Statistical design, formulation, and evaluation of gastroretentive floating tablets for moxifloxacin using natural and semisynthetic polymers

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ABSTRACT

Purpose: The objective of the current study is to develop gastroretentive formulation for moxifloxacin using various drug release modifiers, moxifloxacin, novel synthetic fluoroquinolone, and antibacterial agent. **Materials and Methods:** Floating tablets of moxifloxacin.HCl were prepared using variable amounts of hydroxypropyl methylcellulose (HPMC) K100M and *lannea coromandelica* gum (LCG) with effervescent mixtures as per 3^2 factorial designs by direct compression technique. Amount of release modifiers required to obtain the prolonged release of drug was chosen as independent variables, X_1 and X_2, respectively, whereas time taken for 10%, 50%, 75%, and 90% of drug release were chosen as dependent variables. **Results and Discussion:** Nine formulations were developed and are checked for pharmacopeial tests. Results show that all the factorial batches were lie within the standard limits. Dissolution parameters of all formulations were subjected to kinetic fitting; various statistical parameters were determined. Polynomial equations were developed and verified for dependent variables. **Conclusion:** Formulation (F_5) containing 50 mg of HPMCK100M and 50 mg of LCG is the best formulation showing similarity $f_2 = 71.733$ and $f_1 = 4.272$ with the marketed product (AVELOX). Formulation F_5 follows Higuchi's kinetics, Non-Fickian Diffusion, and first-order kinetics ($n = 1.098$).

Keywords: 3^2 factorial design, first-order kinetics, gastroretentive, hydroxypropyl methylcellulose K100M, lannea coromandelica gum, moxifloxacin, non-Fickian diffusion mechanism

INTRODUCTION

The effective oral drug delivery practice depends on numerous factors such as gastric emptying process, gastrointestinal (GI) transit time, release of drug from dosage form, and absorption site for the drug.[1-3] The design of oral controlled drug delivery systems (DDS) is aimed to obtain desirable and enhanced bioavailability. Gastric emptying is a dynamic process and gastroretentivity of dosage form results improved clinical response.

Numerous factors show the impact on the effectiveness of oral delivery practice such as gastric emptying process, GI transit time, drug release pattern from the formulation and absorption site for the drug. The design of oral controlled DDS is targeted to obtain predictable and improved *in vivo* availability. Gastric transit time in humans, influences absorption of drugs, can result inappropriate drug release from formulation leading to diminished clinical response. Gastric transit time is a dynamic process and ability to sustain the release of drug at a predictive rate, which retains in the acidic environment for a longer period of time than prompt release formulations.

Several difficulties were present in front of researchers for designing controlled release systems for better absorption, improved bioavailability.[4] The controlled gastric retention of solid dosage forms was obtained by numerous mechanisms such as flotation, bioadhesion, high density (sedimentation), modified shape systems, expansion, or by simultaneous administration of pharmacological agents that delay gastric emptying.[5,6]

Floating drug delivery system (FDDS) is also known as hydrodynamically balanced system. FDDS have a bulk density is lower than gastric fluids and thus remain buoyant in the gastric environment for a prolonged period of time, without affecting the gastric emptying rate. The dosage form is stayed in the stomach due to the flotation mechanism, which results in controlled rate of drug release. After the release of the drug, the residual system is run out from the gastro environment; this will increases GRT and better control of fluctuations in plasma drug concentrations.[7-10]

Moxifloxacin, synthetic broad-spectrum antibacterial agent, belongs to the class of fourth-generation fluoroquinolone. It has a narrow absorption window and absorbed primarily in the proximal portions of gut, an ideal candidate for a gastroretentive drug-delivery system that will prolong the gastric transit time of formulation, results enhanced bioavailability.[11,12]

An attempt is made in the current study to develop gastroretentive drug-delivery system (preferably by flotation) with the help of drug release rate modifiers (natural – lannea coromandelica gum [LCG] and semisynthetic – hydroxypropyl methylcellulose [HPMC] K100M) and effervescent mixtures.[13-16] From the literature, very less work reported for LCG, though it is natural more benefits observed from an economy point of view as well as risk incidence also low. Hence, LCG selected as a polymer for the formulation development of moxifloxacin gastroretentive delivery.

A systemic approach for formulation of gastroretentive drug-delivery system of moxifloxacin with the help of polymers which prolong the gastric transit time, improve penetrability of the drug through mucosa thereby improving the clinical efficacy of the active ingredient.

Response surface methodology (RSM) with a polynomial equation has been extensively applied in the design and development of pharmaceutical products. Variables of RSM include 3^2 factorial design, central composite design), and Box-Behnken design. RSM is applied when only a few significant factors are involved in the optimization procedure. Advantage of this method is less experimentation and time, results in more effective and cost-effective than tradition experimentation models.[17,18]

Direct compression is a widely used manufacturing method for the preparation of tablets.[19]

Hence, an attempt is made in this research work to formulate gastroretentive floating (GRF) tablets of moxifloxacin using HPMCK100M and LCG. Instead of the heuristic method, a standard statistical tool design of experiments is utilized to study the effect of formulation variables on the release properties.

A 3^2 factorial design was utilized to study the effect of polymers on the drug release profile (effect of independent variables or factors), i.e., the quantity of HPMCK100M and LCG on the dependent variables ($t_{10\%}$, $t_{50\%}$, $t_{75\%}$, and $t_{90\%}$).[18,20]

A systemic approach for design and development of gastroretentive drug-delivery system of moxifloxacin using polymers which increases the gastric transit time, improve penetrability of drug through mucosa thereby improving the clinical efficacy of the active ingredient.

MATERIALS AND METHODS

Materials

A gift sample of moxifloxacin HCl was procured from Macleods Pharmaceutical Ltd., Mumbai, India. HPMCK100M was obtained from Loba Chemie Pvt. Ltd., Mumbai, India. LCG was gifted from Sarada Pharmaceuticals, Guntur. All other excipients such as Sodium bicarbonate, Emcompress, Magnesium stearate, Talc were obtained from S.D. Fine Chem. Ltd, Mumbai, India.

Formulation Development of Moxifloxacin GRF Tablets

Quantities required for the HPMCK100M, LCG for the preparation of moxifloxacin floating tablets was selected as independent variables (X_1 and X_2, respectively). $t_{10\%}$, $t_{50\%}$, $t_{75\%}$, and $t_{90\%}$ were selected as dependent variables. Polynomial equations were developed for dependent variables as per backward stepwise linear regression analysis.[21]

The three levels of X_1 (HPMCK100M) were 8.75%, 12.5%, and 16.25%. Three levels of X_2 (LCG) were 8.75%, 12.5%, and 16.25% (percentage with respect to dose of active ingredient). Nine moxifloxacin floating tablet formulations were designed using selected combinations of X_1 and X_2, checked for the selection of optimum composition required to meet the primary objective of the study.

Preparation of moxifloxacin HCl floating tablets

Direct compression technique was utilized for the preparation of floating tablets, each containing 400 mg moxifloxacin HCl. Accurately weighed ingredients (except moxifloxacin HCl) were screened for obtaining uniform size to ensure proper mixing, to obtain polymer mixture. The drug was then mixed with the polymer mixture for 10 min for uniform mixing of the powder blend. The blend was lubricated with magnesium stearate. The formulae for moxifloxacin HCl floating tablets are shown in Table 1. The powder blend was subjected to preformulation analysis.

The powder blend was subjected to compression with the help of rotary tablet compression machine (Tablet Minipress). Compressed tablets were processed for quality control measures as per pharmacopeia. Final formulations were transferred to airtight and light resistance containers.

Experimental Design

Experimental design used in the current research study is 3^2 factorial designs, quantity of HPMCK100M was labeled as X_1, and quantity of LCG was labeled as X_2 and presented in Table 1. Three levels for both X_1 and X_2 chosen and coded as $-1 = 8.75\%$, $0 = 12.5\%$, $+1 = 16.25\%$, formulations for factorial trials are presented in Table 2.

Evaluation of Moxifloxacin.HCl GRF Tablets[22]

Hardness

The breaking/crushing strength of the tablets was determined by measuring the diametric breakdown of tablet using a Monsanto Tablet Hardness Tester.

Friability

The friability of the tablets was carried with the help of Roche friabilator. Twenty tablets were weighed noted as initial weight (W_0); these were subjected to 100 free falls from a fixed height and weighed (W) again. Percentage friability was calculated using the following formula. The friability result should not be more than 1 %.

$$\text{Weight loss (\%)} = [W_0 - W/W_0] \times 100$$

Assay

The assay was performed by the triturating stated number of tablets in Indian Pharmacopoeia (20) converted to powder, powder equivalent to 100 mg of drug was added in 100 ml of 0.1 N HCl followed by sonication. The solution was filtered through a 0.45 μ membrane filter, suitable aliquots were prepared, and the absorbance of the resultant solution was measured spectrophotometrically at 288 nm using 0.1 N HCl as blank.

Thickness

Thickness formulations were determined using Vernier calipers, by placing the tablet between two arms.

In vitro buoyancy studies

This test is performed by placing the tablets in a beaker containing 100 mL of 0.1 N HCl (SGF). The time required for the upward movement of the tablet to float on the 0.1 N HCl (SGF) was noted to be floating lag time.[23]

In vitro drug release study

The *in vitro* dissolution rate study for formulation trials was performed using USP XXIII type-II dissolution test apparatus containing 900 ml of 0.1 N HCl operated under conditions such as temperature 37 ± 0.5°C and rotated at a speed of 50 rpm. At predetermined time intervals, 5 ml of the samples were withdrawn as per the pharmacopeial procedure. The resultant samples were analyzed for estimation of drug release by measuring the absorbance at 288 nm using ultraviolet-visible spectrophotometer after suitable aliquots. The samplings were performed in the triplicate manner ($n = 3$).[11,12,24]

The dissolution profile of all the formulations was subjected to kinetic modeling such as zero-order, first-order, Higuchi, and Korsmeyer–Peppas models to know the drug release mechanisms.[25-28]

Swelling index study

To evaluate swelling index, the tablet was placed in USP dissolution apparatus II with 900 ml 0.1N HCl after measuring the weight of tablet (W_1). Then, the weight of tablet (W_2) was determined by virtue of time, i.e., at different time intervals, namely, 0, 2, 4, 6, 8, 10, and 12 h after using blotting paper to remove surplus fluid. Swelling index was calculated using the following formula.

$$\text{Swelling index (\%)} = [(W_2 - W_1)/(W_2)] \times 100$$

RESULTS AND DISCUSSION

GRF tablets of moxifloxacin were formulated with the help of 3^2 factorial designs, for identifying the best composition of drug release modifiers (HPMCK100M, LCG) along with effervescent mixtures. Formulation design is presented in Table 1. Two factors involved for the design are that the quantity of HPMCK100M and LCG was labeled or chosen as independent variables (X_1 and X_2, respectively), and kinetic parameters labeled as dependent variables ($t_{10\%}$, $t_{50\%}$, $t_{75\%}$, and $t_{90\%}$). Nine factorial batches were designed as per the formulae are given in Table 2.

Powder blends were subjected to flow analysis. Results are summarized in Table 3. Pre-formulation results reveal that

Table 1: Experimental design layout

Formulation code	X_1	X_2
F_1	1	1
F_2	1	0
F_3	1	−1
F_4	0	1
F_5	0	0
F_6	0	−1
F_7	−1	1
F_8	−1	0
F_9	−1	−1
C_1	−0.5	−0.5
C_2	+0.5	+0.5

Table 2: Formulae for moxifloxacin gastroretentive floating tablets

Name of ingredients	Quantity of ingredients per each tablet (mg)								
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Moxifloxacin HCl	436.8	436.8	436.8	436.8	436.8	436.8	436.8	436.8	436.8
Emcompress	17.2	32.2	47.2	32.2	47.2	62.2	47.2	62.2	77.2
HPMCK100M	65	65	65	50	50	50	35	35	35
Lannea coromandelica gum	65	50	35	65	50	35	65	50	35
Sodium bicarbonate	50	50	50	50	50	50	50	50	50
Magnesium stearate	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3
Total weight	640	640	640	640	640	640	640	640	640

HPMC: Hydroxypropyl methylcellulose

all formulations are passed the limits and blends show good flow properties.

All trials have 400 mg of moxifloxacin as a GRF tablet dosage form by direct compression technique. All final batches were subjected to various finished product evaluation tests such as drug content, floating lag time, mean hardness, total floating time, mean thickness, and friability as per pharmacopeial methods, and subjective results are summarized in Table 4. Hardness for finished batches was founded to be in the range of 5.19 ± 0.188–5.68 ± 0.22 kg/cm². The thickness for finished batches was founded to be in the range of 6.12 ± 0.03–$6.31 \pm$

0.04 mm. Results for friability test were founded to be <0.35%. Drug content for finished batches was founded to be within the acceptance criterion. All formulation batches passed the weight variation test. The purpose of the swelling study is to determine the water uptake capability of the retardant. The swelling study was performed on all formulation trials about 12 h. From the swelling study, it is found that all formulation trails were shown swelling phenomenon when come in contact with 0.1 N HCl but stayed without breaking during the study period. Formulation F_1 was found to have the highest swelling property and the data for swelling evaluation are presented in Table 5.

Drug release studies were performed for finished batches using pH 1.2 buffer (0.1 N HCl) as a dissolution fluid is operated under a standard set of conditions at 50 rpm (paddle), $37 \pm 0.5°C$. Dissolution plots were presented in Figures 1-4 (kinetic plots), and statistical parameters are summarized in Table 6. Percentage cumulative drug release for finished batches F_1-F_9 at 24 h was found to be 94.815–100.39%. The result revealed that the release rate of the drug was inversely proportional to the quantity of polymers and vice versa.[29] Hence, desired drug release was achieved by manipulating the composition of independent variables.

The difference was seen independent variables due to the change in proportions of X_1 and X_2. Formulation coded F_5 containing 50 mg of HPMCK100M, 50 mg of LCG produced promising dissolution characteristics, which helps in meeting the objective of research by gastric retentive and optimum drug release ($t_{10\%} = 0.453$ h, $t_{25\%} = 1.236$ h, $t_{50\%} = 2.979$ h,

Table 3: Pre-formulation studies for formulation blends

Formulation code	Angle of repose (°)	Compressibility index (%)
F_1	25.155±0.7	16.95±0.3
F_2	25.855±0.6	16.725±0.2
F_3	26.34±1.1	17.205±0.2
F_4	25.1±0.7	16.455±0.3
F_5	26.285±0.6	16.23±0.2
F_6	26.285±1.1	16.71±0.2
F_7	25.815±0.7	16.675±0.3
F_8	26.2±0.6	16.05±0.2
F_9	26.2±1.1	16.53±0.2
Moxifloxacin HCl	36.12±1.1	26.01±0.18

Table 4: Post-compression parameters for the formulations ($n=3$)

Formulation code	Hardness (kg/cm²)	Thickness (mm)	Friability (%)	Average weight (mg)	Drug content (%)	Floating lag time (s)	Total floating time (h)
F_1	5.39±0.198	6.31±0.04	0.195±0.125	641.61±2.05	97.37±0.31	48.25±1.35	>12
F_2	5.19±0.188	6.26±0.02	0.345±0.085	643.62±4.05	97.715±0.36	50.86±1.4	>12
F_3	5.24±0.193	6.25±0.01	0.235±0.12	640.61±3.05	97.26±0.38	52.84±1.5	>12
F_4	5.46±0.18	6.24±0.04	0.18±0.13	642.5±2.15	98.96±0.33	49.34±1.4	>12
F_5	5.263±0.17	6.18±0.03	0.33±0.09	644.5±4.15	99.3±0.39	51.95±1.45	>12
F_6	5.32±0.18	6.18±0.01	0.22±0.125	641.5±3.15	99.95±0.41	53.93±1.55	>12
F_7	5.68±0.22	6.27±0.04	0.175±0.115	641.61±2.05	99.91±0.43	51.86±1.5	>12
F_8	5.48±0.21	6.22±0.02	0.325±0.075	643.62±4.05	99.26±0.49	54.47±1.55	>12
F_9	5.54±0.21	6.21±0.01	0.215±0.11	640.6±3.05	100.6±0.51	56.45±1.65	>12

Table 5: Swelling index of moxifloxacin HCl floating tablets

| Time (h)	% Swelling								
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
0	0	0	0	0	0	0	0	0	0
2	31.97±0.1	31.43±0.3	30.9±0.4	32.97±0.2	32.43±0.3	31.9±0.3	31.97±0.2	31.43±0.3	30.9±0.3
4	53.4±0.2	52.4±0.4	51.47±0.4	55.4±0.1	54.4±0.4	53.47±0.5	54.4±0.1	53.4±0.4	52.47±0.5
6	88.49±0.3	87.28±0.2	85.95±0.25	79.49±0.2	78.28±0.5	76.95±0.6	76.49±0.2	75.28±0.5	73.95±0.6
8	96.0.38±0.3	95.9±0.5	93.23±0.4	88.8±0.2	87.9±0.4	85.23±0.4	86.8±0.2	85.9±0.4	83.23±0.4
10	107.7±0.4	106.95±0.4	103.5±0.3	106.7±0.3	105.95±0.3	102.5±0.3	105.7±0.3	104.95±0.3	101.5±0.3
12	120.83±0.4	119.92±0.3	117.15±0.3	119.83±0.2	118.92±0.4	116.15±0.3	117.83±0.2	116.92±0.4	114.15±0.3
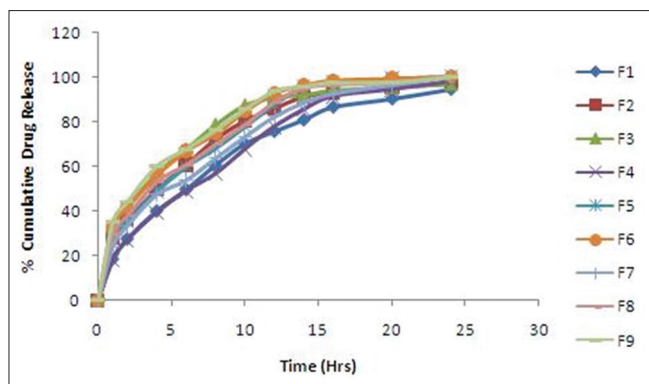
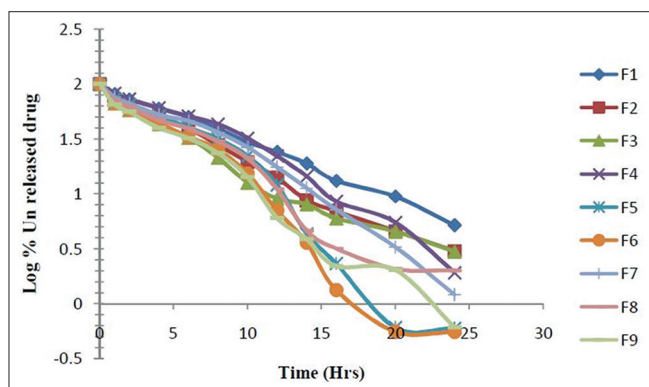**Figure 1:** Comparative zero-order plots

Figure 2: Comparative first-order plots
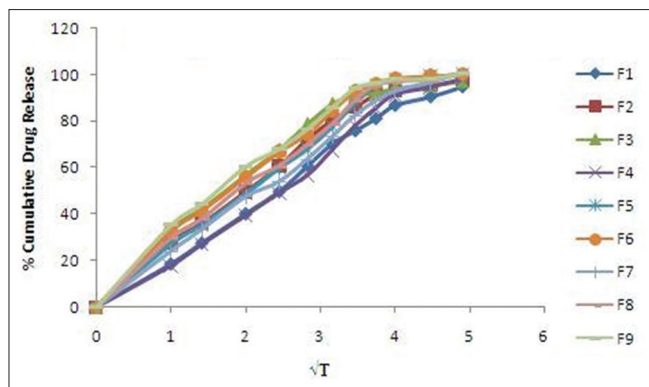

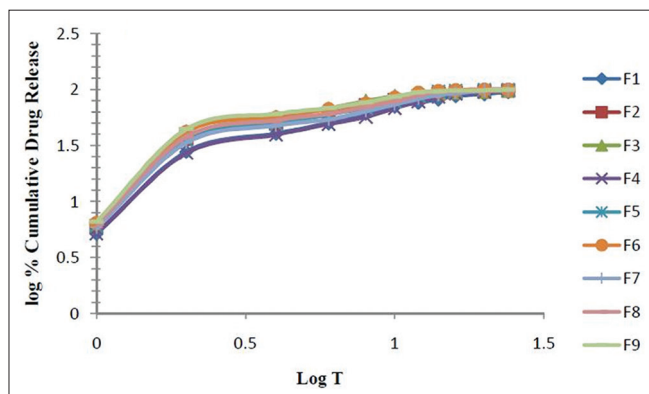**Figure 3:** Comparative Higuchi plots

Figure 4: Comparative Korsmeyer–Peppas plots

$t_{75\%}$ = 5.958 h, and $t_{90\%}$ = 9.899 h). The initial burst release of drug from the formulation was due to change in viscosity of polymer matrix. As the increase in viscosity of stagnant layer results in a corresponding decrease in the drug release (occurred due to thicker gel layer formation). Dissolution profiles of moxifloxacin floating tablets were subjected to kinetic modeling. The results are presented in Table 4 and Figures 1-4. Results reveal that all formulation batches best fitted to first-order kinetics, quantification of r^2 was founded to be in the range of 0.977–0.998. They also fitted to Higuchi's kinetics, r^2 was found to be in the range of 0.964–0.994. From the Peppas treatment, it reveals that all batches follow that shows non-Fickian diffusion super Case-II path (n values 0.986–1.187). Polynomial equations were developed for all dependent variables by linear stepwise backward regression analysis with the help of PCP Disso software, and response morphological plots were constructed using Design-Expert 7.0. The response morphological plots are presented as Figures 5-9 for $t_{10\%}$, $t_{25\%}$, $t_{50\%}$, $t_{75\%}$ and $t_{90\%}$ using X_1 and X_2 on both the axes, to show the effects of independent variables on the dependent variables. Kinetic parameters for trials (F_1 - F_9) are presented in Table 7.

Polynomial equation for 3^2 full factorial designs was presented as follows:

$$Y= b_0+b_1 X_1+b_2 X_2+b_{12} X_1X_2+b_{11} X_1{}^2+b_{22} X_2{}^2\ldots$$

Y – dependent variable, b_0 – mean response of 9 trials, b_1– estimated coefficient for X_1, b_2– estimated coefficient for X_2, b_{12}– interaction term, $X_1{}^2$ and $X_2{}^2$ coefficients for non-linearity.

The equations for dependent variables developed as mentioned below,

$$Y_1 = 0.617+0.102X_1+0.084X_2+0.017X_1X_2+0.142 X_1{}^2+0.055X_2{}^2 \text{ (for } t_{10\%})$$

$$Y_2 = 1.683+0.279X_1+0.227X_2+0.046 X_1X_2+0.388 X_1{}^2+0.152 X_2{}^2 \text{ (for } t_{25\%})$$

$$Y_3 = 4.056+0.672X_1+0.547X_2+0.111 X_1X_2+0.936 X_1{}^2+0.364 X_2{}^2 \text{ (for } t_{50\%})$$

$$Y_4 = 8.111+1.344X_1+1.095X_2+0.222 X_1X_2+1.871 X_1{}^2+0.729 X_2{}^2 \text{ (for } t_{75\%})$$

$$Y_5 = 13.477+2.233X_1+1.820 X_2+ 0.368 X_1X_2+3.11 X_1{}^2+1.21 X_2{}^2 \text{ (for } t_{90\%})$$

The positive sign for coefficient of X_1 in Y_1–Y_5 notifies that, as the amount of X_1 increases, all independent variables values were also increases. In other words, the data demonstrate that both X_1 and X_2 affect dependent variables. From the results, it can be concluded that increase in the amount of the polymer leads to decrease in release rate of the drug and drug release pattern may be altered by changing the quantities of X_1 and X_2 to appropriate levels. The dissolution parameters for predicted from the polynomial equations and those actual observed from experimental results are summarized in Table 8. Closeness of results were seen between actual values and predicted values. This proves that developed polynomial equation was valid. The response surface/surface morphological plots were presented to show the effects of X_1 and X_2 on dependent variables. The final best (based on desirability factor above 0.999) formulation (F_5) is the identical product and shows similarity factor (f2) 71.733, difference factor

Table 6: Regression analysis for factorial trials

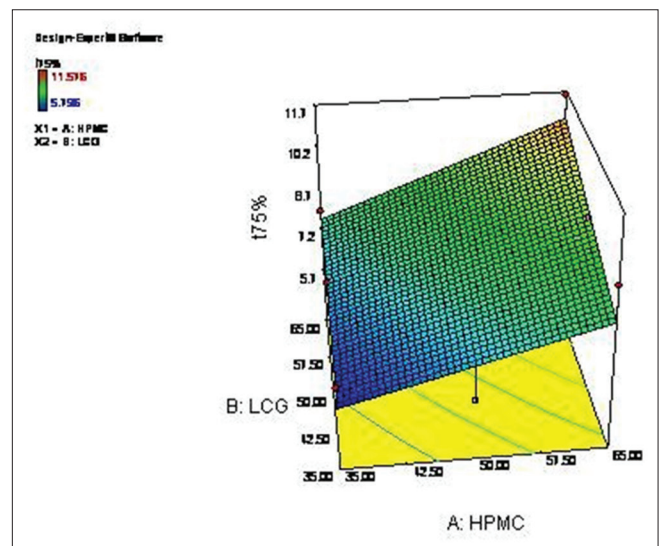| Formulation code	Kinetic parameters											
	Zero-order			First-order			Higuchi			Korsmeyer–Peppas		
	a	b	r	a	b	r	a	b	r	a	b	r
F_1	21.369	3.761	0.938	1.989	0.052	0.998	0.027	20.825	0.994	1.001	0.798	0.934
F_2	30.176	3.651	0.895	1.946	0.065	0.995	7.508	20.913	0.981	1.109	0.743	0.904
F_3	36.290	3.418	0.854	1.871	0.064	0.984	13.452	20.160	0.964	1.171	0.705	0.875
F_4	19.665	4.013	0.949	2.070	0.068	0.986	−2.337	21.941	0.993	0.986	0.817	0.942
F_5	28.582	3.883	0.910	2.108	0.101	0.978	5.282	21.954	0.984	1.098	0.758	0.914
F_6	34.694	3.651	0.876	2.043	0.104	0.982	11.225	21.202	0.973	1.161	0.719	0.887
F_7	25.552	3.838	0.929	2.058	0.076	0.988	3.292	21.421	0.992	1.073	0.761	0.920
F_8	31.127	3.710	0.896	1.981	0.079	0.977	8.172	21.223	0.980	1.130	0.732	0.901
F_9	37.063	3.507	0.861	1.970	0.091	0.990	13.892	20.591	0.967	1.187	0.698	0.874
MP	16.008	7.024	0.966	2.019	0.090	0.970	1.258	26.973	0.999	0.998	0.991	0.920
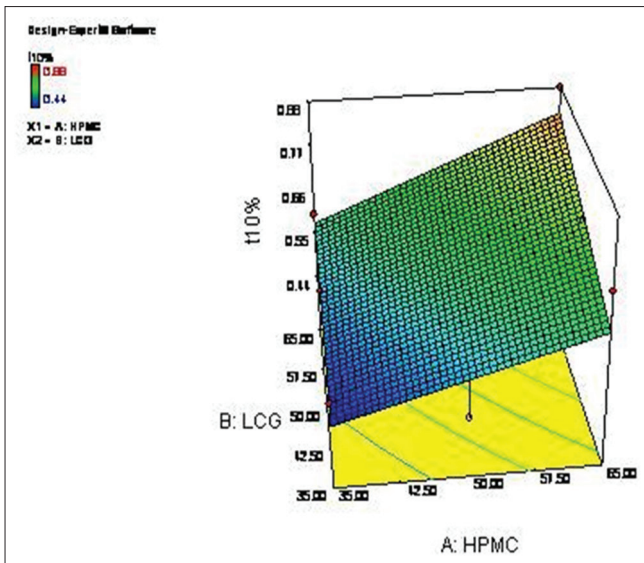
Figure 5: Response morphological plot for $t_{10\%}$
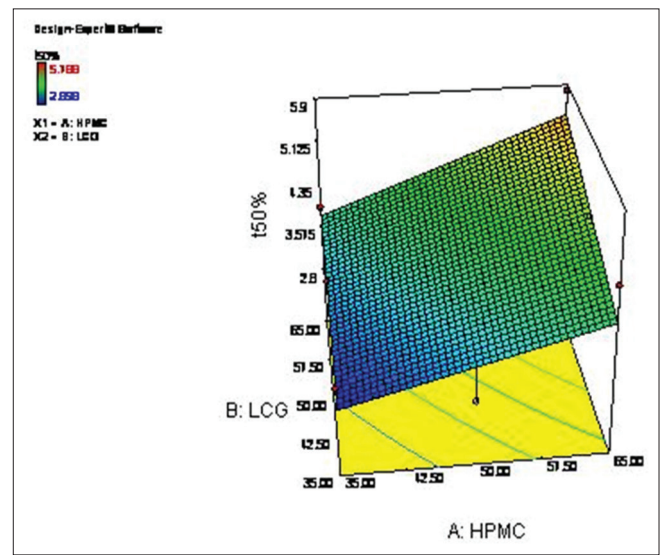
Figure 7: Response morphological plot for $t_{50\%}$
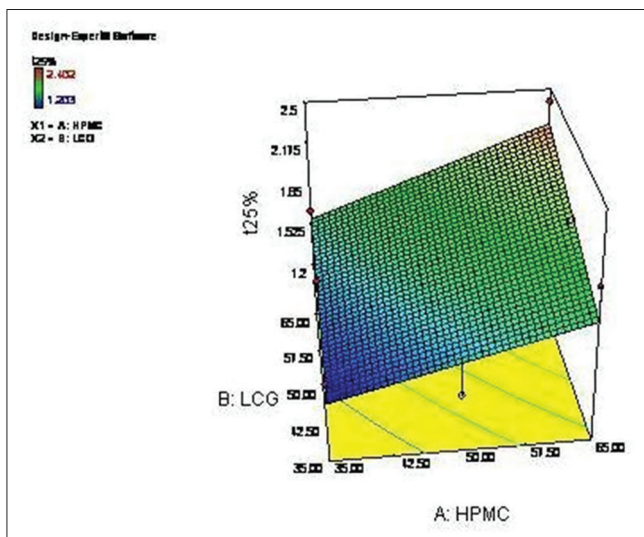
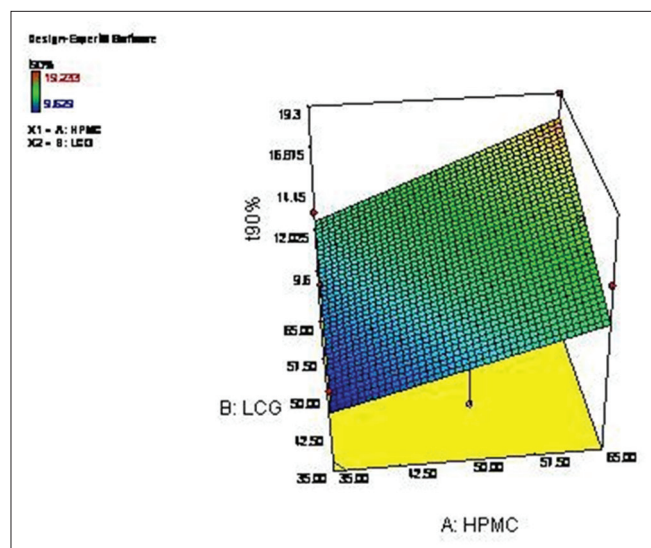**Figure 6:** Response morphological plot for $t_{25\%}$

Figure 8: Response morphological plot for $t_{75\%}$

Table 7: Dissolution parameters of moxifloxacin gastroretentive floating tablets

Formulation code	Kinetic parameters				
	$t_{10\%\,(h)}$	$t_{25\%\,(h)}$	$t_{1/2\,(h)}$	$t_{75\%\,(h)}$	$t_{90\%\,(h)}$
F_1	0.880	2.402	5.788	11.576	19.233
F_2	0.706	1.928	4.645	9.290	15.435
F_3	0.712	1.944	4.685	9.370	15.568
F_4	0.672	1.834	4.419	8.839	14.686
F_5	0.453	1.236	2.979	5.958	9.899
F_6	0.440	1.203	2.898	5.796	9.629
F_7	0.603	1.646	3.966	7.932	13.179
F_8	0.580	1.583	3.815	7.629	12.676
F_9	0.503	1.372	3.306	6.612	10.986
MP	0.510	1.393	3.357	6.715	11.157

Table 8: Dissolution parameters for checkpoint formulations

Formulation code	Predicted value					Actual observed value				
	$t_{10\%}$ (h)	$t_{25\%}$ (h)	$t_{50\%}$ (h)	$t_{75\%}$ (h)	$t_{90\%}$ (h)	$t_{10\%}$ (h)	$t_{25\%}$ (h)	$t_{50\%}$ (h)	$t_{75\%}$ (h)	$t_{90\%}$ (h)
C_1	0.578	1.577	3.799	7.597	12.623	0.581	1.585	3.811	7.610	12.615
C_2	0.764	2.083	5.0183	10.036	16.676	0.771	2.094	5.02	10.05	16.682

Figure 9: Response morphological plot for $t_{90\%}$

Figure10: Comparative *in vitro* dissolution profiles for F_5 – AVELOX

(f1) 4.272, t_{cal} is <0.05 when compared with the marketed product (AVELOX). Comparative dissolution plots for best formulation (F_5) and marketed product, as shown in Figure 10.

CONCLUSION

On the basis of the current research study, the use of macromolecules (Natural and Semisynthetic polymers) in combination had its own advantages of maintaining integrity and buoyancy of tablets. The effervescent based FDDS is a promising formulation to obtain gastroretentivity using gel-forming polymers such as HPMCK100M, LCG employing sodium bicarbonate as gas generating agent using 3^2 factorial design. Among the various FDDS formulations studied, the formulation (F_5) showed the best result in terms of the required percentage cumulative drug release, floating lag time and total floating time were 99.245% within 24 h and are considered as the ideal formulation. Best formulation F_5 follows first-order release, Non-Fickian Diffusion super Case-II transport. The best formulation shows good retaining characteristics. It also avoids the first-pass effect and also improves patient compliance by reducing the dosing frequency, which will ultimately improve the clinical response.

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