 278 nm and absorbance was measured. Percent drug release was calculated for every sample.

Table 2. Conditions for *in-vitro* dissolution study

Particulars	Description/comment
USP dissolution apparatus	type II (paddle method)
Volume of dissolution medium	900 mL
Speed of paddle	50 rpm
Temperature	37 ± 0.5°C
Dissolution medium	0.1N HCl
Sampling interval	1 h
Study time	12 h
Quantity of sample withdrawn	5 mL

Dissolution Efficiency

The dissolution efficiency of a pharmaceutical dosage form is defined as the area under the dissolution curve up to a certain time (t) (measured using the trapezoidal rule), expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time. It was calculated by the following equation [16–19].

$$D.E. = \frac{\int_0^t y \times dt}{y_{100} \times t} \times 100 \ ,$$

where, y is the drug percent dissolved at time t.

Floating Lag Time and Total Floating Duration

The time required for the tablet to rise to the surface and float was noted as the floating lag-time. The floating lag time of the tablets was studied at 37 ± 0.5°C, in 200 mL 0.1N HCl. The total floating duration means total time duration of which the tablet floats on the surface of the liquid; it was noted [20, 21].

Drug Release Models

To describe the kinetics of the drug release from floating tablets, mathematical models such as zero--order, first-order, Higuchi, Hixon-Crowell, Korsmeyer--Peppas models were studied [22, 23].

Zero-order kinetic model

$$M_0 - M_t = K_0 t,$$

First-order model

$$\text{In } (M_0/Mt) = K_1 t,$$

Higuchi's model

$$Mt = K\sqrt{t},$$

Hixon-Crowell Cube root model

$$M_0^{1/3} - M_0^{1/3} = Kt$$

Korsmeyer-Peppas model

$$Mt/M = Kt^n.$$

The drug release data was evaluated by model-dependent (curve fitting) using the PCP Disso v3 software and the model with the highest correlation coefficient was considered to be the best model [24]. The observations were as summarized in Table 3. In order to understand the drug release mechanism, the data was further analyzed by the Korsmeyer-Peppas equation and the value of 'n', i.e. release exponent, was calculated.

Table 3. Infrared spectral assignments for norfloxacin

WAVENUMBER (/CM)	ASSIGNMENT
3600 to 3250	N–H and O–H stretch
2500	hydrogen bonded O–H stretch
1725–1700	carboxylic acid C=O
1250	C–F and carboxylic C–O stretch

Analysis of Data by Design Expert Software

A 3^2 factorial design was selected and the two factors were evaluated at 3 levels [25]. HPMC K100M and Sodium alginate were selected as independent variables. A percent drug release was the dependent variable. The data obtained was evaluated by Design expert 7.1.6 software and analyzed statistically using an analysis of variance (ANOVA). The data was also subjected to 3D response surface methodology optimization to study the interaction of dependent variables.

Results and Discussion

The identification of norfloxacin was performed by organoleptic characteristics, melting point, ultraviolet spectroscopy, infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC).

The melting point of norfloxacin was found to be 221–226°C by digital melting apparatus, and 226.24°C by DSC (Fig. 3) which is in good agreement with reported the melting point of 221–223°C. The UV spectrum of Norfloxacin solution (8 µg/mL) exhibited wavelength of absorbance maximum at 278 nm as shown in Fig. 1. The infrared spectrum of norfloxacin and major frequencies observed are reported in Fig. 2 and Table 3 respectively confirms its identity.

Many different types of angular properties have been employed to assess flowability, of these the angle of repose is the most relevant. The value of an angle of repose (θ) decreased after the addition of a lubricant. The angle of repose (θ) is an indicative parameter of powder flowability from the hopper to the die cavity. The angle of repose was within the range of 29–30°, indicative of good flowability. Bulk density may influence compressibility, tablet porosity, dissolution and other properties and depends on the particle size, shape and tendency of particles to adhere together. The bulk densities of drug and polymers-HPMC K100M and sodium alginate were found to be 0.622 gm/cm^3, 0.354 gm/cm^3, 0.689 gm/cm^3 respectively. The tapped densities of drug and polymers-HPMC K100M and sodium alginate were found to be 0.7176 gm/cm^3, 0.483 gm/cm^3, 0.8733

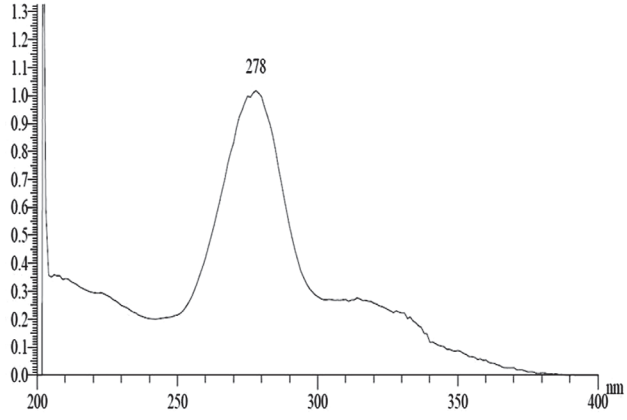

Fig. 1. U.V. Spectrum of norfloxacin

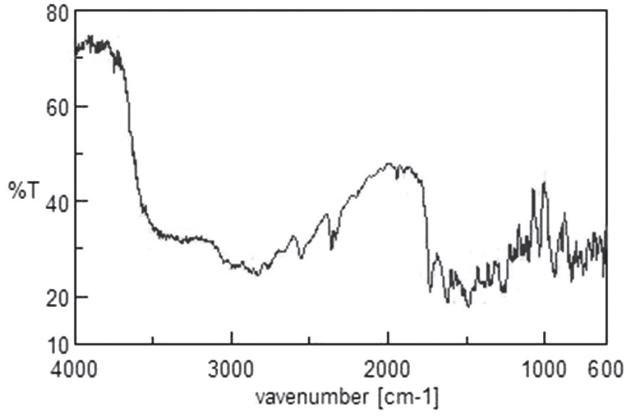

Fig. 2. Infrared spectrum of norfloxacin

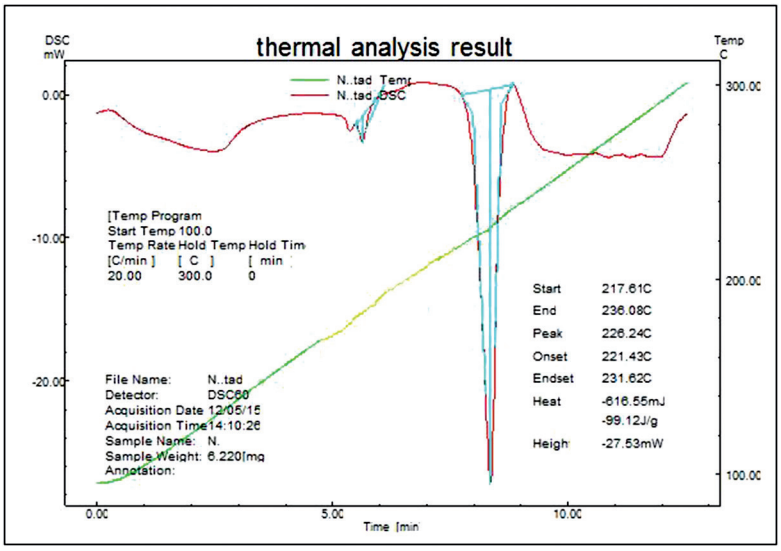

Fig. 3. DSC Thermogram of norfloxacin

Table 4. Flow properties of drug and polymer

Drug/polymer	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carrs index (%)	Hausner ratio	Angle of repose (θ)
Norfloxacin	0.622	0.7176	13.32	1.15	27.34°
HPMC K100M	0.354	0.483	26.7	1.36	32.48°
Sodium alginate	0.698	0.8733	25.11	1.25	29.14°

Table 5. Flow properties of final powder blend

Formulation code	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's index (%)	Hausner ratio	Angle of repose (θ)
F1	0.7978	0.8923	10.56	1.11	26.92
F2	0.8123	0.9812	17.21	1.20	30.12
F3	0.7813	0.8753	10.73	1.12	24.56
F4	0.8319	0.9946	16.35	1.19	28.61
F5	0.8646	0.9753	11.35	1.12	30.59
F6	0.7635	0.8963	14.81	1.17	28.39
F7	0.7862	0.9878	20.40	1.25	29.13
F8	0.7435	0.8475	12.27	1.13	24.30
F9	0.7568	0.8901	14.97	1.17	29.13

gm/cm^3 respectively. The values indicate good packing capacity of powders. The bulk density and tapped density was used to calculate the percent compressibility of the powders. The characterization of flow properties of final blends is important in tablet compression. According to the following results, as shown in Tables 4 and 5, all the formulations from F1 to F9 had shown good flow properties and compressibility as compared to raw materials.

The drug : excipient compatibility testing of norfloxacin with the polymers was performed and the DSC thermogram of a mixture of norfloxacin with HPMC K100M and sodium alginate is depicted in Fig. 4. The melting point as observed in the thermogram was 224.86°C, which is indicative of negligible interaction of norfloxacin with excipients.

The evaluation of floating tablets from experimental factorial batches was as reported in Table 6, showing an acceptable level of parameters.

The *in-vitro* drug release from a tablet of all formulation was performed in triplicate using USP apparatus II (paddle method). The dissolution study was performed in 0.1N HCl for 12 h and the obtained results of all formulations are shown in Fig. 5. From the *in-vitro* drug release study, drug release retardation in the formulation can be attributed to the release retardation property of HPMC K100M and sodium alginate polymers. The higher the concentration of

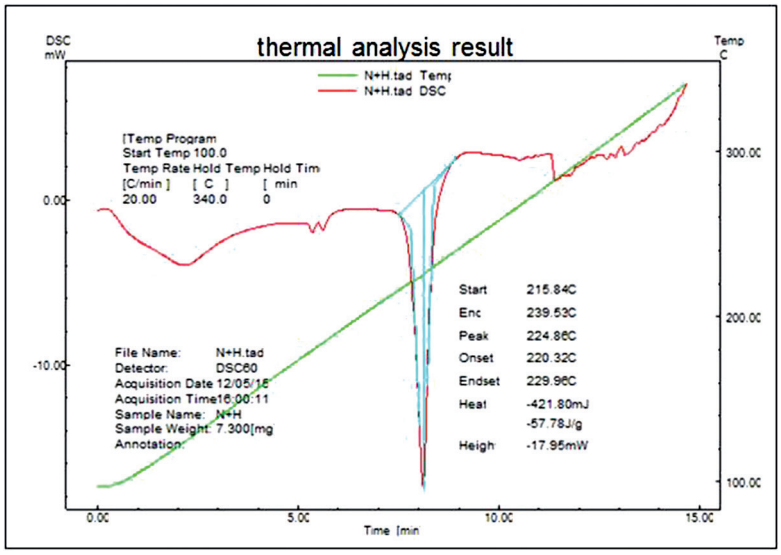

Fig. 4. Thermogram of excipients compatibility study

HPMC, the thicker and viscous is the gel layer, which offers more resistance to the drug diffusion and gel erosion [26]. In the gastric environment of low pH, sodium alginate precipitates in the hydrated gel layer as alginic acid. The precipitated alginic acid provides a firm structure to the gel and acts as a drug release retarding agent [27]. Additionally, it was also postulated that when the combined matrix of HPMC and sodium alginate is exposed to an acidic environment, the HPMC hydrates to form a gel layer at the surface of the tablet while the sodium alginate remains insoluble, acting as a barrier to drug diffusion from the tablets [28]. Norfloxacin is amphoteric in nature and demonstrates a higher solubility at pH below 4 and above 8 [29]. In such case, although the drug is present in solubilized state, the polymeric gel formed by a combined matrix of HPMC and sodium alginate polymers may act synergistically, providing prolonged drug release from the floating tablets.

We can conclude from the *in-vitro* drug release study that, as the concentration of polymer increases, drug release decreases. Dissolution efficiency was cal-

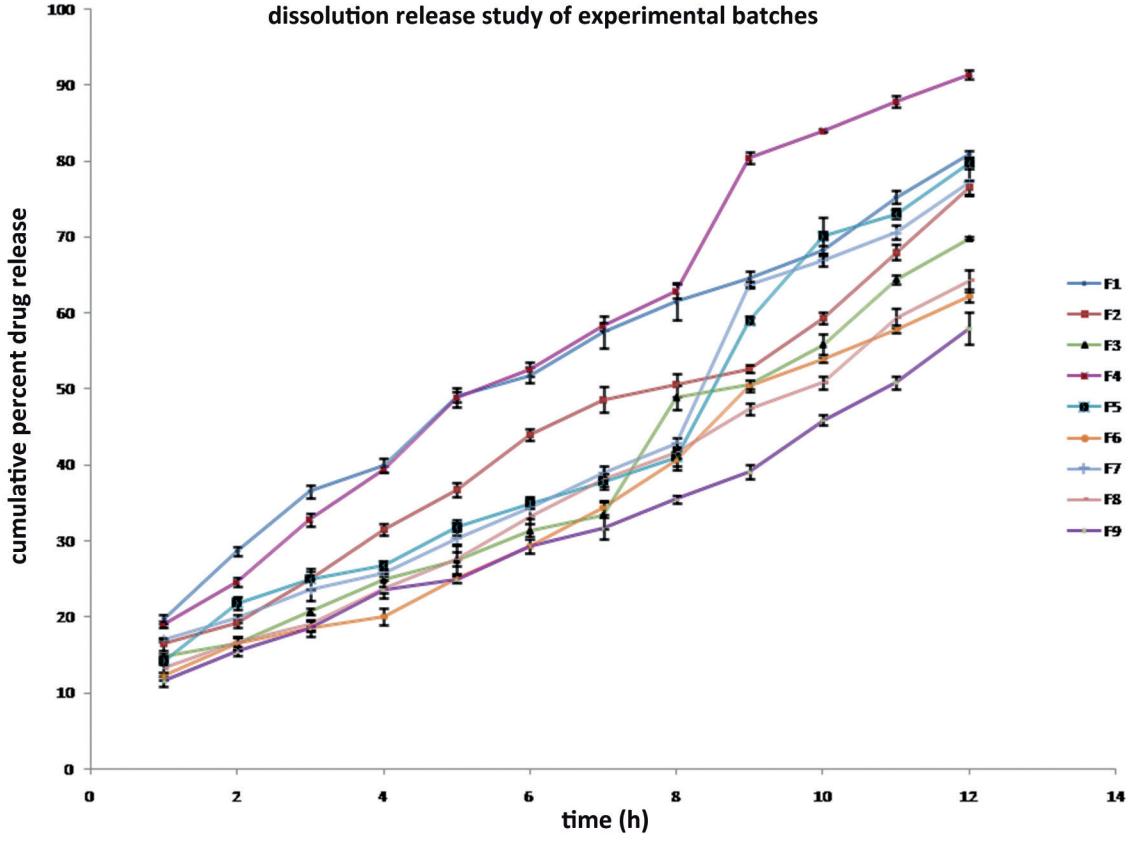

Fig. 5. Drug release study of experimental batches in 0.1N HCl

Table 6. Evaluation of final factorial batches

Formulation	Appearance	Weight Variation mg ± %SD	Hardness (kg/cm^2) ±SD	Friability %	Thickness (mm) ± SD	Assay (%mg) ± SD
F1	Off white, circular, 13 mm, biconvex	800 ± 2.01	7.6 ± 0.288	0.033	6.39 ± 0.057	98.23 ± 0.25
F2	Off white, circular, 13 mm, biconvex	800 ± 2.13	7.5 ± 0.5	0.016	6.32 ± 0.023	99.33 ± 0.53
F3	Off white, circular, 13 mm, biconvex	800 ± 2.04	7 ± 0.288	0.025	6.35 ± 0.01	99.23 ± 0.45
F4	Off white, circular, 13 mm, biconvex	800 ± 1.86	7.5 ± 0.5	0.008	6.41 ± 0.05	101.21 ± 0.63
F5	Off white circular, 13 mm, biconvex	800 ± 1.80	6.5 ± 0.5	0.016	6.36 ± 0.02	99.6 ± 0.81
F6	Off white, circular, 13 mm, biconvex	800 ± 1.59	7.8 ± 0.75	0.008	6.41 ± 0.057	100.66 ± 0.62
F7	Off white, circular, 13 mm, biconvex	800 ± 1.59	6.66 ± 0.76	0.033	6.39 ± 0.03	99.33 ± 1.02
F8	Off white, circular, 13 mm, biconvex	800 ± 1.51	7.16 ± 0.28	0.017	6.38 ± 0.02	100.2 ± 0.85
F9	Off white, circular, 13 mm, biconvex	800 ± 1.54	7.66 ± 0.57	0.008	6.35 ± 0.01	98.66 ± 0.56

culated using PCP-Disso v. 3 software and the graphical representation of the dissolution efficiency was shown in Fig. 6. The drug release kinetics of factorial experimental batches was reported in Table 8. The kinetic data fitting shows Batch F1, F2 and F4 follow Korsmeyer-Peppas kinetic model, Batch F3, F5 and F7 follow Zero order kinetics and Batch F6, F8 and F9.

Although all batches were observed to be intact and float for the duration longer than 12 hrs, the lowest floating lag time was observed with F4 factorial batch

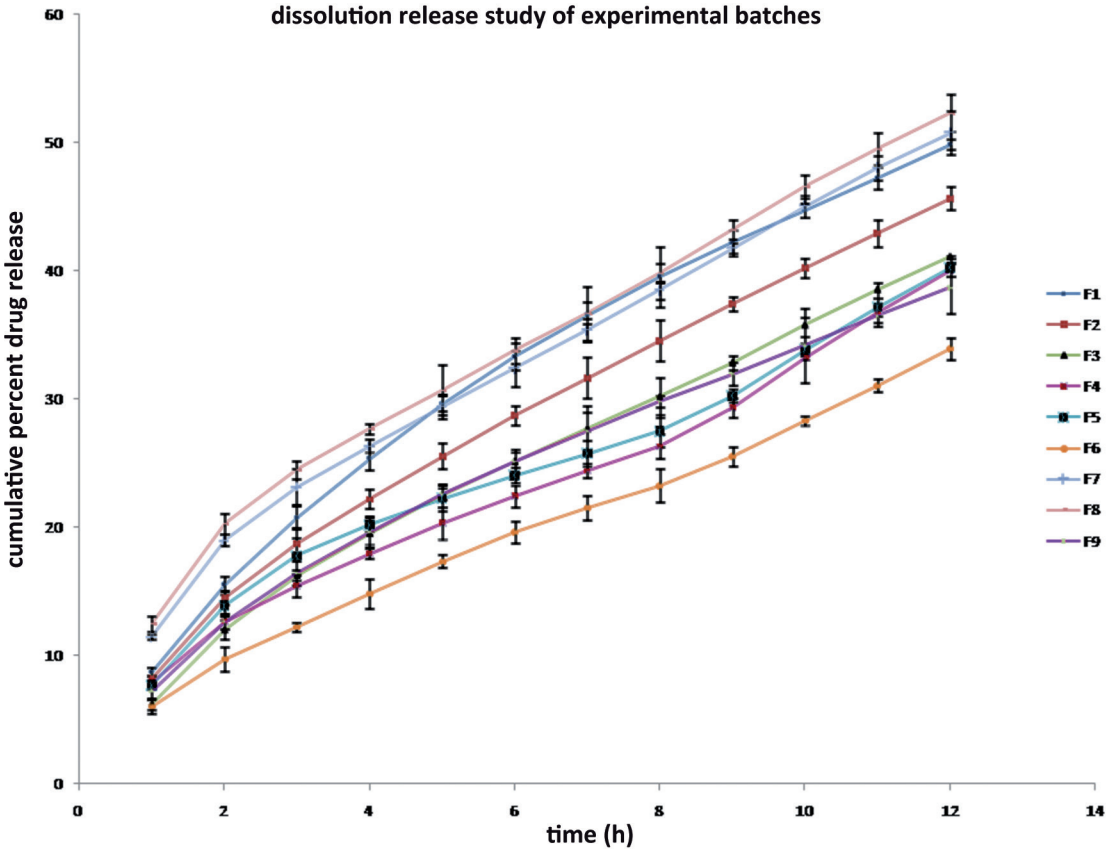

Fig. 6. Dissolution efficiency of experimental batches in 0.1N HCl

Table 7. Floating lag time and total floating duration

Formulation code	Floating lag time (s) ± SD	Floating duration (h)	Tablet integrity
F1	24.00 ± 0.60	> 12	intact
F2	25.36 ± 0.46	> 12	intact
F3	27.40 ± 0.43	> 12	intact
F4	16.67 ± 0.50	> 12	intact
F5	18.74 ± 0.55	> 12	intact
F6	26.22 ± 0.90	> 12	intact
F7	32.71 ± 1.01	> 12	intact
F8	21.15 ± 0.75	> 12	intact
F9	29.62 ± 0.59	> 12	intact

(see Table 7 and Fig. 7). The sodium bicarbonate and citric acid were added to improve buoyancy lag time.

The traditional design process of the pharmaceutical formulations was based on a time-consuming approach of changing one variable at a time, which does not take into consideration the joint effect of independent variables. Thus, factorial design can serve as an essential tool to understand the complexity of the pharmaceutical formulations. The results can be expressed either as simple linear or second order polynomial equations to statistically evaluate the responses obtained after experiments.

The 3^2 factorial design was selected to study the effect of independent variables HPMC K100M and Sodium alginate on dependent variable-cumulative percent drug release. A statistical model incorporating interactive and polynomial terms was utilized to evaluate the responses. The equation conveyed the basis to a study of the effects of variables. The regression coefficient values are the estimates of the model fitting. The r^2 was high, indicating the adequate fitting of the quadratic model. The polynomial equations can also be used to draw conclusions considering the magnitude of the coefficient and the mathematical sign it carries; i.e. positive or negative.

The factorial model equations for drug release at the end first hour and at the end of 12 h were obtained through Design Expert and given below:

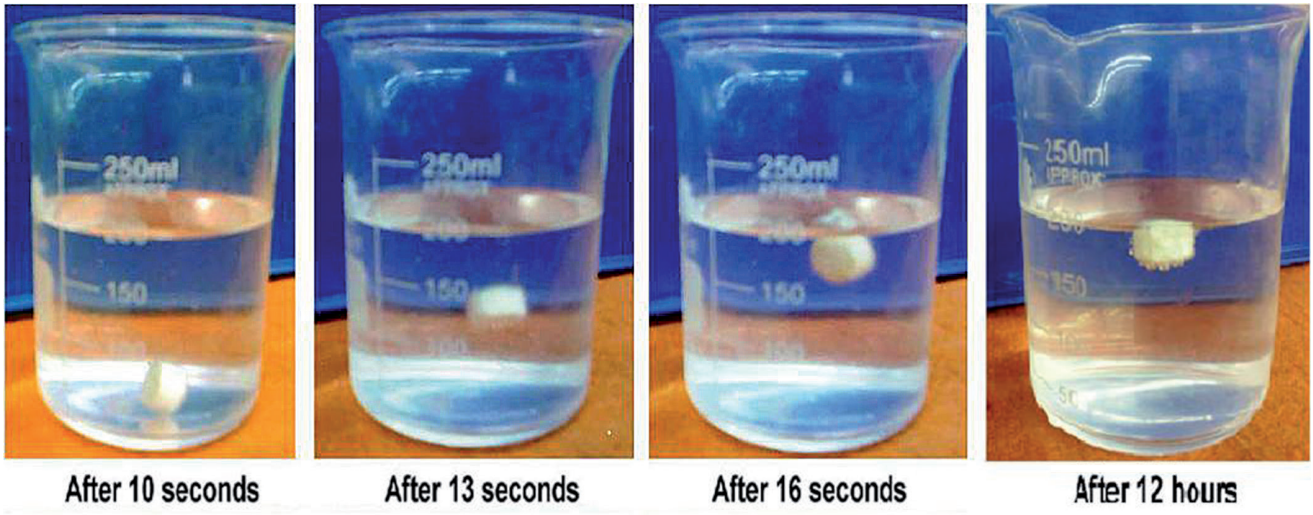

Fig. 7. *In-vitro* floating duration (buoyancy) study of Batch-F4

Table 8. Drug release kinetics

Formulation code	Drug release kinetic model (R^2)					n	K
	Zero order	1st order	matrix	peppas	Hixson-Crowell		
F1	0.9171	0.9868	0.9950	0.9987	0.9893	0.5551	19.8292
F2	0.9709	0.9701	0.9673	0.9832	0.9817	0.6395	13.7286
F3	0.9813	0.9618	0.9296	0.9531	0.9742	0.6645	11.2060
F4	0.9774	0.9554	0.9663	0.9921	0.9827	0.6892	16.1042
F5	0.9613	0.9243	0.9111	0.9127	0.9457	0.5876	14.6301
F6	0.9803	0.9739	0.9318	0.9355	0.9805	0.6371	10.8751
F7	0.9713	0.9419	0.9300	0.9591	0.9568	0.6312	13.2556
F8	0.9817	0.9794	0.9510	0.9605	0.9851	0.6310	11.4402
F9	0.9682	0.9726	0.9527	0.9579	0.9759	0.5793	11.2133

Final Equation in Terms of Actual Factors

% DR at first hour = 15.3667 – 2.83833* HPMC K100M – 1.54833 sodium alginate +1.00206597 HPMC K100M* sodium alginate – 0.649564*(HPMC K100M)^2 2.002636576 (sodium alginate)^2 [r^2 = 0.93883]

% DR at 12th h = 73.34 – 9.8933* HPMC K100M – 4.63833 * sodium alginate –0.045451 HPMC K100M* sodium alginate – 0.180094*(HPMC K100M)^{2*} 0.752003 (sodium alginate)^2 [r^2 = 0.9648]

The negative coefficient of variable HPMC K100M and Sodium alginate in a case of response drug release indicated negative effect, i.e. increase in the concentration of these two variables results in a decrease in drug release confirmed from the experimental design. The mutual interaction of HPMC K100M and sodium alginate was positive in factorial equations, indicating synergistic release retardation, as stated in the earlier discussion.

The study data regarding the variance of dissolution of all formulations was analyzed. The coefficients of HPMC K100M and sodium alginate were found to be significant at $P < 0.05$, thereby confirming the significant effect of both the variables on the selected response. ANOVA and multiple regression analysis were done using Design Expert 7.1.6 software.

The quadratic model obtained from the regression analysis used to build 3-D graphs in which the responses were represented by curvature surface as a function of independent variables. The relationship between the response and independent variables can be directly visualized from the response surface plots. The response surface plots were generated using Design Expert 7.1.6 software presented in Fig. 9 and 10. The effect of independent variables, HPMC K100M and sodium alginate on a selected response was studied. A graphical presentation of the data helped to show the relationship between the response and the independent variables. The information given by the graph was similar to that of mathematical equations obtained from the statistical analysis. The response surface plots showed that various combinations of independent variables HPMC K100M and sodium alginate may satisfy any specific requirement (i.e. max drug release up to 12 h) while taking into consideration various factors involved in dosage form [30].

Conclusion

The preformulation studies indicated improved characteristics of norfloxacin in a blend prepared for tablet compression. *In-vitro* release rate studies demonstrated that the maximum drug release was observed in Batch-F4 formulation, i.e. 91.36% at the end of 12 h with less floating lag time and increased matrix integrity. The integrity of the matrix was due to a combined matrix of HPMC K100M and sodium alginate. Hence, Batch-F4 forumlation was selected as optimized formulation batch. It shows best curve fitting with the Kors-

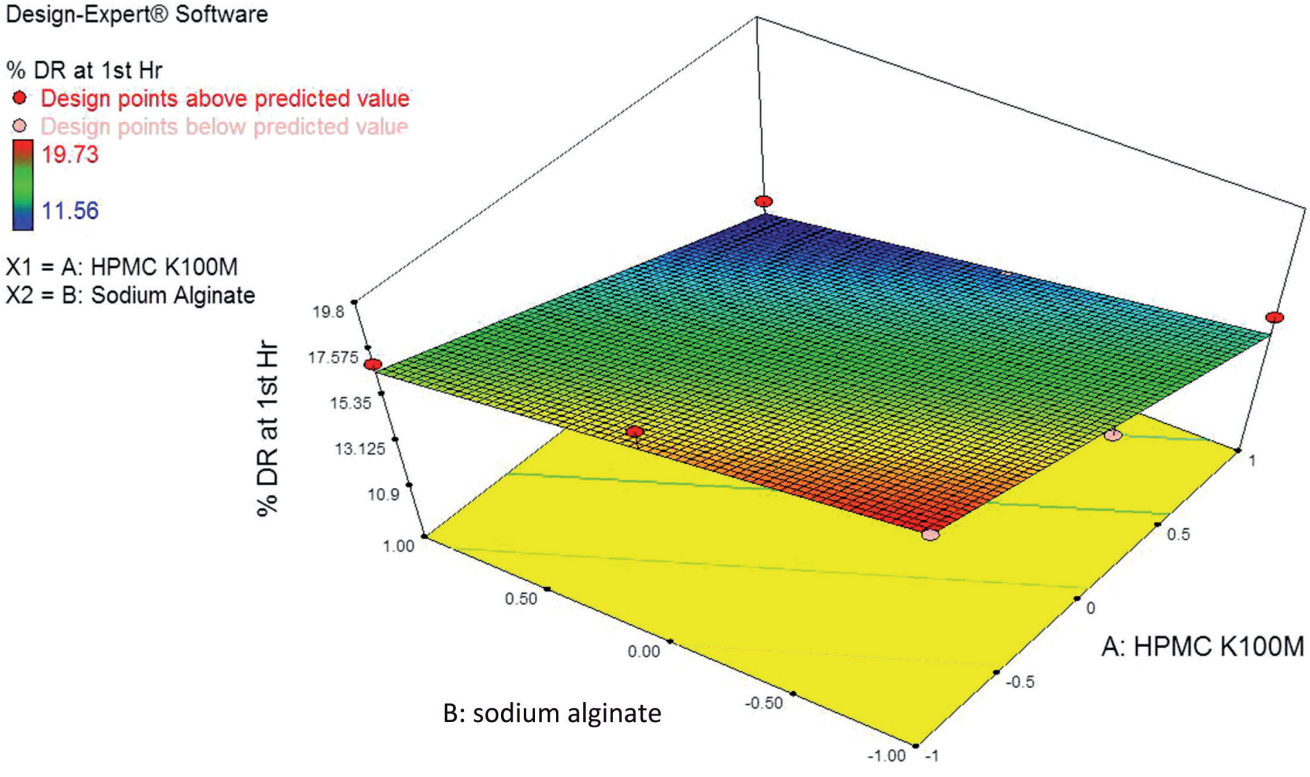

Fig. 8. Response surface plot for percent drug release at first hour

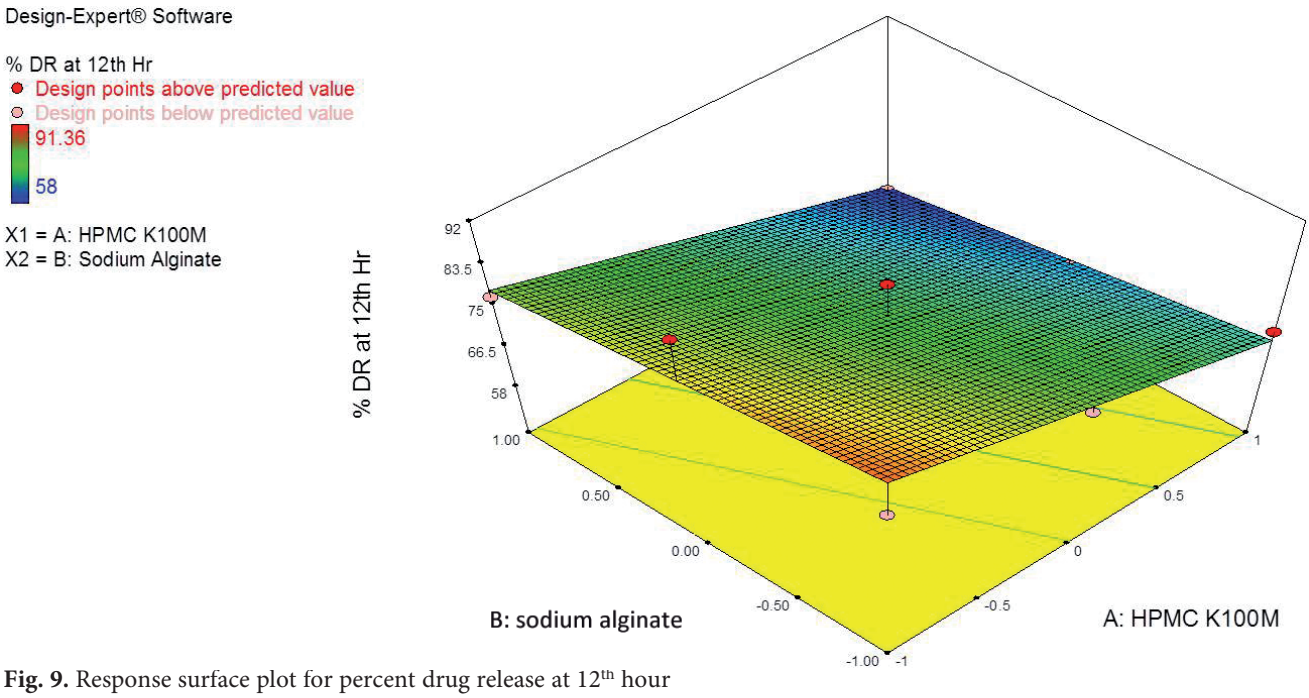

Fig. 9. Response surface plot for percent drug release at 12th hour

meyer-Peppas model for which the R2 value was 0.9921 and the release exponent value was 0.6892, indicating release of the drug is by diffusion followed by erosion mechanism from formulation. The drug release study shows that there was a desirable effect of release retardation polymers used in the formulation providing the required release profile from norfloxacin floating tablet formulations. An *In-vitro* drug release data was analyzed by design expert software for drug release at first hour and at the end of the twelfth hour and confirms that the selected independent variables HPMC K100M and sodium alginate concentration had a significant effect on drug release of norfloxacin**.** HPMC K100M and sodium alginate can be combined together, as they work synergistically, thus providing prolonged release at the upper part of the gastrointestinal tract in floating tablets.

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