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Research Article

DESIGN, OPTIMIZATION, AND EVALUATION OF A Rutin–*Glycyrrhiza Glabra In-Situ* FLOATING GEL FOR GASTRIC ULCER MANAGEMENT USING A QbD APPROACH

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ABSTRACT

The aim of this study was to develop and optimize an oral *in-situ* floating gel containing Rutin and *Glycyrrhiza glabra* (*Liquorice*) extract for the effective management of peptic ulcer disease. The *Liquorice* extract was obtained using the Soxhlet extraction method, while the solubility of Rutin was enhanced by preparing solid dispersions with hydroxypropyl methylcellulose (HPMC) as a carrier in varying concentration ratios (1:1, 1:2, 1:3, and 1:4). Among these, the 1:3 ratio exhibited the highest solubility enhancement, showing a six-fold increase in solubility and achieving 90% drug release. A 3^2 full factorial design based on Quality by Design (QbD) principles was employed to optimize the formulation. The independent formulation variables were the concentrations of gellan gum and calcium carbonate, while the dependent variables were floating lag time and viscosity. A total of nine formulations were prepared and evaluated for physicochemical characteristics, drug content, pH, floating behaviour, viscosity, and drug release profile. Among the formulations, Batch F9 was identified as the optimized formulation, demonstrating a floating lag time of 25 seconds, viscosity of 55.1 cp, drug release of 98%, drug content of 97%, pH of 7.1, and water uptake capacity of 89%. The optimized in-situ gel showed excellent floating properties and sustained drug release, indicating prolonged gastric residence and enhanced bioavailability. The findings suggest that the combination of Rutin and *Liquorice* extract in an optimized in-situ floating gel provides a stable gastro-retentive drug delivery system with significant potential for sustained localized therapy in the management of peptic ulcer disease. This formulation approach offers an effective strategy for improving the therapeutic efficacy and patient compliance in ulcer treatment.

INTRODUCTION

Peptic ulcer disease (PUD) is a widely occurring digestive disorder characterised by the formation of painful, ulcerative lesions on the inner lining of the gastric region or the proximal part of the small intestine. A major causative factor is Helicobacter pylori infection, which disrupts the stomach's protective mucus barrier. Under normal conditions, this mucus layer serves as a defence mechanism, protecting the gastric epithelium from corrosive gastric acids. However, when this barrier is compromised, mucosal erosion occurs, resulting in ulcer formation. In addition to H. pylori, several external factors, such as excessive alcohol consumption, poor diet, chronic stress, smoking, and prolonged use of nonsteroidal anti-inflammatory drugs (NSAIDs), additionally compromise the stomach's protective mechanisms and increase the risk of ulcer development.[1]

Gastric ulcers affect millions of individuals globally, posing a significant public health concern. Despite the availability of several pharmacological treatments both conventional (proton pump inhibitors, H_2 blockers, and antibiotics) and non-conventional many therapies are associated with drawbacks such as

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adverse side effects, drug resistance, limited efficacy, and high treatment costs. This has sparked growing interest in herbal and natural therapies as safer, cost-effective, and holistic alternatives. The World Health Organization (WHO) reports that about 80–85% of people worldwide depend on herbal remedies for both treatment and nutrition, highlighting their growing significance in contemporary healthcare.[2]

Rutin (3,3′,4′,5,7-pentahydroxyflavone-3-Rutinoside) is a naturally occurring and non-toxic flavonoid glycoside widely present in various dietary sources, including tomatoes, oranges, carrots, sweet potatoes, black tea, and apple peels. Its multiple hydroxyl groups contribute to its potent antioxidant and biological activities. Extensive research has demonstrated its diverse pharmacological properties, including anti-carcinogenic, anti-thrombotic, cardio-protective, neuroprotective, and hepatoprotective effects. Importantly, Rutin exhibits strong gastroprotective potential by enhancing mucosal defence, reducing oxidative stress, and promoting ulcer healing making it a promising candidate for managing peptic ulcer disease.[4]

Liquorice, scientifically known as *Glycyrrhiza glabra*, is a medicinal herb belonging to the family Fabaceae. It has been widely recognized for its anti-ulcer, antioxidant, anti-inflammatory, and antimicrobial properties. The plant is rich in bioactive constituents, among which glycyrrhizin is predominant. Glycyrrhizin imparts the characteristic sweetness of *Liquorice* approximately 50 times sweeter than sucrose and contributes to its pharmacological efficacy. Traditionally, *Glycyrrhiza glabra* roots have been used to treat gastrointestinal, respiratory, and hepatic disorders. In the context of gastric ailments, its soothing and demulcent properties help protect the gastric mucosa, reduce acidity, and promote ulcer healing.[5]

Oral administration continues to be the most favoured route for systemic drug delivery because it is non-invasive, convenient, and highly acceptable to patients. However, conventional oral dosage forms often suffer from poor gastric retention, resulting in reduced bioavailability, especially for drugs with narrow absorption windows. To address this limitation, *in-situ* gel-forming systems have gained attention as an innovative approach for sustained and localized drug delivery.[7]

In-situ gels are delivered as liquid formulations (sols) that convert into a gel upon exposure to physiological triggers like variations in pH, temperature, or ionic content. After gelation, the system stays localized at the target site, promoting extended gastric retention and sustained drug release. Compared to conventional systems, *in-situ* gels offer advantages such as simple preparation, reduced dosing frequency, enhanced bioavailability, and improved patient comfort. These properties make them particularly suitable for gastro-retentive delivery systems aimed at treating gastric disorders like PUD.[7]

Quality by Design (QbD) represents a paradigm shift from end-product testing to incorporating quality into the product from the earliest stages of Design. QbD is "a systematic approach to pharmaceutical development that begins with predefined objectives and emphasises product and process understanding and control, based on sound science and quality risk management." QbD focuses on identifying critical formulation and process parameters that influence product performance, ensuring consistent quality. through design of experiments (DoE), quality risk management (QRM), and the use of process analytical technology (PAT). Its implementation enhances process efficiency, product safety, and regulatory flexibility, ultimately leading to robust formulations and reproducible outcomes. In the context of this study, QbD principles were applied to optimise the formulation parameters of an oral *in-situ* floating gel containing Rutin and *Glycyrrhiza glabra* extract to ensure effective clinical control of peptic ulcers.[9]

MATERIALS AND METHODS

Materials

Rutin was procured from Yucca Enterprises, while *Glycyrrhiza glabra* (*Liquorice* extract) was obtained from Shri B. M. K. Ayurveda Mahavidyalaya. All other materials and chemicals used were of either pharmaceutical or analytical grade.

Methods

Soxhlet extraction of *Liquorice* root

One hundred grams of coarse *Liquorice* root powder was packed in a muslin bag and placed in the Soxhlet extractor, with 500ml of ethanol added to the round-bottom flask. The apparatus was assembled with a condenser and continuous water flow, and the solvent was heated to allow repeated cycles of evaporation, condensation, and siphoning through the plant material for six hours. After completion, the ethanol was evaporated on a water bath at 40°C to obtain a small concentrated extract, which was further dried in a porcelain dish, weighed to determine extractable matter, and finally stored in a refrigerator for later use.[22]

Solvent Evaporation Method for Rutin

Solid dispersions (SDs) of Rutin with HPMC E5 were formulated in weight compositional ratios ranging from 1:1 to 1:4 using the solvent evaporation technique. A measured quantity of Rutin was dissolved in 25 ml of ethanol, followed by the addition of the required amount of HPMC E5 was added according to

the specified ratios. The sample was magnetically stirred without interruption for 30 minutes, then heated on a water bath until the solvent completely evaporated. The dried mass was scraped to obtain the solid dispersion, which was subsequently stored in a desiccator for future use.[23]

Formulation of an oral herbal *in-situ* suspension

For preparing the for the *in-situ* floating gel, 50 ml of distilled water was initially combined with 0.25% sodium citrate, and the mixture was raised to 80°C under constant stirring to promote homogeneous dispersion. Gellan gum was subsequently introduced as the main gelling polymer, and the mixture was allowed to slowly reduce in temperature to about 40°C. At this temperature, calcium carbonate (0.5–1%) was added to the formulation. Its addition produced a milky suspension due to the release of calcium ions, which later help in gel formation. The mixture was kept at 40°C and stirred continuously to maintain uniformity and achieve a smooth, homogeneous dispersion.[16]

Table 1: Formulation Table of Herbal *In-Situ* Gel

Formulation Code	Rutin	*Liquorice*	Gellan Gum %	Calcium Carbonate %	Sodium Citrate %	Methyl Paraben	Propyl Paraben
F1	250mg	500mg	0.5%	0.5%	0.25%	0.03%	0.01%
F2	250mg	500mg	0.5%	1%	0.25%	0.03%	0.01%
F3	250mg	500mg	0.4%	0.7%	0.25%	0.03%	0.01%
F4	250mg	500mg	0.6%	0.7%	0.25%	0.03%	0.01%
F5	250mg	500mg	0.6%	1%	0.25%	0.03%	0.01%
F6	250mg	500mg	0.4%	1%	0.25%	0.03%	0.01%
F7	250mg	500mg	0.6%	0.5%	0.25%	0.03%	0.01%
F8	250mg	500mg	0.4%	0.5%	0.25%	0.03%	0.01%
F9	250mg	500mg	0.5%	0.7%	0.25%	0.03%	0.01%

Design of experiments (DOE)

A structured, coordinated strategy for determining the link between process inputs and process output. Also known as "Design of experiment".

The herbal in-situ floating gel was designed and optimized using a conventional 3^2 factorial design. Gellan gum and calcium carbonate were selected as independent variables and tested at three specified coded levels (−1, 0, +1, denoting low, medium, and high). The responses assessed included viscosity (Y_1) and floating lag time (Y_2). Design-Expert software version 13.0 (Stat-Ease Inc., Minneapolis, MN, USA) was employed to generate nine experimental runs, supporting the optimization of formulation parameters to attain the expected product performance

Table 2: Design of Experiments (DoE)

Independent variables	Levels			Responses (Dependent Variables)
	Low (-)	Medium (o)	High (+)	
Gellan gum	0.4%	0.5%	0.6%	Viscosity
Calcium carbonate	0.5%	0.7%	1%	Floating lag time

UV- spectrophotometer analysis of Rutin

Spectrophotometric Condition

The Shimadzu UV 1800 double beam spectrophotometer was employed, along with paired 10mm quartz cuvettes. Spectrophotometric tests were carried out using analytical grade methanol.

Wavelength Detection

Lambda max (λ max) of Rutin was estimated by running a 10µg/ml concentration solution in the UV Spectrophotometer over the wavelength range of 400-200nm.

Preparation of the Standard Stock Solution of Rutin

Accurately weighed 10mg of Rutin and dissolved in 10ml of Methanol [1000µg/ml] and then ultrasonicated for 10 minutes. From the first stock pipette out separately 1ml solution and transferred into 10ml of volumetric flask and make up the volume with methanol[100µg/ml]. the final stock solution was prepared by pipetting out 1ml of solution and poured into a volumetric flask and make up the volume with methanol [10µg/ml]. all stock solutions were kept in firmly stoppered, amber-coloured volumetric flasks that were impervious to light.

Preparation of Serial Dilution from the Stock solution

Aliquots equivalent to 2, 4, 6, 8, and 10µg/ml from the standard stock solution were placed into amber coloured 10 ml volumetric flasks to prepare sample concentrations ranging from 2 to 10µg/ml. The volume in each flask was then adjusted to 10 ml using the optimized mobile phase for UV spectrophotometric linearity assessment.[16]

Evaluation Parameters

pH

The pH of the formulated *in-situ* suspension was assessed at room temperature by using a digital pH meter. For each formulation, readings were collected in three replicates, and average results were noted.[15]

Viscosity determination

The viscosity of the formulated *in-situ* suspension was evaluated by using a digital rotational viscometer. (Model LMDV-100). A 10ml sample was subjected to shear at 50 rpm using the S1 spindle at room temperature, with each reading recorded over approximately 30 seconds.[14]

Floating lag time

The *in-vitro* buoyancy assessment was performed by gently introducing 5ml of the prepared formulation into a beaker containing 100 ml of 0.1 N HCl (pH 1.2), maintained at 37°C. The floating lag time, defined as the interval required for the formulation to ascend to the surface, was measured, along with the total floating duration during which the system remained buoyant in the medium. The system exhibited a floating duration of up to 12 hours, indicating the formation of a thick, stable gel with excellent floating behaviour. [25]

***In-vitro* Drug Release Study**

The *in-vitro* drug study was assessed using a USP Type II (paddle) dissolution apparatus, maintained at 37±0.5°C at 50 rpm. A total of 900ml of 0.1N HCl (pH 1.2) was used as the dissolution medium. The medium received a 5ml sample of the in-situ gel formulation, which consisted of 12.5mg Rutin along with 25 mg *Liquorice*. At each sampling time, a 5ml portion was withdrawn, filtered, diluted as necessary, and measured spectrophotometrically at 256 nm with a SHIMADZU UV-1800. To maintain sink conditions, an equal volume of fresh medium was added right after sampling to maintain sink conditions. The release study was carried out for a total duration of 12 hours.[14]

Stability study

The herbal *in-situ* formulation was successfully maintained at a consistent temperature between 8°C, 25°C and 40°C for 30 days as part of the stability tests. This formulation's pH, viscosity, and Floating lag time were all assessed. It was also subjected to different temperatures.[20]

Drug Content

For drug content analysis, 1ml of the in-situ gel was diluted to 50 ml with methanol, sonicated for 15 minutes, and filtered. The filtrate was then analysed at 256 nm using a UV–Visible spectrophotometer.[14]

Water Uptake Capacity

Water absorption was assessed by mixing 10ml of the formulation with 40ml of 0.1 N HCl, isolating the formed gel, and blotting excess moisture. The gel was placed in a petri dish, and 10ml of distilled water was added every 30 minutes. Its initial weight was measured before every subsequent water addition. After 30 minutes, the water was decanted and measured to evaluate absorption. Fresh distilled water was added at 0.5, 1.0, and 1.5 hours to continue the assessment.[16]

Calculation and recording of the weight difference were done.

$$\textbf{Water uptake capacity} = \frac{\textbf{Final weight} - \textbf{Intial weight}}{\textbf{Intial weight}} \times \textbf{100}$$

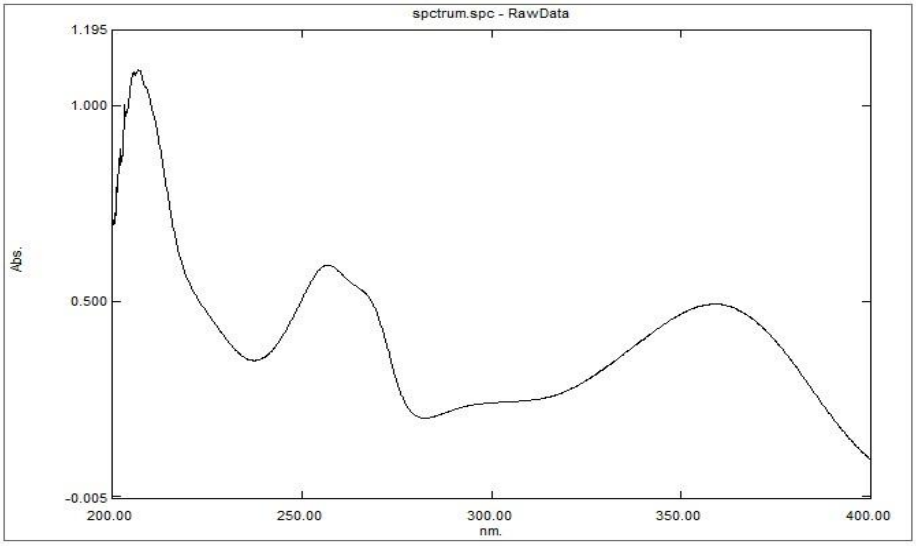
RESULTS

UV spectrophotometric analysis

Wavelength has been determined for the concentration of 10µg/ml, and maximum absorbance was observed at 256nm.

Spectra of Rutin in Methanol

Figure 1: Spectra of Rutin



Solvent Evaporation Method of Rutin

Table 3: *In-Vitro* Drug Release Study of Rutin in Various Ratios

S.no	Time (min)	%CDR				
		Pure drug	1:1	1:2	1:3	1:4
1	45	11.90	38.06	40.20	65.41	39.19
2	60	15.04	57.75	65.66	90.87	60.87

Preliminary Phytochemical Screening

Table 4: Preliminary Phytochemical Screening of Liquorice

S.no	Phytochemical Tests	Liquorice
1	Flavonoids	Present
2	Alkaloids	Absent
3	Saponin	Present
4	Tannins	Present
5	Polyphenols	Present
6	Glycosides	Present

Table 5: Contains the Independent Variables X1 & X2 I.E., Concentrations of Gellan Gum and Calcium Carbonate, along with the Dependent Variables Y_1 (Floating Lag Time) and Y_2 (Viscosity of the *In-Situ* Suspension) as Determined using Doe Software

Formulation Code	Gellan Gum Concentration (%) – X_1	Calcium Carbonate Concentration (%) – X_2	Floating Lag Time – Y_1	Viscosity of *In-situ* Suspension – Y_2
F1	0.5%	0.5%	65.25	41.2
F2	0.5%	1%	15.67	53.9
F3	0.4%	0.7%	43.1	24.2
F4	0.6%	0.7%	30.89	67.1
F5	0.6%	1%	18.28	104.7
F6	0.4%	1%	15.85	46.7
F7	0.6%	0.5%	67.1	89.9
F8	0.4%	0.5%	40.73	44.2
F9	0.5%	0.7%	25	55.1

Statistical Optimisation & ANOVA test results

Optimisation of the oral herbal in-situ gel was achieved through analysis of statistical data provided by Design-Expert 13.0. Table 6 presents the statistical outputs of the experimental design. ANOVA assessed the significance of the independent variables on viscosity (Y_1) and floating lag time (Y_2). Polynomial models describing factor response relationships were generated, and the corresponding regression coefficients are listed in Table 7. Coefficients for X_1 and X_2, including interaction and quadratic terms, indicate the direction and magnitude of each variable's effect positive values reflecting synergism and negative values indicating antagonism. Response surface and contour plots were constructed to visualise the influence of formulation factors on the responses.

Table 6: Summary of Statistical Parameters Analysis of Variance Test (Anova)

Response	Sum of squares	Mean square	df	f-value	p-value	Model significant
Floating Lag time Y_1	2478.67	1239.34	2	10.67	0.0106	significant
Viscosity Y_2	3793.35	1896.68	2	9.08	0.0153	significant

Table 7: Regression Equation Coefficient (Polynomial Equation)

Response	Regression Equation Coefficient
Floating Lag time Y_1	$+80.61465+2.77X_1-20.00X_2$
Viscosity Y_2	$+58.95+24.43X_1+590X_2$

Response Y1- Floating lag time

Based on the ANOVA regression coefficient (Fig. 3), both X1 and X2 showed positive signs. This indicates a synergistic influence of X1 and X2 on the response Y1. ANOVA also confirmed that both variables had a significant effect on Y2 according to the regression equation. When X1 and X2 were used together, a clear synergistic impact was observed. The response surface and contour plots (Figs. 2 and 3) visually confirmed these observations. An increase in both X_1 and X_2 levels resulted in a corresponding rise in the Y_1 response. This indicates that higher concentrations Increasing concentrations of gellan gum and calcium carbonate resulted in a rise in floating lag time. However, the effect of calcium carbonate alone on floating lag time was relatively minor. Thus, X1 contributed more strongly to changes in Y1 than X2. Overall, X1 was identified as the main factor affecting response Y1.

Figure 2: Contour Plot for Response Y1: Floating Lag Time

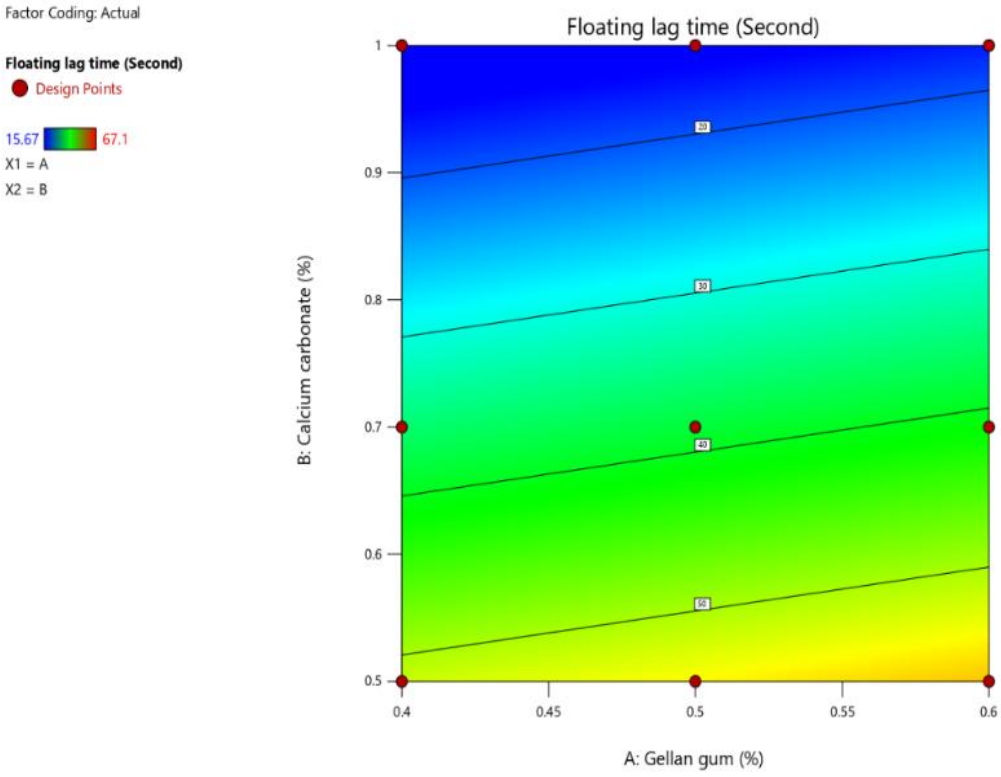
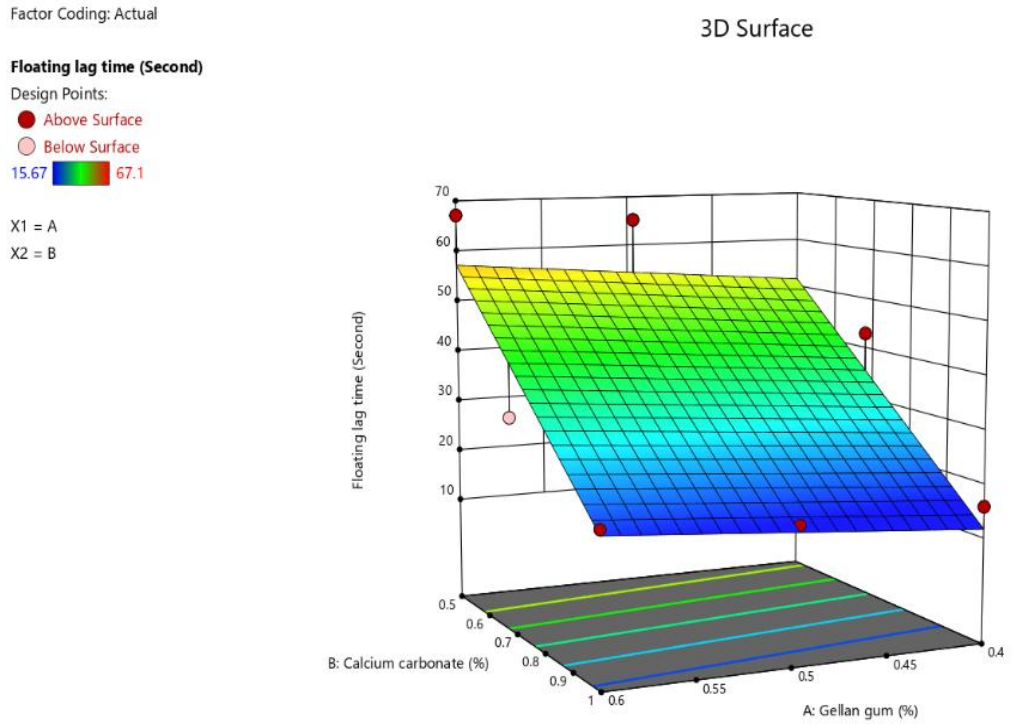


Figure 3: Surface Plot for Response Y1: Floating Lag Time



Response Y2- Viscosity of *In-situ* suspension

The ANOVA results (Table 3) revealed that variable X_1 showed a positively signed coefficient, signifying a direct enhancement of Y_2. In contrast, variable X_2 showed a negative regression coefficient, suggesting an antagonistic effect on the response. This reflects an antagonistic effect of X2 on the response Y2. The regression equation confirmed that X1 exerts a stronger influence on Y2 than X2. Response Surface and Contour plots (Figs. 4 & 5) supported these findings graphically. Increasing X1 (Gellan gum concentration) increased the viscosity of the *in-situ* suspension. An elevation of X_2 (calcium carbonate concentration) resulted in a reduction in the viscosity of the *in-situ* suspension. Hence, X1 contributed more significantly to viscosity changes than X2. Overall, X1 was identified as the dominant factor affecting the response Y2.

Figure 4: Contour Plot for Response Y2: Viscosity

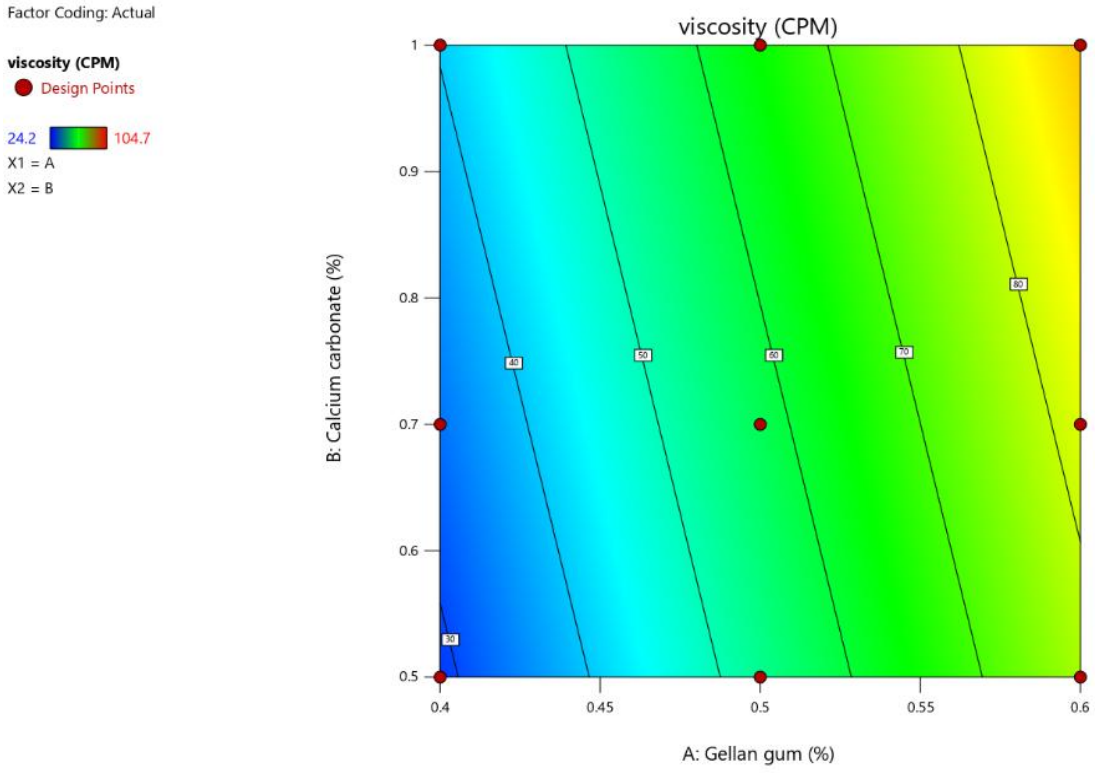
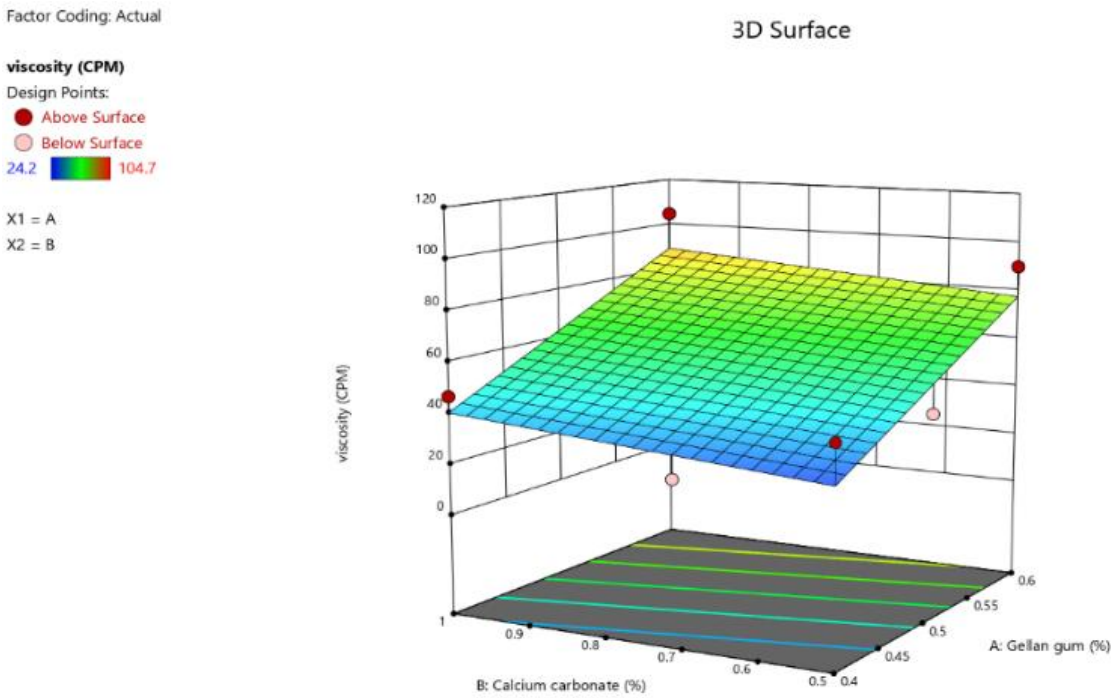


Figure 5: Surface Plot for Response Y2; Viscosity



Generating Design Space

The design space represents the range of formulation variables within which a product meeting the desired quality attributes can be reliably produced. In this study, graphical optimization in Design-Expert 13.0 was employed to establish the design space. indicating that both gellan gum and calcium carbonate concentrations exerted significant effects on viscosity, lag time, and gel formation. The targeted criteria for optimization were set as viscosity of the *in-situ* suspension ≤ 55 cps and floating lag time ≤ 2 minutes. Achieving these targets identified a multidimensional region of excipient combinations that constituted the acceptable operating range for formulating the oral herbal in-situ gel to meet the target product profile. Ensuring that the critical quality attributes (CQAs) remained within specification depended on maintaining the formulation variables within this defined design space. The yellow-coloured zone in the design space overlay-plot indicates the zone where optimal operating conditions were achieved.

Figure 6: Overlay Plot of the Design Space

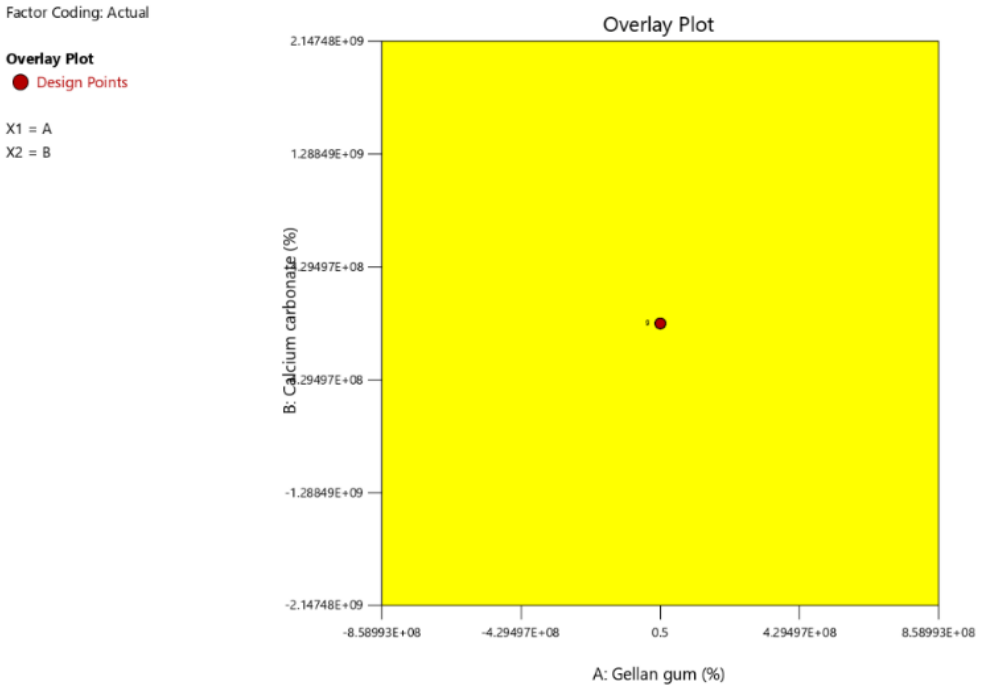


Table 8: pH of Formulation F1 to F9

Formulation code	F2	F2	F3	F4	F5	F6	F7	F8	F9
pH	7.2	7.2	7.1	7.1	7.2	7.2	7.1	7.1	7.1

Table 9: Water Uptake Capacity of F9

Formulation code	Hour	Water uptake Percentage %
F9	0.5	46.96
	1	79.46
	1.5	89.77

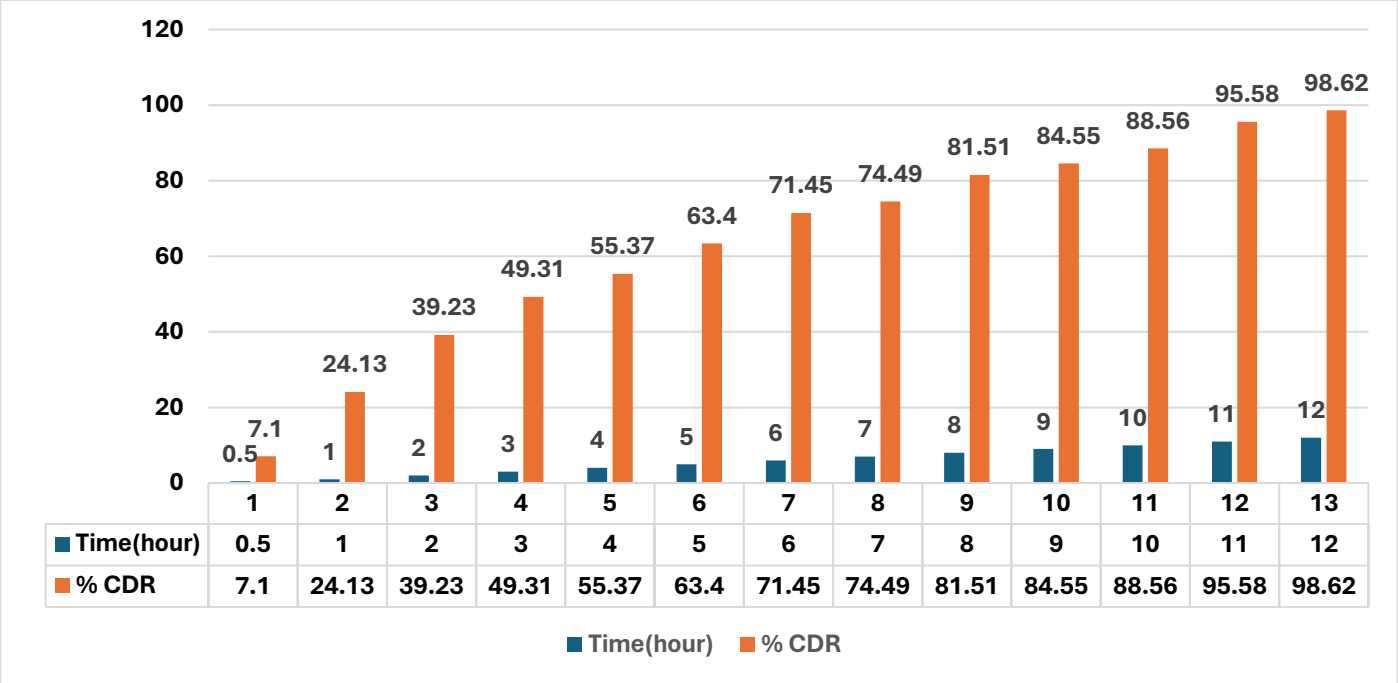
Table 10: Determination of Viscosity, Floating Lag Time and Total Floating Duration

Batch code	Viscosity	Floating Lag Time	Total Floating Duration
F1	41.2	65.25	>12 hours
F2	53.9	15.67	>12 hours
F3	24.2	43.1	>12 hours
F4	67.1	30.89	>12 hours
F5	104.7	18.28	>12 hours
F6	46.7	15.85	>12 hours
F7	89.9	67.1	>12 hours
F8	44.2	40.73	>12 hours
F9	55.1	25	>12 hours

Table 11: In-Vitro Drug Study of the Optimized Batch F9

S.No	Time (min)	Absorbance	Concentration	DR in 900	CLA mcg/5ml	CDR mg	% CDR
1	30	0.015	0.0986	887.50	0.0000	0.8875	7.1000
2	60	0.032	0.3347	3012.50	4.9306	3.0174	24.1394
3	120	0.047	0.5431	4887.50	16.7361	4.9042	39.2339
4	180	0.057	0.6819	6137.50	27.1528	6.1647	49.3172
5	240	0.063	0.7653	6887.50	34.0972	6.9216	55.3728
6	300	0.071	0.8764	7887.50	38.2639	7.9258	63.4061
7	360	0.079	0.9875	8887.50	43.8194	8.9313	71.4506
8	420	0.082	1.0292	9262.50	49.3750	9.3119	74.4950
9	480	0.089	1.1264	10137.50	51.4583	10.1890	81.5117
10	540	0.092	1.1681	10512.50	56.3194	10.5688	84.5506
11	600	0.096	1.2236	11012.50	58.4028	11.0709	88.5672
12	660	0.103	1.3208	11887.50	61.1806	11.9487	95.5894
13	720	0.106	1.3625	12262.50	66.0417	12.3285	98.6283

Figure 7: Evaluation of the in-vitro drug study of the optimised batch f9



	1	2	3	4	5	6	7	8	9	10	11	12	13
Time(hour)	0.5	1	2	3	4	5	6	7	8	9	10	11	12
% CDR	7.1	24.13	39.23	49.31	55.37	63.4	71.45	74.49	81.51	84.55	88.56	95.58	98.62

Drug Content

The F9 formulation exhibited a drug content of 97.8%.

Table 12: Stability Study of Optimised Batch F9

Parameters	Stability study duration					
	15th day			30th day		
Temperature	8°C	25°C	40°C	8°C	25°C	40°C
Floating lag time	25 sec	23 sec	27sec	26 sec	22 sec	28 sec
Viscosity (Cp)	55.1	51.2	56.8	56.9	53.2	58.1
pH	7.1	7.1	7.1	7.1	7.1	7.1
Drug content (%)	97.86	97.72	97.58	97.83	97.22	97.46

DISCUSSION

The present study focused on formulating an herbal *in-situ* floating gel prepared with Rutin and *Glycyrrhiza glabra* extract to achieve sustained and localized delivery in the gastric region for effective ulcer management. The rationale behind selecting these phytoconstituents was their well-documented antiulcer, antioxidant, anti-inflammatory, and mucosal-protective activities, which offer a safer alternative to synthetic antiulcer agents.

The formulation was based on gellan gum, a naturally occurring polysaccharide known for its capacity to undergo gelation in the presence of cations. The addition of calcium carbonate played a dual role: (i) providing calcium ions for ionic crosslinking of gellan at gastric pH, enabling *in situ* gelation, and (ii) generating carbon dioxide, contributing to the floating mechanism. Sodium citrate acted as a calcium-sequestering agent, preventing premature gelation during preparation and ensuring controlled gel formation within the gastric environment. The optimized formulation showed immediate gelation when exposed to simulated gastric fluid, confirming its suitability for gastric-retentive delivery. The floating lag time was minimal, and buoyancy was maintained for prolonged periods, indicating that the generated gel possessed a low density and adequate matrix strength to remain afloat. This is crucial in ulcer therapy as floating systems ensure longer gastric residence time, allowing the actives to act directly on the ulcer site.

Drug content analysis confirmed uniform dispersion of both Rutin and *Glycyrrhiza glabra* extract, ensuring dose consistency. The *in-vitro* drug release studies revealed a sustained release, attributed to the gellan gum matrix, which controls diffusion of the phytoconstituents. The biphasic release behaviour observed an initial mild burst followed by prolonged release may be advantageous for immediate soothing action followed by long-term mucosal protection.

The antioxidant and anti-inflammatory nature of both Rutin and *Glycyrrhiza glabra* suggests a synergistic therapeutic effect. Rutin helps in reducing oxidative damage to the gastric mucosa, while glycyrrhizin glabra enhances mucus secretion and inhibits gastric acid. Their combined use in a localized, sustained-release system potentially enhances ulcer healing efficiency while minimizing systemic exposure and adverse effects.

Overall, the developed *in-situ* floating gel demonstrated excellent physicochemical properties, gastro-retentive behaviour, and controlled drug release, validating the design strategy. The formulation provides an effective platform for the gastric delivery of herbal actives and represents a promising option for the treatment of peptic ulcer disease. Future work may involve *in-vivo* evaluation, stability studies, and clinical validation to establish its therapeutic potential.

CONCLUSION

A QbD approach was efficiently employed in this study to design and optimize an oral in-situ floating gel targeted for peptic ulcer therapy, incorporating Rutin and *Liquorice* as the key herbal actives. The solubility of Rutin was improved through the preparation of solid dispersions, while *Liquorice* extract was obtained as a standardized ethanolic extract using the Soxhlet extraction method.

The QTPP and CQAs were pre-defined, and systematic risk evaluation highlighted the concentrations of gellan gum and calcium carbonate as major formulation factors. Optimization using Design of Experiments (DOE) software, followed by ANOVA and response surface analysis, confirmed the robustness and reproducibility of the optimized formulation.

Phytochemical screening of *Liquorice* confirmed the presence of bioactive compounds, and Rutin was quantitatively analyzed using a validated UV spectrophotometric method. The developed formulation met the desired QTPP and exhibited consistent performance.

Overall, the QbD based approach ensured product quality, scalability, and reproducibility, while the use of Rutin and *Liquorice* provided a safe and effective herbal alternative for the management of peptic ulcer.

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REFERENCES

1. Savarino E, Zingone F, Barberio B, Marasco G, Akyuz F, Akpinar H, Barboi O, Bodini G, Bor S, Chiarioni G, Cristian G. Functional bowel disorders with diarrhoea: Clinical guidelines of the United European Gastroenterology and European Society for Neurogastroenterology and Motility. United European gastroenterology journal. 2022 Jul; 10(6): 556-84.
2. Carretero C, Bojorquez A, Eliakim R, Lazaridis N. Updates in the diagnosis and management of small-bowel Crohn's disease. Best Practice & Research Clinical Gastroenterology. 2023 Jun 1; 64: 101855.
3. Gupta M, Kapoor B, Gupta R, Singh N. Plants and phytochemicals for treatment of peptic ulcer: An overview. South African Journal of Botany. 2021 May 1; 138: 105-14.
4. Akash SR, Tabassum A, Aditee LM, Rahman A, Hossain MI, Hannan MA, Uddin MJ. Pharmacological insight of Rutin as a potential candidate against peptic ulcer. Biomedicine & Pharmacotherapy. 2024 Aug 1; 177: 116961.
5. Sreelakshmy V, Deepa MK, Mridula P. Green synthesis of silver nanoparticles from Glycyrrhiza glabra root extract for the treatment of gastric ulcer. J Dev Drugs. 2016; 5(2): 152.
6. Aslam B, Awan T, Javed I, Khaliq T, Khan JA, Raza A. Gastroprotective and antioxidant potential of Glycyrrhiza glabra on experimentally induced gastric ulcers in albino mice. Int J Curr Microbial App Sci. 2015 Mar 11; 4(2): 451-60.
7. Rao MR, Shelar SU. Controlled release ion sensitive floating oral in situ gel of a prokinetic drug using gellan gum. Ind J Pharm. 2015 Apr 1; 49(2): 158-67.
8. Antony JE, Nair SS. Formulation and Evaluation of Stomach specific Floating in situ gel of Clarithromycin. IJPSR. 2018; 11(3): 1479-87.
9. Bhutani H, Kurmi M, Singh S, Beg S, Singh B. Quality by design (QbD) in analytical sciences: an overview. Quality Assurance. 2004 Sep; 3: 39-45.
10. Patel MS, Patel AD, Doshi NR, Vyas G. Design and development of novel floating in situ gel of amoxicillin for the treatment of peptic ulcer disease caused by Helicobacter pylori. Acta Scientific Pharmaceutical Sciences 2021 Sep; 5(9).
11. Ranade A, Birajdar P, Punde P. Repositioning of eugenol in treatment of gastric ulcers through development of floating in situ gel. Indian J Pharm Educ Res. 2016 Jul 1; 50(3): 244-53.
12. Jafar M, Salahuddin M, Bolla SR. Gastric floating in-situ gel as a strategy for improving anti-inflammatory activity of meloxicam. Journal of Applied Pharmaceutical Science. 2018 Nov 30; 8(11): 095-102.
13. Bothiraja C, Kumbhar V, Pawar A, Shaikh K, Kamble R. Development of floating in situ gelling system as an efficient anti-ulcer formulation: in vitro and in

vivo studies. RSC Advances. 2015; 5(37): 28848-56.

14. Rao MR, Shelar SU. Controlled release ion sensitive floating oral in situ gel of a prokinetic drug using gellan gum. Ind J Pharm. 2015 Apr 1; 49(2): 158-67.
15. Antony JE, Nair SS. Formulation and Evaluation of Stomach specific Floaring in situ gel of Clarithromycin. IJPSR. 2018; 11(3): 1479-87.
16. Malge, R.P., Mannur, V.S. & Koli, R. Quality by Design (QbD) Enabled and Central-Composite Design Assisted Approach for Formulation of Oral Herbal Gastro-retentive In-situ Gel. J Pharm Innov 19, 60 (2024). https://doi.org/10.1007/s12247-024-09863-5
17. Yadiki KK, Kokatanur U, Dandagi PM, Hulyalkar S. Formulation and evaluation of floating oral in-situ gel of Liquorice extract. Indian J Pharm Educ Res. 2024 Jan 1; 58(1s): 167-75.
18. Basu A, Masareddy RS, Patil A, Bolmal U. Design and characterization of sustained release in situ gastric floating gel of ropinirole hydrochloride. Indian J Pharm Educ Res. 2021 Apr 1; 55(2): 374-82.
19. HB N, Bakliwal S, Pawar S. In-situ gel: new trends in controlled and sustained drug delivery system. International Journal of Pharm Tech Research. 2010 Apr; 2(2): 1398-408.
20. Vijayashree R, Priya S, Yothi D, Jainey PJ. formulation and characterisation of gastro-retentive in situ gel loaded with Glycyrrhiza glabra l. extract for gastric ulcer. int j app pharm. 2024; 16(2): 76-85.
21. Vipul V, Basu B. Formulation and characterization of novel floating in-situ gelling system for controlled delivery of ramipril. International Journal of Drug Delivery. 2013 Jan 1; 5(1): 43.
22. Sankeshwari RM, Ankola AV, Bhat K, Hullatti K. Soxhlet versus cold maceration: Which method gives better antimicrobial activity to licorice extract against: Streptococcus mutans:? Journal of the Scientific Society. 2018 May 1; 45(2): 67-71.
23. Ismail A, El-Biyally E, Sakran W. An innovative approach for formulation of Rutin tablets targeted for colon cancer treatment. AAPS Pharm Sci Tech. 2023 Feb 15; 24(2): 68.
24. Zatla AT, Hammoudi A. Phytochemical Screening and Inflammatory Activity Evaluation of Hydroalcoholic Extract of Glycyrrhiza glabra Root. Chemistry Proceedings. 2024 Nov 14; 16(1): 5.
25. Thomas LM. Formulation and evaluation of floating oral in-situ gel of metronidazole. Int J Pharm Pharm Sci. 2014; 6(10): 265-9.

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