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Response Surface Design for Formulation and Evaluation of Floating Oral *In Situ* Gelling System oof Famotidine For Ulcer

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ABSTRACT
The aim of the present investigation was the development and evaluation of Famotidine oral insitu gel to treat upper gastro intestinal ulcers. In the present work, a three-factor at three-level Box-Behnken design was adopted to inspect the effects of three factors viz. sodium alginate [A], sodium bicarbonate [B], and sodium citrate [C] on the dependent variables like in vitro gelation, in vitro floating, percentage water uptake, and percentage drug release. The Box-Behnken model suggests that the development of a famotidine oral in situ gelling device was a complete success. The optimized in situ gel floated and gelled as desired, releasing a sufficient dose of medication into the stomach. pH values for all the preparations have been between 6.34 and 7.15, within a margin of error of 0.19 and 0.13. With immediate invitro gelation, the drug concentration was found to be between 96.31±0.18 and 99.02±0.14%, and it remained stable for a long time. There was an observed range of 7.36±0.28 to 29.41±0.24% in terms of water intake, and an estimated range of 8.95±0.28 to 56.35±0.34s in terms of floating lag time. All formulations had released over 90% of the medication during the 8-h time frame, with F1 and F2 showing floating even after 12 h. The impact of the chosen independent variables on the dependent ones were found to be quite large. Responses such floating lag time, percentage water absorption, and % drug release at 12 h and 24 h have shown significant changes in response to slight changes in concentrations of components A, B, and C. Results suggest that oral floating in situ gel formulated with Famotidine tartrate promotes sustained medication release.
Keywords: *Famotidine, NSAIDs, oral In Situ gel, H2 receptor antagonist, Box-Behnken design, Drug release studies.*

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INTRODUCTION

For the regulated release of medications over a range of predetermined time intervals, numerous oral drug delivery systems have been created in recent years. The real challenge in creating an oral controlled-release drug delivery system is to extend the dosage form's time in the gastrointestinal tract (GIT) so that the entire drug is released in the required amount of time [1]. To achieve site-specific drug release in the upper GIT for a local or systemic effect, the stomach residence duration is increased using the gastroretentive drug delivery method [2].

The formation of a gastroretentive in situ gelling device has sparked increased interest in both academics and business. This is mostly attributable to the in-situ gelling system's significant benefits, which include ease of administration and decreased administration frequency and hence aid to improve patient compliance [3]. Controlled medication delivery with improved gastroretention can be achieved via gastroretentive in situ gelling devices, also referred to as stomach-specific systems. When in contact with bodily fluids or when the pH changes, in situ gelling systems, which are liquid at room temperature, begin to gel [4]. Due to the bioadhesive nature of the polymer and the fact that the gel produced by the in-situ gelling system is lighter than gastric fluids, it floats over the stomach contents or sticks to the gastric mucosa, producing gastric retention of the dosage form and increasing gastric residence time, which prolongs the time that the drug is delivered to the gastrointestinal tract [5]. The system uses polymers that go through a sol-gel phase transition as a result of modifications in particular physicochemical characteristics.

A histamine H2-receptor antagonist is Famotidine. Local administration of Famotidine improves the drug's bioavailability at the receptor site on the stomach wall and boosts its effectiveness in lowering acid secretion [6]. In order to distribute drug in the stomach for extended periods of time, the current work set out to generate and evaluate a floating in situ gelling system containing Famotidine.

MATERIAL AND METHODS

Materials

Famotidine was gifted by Zuventus Healthcare Ltd., Sodium bicarbonate, Sodium citrate, calcium carbonate, were purchased from Loba Chemie, Mumbai, India. Sodium alginate and HPMC K100 were obtained from Himedia laboratories, Mumbai and Yarrow chem Products, Mumbai, India, respectively.

Methods

Preformulation Studies

Determination of Melting Point

Capillary tube melting point analysis was used to establish the melting point of Famotidine in accordance with USP standards. The capillary tube was loaded with enough Famotidine powder to form a compact column of between 4 and 6 mm in height. The tube was then heated to its melting point in an electrical melting point device and temperature at which the final remaining solid particle in the tube turned into a liquid, was measured [7].

Drug-Excipient Compatibility Studies

The spectrum was acquired and measured using Fourier transform infrared (FTIR) spectroscopy. The sample is dispersed in KBr (200–400 mg), and then compressed to a disc shape at a pressure of 5 tons in a hydraulic press. After positioning the pellet in the beam of light, a spectrum was taken [8].

Differential scanning calorimetry studies

A differential scanning calorimeter connected to a data acquisition system from Mettler Toledo was used to conduct the thermal investigation. Using a scanning rate of 10°C/min between 40 and 200°C and a nitrogen flow rate of 40 ml/min, a sample of pure drug, a physical combination of drug and polymer was heated [9].

Preparation of Oral In Situ Gel of Famotidine

On a magnetic stirrer at 70°C, dissolved several amounts of gelling polymer (Sodium Alginate or Gellan Gum) in deionized water with a weighed quantity of Sodium Citrate. In a separate process, iota carrageenan was dissolved in Sodium Citrate-treated deionized water and heated to 80 °C with continuous stirring. The necessary amount of HPMC K4M release retardant polymer was dissolved in deionized water in another beaker. Then, while swirling constantly, the three solutions were combined. The aforementioned solution was chilled to 40 °C before the addition of Calcium Carbonate, Sodium bicarbonate, and Famotodine [10] . Preservatives were used with sodium saccharin. After making any necessary adjustments to the volume with the deionized water, the resulting solution was given a good stir and placed in amber bottles for later use.

Experimental Design

The connection and interaction between independent and dependent variables may be studied using an experimental Design Expert® (version 12.0.3.0) by StatEase Inc., Minneapolis, MN. The optimization of the formulas was inferred to take place using a Box-Behnken design [11]. Low (-1) and high (+1) values were assigned to three independent variables (factors): sodium alginate (A), sodium bicarbonate (B), and sodium citrate (C).

Evaluation

Drug Content Determination

A total of ten milliliters of the formulation (equal to forty milligrams of Famotidine) was taken from each batch and placed in a 100 milliliter volumetric flask. Using a UV-visible spectrophotometer (UV-1800, Shimadzu, Kyoto, Japan), the concentration of famotidine was measured at 263 nm.

Measurement of pH

The pH of the finished formulations was measured by submerging the probe end of a calibrated digital pH meter (Mettler Toledo MP 220, Greifensee, Switzerland) into them at room temperature.

In Vitro Gelation

The colored formulation, measured out to be 1 ml, was mixed with 5 ml of 0.1 N HCl at pH 1.2 and 37 ±0.5 °C in a test tube with gentle stirring to avoid breaking the gel that had formed. Based on the stiffness of the formed gel, the time of gelation, and the stability of the gel, the gelling capacity was classified as follows [12]: () no gelation, (+) gelation after few minutes following rapid dispersion, (++) immediate gelation persist for few hours, and (+++) immediate gelation persist for extended period of time.

Determination of viscosity

The Brookfield DV-II+Pro digital viscometer was used to measure the compositions' viscosities using an S21 spindle at 50 rpm over the course of three separate measurements, with each sample replaced between tests.

***In vitro* buoyancy study**

The research was done at a temperature of 37± 0.5°C in a simulated gastric fluid medium (pH 1.2) utilizing a USP Type II dissolving device. The In situ gel formulation, about 10 ml, was added to the medium and floating lag time ,floating duration were recorded [13].

Measurement of water uptake by the gel

The In situ gel was prepared in 40 ml of 0.1N HCl (pH 1.2). The gel component of each formulation was isolated from the buffer, and the buffer was removed by blotting using Whatman filter paper. After determining the gel's mass, 10 cc of distilled water were added to it. The weight of the gel was recorded and the time gap between decanting the water and recording the final weight of the gel was recorded [14].

Measurement of density of gel

Thirty milliliters of the In situ formulation were added to fifty milliliters of 0.1N HCl in a beaker. weighed 10 ml of the gel that had formed in a measuring cylinder. The density was determined by using both the gel's mass and its volume [15].

Measurement of gel strength

A weight of 50 grams was put in the middle of the gel's surface in a 50 ml beaker and allowed to sink through the gel. For each gel formulation, the time it took for a 50 g weight to sink 5 cm into the gel was recorded. Each new formulation was tested three times using the same procedure, and the average time was recorded [16].

In vitro drug release study of the In situ gel formulation

The USP type II (paddle technique) dissolving equipment was used for the dissolution investigations. 900 m; of 0.1 N HCl (pH 1.2) at 37 ℃ was utilized as the dissolving media. The mixing speed was set at 50 revolutions per minute [17]. This was deemed slow enough to prevent the gelled mixture from breaking and mimic the current modest agitation in vivo. Using a UV-Visible Spectrophotometer, 10 ml samples were taken at regular intervals, the dissolving media was changed out, the samples were filtered using Whatman filter paper, diluted, and finally tested for maximum absorbance at 263 nm.

Release Kinetics of the Optimized Formulation

Data obtained from the dissolving research were plotted in several kinetics models to investigate the In vitro release kinetics of the improved formulation of Famotidine tartrate oral In situ gel [18,19].

Zero-order equation

By graphing the cumulative proportion of medicine released against time in hours, we may calculate the zero order release.

$C=K0t$

Where, K0= Zero order constant, t= Time in hours

First order equation

The graph was plotted as log % cumulative drug remaining vs. time in hours.

$$\text{Log } C = \log C0 - Kt/2.303$$

Where, C0= Initial concentration of drug, K= First order, t= Time in hours

Higuchi kinetics

The graph was plotted with % cumulative drug released vs. square root of time

$$Q = Kt^{½}$$

Differential rate constant (K) represents the system of design variables; time (t) represents elapsed time. Ratio of drug release to the square root of time is negative.

Hixson and Crowell erosion equation

Data were displayed using the Hixson and Crowell rate equation to examine the relationship between particle surface area and diameter and drug release.

$$Q01/3 - Qt1/3 = KHCt$$

Where,

In this context, Qt= the dose released at time t. KHC = Rate constant for the Hixson Crowell equation, where Q0 = initial drug amount.

Korsmeyer-Peppas equation

It was then plotted in the Korsmeyer-Peppas equation as Log cumulative percent of drug released vs. Log time to assess the drug release mechanism.

$$Mt/M\alpha = Ktn$$

Where

$Mt/M\alpha$ = Fraction of drug released at time t, t = Release time, K= Kinetics constant (Incorporating structural and geometric characteristics of the formulation), N= Diffusional exponent indicative of the mechanism of drug release.

Stability studies

The In situ gel, now in its optimal state, was stored in a container of amber hue. It had a good, solid seal. Accelerated temperature 40± 2 °C / 75 5% RH for 1 month was used for the stability research, as recommended by the ICH. At 0 and 30 days, samples were taken to analyze for color, pH, floating behavior, gelling capability, drug content, and In vitro drug release [20].

RESULTS & DISCUSSION

Preformulation Studies

Melting Point

Using a glass capillary technique and a melting point apparatus, the melting point of Famotidine was determined to be 163.25±1.59 ℃. This value agrees with the melting point of Famotidine that has been published in the scientific literature (163-164 ℃)

Determination of solubility of Famotidine

Famotidine's solubility in various aqueous buffers varied with pH. Famotidine solubility was found to be highest at acidic pH values, and it quickly decreased when the pH was raised.

Table 1: Solubility determination in different mediums

S. No	Medium	Solubility determination Concentration (mg/mL)
1	Methanol	28.36±0.12
2	Dichloromethane	22.34±3.45
3	PEG 200	15.36±3.21
4	PEG 400	18.39±2.46
5	PEG 600	12.84±1.27
6	Ethanol	5.39±1.25
7	Chloroform	16.43±0.83
8	0.1 N HCl pH 1.2	28.37±0.07
9	Buffer pH 6.8	2.35±0.023
10	Buffer pH 7.4	1.26±0.053
11	water	In soluble

Drug - Excipient Compatibility Study

FT-IR spectroscopy was used to conduct a chemical compatibility analysis, and the results showed that the medicine and excipients did not interact with one another.

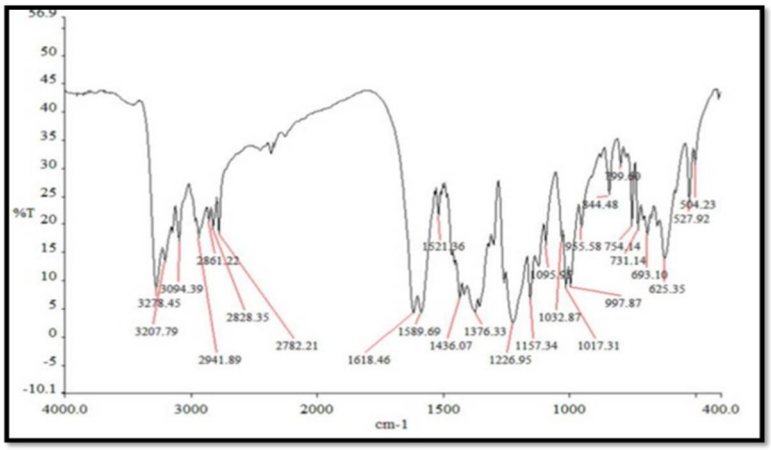

Fig. 1. FTIR spectrum of Famotidine

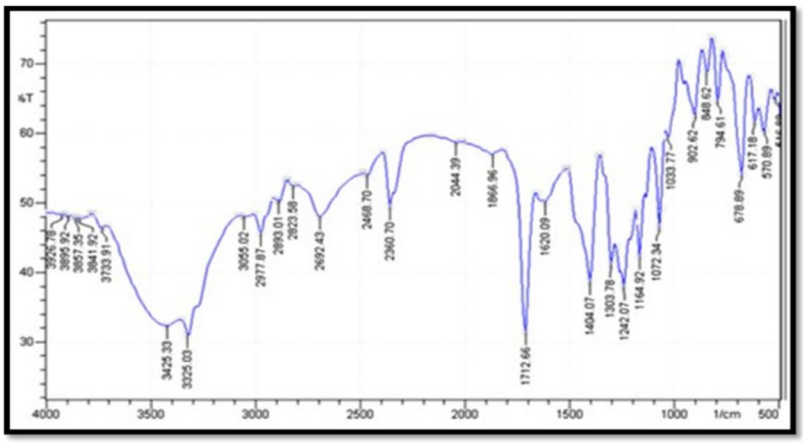

Fig. 2. FTIR spectrum of Optimized formulation

Differential Scanning Calorimetric (DSC) studies

DSC showing a clear endothermic peak at 130.2°C, which corresponds to the melting point of pure famotidine.

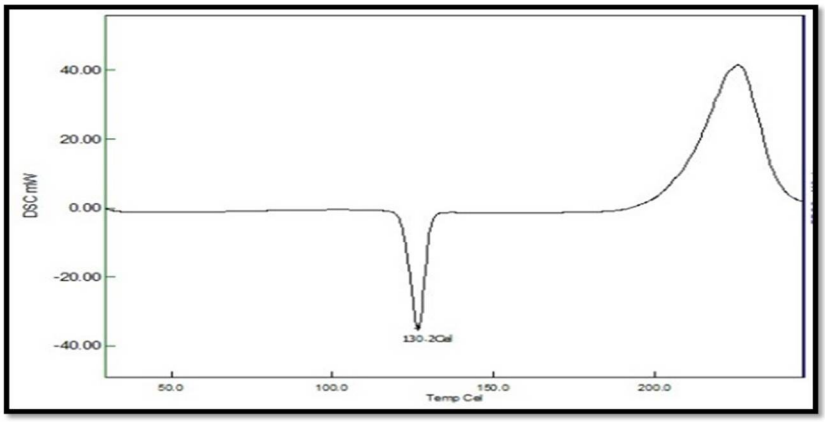

Fig. 3. DSC thermogram of Pure Drug (Famotidine)

Table 2: Formulation of Famotidine in situ gel

Name of ingredient	Quantity in 100 ml (% w/v)							
	F-1	F-2	F3	F4	F5	F6	F7	F8
Famotidine	40	40	40	40	40	40	40	40
Sodium alginate	3	2	2	1	2	1	3	3
Sodium bicarbonate	1.5	1.5	1.5	0.5	0.5	0.5	1	0.5
Sodium citrate	1	0.5	1	1	1	0.5	0.5	0.5
HPMC K100	0.5	0.5	0.5	1	1	1	1	1
Methyl paraben	0.5	0.5	0.5	0.8	0.8	0.8	1	1
Deionised water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

In Vitro Gelation

Sodium alginate formulations with lower concentrations (F4) have formed weak gels that may not resist peristaltic waves in the GI tract and would be transported to the colon along with stomach contents [18]. In the presence of gel-forming polymers, all of the formulations experienced a sol-to-gel transition upon contact with the gelation medium. All the formulations using sodium alginate or sodium bicorbonate as the principal polymer resulted in the formation of rigid gels, with the exception of formulation F4, which used a lower concentration of sodium alginate as the gelling polymer and resulted in a more quickly dispersing gel.

pH Measurement

The pH of all the finished products was between 6.23 and 7.15, which is within acceptable range. [19].

Viscosity of Famotidine Oral In situ Gel

All In situ gelling compositions viscosity measured using a Brookfield Viscometer DV-II+Pro at 50 rpm and 25 °C. Formulations with a high concentration of Sodium alginate and HPMC K100 increased in viscosity.

In Vitro Floating Study

Formulations F1, F4, F7, and F8 with a greater polymer content stayed afloat for at least 6 hours. Enhanced cross-linking density at higher polymer concentrations successfully traps the released CO_2 bubbles, resulting in a less dense gel and, ultimately, superior buoyancy [22]. These formulations have also shown a floating lag time of less than 30 s.

Density of Famotidine Oral In situ Gel

The formulation has to be lighter than the gastric contents (1.004 gcm^3) or have the same density as the gastric contents in order to float on top of the stomach. All the formulations have densities that are lower than stomach fluid (1.004 gcm^3). This encourages the in situ gastroretentive gel to float freely in the stomach.

Measurement of Gel strength

Good gel strength was demonstrated by all of the formulations; values ranged from 14.7 s for the formulation with only Iota carrageenan as the main polymer to 44.3 s and 52.6 s for the formulations with a combination of three polymers (i.e., Sodium Alginate, Gellan gum, and Iota carrageenan).

Drug Content

All formulations had a drug content between 98.04 and 99.83%, showing that the drug was distributed evenly throughout the products.

Table 3: Evaluation parameters of Famotidine floating oral in situ gelling system

F. Code	pH	Drug content (%)	In vitro gelation	Floating lag time (s)
F1	7.01±0.21	97.23 ±0.21	+++	16±0.25
F2	7.23 ±0.23	96.84±0.35	+++	8±0.43
F3	7.04 ±0.15	98.01 ± 0.14	+++	6±0.26
F4	6.95 ±0.24	97.42 ±0.16	+++	10±0.19
F5	6.83±0.22	96.31 ±0.18	+++	3±0.51
F6	6.34 ±0.19	97.28 ±0.26	+++	5±0.38
F7	6.59 ±0.16	99.02 ±0.14	+++	19±0.42
F8	7.15 ±0.13	98.24 ±0.29	+++	8±0.16

(+++) indicates immediate gelation which persist for extended period of time

Table 4: Evaluation parameters of Famotidine floating oral in situ gelling system

F. Code	Total floating time (h)	% Drug Release (at 24 h)	Mucoadhesive strength (dyne/cm^2)	Viscosity (cps)	Gel strength (sec)
F1	≥24	78.36±0.21	968.47±0.42	986.34±1.05	201.43±0.56
F2	3	79.13±0.14	1234.87±0.56	876.01±1.34	175.38±1.42
F3	6	89.01±0.16	965.84±0.38	1384.01±1.32	246.38±0.34
F4	≥24	83.64±0.18	1157.43±0.39	1126.35±1.09	300.51±0.11
F5	≤12	79.16±0.35	1068.94±0.47	891.24±0.96	264.82±0.36
F6	5	85.62±0.17	978.21±0.35	583.47±1.52	231.54±0.25
F7	≥24	91.36±0.11	895.36±0.43	326.95±0.48	115.62±0.22
F8	≤12	80.95±0.21	1136.85±0.35	1035.27±0.69	236.51±0.04

Data Analysis and Optimization

Using a 2^3-factor complete factorial design, we looked at how different amounts of sodium alginate (A), sodium bicarbonate (B), and sodium citrate (C) affected outcomes such floating lag time, water absorption, and drug release.

Table 5. Formulation composition with their results used for optimization

Run	X1	X2	X3	Y1	Y2	Y3
1	3	1	1	18.27±0.21	26.53±0.01	70.21±0.28
2	3	1	0.5	56.35±0.34	28.34±0.01	72.48±0.11
3	2	1	0.75	10.35±0.18	20.46±0.05	52.31±0.14
4	2	0.5	1	13.48±0.11	10.67±0.04	49.32±0.13
5	2	1	0.75	11.02±0.17	16.52±0.13	50.36±0.26
6	2	1.5	0.5	18.37±0.26	8.94±0.16	68.31±0.28
7	2	1	0.75	10.25±0.23	7.36±0.28	50.43±0.17
8	3	0.5	0.75	25.94±0.26	28.39±0.13	83.61±0.14
9	3	1.5	0.75	27.03±0.14	16.82±0.32	81.07±0.15
10	2	1.5	1	16.34±0.11	29.36±0.24	69.37±0.16

11	2	1	0.75	10.35±0.13	13.52±0.16	62.15±0.31
12	1	1.5	0.75	8.95±0.28	21.03±0.25	83.06±0.15
13	1	1	0.5	12.35±0.19	23.59±0.34	75.19±0.24
14	1	0.5	0.75	6.25±0.37	16.52±0.15	70.42±0.15
15	2	0.5	0.5	19.52±0.15	29.41±0.24	83.51±0.19
16	1	1	1	16.52±0.12	28.63±0.22	52.38±0.14
17	2	1	0.75	9.62±0.24	15.39±0.19	63.28±0.25

The program has generated a total of 8 iterations of the formulation by supplying the independent variables at two levels. Multiple regression analysis revealed linear, with interaction terms, coefficients of second-order polynomial equations and mathematical correlations for all answers. The answers have varied from 7 seconds to 57 seconds for the floating lag time, 9.01 percent to 31.01% for the water absorption percentage, and 51.3 percent to 99.2 percent for the medication release percentage. In a polynomial equation, a negative number indicates an inverse link between the factor and the response, whereas a positive value indicates a direct association between the factor and the response.

Impact of Factors in Floating Lag Time

Floating lag time R1= +10.32 +4.19A +0.6875B -1.50C -0.4025AB -3.06AC +1.00BC +1.58A2 +0.1397A2 +6.47C2

Increasing the amounts of A and B would increase the floating time, while increasing the quantity of C would lower the floating lag time of the formulations; this is because all three independent variables, A, B, and C, have shown negative influence on R1 (floating lag time).

When comparing formulations F15 and F2, both of which include the same amounts of sodium alginate and sodium citrate but different amounts of sodium bicarbonate, it has been shown that a greater concentration of sodium citrate results in a shorter floating lag time. The F3 formulation was dispersed after 3 hours, but the F5 formulation was still afloat 24 hours later. It is clear from the results that increasing the sodium bicarbonate content shortens the formulation's floating lag time and floating duration. These results were more in line with what has been reported in the past [21]. Despite both F8 and F9 containing the same amounts of sodium alginate and sodium bicarbonate, the floating lag time and floating duration were drastically different for these two formulations at 15 and 57 s, 24 and 5 hours. Even with the formulations F7 and F4, with less than 12 h and more than 24 h of floating, respectively, similar floating duration outcomes were obtained. Based on the data presented above, it is clear that increasing the concentration of sodium citrate shortens the lag time required for buoyancy and allows for floating for up to 24 hours. In conclusion, sodium citrate shortens the delay before floating and lengthens the time spent in the water.

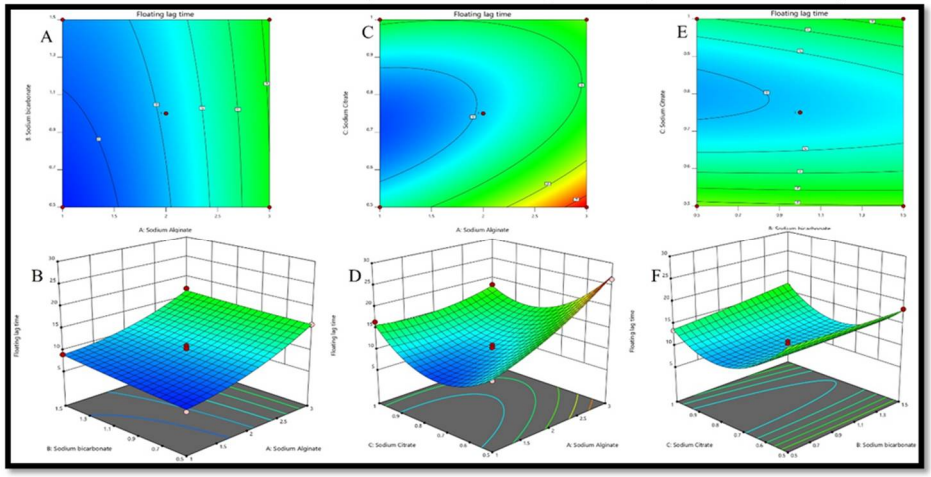

Fig. 4: Response surface plot independent variables on Floating lag time (Y1)

Effect of Independent Variables on Percentage Water Uptake

After 180 minutes, the percentage of water absorption was calculated, and a positive correlation between sodium bicarbonate concentration and water uptake was found. This has been further proven by the findings of a water intake research conducted with formulations F8 and F8 (with different sodium bicarbonate concentrations and the same concentrations of sodium alginate and sodium citrate). According to Eq. (2), the response two (R2), i.e. the percentage water absorption, has been dramatically influenced by the addition of sodium alginate, sodium citrate, and sodium bicarbonate.

Percentage water uptake R2 = +14.62 +1.29A -1.10B +0.6137C -4.02AB -1.71AC +9.79BC +6.61A2 -0.5688B2 +5.51C2

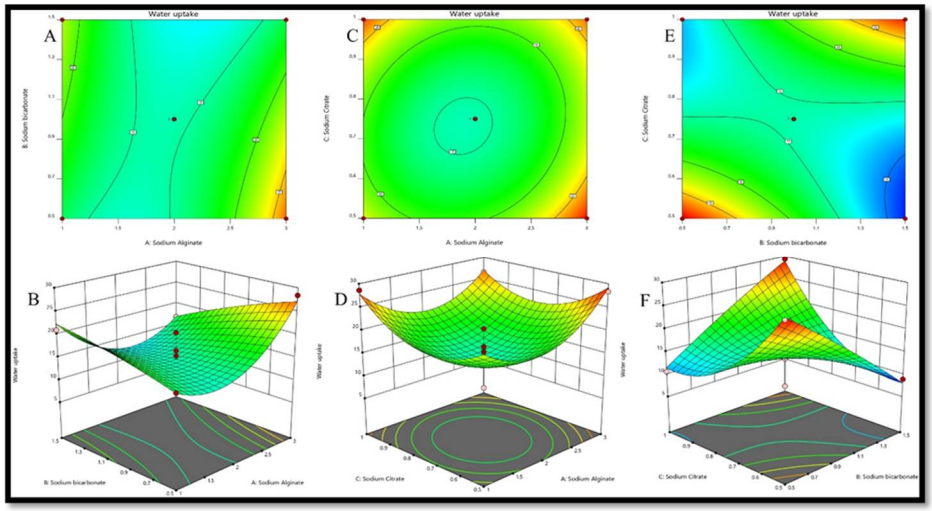

Fig. 5: Response surface plot of independent variables on water uptake studies (Y2)

Formulations F2 and F8 exhibit a positive relationship between sodium bicarbonate concentration and % hydration. Formulation F5, with a higher sodium citrate content, has shown 26% water absorption, whereas Formulation F6, with a lower sodium citrate concentration, has shown just 7.62% water uptake. Therefore, it was clear from both the observed data and the polynomial equation that sodium citrate stimulates cellular water uptake.

Effect of Independent Variables on Percentage Drug Release

The rate and amount of Famotidine release were shown to be decreased with increased polymer concentration. Dissolution of famotidine at the gel surface, which might have been released quickly upon contact with the dissolution medium (0.1 N HCl), may account for the large burst release seen in all in situ gel formulations during the first 2 h. Sodium citrate was shown to have a significant impact on the proportion of medicine released, and it also helped to keep the solution from gelling up just before administration. According to Eqs. (3), the responses 3, i.e. the percentage drug release at 24 h, are significantly impacted by the presence of sodium alginate, sodium citrate, and sodium bicarbonate, in that order.

Percentage drug release at 24 h R3 = +55.71 +3.29A +1.87B -7.28C -3.80AB +5.13AC +8.81BC +11.89A2 +11.95B2 -00267C2

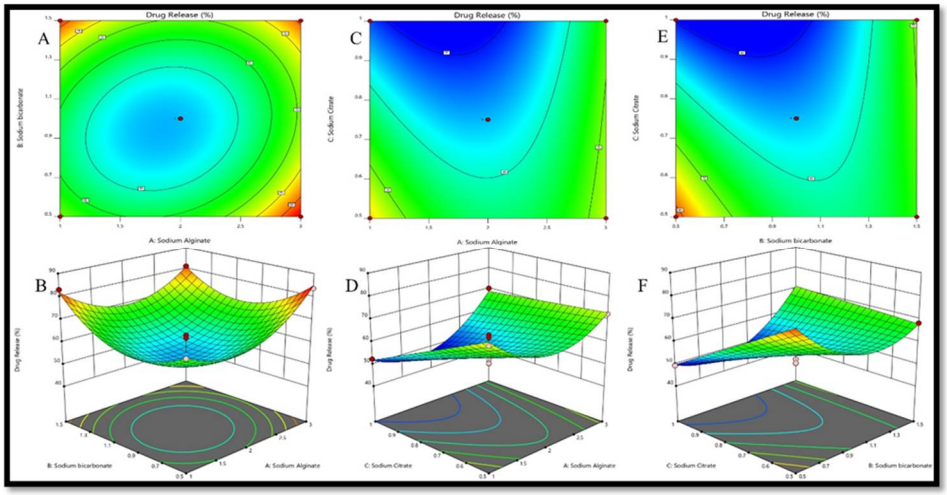

Fig. 6: Surface plot of independent variables on % drug release (Y3)

As sodium citrate concentration increased, medication release reduced proportionally. As shown in Eqs. (3), sodium bicarbonate had a beneficial influence on drug release after 24 hours. In Fig. 2, we see three-dimensional response surface plots that depict the influence of the independent variables on the dependent ones. By using optimization techniques and a desirability method, we were able to zero in on the optimal level of the independent variables that would have the greatest effect on the dependent ones. Applying limits on replies (to a predetermined goal value) and creating desirability plots (Fig. 3) yielded the optimum

formulation. 15 seconds was set as the maximum allowed floating lag time, 20% water absorption, 50% drug release after 4 hours, and 80% drug release after 8 hours were the other limits used.

The best results were found with A = 2.895%, B = 0.519%, and C = 0.504% as the values of the dependent variables. Famotidine 40 mg, sodium alginate 2.5% (as a gelling agent), sodium bicarbonate 1% (as a gas forming agent), sodium citrate 0.75 (as a preservative), HPMC K 100 0.5% (as a thickening agent), methyl paraben 0.25% (as a preservative), and distilled water (as a vehicle) made up the final composition of the floating in situ gel formulation. The optimal formulation was determined to have a preferability factor of 0.986. The theoretical prediction was tested by measuring the improved formulation's floating lag time, % water absorption, and percentage drug release at 24 hours. Data showed values similar to the model perdition for floating lag time (26.526 s), water absorption (40.588%), and medication release (91.631%) after 24 hours. It was found that the deviation (in %) between the anticipated and observed experimental values was small (within the range of 5%). All of these results show that the complete factorial design used in the current study is effective for optimizing the variables being studied.

Drug Release Kinetics

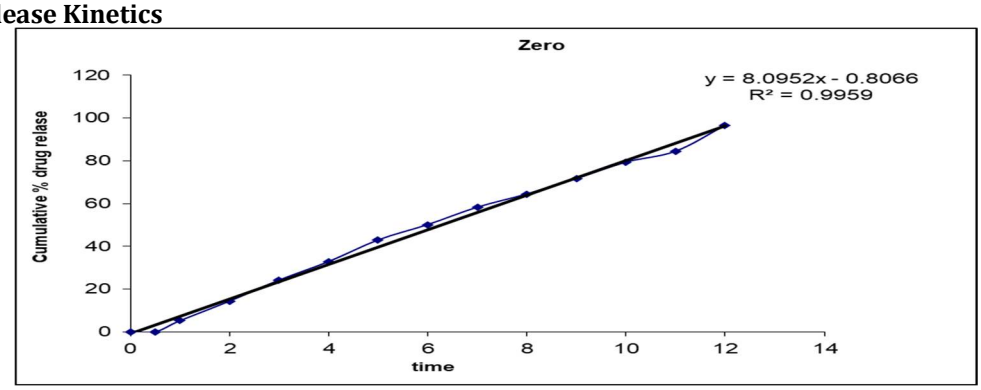

Fig. 7: Zero order release kinetics

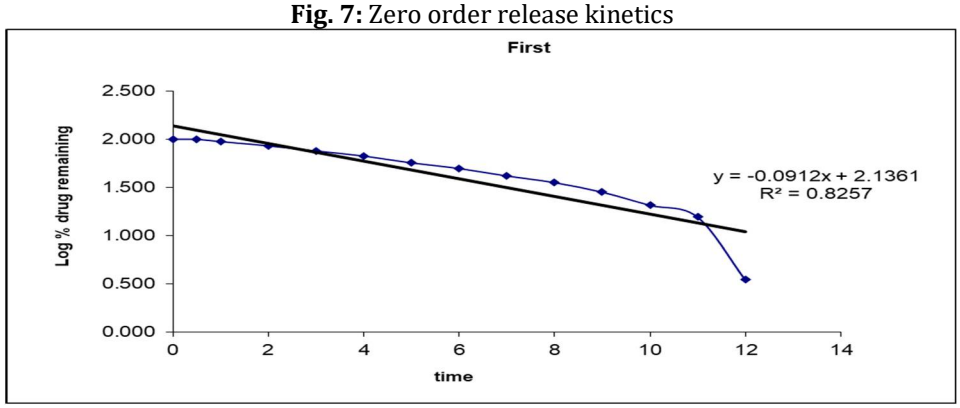

Fig. 8: First order release kinetics

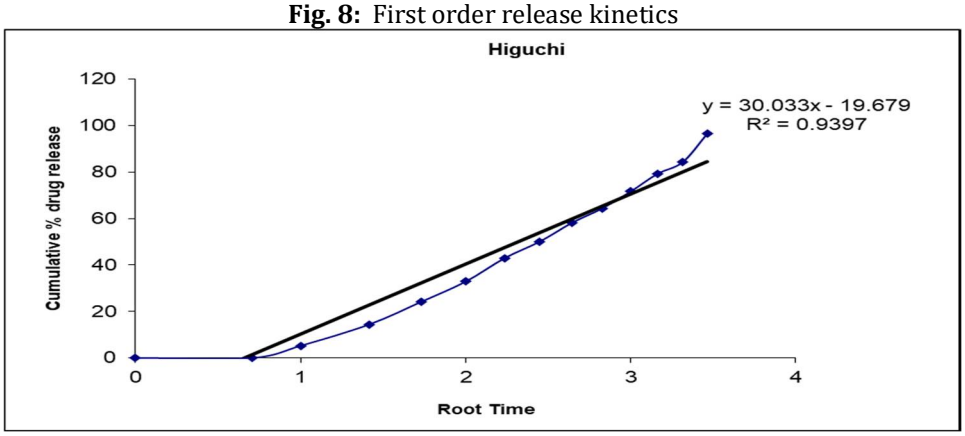

Fig. 9: Higuchi release kinetics

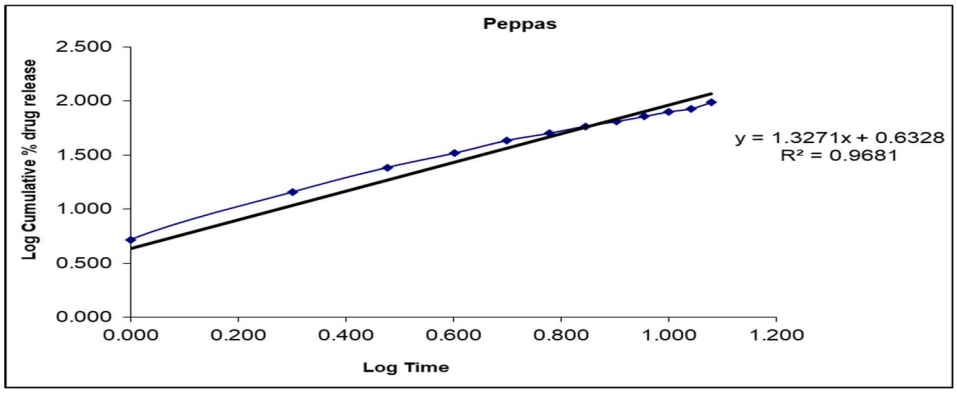

Fig. 10: Peppas release kinetics

It was clear from the release kinetics data that the optimized method for calculating release rates was used.

Stability Studies

The optimized formulations (F2) subjected to stability studies as per ICH guidelines.

Table 6: Stability data for Optimized Formulation

Parameter	**Condition: 40±2ºC/75±5%RH**	
	Initial	**After 3 months**
Visual Appearance	Milky-white	Milky-white
Pourability	Easily pourable	Easily pourable
pH	7.23 ±0.23	6.82
Gelling capacity	+++	+++
Floating Lag time	16±0.25	19±1.02
Floating duration	≥12	≥12
Viscosity (cps)	876.01±1.34	880.31±0.27
Drug content (% w/v)	99.02 ±0.14	98.64±0.21

CONCLUSION

Sodium Alginate, sodium bicarbonate, sodium citrate, and HPMC K4M were used as gelling agents in the formation of an oral in situ gel containing Famotidine tartrate. The drug and excipients were shown to be compatible by the FT-IR spectroscopy and did not interact with one another. There are a total of 8 Famotidine preparations (F1, F2, F3, F4, F5, F6, F7, and F8). Sodium Alginate, sodium bicarbonate, and sodium citrate were used as polymers, while HPMC K4M (0.5% w/v) was used as a release retardant, to make in situ gels with varied concentrations. Floating lag time was less than 2 minutes across all formulations, while floating time was larger than 12 hours. Gel strength was greater in formulations F1 and F2 and their densities were lower than that of stomach fluid (1.004 gcm^3). The Box-Behnken model suggests that the development of a famotidine oral in situ gelling device was a complete success. The optimized in situ gel floated and gelled as desired, releasing a sufficient dose of drug into the stomach. With immediate invitro gelation, the drug concentration was found to be between 96.31±0.18 and 99.02±0.14%, and it remained stable for a long time. There was an observed range of 7.36±0.28 to 29.41±0.24% in terms of water intake, and an estimated range of 8.95±0.28 to 56.35±0.34s in terms of floating lag time. All formulations had released over 90% of the drug during the 8-h time frame, with F1 and F2 showing floating even after 12 h. The impact of the chosen independent variables on the dependent ones were found to be quite large. Responses such floating lag time, percentage water absorption, and % drug release at 12 h and 24 h have shown significant changes in response to slight changes in concentrations of components A, B, and C. As a result of its development, optimization, and thorough evaluation, the suggested formulation for increasing Famotidine's anti-inflammatory activity and decreasing its gastrointestinal ulceration potential has the potential to become a favored prospective dosage form in the near future. Results suggest that oral floating in situ gel formulated with Famotidine tartrate promotes sustained medication release.

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