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Research Article

FLOATING IN-SITU GELLING SYSTEM FOR STOMACH SPECIFIC ORAL DRUG DELIVERY OF VALACYCLOVIR

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ABSTRACT

The present investigation deals with the formulate and evaluate oral in situ floating drug delivery system for Valacyclovir which undergoes ion dependent sol - gel transition at gastric physiological conditions, thereby prolonging the retention of the system in stomach. Sodium alginate as gelling agent whose gelation is triggered by source of Calcium ions in the form of calcium carbonate. The study demonstrates the feasibility of prolonging gastric residence time and release rate of Valacyclovir by preparing floating in situ gel system using ion- cross linking in situ gel forming polymers. The formulated batches were further studied for Floating lag time, Gelling lag time, Viscosity and in vitro drug release was carried out. The prepared floating oral in situ gel formulation was optimized using 3^2 full factorial experimental design. Floating oral in situ gel formulation optimized for amount of sodium alginate(X_1) and amount of calcium carbonate(X_2) independent variables) in order to achieve desired response of floating lag time(Y_1), viscosity(Y_2), %CDR at 1 hour(Y_3) and %CDR at 8 hour(Y_4)(dependent variables). The experimental results of optimized batch (F6) revealed that floating lag time = 54 sec, viscosity = 218 cP, 39.83 %CDR = 1hour and 88.96 %CDR = 8 hour. The improved characteristics of the selected floating oral in situ gel system make them excellent candidates for gastric retention.

Keywords: In situ gel, Floating, Valacyclovir, Sodium alginate, 3^2 Full Factorial Design.

INTRODUCTION

In-situ gel forming systems has been widely investigated as vehicle for the sustained and controlled delivery of drug. The in-situ forming polymeric delivery systems have advantages such as can be administered easily and reduced dosing frequency, which increases patient compliance and comfort, has drawn considerable interest in their development. In situ gel formulations offers an interesting alternative for achieving systemic drug effects of parenteral routes, which can be inconvenient or oral route, which can result in unacceptably low bioavailability and passes the hepatic first-pass metabolism, in particular of proteins and peptides. This novel drug delivery system promotes the importantly ease and convenience of administration, deliverance of accurate dose as well as to prolong residence time of drug in contact with mucosa, that problems generally encountered in semisolid dosage forms. In situ gel formation occurs due to one or combination of different stimuli like pH change, temperature modulation and solvent exchange. Smart polymeric systems represent promising means of delivering the drugs; these polymers undergo sol-gel transition, once administered.

Valacyclovir has biological half-life (2.5 to 3.3hour) which is ideal for the development of a sustained release formulation. Valacyclovir is rapidly absorbed and oral bioavailability is 55%. Valacyclovir is BCS class I drug so it is ideal for controlled release of drug. It has absorption window in the stomach and upper gastrointestinal tract. For herpes infection Valacyclovir immediate release tablets are available in market. Hence, a floating controlled release formulation was prepared for the treatment of herpes virus. Valacyclovir is a water soluble drug, therefore the polymers like Sodium alginate play an important role in retarding the release of drug from the formulation. Calcium carbonate and sodium citrate can be added to the formulation as gas generating agent for the formulation to remain floated[1].

MATERIALS AND METHODS

Materials

Valacyclovir was provided as a gift sample from Yarrow chemicals, Mumbai (India), Sodium alginate was obtained from Chemdyes Corporation, Rajkot (India), other excipients as sodium citrate, calcium carbonate obtained from S d fine – chem limited, Mumbai (India).

Preformulation Studies

Preformulation can be defined as investigation of physical and chemical properties of drug substance alone and when combined with excipients.

Preformulation studies are designed to identify those physicochemical properties of drug and excipients that may influence the formulation design, method of manufacture, pharmacokinetic and biopharmaceutical properties of the resulting product[2].

Determination of Drug and its Compatibility with Excipients FTIR Studies

Drug- excipients interactions play a vital role in the release of drug from formulation. Fourier transform infrared spectroscopy

has been used to study the physical and chemical interactions between drug and the excipients used. FTIR spectra of Valacyclovir and polymer were recorded using KBr mixing method on FTIR instrument. The samples were scanned between 400-4000 cm^{-1} range of monochouromatic light beam, which is known as IR radiation[3].

Differential Scanning Calorimetry

Purity of drug was determined by DSC analysis. DSC measurement was carried out using DSC-60 (Shimadzu Corporation Kyoto, Japan) under nitrogen flow. DSC run was conducted over a temperature range of 25 to 300 ^{0}C min^{-1} under nitrogen flow rate 20ml/min. An empty aluminium pan was used as reference and pure drug was cramp in DSC pan and records the peak.

Preparation of *in situ* gelling solution of Valacyclovir

Sodium alginate solution was prepared by adding sodium alginate in purified water containing 1 %w/v sodium citrate with constant stirring. Calcium carbonate was dissolved in another beaker. Calcium carbonate was added in polymeric solution and dispersed well with constant stirring. Add required quantity of drug mixed and well. After that final volume was made up to 50 ml with distilled water[4].

Dose calculation

Dose of Valacyclovir was calculated on the basis of pharmacokinetic parameters as follows:

Dose of immediate release part = Css.Vd/F…..Equation 2
Where,
Css = steady state plasma concentration (2.02 mg/L),
Vd = volume of distribution (0.7 L/Kg),
F= bioavailability (55 %).
Dose of immediate release part = 2.02 x 0.7 x 70 x 100/55 = 179.96 mg.
To maintain the drug concentration in the blood, rate of elimination of drug should be equal to rate of drug absorption hence rate of drug release from the dosage form.

Rate of elimination = Ke.Cd.Vd…..Equation 3
= 0.301 x 2.02 x 0.7 x 70 = 29.79 mg/hour.
Where; Ke= elimination rate constant (0.693/t1/2 = 0.693/2.3 = 0.301 $hour^{-1}$),
Cd= desired drug level in the body (4.04 mg/L),
Vd= volume of distribution (0.7 L/Kg).
Bioavailability of Valacyclovir is 55 %, so amount required to release from dosage form to maintain the steady state concentration of drug in plasma is
=29.79 x 100/55 = 54.16 mg/ hour.
Hence, the formulation should release 179.96 mg in 1 hour and 54.16 mg per hour up to 12 hour.
Total dose = 179.96+ (54.16 x 11)
= 179.96 + 595.76
= 775.2 mg
Now, 775.2 mg dose is given in 1 table spoonful (i.e. 15ml). So, for 50ml solution
50 × 775.2/15 = 2585 mg Valacyclovir is required.

Preliminary screening

Selection of *in situ* gelling polymer was carried out on the basis of compatibility and novelty in polymer. Selection of floating agent was carried out on the basis of floating lag time, total floating time etc. The preliminary screening of polymer and floating agent were performed to determine the effect of polymer concentration and floating agent concentration on formulation respectively[5,6].

Table 1: Preliminary screening

Evaluation parameter	P1	P2	P3	P4	P5	P6	P7	P8	P9
Drug (mg)	2585	2585	2585	2585	2585	2585	2585	2585	2585
Sodium alginate (%)	0.5	1	1.5	2	2.5	3	2	2	2
Calcium Carbonate (%)	1	1	1	1	1	1	1	1	1
Sodium citrate (%)	0.75	0.75	0.75	0.75	0.75	0.75	0.75	1	1.5

Evaluation parameter	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19
Drug (mg)	2585	2585	2585	2585	2585	2585	2585	2585	2585	2585
Sodium alginate (%)	2	2	2	2	2	2	2	2	2	2
Pectin (%)	0.5	1	-	-	-	-	-	-	-	-
Calcium carbonate (%)	1	1	0.5	0.75	1	1.5	2	1	1	1
Sodium citrate (%)	1	1	1	1	1	1	1	1	1	1
Calcium chloride (%)	-	-	-	-	-	-	-	0.025	0.05	0.075

Evaluation
pH

The pH of the developed gel base was measured on a digital pH meter at room temperature.

Viscosity

The viscosity of the prepared solutions was determined by Brookfield viscometer. The samples were sheared at speed (50 RPM) using (spindle no: 31) at room temperature.

***In Vitro* Drug Release study**

The *in vitro* release rate of Valacyclovir from sustained release *in situ* gel was performed using USP apparatus (model TDT-08L, Electrolab, Mumbai, India) fitted with paddle over disk (50 rpm) at 37±0.50C using 900 ml of 0.1N HCl as a dissolution medium. At the predetermined time interval, 10 ml samples were withdrawn, filtered thourough a whatman filter paper membrane filter, diluted and assayed at λmax (254 nm) using UV-spectrophotometer and cumulative percentage rate was calculated

Gelling time and gelling capacity

To evaluate the formulations for their *in-vitro* gelling capacity by visual examination, coloured solutions of *in situ* gel forming drug delivery system were prepared. The *in-vitro* gelling capacity of prepared formulations were measured by placing five ml of the gelation solution (0.1N HCl, pH 1.2) in a 15 ml borosilicate glass test tube and maintained at 37 ± 1˚C temperature. One ml of coloured formulation was added with the help of pipette. The

formulation was transferred in such a way that touched the pipette at surface of fluid in test tube and formulation was slowly released from the pipette. As the solution comes in contact with gelation solution, it was converted into stiff gel like structure. The gelling capacity of solution was evaluated on the basis of stiffness of formed gel and time period for which formed gel remains as such. Colour was added to give visualized appearance to formed gel. The *in-vitro* gelling capacity was graded in thouree categories on the basis of gelation time and time period for which formed gel remains.

(+) Gels after few minutes, dispersed rapidly.
(++) Gelation immediate remains for few hours.
(+++) Gelation immediate remains for more than 12 hours[8].

In Vitro Floating Study

Floating study of *in situ* gelling solutions was carried out in 900 ml of 0.1 N HCl (pH 1.2) in a Dissolution jar. Time required for floating on surface after adding solution (floating lag time) and total floating time were measured[9].

Gel strength

Texture profile analysis of the prepared gel was performed using QTS-25 Texture Analyzer. (Brookfield Engineering Labs., USA) An analytical probe of diameter 38mm was depressed twice into sample to a defined depth (8 mm), at a defined rate (10 mm/min), with a defined recovery period (15 sec) between the end of the first compression and the beginning of the second.
A trigger force of 1 g was applied. Data were collected and calculated by Texture pro software, version 2.1 (Biozon Food Innovations GmbH, Bremerhaven, Germany)[10].

Release kinetics

Different kinetic studies were used to analyse the mechanism of drug release. Release rate data were fitted into different release kinetics mechanism like zero order, first order, Higuchi matrix, Korsmeyer and Peppas. Based on R^2 -value; the best fit model was selected[11].

Experimental design

A 3^2 randomized full factorial design was in the present study. In this design, 2 factors are evaluated, each at 3 levels and experimental trials were performed for all 9 possible combinations. The concentration of sodium alginate (X_1) and Concentration of calcium carbonate (X_2) were chosen as independent variables in 3^2 factorial design, while floating lag time, Viscosity, % drug release after 1, 8 hours respectively and viscosity were taken as dependent variables. The formulation layout for the factorial design batches (F1-F9) is shown in table 1[12,13,14].

Table 2 Selection of independent and dependent variable

Translation of coded values in actual units			
Independent variable	**Levels used, actual(coded)**		
	Low(-1)	Medium(0)	High(+1)
X_1= concentration of Sodium alginate	1.5	2	2.5
X_2= concentration of Calcium carbonate	0.75	1	1.5
Dependent variable Y_1= Floating time Y_2= Viscosity Y_3= Drug release at 1 hour. Y_4= Drug release at 8 hour.			

Table 3 3^2 full factorial design

Batch	**Factor**		**Response**			
	X_1	**X_2**	**Y_1(FLT) sec**	**Y_2(Viscosity) cP**	**Y_3 (%CDR at 1hour)**	**Y_4 (%CDR at 8 hour)**
F1	1.5	0.75	59	99	43.12	97.36
F2	1.5	1	54	105.8	40.83	96.93
F3	1.5	1.5	52	142	40.53	93.51
F4	2	0.75	65	154	37.83	92.60
F5	2	1	60	185	37.71	89.38
F6	2	1.5	54	210	36.09	86.67
F7	2.5	0.75	70	245.3	35.76	85.84
F8	2.5	1	66	259.3	33.02	82.08
F9	2.5	1.5	61	285	31.42	80.43

RESULTS AND DISCUSSION

FTIR spectroscopy of drug

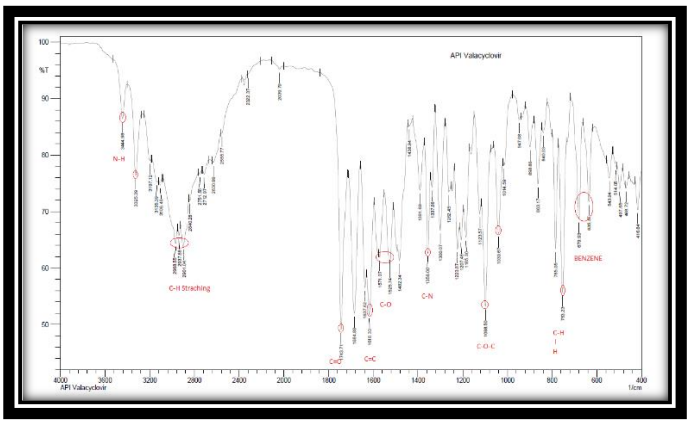


Figure 1 FTIR spectroscopy of Valacyclovir

The IR spectrum of the drug was recorded using FTIR – Bruker Alpha E model and the functional groups were interpreted as per the structure, they were found to be appropriate and matching the structure of drug and standard peaks of drug shown in the Figure 1.

FTIR spectroscopy of drug and excipients

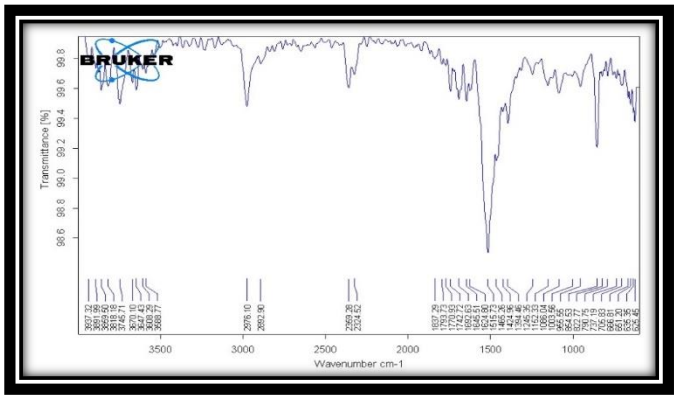
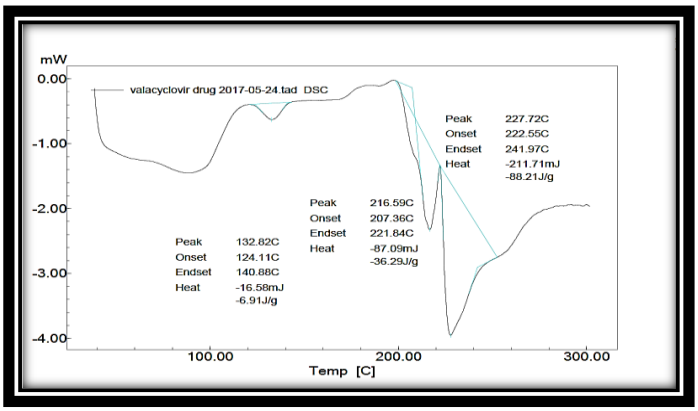


Figure 2 FTIR spectroscopy of drug and excipients

All the characteristic peaks of Valacyclovir were present in spectra at respective wavelengths thus indicating compatibility between drug and excipients. It was confirmed that there was no significant change in the chemical integrity of the drug.

Differential Scanning Calorimetry



Preliminary screening

Table 4 Evaluation parameter of preliminary batches

Evaluation parameter	P1	P2	P3	P4	P5	P6	P7	P8	P9
Floating lag time (sec)	43	46	54	59	67	71	-	-	-
Gelling time (sec)	18	15	11	7	3	2			
Pourability	Very fluidly	Fluidly	Pourable	Pourable	Viscous	Very viscous	-	-	-
Gelling capacity	+	++	++	+++	+++	+++	++	+++	+++

Evaluation parameter	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19
Floating lag time (sec)	46	60	59	53	45	40	34	47	46	48
Gelling time (sec)	11	8	22	19	16	11	8	18	16	16
Pourability	Pourable	Pourable	Pourable	Pourable	Pourable	Pourable	Pourable	Pourable	Pourable	Pourable
Gelling capacity	++	+++	++	++	+++	+++	+++	+++	+++	+++

NOTICE (+) Gels after few minutes, dispersed rapidly.
(++) Gelation immediate remains for few hours.
(+++) Gelation immediate remains for more than 12 hours

- Batch P1-P6 showed the increase concentration of sodium alginate which lead to increase in gelling capacity, increase in floating lag time, decrease in gelling time and decrease in pourability which was showed in table 4.
- From table 4 it was concluded that 2% concentration Sodium alginate showed appreciable gelling properties.
- Batch P7, P8, P9 showed problem was solved by increasing concentration of sodium citrate up to 1.5%.
- Batch P10, P11 showed that sodium alginate and pectin Form gel which was almost constant in all parameters as form by alone sodium alginate.
- So, alone Sodium alginate selected as an *in-situ* gelling polymer.
- Batch P12-P17 showed that as increase in concentration of $CaCO_3$, decrease in floating lag time, decrease in gelling time was observed but gelling capacity and pourability not affected which was showed in table 4. From table 4 it was concluded that 1 % concentration of $CaCO_3$ showed appreciable gelling properties
- Batch P17-19 showed effect of calcium chloride on formulation. All parameter of batch P16 containing calcium carbonate and batch P17-P19 containing calcium carbonate and calcium chloride were almost same as showed in table 4. From this it was concluded that there was no effect of calcium chloride since calcium carbonate was sufficient to form gel.

Table 5 Evaluation of full factorial design batches

Evaluation parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Physical Appearance	White milky solution	White milky solution	White milky solution	White milky solution	White milky solution	White milky solution	White milky solution	White milky solution	White milky solution
Floating Lag time (sec)	59	54	52	65	60	54	70	66	61
pH	7.0	7.3	7.0	7.1	7.2	7.2	7.3	7.0	7.3
Gelling time(sec)	12.33 ±0.47	11.33 ±0.47	9.66 ±0.81	12.33 ±0.47	10.66 ±0.94	10.33 ±0.47	10.66 ±0.94	10.66 ±0.47	9.00 ±0.47
Gelling capacity	+++	+++	+++	+++	+++	+++	+++	+++	+++
Viscosity (cP)	99	105.8	142	154	185	210	245.3	259.3	285
Total Floating Time(hour)	>12	>12	>12	>12	>12	>12	>12	>12	>12

All the batches was found to be milky white solution due to calcium carbonate which was suspended in to gelling solution. The pH of all the batches was found to be around 7 to 7.3 which suitable for oral administration and not produce any irritation. Gelling time was studied for F1-F9 batches was found to be 12-9 sec. F4, F7 batches were showed higher gelling time as compared to other batches which was due to low concentration of calcium carbonate. Since entanglement of G- block (L-guluronic acid) occur at higher concentration of sodium alginate. It was also found that F8, F9 has comparatively lower gelling time as compared to other respective batches. Since calcium carbonate has capacity to form faster complex with sodium alginate at higher concentration. Gelling capacity of all batches were almost same, the reason behind that sodium alginate was formed appreciable gel in the range of 1.5-2.5 % concentration.

The result of floating lag time, total floating time, and viscosity of F1, F4, F7 batches was (59,65,70 sec) exhibited higher floating lag time than other batches as it contains 0.75 % calcium carbonate which was insufficient to reach targeted floating lag time. F2, F3; F5, F6; F8, F9 batches were exhibited acceptable floating lag time since it was contained higher amount of calcium carbonate. Viscosity of formulation was depended on concentration of polymer and very slightly depended on

concentration of calcium carbonate. Formulation F1 has lowest viscosity and formulation F9 has highest viscosity. All the batches have total floating time more than 12 hours.

***In vitro* drug release**

From the results it could be concluded that *in vitro* drug release was clearly affected by sodium alginate and calcium carbonate. F1 batch was contained lowest amount of sodium alginate and calcium carbonate therefore it was showed higher drug release 99.71 % in 9 hours. F9 batch was contained highest amount of sodium alginate and calcium carbonate therefore it was showed lower drug release 99.2 % in 12 hours. The initial burst release was also decreased as increased in concentration of sodium alginate because of increased in viscosity as F1 batch was showed 36.69 % drug release in 0.5 hour and F9 was showed 25.56 % in 0.5 hour. From the results it could be concluded that as concentration of sodium alginate increased, drug release and burst release (effect) was decreased. Furthermore F2; F3, F5; F6 and F8; F9 batches were showed almost same drug release profile, it was indicated that higher amount of calcium carbonate 1.5 % was not extend the drug release. The reason behind that was lower amount of calcium carbonate 0.75 % was not sufficient to produce strong crosslinking between polymer and calcium but 1 % was sufficient and higher amount of calcium carbonate 1.5 % may be excessive and useless. So that excess amount of calcium carbonate was not extending the drug release.

Table 6 *in vitro* drug release of full factorial design batches

Cumulative Percentage Release (%)									
Time (hour)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0.5	36.69 ± 0.12	35.43 ± 0.28	33.75 ± 0.22	31.45 ± 0.35	30.76 ± 0.24	30.49 ± 0.16	29.10 ± 0.22	28.73 ± 0.25	25.56 ± 0.19
1	43.12 ± 0.16	40.83 ± 0.25	40.53 ± 0.28	37.83 ± 0.48	37.71 ± 0.39	36.9 ± 0.19	35.76 ± 0.2	33.2 ± 0.22	31.42 ± 0.23
2	49.69 ± 0.16	45.80 ± 0.25	43.86 ± 0.20	41.89 ± 0.28	41.22 ± 0.33	39.26 ± 0.25	38.45 ± 0.35	37.71 ± 0.22	35.21 ± 0.3
3	53.27 ± 0.18	50.71 ± 0.22	49.80 ± 0.35	47.17 ± 0.3	45.85 ± 0.19	41.27 ± 0.2	41.77 ± 0.23	40.82 ± 0.25	39.60 ± 0.28
4	61.82 ± 0.25	60.36 ± 0.32	59.11 ± 0.28	55.78 ± 0.38	53.85 ± 0.35	49.18 ± 0.28	48.95 ± 0.28	47.93 ± 0.18	45.08 ± 0.21
5	69.86 ± 0.22	68.63 ± 0.48	67.29 ± 0.4	64.24 ± 0.34	62.72 ± 0.28	58.32 ± 0.19	57.80 ± 0.22	56.24 ± 0.23	54.15 ± 0.29
6	78.11 ± 0.34	76.14 ± 0.15	76.01 ± 0.27	74.94 ± 0.32	74.74 ± 0.19	72.22 ± 0.24	69.57 ± 0.19	68.19 ± 0.21	66.52 ± 0.34
7	89.80 ± 0.28	87.58 ± 0.26	85.24 ± 0.19	84.15 ± 0.18	78.72 ± 0.28	76.64 ± 0.30	75.05± 0.28	74.53 ± 0.31	72.52 ± 0.26
8	97.36 ± 0.31	96.93 ± 0.22	93.51 ± 0.21	92.6 ± 0.14	89.38 ± 0.31	86.67 ± 0.29	85.84± 0.29	82.08 ± 0.25	80.43 ± 0.31
9	99.71 ± 0.19	99.62 ± 0.28	99.46 ± 0.25	97.56 ± 0.33	96.20 ± 0.24	94.45 ± 0.17	92.34± 0.21	90.41 ± 0.25	86.94 ± 0.31
10			99.75 ± 0.18	99.1 ± 0.22	99.66 ± 0.25	97.1 ± 0.22	99.3.± 0.31	94.35 ± 0.27	91.91 ± 0.35
11					99.55 ± 0.36	99.59 ± 0.32		99.81 ± 0.35	97.44 ± 0.27
12						99.42 ± 0.27			99.2 ± 0.33

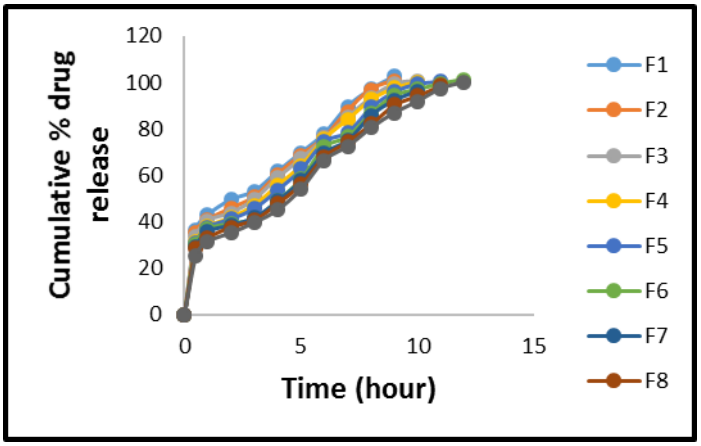


Figure 3 *In vitro* drug release of full factorial design batches

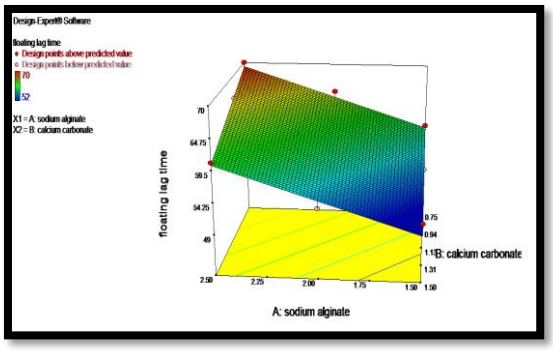


Figure 4 3D Response surface plot for Floating Lag Time

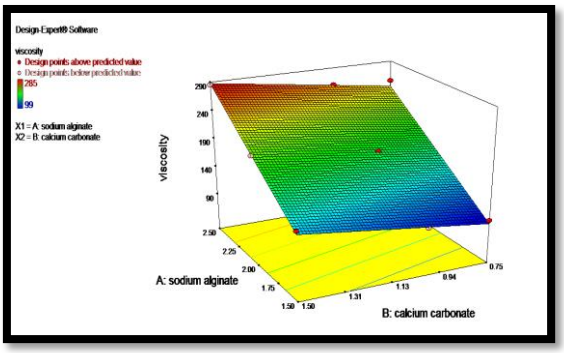


Figure 5 3D Response surface plots for Viscosity

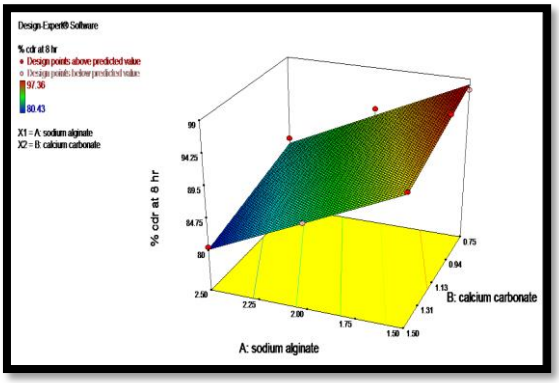


Figure 6 3D Response surface plot for Drug release at 1 hour

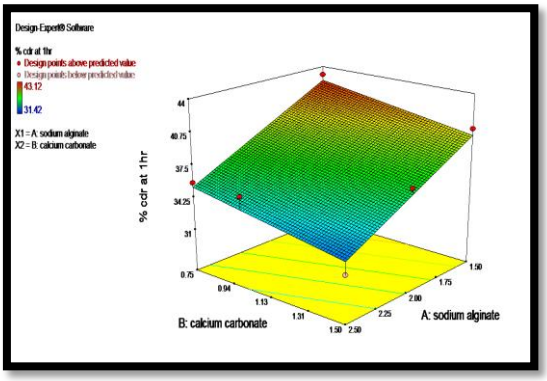


Figure 7 3D Response surface plot for Drug release at 8 hour

Statistical analysis floating lag time

From the above 3D graph, it can be interpreted that factor SA and CC do not have significant quadratic effect.

Statistical analysis viscosity

There is no curvature effect in the 3D graph. So, it can be interpreted that factor SA and CC have positive linear relationship with no significant quadratic effect.

Statistical analysis Drug release at 1 hour

There is no curvature effect in the 3D graph. So, it can be interpreted that factor SA and CC have positive linear relationship with no significant quadratic effect

Statistical analysis Drug release at 8 hour

There is no curvature effect in the 3D graph. So, it can be interpreted that factor SA and CC have positive linear relationship with no significant quadratic effect.

Optimization of design batch by design expert software (trial version)

The optimum formulation was selected based on the criteria of attaining targeted value with the minimum and the maximum limit of formulation variables. An overall desirability function dependent on all the investigated formulation variables were used to predict the ranges of variables where the optimum formulation might occur. The desirable ranges are from zero to one (least to most desirable, respectively). The optimize batch is presented in Table5.22.

Based on studying the effect of independent variables on the responses the levels of variables which contribute optimum response (Y_1=54sec, Y_2=218cp, Y_3=39.83% and Y_4=88.96%) were determined and shown in table 5.22. Keeping all points in view, from contour plot (overlay) the level of X_1X_2 were selected using design expert software 10(trail version). The level of X_1X_2 were kept at -1, 0, +1 respectively, with target floating lag time (range= 52 - 70 sec), viscosity (range=99 - 285cp), % CDR at 1hour (range= 31 - 43 %) and % CDR at 8hour (range= 80 - 97 %). The optimum batch can be formulated with desirability 1 by selecting X1=2 % sodium alginate and X_2=1.5 % Calcium carbonate, to get model prediction value of Floating lag time (55 sec), Viscosity (212cp), %CDR at 1 hour (39.83), %CDR at 8 hour (86.70).

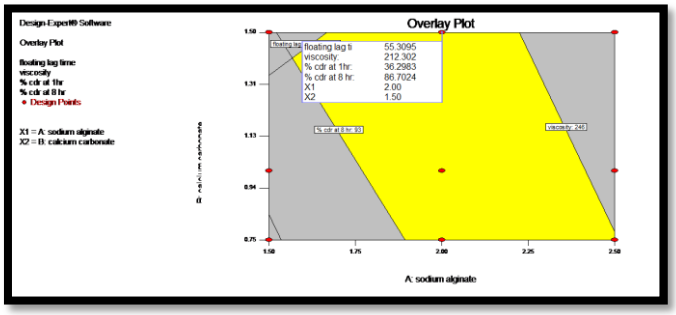


Figure 8 overlay plot for prediction of optimized batch

Floating oral *in situ* gelling system was design and evaluated by using sodium alginate *in situ* gelling polymer. Gum was designed and evaluated, for their buoyancy, *in situ* gelation and sustaining capacity for the release of Valacyclovir, aiming to meet the requirements for designing a gastro retentive dosage forms. The floating oral *in situ* gel system of Valacyclovir was successfully formulated using sodium alginate gum as *in situ* gel forming polymer. The optimization of amount of Sodium alginate and amount of calcium carbonate in the floating oral *in situ* gel formulation was carried using 3^2 full factorial design. The optimized batch showed the promising results with viscosity 218 cP. The % CDR at 1 hour & 8 hour of optimized batch was found to be 39.83 % &88.96 %respectively. It can be concluded that as the concentration of Sodium alginate increases, drug release decreases. As the concentration of Sodium alginate gum goes up, gel strength increases. Sodium alginate have significant effect on viscosity. The developed formulation holds promising future due to reduction in dosing frequency and thus reduces dose related side effects and improved patient compliance.

CONCLUSION

In this study *in situ* floating gel of Valacyclovir, an anti-viral agent used in the treatment of herpes infection was successfully formulated using sodium alginate and calcium carbonate. The formulation was liquid before administration and produce rapid gelation upon contact with gastric fluid and it was found milky white appearance, immediate gelation, acceptable viscosity, good gelling capacity and remain for extended period. FT-IR and DSC studies revealed that there was no interaction between the drug and polymer. 3^2 full factorial design was used for optimization of variables. The drug was released by fickian diffusion transport mechanism because all formulation (F1 to F9) showed release exponent n value below 0.5. The experimental design batches were showed R^2 values for higuchi model. The drug was released in a sustained and controlled manner over a period of time 12 hours. F6 (2 %w/v sodium alginate and 1.5 %w/v calcium carbonate) was selected as variables for optimized batch using desirability approach in Design expert10 (trial version).

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