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Formulation and Evaluation of Floating Sustained Release In situ Gel as Carrier for Stomach Specific Drug Delivery of Alfuzosin

Abhijeet P. Shirguppe
abhi.shirguppe@gmail.com
Kolhapur District Chemists Association's Institute of Pharmacy, Kolhapur, Maharashtra

Amit M. Belekar
amitbelekar19@gmail.com
Kolhapur District Chemists Association's, Institute of Pharmacy, Ujalaiwadi, Kolhapur, Maharashtra

Prashant S. Salian
prashantsalian31@gmail.com
Kolhapur District Chemists Association's, Institute of Pharmacy, Ujalaiwadi, Kolhapur, Maharashtra

ABSTRACT

In-situ forming polymeric formulations drug delivery systems are in sol form before administration in the body, but once administered, undergoes gelation in-situ to form a gel, from which drug gets released in sustained and controlled manner. The formulation of gel depends upon factors like temperature modulation, pH changes, the presence of ions and ultra-violet irradiation. The objective of this study was to develop a novel in- situ gel system for sustained drug delivery of Alfuzocin using natural biodegradable polymers. The system utilizes polymers that exhibit sol-to-gel phase transition due to change in specific physicochemical parameters. The in-situ gel was formed at a biological pH. Gellan gum used as a polymer and $CaCO_3$ was used as a cross-linking agent. In vitro release studies were conducted in 0.1 N HCl and the cumulative amount of drug release was analyzed by spectrophotometry. From the designed set of experiments, it was evident that formulation containing Gellan gum control the release of drug for a longer duration. The in-situ gel exhibited the expected viscosity, drug content, pH, in vitro gelling capacity, in vitro floating ability and sustained drug release. The stability studies were carried out for 3 months.

Keywords: *Alfuzosin, Floating, Gellan Gum, In situ Gel, Sustained, etc.*

1. INTRODUCTION

Alfuzosin hydrochloride, a selective alpha adrenergic antagonist is used against benign prostatic hypertrophy (BPH) in elderly males. The prostate gland of the patient enlarges in BPH and prevents urine flow from bladder which results in urinary retention. The treatments available are surgical removal of excess tissue or drug therapy. Two classes of drugs are used, 5-alpha reductase inhibitors and alpha adrenergic antagonists. The second class includes terazosin, doxazosin, tamsulosin, and alfuzosin. [1, 2] Alfuzosin is freely soluble in water and thus readily absorbed after administration. The oral absorption is significantly aided by the presence of food. The dose of immediate release alfuzosin tablet is 2.5 mg thrice daily. Recently 10 mg once daily extended release formulation has become available in the market which is more convenient for older patients.

Marketed alfuzosin formulation is a three-layered Geomatrix tablet that requires special facilities, high cost, more time and complex operation than conventional formulations. An easier directly compressible formulation was reported by Nair *et al.* which is also followed in the current experiment. As the drug is recently introduced, the data regarding the formulation and drug excipients compatibility are inadequate. Low viscosity hydroxyl propyl methyl cellulose (HPMC) was used to prepare controlled release alfuzosin tablet (10 mg) that sustained drug release only for 12 h. To obtain once daily dosage form, high viscosity HPMC (such as Methocel K15M) should be used which can sustain drug release for a longer period. For freely soluble drugs like alfuzosin, a large quantity of HPMC is required to control the release that ultimately results in tablets which are difficult to swallow. This problem can resolve by using *in situ* gel. [3]

In situ gel forming systems used for sustained drug delivery. *In situ* forming polymeric delivery systems provides some advantages such as ease of administration, reduced frequency of administration, improved patient compliance and comfort.[4] *In situ* gel formation occurs due to one or combination of different stimuli like pH change, temperature modulation, and solvent exchange.[5] Various natural and synthetic polymers such as gellan gum, alginic acid, xyloglucan, pectin, chitosan, poly (DL lactic acid), poly (DL-lactide-co-glycolide) and poly-caprolactone are used for formulation development of *in situ* forming drug delivery systems.[6] Gastroretentive *in situ* gelling system helps to increase the bioavailability of drug compared to the conventional liquid dosage form.[7] The gel formed from *in situ* gelling system, being lighter than gastric fluids, floats over the stomach contents or adhere to

gastric mucosa due to the presence of bioadhesive nature of the polymer and produce gastric retention of the dosage form and increase gastric residence time resulting in prolonged drug delivery in gastrointestinal tract.[8]

2. MATERIALS AND METHOD

2.1 Materials

Low acyl gellan gum, was supplied by C.P. Kelco PVT. India, and was used as received. Alfuzosin was obtained from Cipla R & D, sodium citrate calcium carbonate & all reagents used were of analytical grade.

2.2 Differential Scanning Calorimeter (DSC) Studies

Thermograms were recorded for Alfuzosin and Gellan gum individually and as physical mixture using Differential Scanning Calorimeter. Accurately weighed samples (3.00 mg) were placed on aluminum plates sealed with aluminum seals and heated at a constant temperature of 5 °C/min over a temperature range of 0- 250 °C.[12]

2.3 Fourier Transform Infrared Spectroscopy

Fourier transform infrared (FTIR) spectra of Alfuzosin, a physical mixture of Alfuzosin –gellan gum were recorded using KBr mixing method on FTIR instrument (FTIR-4100, Jasco, Kyoto, Japan).[13]

2.4 Preliminary Study

Preliminary studies were carried out to determine the concentration of calcium carbonate and gellan gum necessary for drug delivery. Batches P1 to P7 were prepared to study the effect of polymer and calcium carbonate concentration on the floating lag time and gel strength, pH and the physical properties of the gel in pH 1.2 buffer. The concentration of calcium carbonate was varied from 0, 0.25, 0.5, 0.75, 1.0, 1.25 and 1.5 % in batches of P1 to P7 respectively. The concentration of gellan gum was varied from 0.1, 0.2, 0.4, 0.6, 0.8 and 1.0 % in batches P8 to P13. The concentration of sodium citrate and Calcium chloride were kept constant 0.25 % w/v and 0.016 % w/v respectively in all the batches.

2.5 Preparation of *In-situ* Gel

On the basis of conclusions from the preliminary study, a 3^2 full factorial design (Table 1) was employed to study the effect of independent variables, i.e. concentration of gellan gum (X1) and concentration of calcium carbonate (X2) on dependent variables. Formulations from F1 to F9 were prepared as given in Table 2. Gellan gum at solution concentrations of 0.2, 0.4, 0.6 % w/v were prepared in deionized water containing sodium citrate (0.25 % w/v) and calcium chloride (0.016 % w/v). Low level of cations present in the solution was sufficient to hold the molecular chains together and inhibit hydration. The gellan gum solutions were heated to 90 °C with stirring. After cooling below 40 °C, various concentrations of calcium carbonate (0.7, 1, 1.25 % w/v) and 1 % w/v of Alfuzosin was added and dispersed well with continuous stirring. The resulting gellan gum *in situ* gel solution containing Alfuzosin was finally stored in amber color narrow mouth bottles until further use. [9,10,11]

2.6 Measurement of Viscosity of In-situ Gelling Solution

The viscosities of the prepared solutions were determined by brook field viscometer (Brookfield viscometer, model- LVDV-II pro, USA). The samples (100 mL) were sheared at a rate of 100 r/min using suitable spindle at room temperature. Viscosity measurement for each sample was done in triplicate, with each measurement taking approximately 30 s. [14]

2.7 In Vitro Gelation Study

Gelation of in situ gelling solutions was carried out by taking 500 mL of 0.1N hydrochloric acid (HCl, pH 1.2) in a beaker. Accurately measured 10 mL of solution was added to 0.1 N HCl with mild agitation that avoids breaking of formed gel. Gelling was observed visually by qualitative measurement. The gelling capacity was evaluated on the basis of the stiffness of formed gel and time period for which the formed gel remain as such. The in-vitro gelling capacity was graded in three categories on the basis of gelation time and time period for which the formed gel remains. (+) Gel after few minutes dispersed rapidly, (++) Gelation immediate remains for 12 hours, (+++) Gelation immediate remains for more than 12 hours [15,16]

2.8 In Vitro Floating Study

Floating study of in situ gelling solutions was carried out in 500 mL of 0.1N HCl (pH 1.2) in a beaker. Accurately measured 10 mL of solution was added to 0.1 N HCl with mild agitation. Time required for floating on surface after adding solution (floating lag time) and total floating time were measure.[17,18]

2.9 In Vitro Drug Release Study

The in vitro release rate of Alfuzosin from sustained release in situ gel was performed using USP apparatus (model TDT-08T, Electrolab, Mumbai, India) fitted with paddle (50 r/min) at 37 ± 0.5◦C using 500 mL of 0.1N HCl as a dissolution medium. This speed was slow enough to avoid the breaking of gelled formulation and was maintaining the mild agitation conditions believed to exist in vivo. At the predetermined time intervals, 1 mL samples were withdrawn, filtered through a 0.45 µm membrane filter, diluted, and assayed at 245 nm using a Jasco UV V630 double-beam spectrophotometer (Jasco, Kyoto, Japan). Cumulative percentage drug release (CPR) was calculated using an equation obtained from a calibration curve.[19]

2.10 Optimization of Variables Using Full Factorial Design

A 3^2 randomized full factorial design was used in the present study. In this design, 2 factors were evaluated, each at 3 levels and experimental trials were performed for all 9 possible combinations. The concentration of gellan gum (X1) and Calcium carbonate (X2) were chosen as independent variables in 32 full factorial design, while FLT (floating lag time), Q1, Q6, Q12 and Q24 (% drug release after 1, 6, 12 and 24, hours, respectively) were taken as dependent variables. The formulation layout for the factorial design batches (F1–F9) is shown in Table 1. [20]

2.11 Kinetic Modeling of Dissolution Data

The dissolution profile of all batches was fitted to various models such as zero order, first order, Higuchi, Hixon and Crowell, and Korsemeyer et al., to ascertain the kinetic of drug release. The method described by Korsemeyer et al. was used to describe the mechanism of drug release.[21]

2.12 Stability Studies

The stability studies for gel were done by keeping the sample gel from optimized batches for 3 months. The gel was packed in air tight containers coated inside with polyethylene and kept in a humidity chamber maintained at 40˚C temperature and 75% relative humidity for 3 months. At the end of 3 months, the samples were analyzed for different parameters like physical appearance, Percentage drug content, floating duration, viscosity, pH, and Percentage drug release studies [22]

3. RESULTS AND DISCUSSION

3.1 Differential Scanning Calorimeter (DSC) Studies

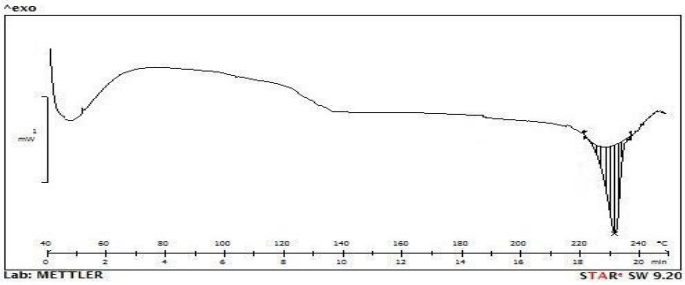

Figure-1 DSC Thermogram of Alfuzosin

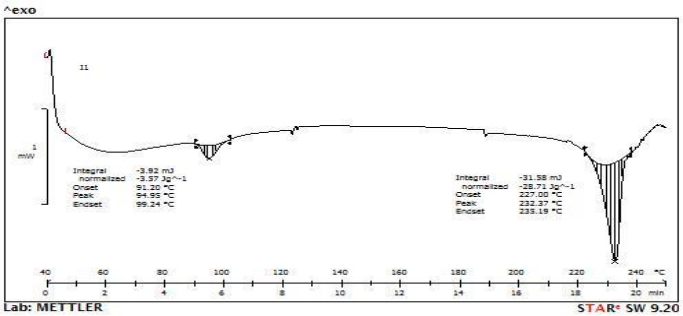

Figure-2 DSC Thermogram of Gellan Gum and Alfuzosin

DSC thermograms of alfuzosin, gellan gum and physical mixture of alfuzocin with gellan gum were illustrated in the figure 1 and 2 respectively. The physical mixture was showing similar identical melting endotherm and spectra were overlapped which indicates compatibility of the drug with the polymer.

3.2 Fourier Transform Infrared Spectroscopy

The FTIR study revealed no physical or chemical interaction of alfuzosin with a polymer as shown in figure 4.

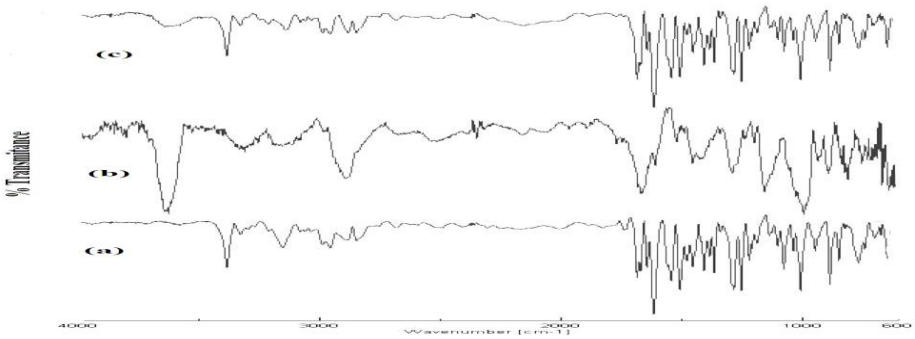

Figure-3 FTIR Spectra for Compatibility Study: (a) Alfuzosin (b) Gelln Gum (c) Gellan Gum and Alfuzosin

3.3 Preliminary Screening

Preliminary studies were carried out to determine the concentration of calcium carbonate and gellan gum necessary for drug delivery. Batches P1 to P7 were prepared to study the effect of polymer and calcium carbonate concentration on the floating lag time and gel strength, pH and the physical properties of the gel in pH 1.2 buffer. P1 formulation which did not contain calcium carbonate shown no floating behavior. P2 to P3 shown improper gelation which leads to a rapid flow of the formulation and also the time required for gelation was also very low. In P7 batch viscosity of the solutions was very high because of the higher concentration of calcium carbonate which was difficult to pour the solution. In the batches P3 and P5 all the characteristics of the gels were good. Thus it was concluded that 0.75 to 1.25 % calcium carbonate was the optimum concentration. P8 formulation showed improper gelation which leads to a rapid flow of the formulation and also the time required for gelation was also very lower than the other batches. In the batches, P9 to P11 all the characteristics of the gels were good while in the batches of P12 and P13 the viscosity of the solutions was very high because of the higher concentration of gellan gum which was difficult to pour the solution. Thus it was concluded that 0.2 to 0.6 % gellan gum was the optimum concentration. There was no significant effect of concentration of sodium citrate and calcium chloride hence their concentration was kept constant as 0.25 % w/v and 0.016 % w/v respectively.
On the basis of the preliminary trials in the present study a 3^2 full factorial design (Table 1) was employed to study the effect of independent variables, i.e. concentration of gellan gum (X1) and concentration of calcium carbonate (X2) on dependent variables viscosity, drug content, drug released at 24 h and formulations F1 to F9 were prepared. The formulations were evaluated for various parameters.

3.4 Physical Appearance

The developed in situ gelling floating system gelled and floated instantaneously at the pH condition of the stomach. The calcium carbonate present in the formulation as insoluble dispersion is dissolved and releases carbon dioxide on reaction with an acid of the stomach and the in situ released calcium ions results in the formation of a gel with floating characteristics. The released carbon dioxide is entrapped in the gel network of the formulation, and gel rises to the surface of the dissolution medium or the stomach fluid. It is established that formulations containing calcium carbonate produce a significantly stronger gel than those containing sodium bicarbonate. This is due to internal ionotropic gelation effect of calcium on gellan. [23] The photographs showed the formation of well-defined irregular shaped gellan gel in pH 2.0 (Fig.4).

Figure-4 Photograph Showing the Appearance of Gellan Gel Formed in 0.1N HCl.

Table-1: Full Factorial Design X1- Calcium Carbonate & X2 Gellan Gum

Code Values	Variable Levels in Coded Form	
	X_1	X_2
-1	0.2 %	0.75 %
0	0.4 %	1 %
1	0.6 %	1.25 %

3.5 Evaluation of Formulations

Two main pre-requisites of in situ gelling systems are optimum viscosity and gelling capacity i.e. speed and extent of gelation. The formulation should have an optimum viscosity that will allow easy swallowing as a liquid, which then undergoes a rapid sol-gel transition due to ionic interaction. Moreover, the in situ formed gel should preserve its integrity without dissolving or eroding for a prolonged period to facilitate sustained release of drugs locally. The developed formulations met all prerequisites to become an in situ gelling floating system, gelled and floated instantaneously in the pH conditions of the stomach. Sol to gel transformation of gellan occurs in the presence of either monovalent or divalent cation in contact with the gastric fluids. [24]

3.6 Viscosity Study

For oral administration, rheological properties of the solution are most important. As gellan gum and Calcium carbonate ratio increases from 0.75:1.25 & 0.2:0.6 to the viscosity increases from 98 to 182 cps. Increasing the concentration of a dissolved or dispersed substance generally give rise to increasing viscosity.

3.7 pH Measurement

It was observed that an increase in the ratio of gellan gum: gas forming agent Calcium carbonate from 0.75:1.25 & 0.2:0.6 resulted in increased pH in a range of 6.5-7.9.

3.8 In vitro Gelation Study

Gelling studies were carried out in 0.1 N HCl (pH 1.2). In this study, the gelling capacity for all formulations was determined. F1 batch showed immediate gelation that remains for 12 h (++) while F2 to F9 batches showed immediate gelation that remains for more than 12 hours (+++).

Table-2: Evaluation of Formulations

Formulation	Variable Levels in Coded Form		Floating lag time (sec.)	Viscosity (cps)	% Drug Content	Floating duration	pH
	X_1	X_2					
F1	-1	-1	122±5.4	98±2.4	92.02±2.82	>24	7.84±0.03
F2	-1	0	97±8	136±1.5	96.76±2.37	>24	7.06±0.03
F3	-1	1	49±4.1	158±1.7	94.68±2.12	>24	6.9±0.04
F4	0	-1	108±8	107±2.6	95.44±2.33	>24	7.34±0.02
F5	0	0	96±0.2	131±3.2	98.84±0.56	>24	7.1±0.02
F6	0	1	83±5.4	164±1.9	98.35±1.18	>24	7.4±0.02
F7	1	-1	106±8	112±4.5	93.74±1.62	>24	7.34±0.04
F8	1	0	91±8	151±3.8	96.38±1.22	>24	6.88±0.09
F9	1	1	87±1.6	182±4.1	92.06±0.93	>24	7.01±0.05

3.9 In vitro Floating Properties

The formulations were tested for the time taken by formulation to emerge on the surface of the medium (floating lag time). It was observed that an increase in the concentration of gas forming agent Calcium carbonate from 0.2 to 0.6 resulted in a decrease in the floating lag time of floating gel. During gelation, Calcium carbonate forms effervescence releasing carbon dioxide and calcium ions. The released carbon dioxide is entrapped in the gel network producing buoyant formulation and then calcium ion reacted with gellan to produce a crosslinked three-dimensional gel network that might restrict the further diffusion of carbon dioxide and drug molecules and has resulted in an extended period of floating and drug release respectively.

3.10 Drug Content

Data of drug content for all the batches (F1 to F9) are mentioned in Table 2. The drug content varied from 92.02±2.82 to 98.84±0.56 in batches F1 to F9 gellan gum based in situ gel.

3.11 In vitro Drug Release

The effect of polymer concentration on in vitro drug release from *in situ* gels was given in Table 3 and shown in Figure 5. A significant ($P<0.01$) decrease in the rate and extent of drug release was observed with the increase in polymer concentration in *situ* gels and is attributed to increasing in the density of the polymer matrix and also an increase in the diffusional path length which the drug molecules have to traverse. The release of drug from these gels was characterized by an initial phase of high release (burst effect). However, as gelation proceeds, the remaining drug was released at a slower rate followed by a second phase of moderate release. This bi-phasic pattern of release is a characteristic feature of matrix diffusion kinetics. Though the cross-linking of the gellan network and eventually the gelation due to the Ca^{++} ions occurs instantaneously, a lag time is still evident before the complete gel formation. This could explain the initial high release of Alfuzosin, which is soluble in lower pH. Further, the systems were formulated in an aqueous vehicle, hence the matrix formed before the complete gelation/cross-linking would already be in a hydrated state thereby discounting the matrix hydration and water permeation that would normally limit drug release during the initial stages. With the increase in calcium carbonate concentration in formulations decreased, the percentage of drug release was observed.

The dissolution data for formulations F1 to F9 was fitted to various drug release kinetic models like Zero order, First order, Korsemeyer Peppas and Higuichi model. Correlation coefficients (R) obtained for various models are listed in Table 4. The model that gives high 'R' value is considered as the best fit model for the release data. It was found that Korsemeyer Peppas was best-fit model for all the formulations tested. The results of dependent variables like Percentage drug content, viscosity, Percentage drug release after 24 h. from nine formulations were used to generate polynomial equation from ''Design of Expert''. All the formulations prepared within the experimental design layout of gel. Mathematical relationships generated using MLRA for the studied response variables are expressed in equation 1 to 3.

Percentage drug content

$$(Y1) = 99.51 - 0.21X_1 + 0.65X_2 - 1.09\ X_1.X_2 - 3.27\ X_1^2 - 2.94\ X_2^2 \ldots (1)$$

Viscosity

$$(Y2) = 168 + 6.50X_1 + 61.33X_2 - 0.75\ X_1.X_2 - 1.83\ X_1^2 - 22.33\ X_2^2 \ldots (2)$$

Percentage drug release after 24 h

$$(Y3) = 101 + 2.26X_1 - 2.18X_2 + 3.18\ X_1.X_2 - 2.75\ X_1^2 - 1.72\ X_2^2 \ldots (3)$$

Formulation	**$Q_{3(hr.)}$**	**$Q_{6(hr.)}$**	**$Q_{12(hr.)}$**	**$Q_{24(hr.)}$**	**$t_{50\%(hr.)}$**	**$t_{80\%\ (hr)}$**
F1	73.90±0.2	84.31±1.1	98.32±0.64	99.34±0.48	1	5
F2	68.41±0.38	82.27±0.72	97.67±0.04	98.35±0.28	1	6
F3	70.84±0.64	77.83±0.24	85.68±0.64	87.73±0.48	1	6
F4	85.87±0.4	97.67±0.87	101.83±0.06	102.47±0.4	1	2
F5	69.63±1.2	80.3±0.96	94.9±0.48	98.15±1.4	1	4

F6	67.93±0	83.12±0.87	94.9±0.22	99.86±0.63	1	3
F7	71.34±0.24	85.85±0.63	95.93±1.69	97.98±0.48	1	5
F8	73.03±3.64	83.8±0.72	96.98±1.24	101.74±0.48	1	4
F9	48.28±0.87	61.43±2.41	96.61±1.5	99.1±1.2	4	6

Table-3: Average*(±SD) Cumulative Percentage Drug Release from Alfuzosin Containing Floating *In situ* Gel

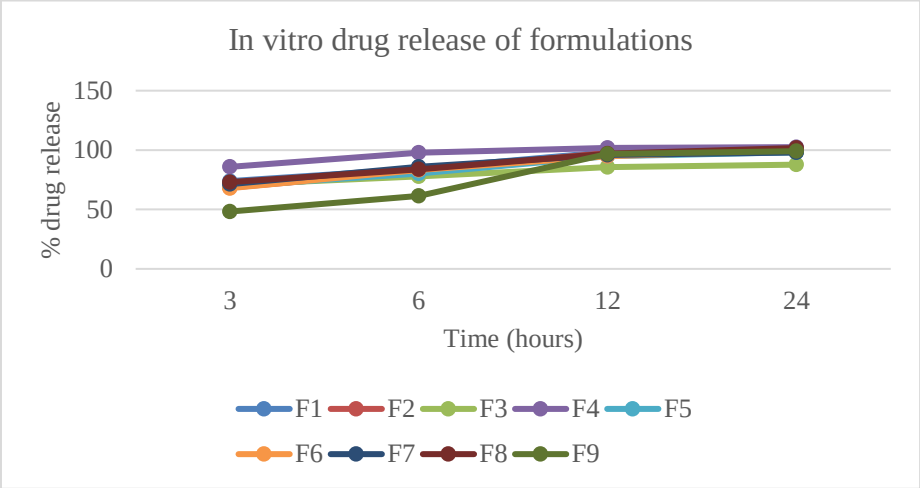

Figure-5: In vitro Drug Release of Formulations

Table-4: Values of Correlation Coefficients (R) for Release from Alfuzosin Contenting Gellan Gum *In situ* Gel

Formulation	Zero Order	First Order	Korsemeyer Peppas	Higuichi Model
	(R)	**(R)**	**(R)**	(R)
F1	0.9296	0.8995	0.9456	0.9797
F2	0.926	0.8808	0.9312	0.9738
F3	0.7697	0.6999	0.7834	0.8964
F4	0.7520	0.68882	0.7599	0.8793
F5	0.8232	0.7812	0.8610	0.9309
F6	0.9129	0.8842	0.9260	0.9616
F7	0.8952	0.8801	0.9207	0.9439
F8	0.8288	0.7802	0.8546	0.9276
F9	0.9917	0.9891	0.9358	0.9503

The significance test for regression coefficients was carried out by applying Students *t* test. A coefficient is significant if the calculated 't' value is greater than the critical value of 't'. All coefficient β_0, β_1, and β_2 showed significant values less than 0.1 and hence they were retained in full model. [25] The results of multiple regression analysis and analysis of variance test (ANOVA) are summarized in Table 5.

3.12 FM – Full Model

For the Percentage drug content, viscosity and percentage drug release after 24 h calculated F-values were 9.39, 292.63 and 2.85 respectively as shown in Table No. 6. Hence it can be concluded that the variables selected contributes significantly to the regression of measured responses Y_1, Y_2, and Y_3. For Percentage drug content, equation 1 was obtained from the design model. Positive coefficient of X_2 increases in Percentage drug content of gel with an increase in calcium carbonate: polymer ratio and Positive coefficient of X_1 indicated an increase in response of Y_1 i.e. increases Percentage drug content with increase in calcium carbonate: polymer ratio. But in combination, it gives negative coefficient effect. The equation obtained was a Quadratic equation. For viscosity, equation 2 was obtained from the design model. Positive coefficient of X_2 indicated increases in viscosity from the gel with an increase in calcium carbonate: polymer ratio and positive coefficient of X_1 indicated increases in the response of Y_2 i.e. increases viscosity with an increase in calcium carbonate: polymer ratio. The equation obtained was a linear equation, which means there was no significant effect of the interaction of two variables on the response. For, Percentage drug release after 24 h, equation 2 was obtained from the design model. The negative coefficient of X_2 indicated decrease in Percentage drug release from gel and positive coefficient of X_1 indicated increases in response of Y_3 i.e. increases Percentage drug release after 24 h with an increase in calcium carbonate: polymer ratio. The equation obtained was linear equation, which means there was no significant effect of interaction of two variables on the response. These effects can be further explained by Response surface plots generated using equations 1, 2 and 3. The response surface are shown in Figure 6, Figure7, & Figure 8 respectively.

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Table-5: Regression Analysis Data for Measured Responses

Coefficients	% drug content	Viscosity	%drug release after 24h.
	FM	FM	FM
β_0	+91.51	+168	+101.30
β_1	-0.21	+6.50	+2.2616
β_2	+0.65	+61.33	-2.1833
β_{12}	-1.09	-0.75	+3.1825
B_{11}	-3.27	-1.83	-2.76
B_{22}	-2.94	-22.33	-1.72
R^2	0.9400	0.9980	0.8261
Significance	0.0473	0.0003	0.2089
F- value	9.39	292.63	2.85

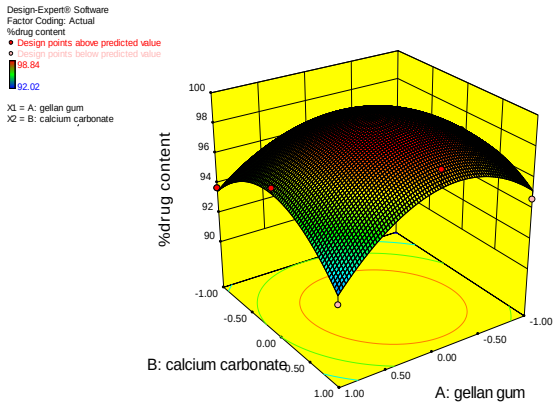

Figure-6: Response Surface Plot of % Drug Content

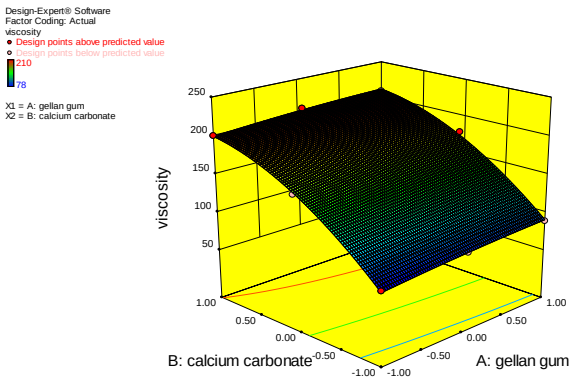

Figure-7: Response Surface Plot of Viscosity

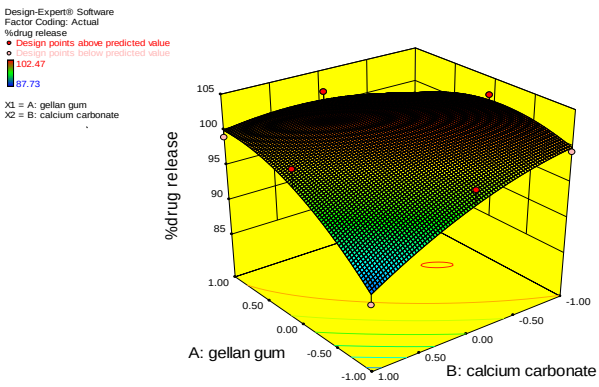

Figure-8: Response Surface Plot of % Drug Release

3.13 Stability Study

The stability studies were carried out on optimized formulation F6. The formulation was stored at 40 ± 2°C/75 ± 5 % RH (Climatic zone IV condition for accelerated testing) for 90 days to assess its stability. After 15, 60 and 90 days samples were withdrawn and

retested for pH, Viscosity, Floating lag time, Floating duration, Percentage cumulative drug release studies as shown in Table 7. The result indicated that the formulation was stable to retain its stability for three months.

Table 6: Result of Optimized Batch F6 after Three Month Storage

Days	pH	Viscosity (cps)	Floating lag time (sec.)	Floating duration (h.)	% Drug release after 24h.
0	7.4±0.02	164±1.9	83±5.4	>24	99.86±0.63
15	7.4±0.13	159±3.5	83±5.8	>24	99.18±1.24
60	7.5±0.45	174±4.5	85±3.4	>24	99.07±0.74
90	7.6±1.09	174±3.9	87±2.3	>24	99.02±1.98

4. CONCLUSION

The floating in situ gel containing Alfuzosin is prepared. Optimization helped to predict the best possible formulation. The design is chosen, i.e., full factorial design, a mathematical model for a generation of polynomial, i.e., MLRA, and method for locating the optimum, i.e., grid search, were successfully utilized for embarking upon the optimal formulations. The in situ gel demonstrated the feasibility of forming a gel in the stomach by the oral administration of an aqueous solution of gellan gum containing Ca^{++} ions in a complexed form. It proves in situ gelling system as a liquid formulation for sustained delivery of drug to improve patient compliance and bioavailability. In vitro release study of F6 indicated that Alfuzosin was released in a controlled manner up to 24 hours. Gellan floating gel is a potential candidate to prolong the residence time in the stomach.

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