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From Concept to Assessment:
Creating an Oral In-Situ Gelling System with Sucralfate

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Abstract

The study aimed to develop and assess an oral in situ gelling system for Sucralfate through a comprehensive approach. Preformulation studies were conducted, encompassing API characterization, solubility, melting point, and absorption maxima determination, along with compatibility assessments. Employing an ion-activated method, a range of formulations (F1-F9) were created, with varying concentrations of Gelrite and HPMC K100M as excipients. Evaluation of these formulations covered numerous physicochemical attributes, such as appearance, clarity, pH, gel strength, viscosity, in-vitro gelling capacity, gelling time, in-vitro floating behavior, drug content, and drug release profiles. The concentration of polymers significantly influenced properties, with increased polymer concentration enhancing gel strength and viscosity but reducing cumulative drug release. Among the formulations, F4 was identified as the optimal choice, exhibiting balanced gelling capacity, viscosity, and high drug content (99.85%), ensuring sustained drug release for over 12 h. The drug release pattern adhered to a zero-order kinetic model, while the release mechanism followed Fickian diffusion, implying diffusion-controlled drug release through the polymer matrix. In conclusion, the study's systematic approach successfully delivered a promising in situ gelling system for Sucralfate, shedding light on polymer effects and drug release behaviors.

Keywords: Dosage form, Gel, Floating, Stomach, Sucralfate, Viscosity

1. Introduction

"In-situ," a term rooted in Latin, conveys the concept of something being "in its original place" or "in position." This notion finds application in the realm of drug delivery through the development of in-situ gelling systems. These systems are designed to sustain drug release and maintain consistent plasma profiles. The distinctive feature of in-situ gelling systems lies in their ability to transition from a liquid state at room temperature to a gel state upon encountering body fluids or a change in pH. This transition provides the advantage of easy administration in liquid form at the site of application, which contrasts with the challenges posed by rigid gels (Rathod et al., 2014).

These gels offer the benefit of extended drug residence time at the absorption site. This is facilitated by their transformation into strong gels following swelling. Several formulation methods can be employed to create in-situ gels, including pH-triggered, ion-activated, photo polymerization, temperature-triggered, and enzymatic cross-linking methods. Each of these techniques capitalizes on specific triggers or conditions to

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achieve gelation at the intended site of action. Ultimately, the strategic implementation of in-situ gelling systems holds promise for enhancing drug delivery by ensuring sustained release and optimal drug presence at target locations (Kousar et al., 2022).

Peptic ulcer refers to a lesion caused by excessive stomach acid exposure in the digestive tract, typically found in the stomach or upper part of the small intestine (proximal duodenum). This condition is characterized by the erosion of the protective mucosal layer, leading to exposed tissue that can extend into deeper layers like the submucosa or muscularis propria. The prevalence of peptic ulcer disease in the general population is estimated to be around 5-10%. However, recent epidemiological studies have demonstrated a decline in its occurrence, rates of hospitalization, and related mortality. This decrease is attributed to the introduction of novel therapeutic approaches and improved hygiene practices, leading to a reduction in *Helicobacter pylori* infections, a key contributing factor to peptic ulcers (Sowjanya & Ahad, 2022).

Traditionally, mucosal damage in individuals with acid peptic disease was understood to result from a combination of factors. These factors included excessive acid production in the stomach, dietary influences, and stress. The acidic environment of the stomach was thought to contribute to the breakdown of the protective mucosal layer, making it susceptible to damage. Alongside this, dietary choices and stress were believed to exacerbate the condition. However, with advancements in our understanding of peptic ulcer etiology, the role of *H. pylori* infection and its subsequent inflammation has gained prominence as a significant cause of peptic ulcers. This shift in focus has led to improved treatment strategies and a decrease in the prevalence and severity of peptic ulcer disease (Ahad et al., 2011).

Sucralfate is categorized as an ulcer protective medication, belonging to the class of anti-ulcer agents known as ulcer protectives. This drug operates by a dual mechanism: inhibiting the activity of pepsin and absorbing bile salts. These specific functions of sucralfate grant it the capacity to function as a potent barrier against the intrusion of acid, pepsin, and bile salts. The efficacy of sucralfate in creating a comprehensive protective shield is supported by substantial evidence (Takabayashi et al., 2004). Sucralfate's mode of action involves its interaction with both duodenal and gastric ulcers, as well as with gastric erosions that can arise from factors such as ethanol and nonsteroidal anti-inflammatory drugs (NSAIDs). By binding to these ulcer sites, sucralfate exerts its protective effects, aiding in the prevention of further damage and supporting the natural healing process. This property makes sucralfate a valuable therapeutic option in the management of gastrointestinal ulcers and erosion caused by a range of factors (Jackson et al., 2001).

2. Materials and methods

2.1 Material

Sucralfate was obtained as a gift sample from SAMCHEM Health Care Pvt. Ltd. The excipients used in the formulation, namely HPMC K100M, Sodium Citrate, and Calcium Carbonate, were acquired from Balaji Drugs. It's important to note that all the chemicals and solvents utilized in the study were of analytical grade, ensuring a high level of quality and accuracy in the experimental procedures.

2.2 Preformulation Studies

2.2.1 Solubility

The solubility of the chosen drug was assessed using standard methods in three different solvents: Distilled water, NaOH solution, and 0.1N HCl solution. This investigation aimed to understand the drug's solubility profile across a range of pH conditions and solvent compositions (Annepogu et al., 2020).

2.2.2 Melting point

To determine the melting temperature of sucralfate powder, a specific procedure was followed. Firstly, sucralfate powder was placed inside a glass capillary tube, which had been sealed at one end. This capillary

tube, with the sucralfate sample, was then attached to a thermometer using a rubber band. The entire setup was submerged in a container filled with liquid paraffin, specifically within a Thiel's tube (Nizamuddin et al., 2020).

The process involved heating Thiel's tube, which in turn heated the liquid paraffin and consequently the capillary tube with the sucralfate sample. As the temperature increased, the sucralfate within the capillary tube would undergo a phase transition from solid to liquid, i.e., it would melt. The thermometer was used to monitor the temperature of the liquid paraffin, which reflected the temperature of the sample inside the capillary tube.

By observing the temperature at which the sucralfate sample underwent the phase transition and turned into a liquid, the melting temperature of sucralfate could be determined. This information is valuable for understanding the drug's physical characteristics and behavior under different temperature conditions.

2.2.3 Fourier Transform Infrared Radiation (FTIR)

FTIR (Fourier Transform Infrared) spectroscopy studies were conducted to investigate the interaction between the pure drug and various excipients, including Gellan gum, HPMC K100M, Sodium Citrate, and Calcium Carbonate, which were components of an in-situ gel formulation. The spectra of the pure drug were compared to those of the drug mixed with different polymers. The FTIR analysis was performed using an instrument called Tensor 27, and the KBr pellets method was employed for sample preparation. This analytical approach allows for the identification of spectral peaks and shifts, revealing any chemical interactions or bonds formed between the drug and the excipients. The study aimed to understand the compatibility and affinity between the drug and the mentioned polymers, which are crucial for the successful formulation of the in-situ gel product.

2.3 Estimation of Sucralfate

The spectrophotometric estimation of Sucralfate involves measuring the extinction of light at 281nm in a 0.1N HCl solution. This method is used to determine the concentration of Sucralfate, a medication for gastrointestinal ulcers. The absorbance at 281nm corresponds to the presence of Sucralfate, and a calibration curve is constructed using known concentrations of Sucralfate to relate absorbance to concentration. The choice of 281nm is based on the molecule's absorbance properties, while the solvent, 0.1N HCl, facilitates analysis. Potential limitations include interference and impurities, but overall, this spectrophotometric approach offers a reliable means of quantifying Sucralfate in solution (Turssi et al., 2019).

2.4 Standard Calibration curve of Sucralfate in 0.1N HCl

Sucralfate weighing 100mg was added to a 100ml volumetric flask and dissolved in 0.1N HCl to create Stock Solution 1. From this stock, 10ml was pipetted into another volumetric flask and diluted to 100ml with 0.1N HCl, resulting in the preparation of a secondary solution. By pipetting appropriate volumes from this secondary solution, a series of concentrations (5, 10, 15, 20, and 25µg/ml) were prepared. The absorbance of these solutions was measured using a UV Spectrophotometer at 281nm, allowing for the construction of a calibration curve relating absorbance to concentration for Sucralfate. This method enables the quantitative determination of Sucralfate concentrations using spectrophotometric analysis based on its absorbance properties at 281nm wavelength (Ahmed & Ahmed, 2022).

2.5. Method of preparation of In-situ gel

The Sucralfate In-situ gel was formulated using the Ion-activated method. The preparation involved the following steps: Gellan gum, HPMC K100M, and Sodium Citrate were added to a beaker containing 1/3rd of the

required amount of water. The mixture was stirred using a magnetic stirrer at a temperature of 60°C. In a separate beaker, Sucralfate, calcium carbonate, and Sacharrin were combined and stirred on a magnetic stirrer(Kesarla *et al.*, 2016). The solutions from both beakers were then mixed, and the volume was adjusted to a final volume of 100ml. This method allows for the creation of a gel that responds to ion activation, with the components coming together to form the desired In-situ gel containing Sucralfate (Table 1).

Table 1 Formulation of In-situ Gel of Sucralfate

Ingredients (g)	Formulations								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Sucralfate	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Gellan gum	0.25	0.25	0.50	0.50	0.85	1.25	1.25	1.50	1.75
HPMC K-100M	0.50	0.75	1.0	0.50	0.75	1.0	0.50	0.75	1.0
Sodium citrate	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Calcium chloride	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Sodium saccharine	0.005	0.005	0.005	0.005	0.005	0.005	0.005	0.005	0.005
Methyl Paraben	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Deionized water	100	100	100	100	100	100	100	100	100

2.6 Evaluation of in-situ gel

2.6.1 Physical Appearance & Clarity

The appearance of all the formulated solutions was visually assessed for clarity and overall physical characteristics. This evaluation involved observing the visual clarity and homogeneity of the solutions. The purpose of this assessment was to determine if the formulations resulted in clear and uniform solutions or if there were any signs of precipitation, phase separation, or other undesirable changes in appearance. This visual inspection provides initial insights into the compatibility and stability of the prepared formulations, which are important factors in the development of pharmaceutical products like In-situ gels (Abdul Ahad et al., 2011).

2.6.2 pH measurement

The pH of each prepared solution in all formulations was determined using a digital pH meter at a temperature of 25±0.5°C. Prior to measuring the pH, the pH meter was calibrated using standard buffer solutions with pH values of 4, 7, and 9.2. After calibration, the pH meter was used to measure the pH of the prepared solutions. The pH measurements were taken as an average of three independent measurements to ensure accuracy and consistency. This procedure was carried out to assess the acidity or alkalinity of the solutions, which is a critical parameter in pharmaceutical and chemical formulations as it can influence the stability, efficacy, and potential interactions of the products (Shravani et al., 2021).

2.6.3 Viscosity Study

Viscosity determination was conducted using a Brookfield DVT viscometer equipped with an LV-3 spindle. The sample was placed in a sample holder, and the angular velocity was incrementally increased for measurement. The angular velocities used were 0.3, 0.6, 1.5, 3, 6, 12, 30, and 60 rpm. Each angular velocity was applied after a 30-second interval. These measurements were performed at room temperature. The viscometer's LV-3 spindle is designed to provide specific rotational speed and torque conditions for viscosity assessment. This experimental setup allowed for the characterization of the flow properties and viscosity of the prepared solutions, which is crucial information for understanding their behavior and potential applications (Sree et al.).

2.6.4 Floating Behaviour

The time required for the gel to travel from the bottom to the top position of the dissolution flask is referred to as the "floating lag time" or "buoyant time." This parameter is particularly relevant for floating dosage forms or formulations that are designed to remain buoyant on the surface of a dissolution medium (Bashir *et al.*, 2019).

To assess the floating lag time, a visual inspection can be conducted using the USP dissolution apparatus. In this setup, the dissolution apparatus contains 900 ml of a dissolution medium, specifically 0.1N HCl, which is maintained at a temperature of 37±0.5℃. The test involves placing the formulated gel in the dissolution medium and observing the time it takes for the gel to rise from the bottom to the top position of the dissolution flask. This floating lag time is an important parameter for evaluating the performance of floating dosage forms and their ability to remain buoyant in the gastric environment. By measuring and analyzing the floating lag time, researchers and pharmaceutical formulators can gain insights into the effectiveness of the formulation in achieving its intended floating behavior and potentially controlling the release of the active pharmaceutical ingredient (Rajinikanth et al., 2007).

2.6.5 Gelling Time

A 5ml aliquot of the prepared formulation was combined with 0.1N HCl in a beaker. The mixture was then observed for the process of gelation. The time taken for the gelation process to initiate and complete was recorded, and this time interval is referred to as the "gelling time." Additionally, the overall integrity and consistency of the formed gel were visually inspected. The gelling time provides valuable information about the kinetics of the gelation process, indicating how quickly the formulation transitions from a liquid to a gel-like state. This parameter is significant in understanding the formulation's behavior upon interaction with the environment it is intended for. Furthermore, the visual assessment of the gel's integrity allows for an evaluation of its stability, cohesion, and ability to maintain its structure during gelation. These observations are critical for ensuring the reliability and performance of the in-situ gelling system, which aims to provide controlled and sustained drug release or other targeted effects (Devasani et al., 2016).

2.6.6 In Vitro Gelling Capacity

The formulation was mixed with 0.1N HCl in a specific ratio of 3 parts formulation to 15 parts HCl. The mixture was then observed for the occurrence of gelation. To denote the gelling capacity or characteristics, different symbols were used (Pandya et al., 2013):

(+): Gelation occurred after a few minutes, resulting in a weak gel formation.

(+ +): Immediate gelation was observed, and the gel formation was good.

(+ + +): Immediate gelation occurred, and the resulting gel formation was stiff.

These symbols represent a visual shorthand for indicating the speed and strength of the gelation process. The combination of symbols and descriptions helps communicate the gelling behavior and capacity of the formulated in-situ gelling system. This qualitative observation provides insights into the formulation's ability to form a gel under specific conditions, which is essential information for further development and optimization of the in-situ gel product.

2.6.7 Drug Content Uniformity

A 1 ml aliquot of the solution was added to 100 ml of 0.1N HCl and stirred for a duration of 1 h using a magnetic stirrer. Following the stirring period, the solution was filtered to remove any particulate matter. The filtered solution was then appropriately diluted using 0.1N HCl. To determine the drug content within the solution, a UV Visible Spectrophotometer was employed. The spectrophotometer measurements were taken

at a wavelength of 253 nm, which is the specific wavelength for detection. A blank solution, serving as a reference, was also measured. By comparing the absorbance of the sample solution to the blank, the drug content within the solution could be quantified (Shaik & Rajasekaran, 2021). This method is commonly utilized to assess the concentration of a specific compound, in this case, likely the drug present in the solution, using its characteristic absorbance properties (e.q.1).

$$\% \text{ Drug Content} = \frac{Drug\ content}{Labelled\ clain} X100 \text{--- (1)}$$

2.6.8 In Vitro Dissolution Studies

For drug release studies, a USP type II apparatus was utilized. The studies were conducted at a controlled temperature of 37±0.5°C, and the rotation speed of the apparatus was set at 50 rpm. As the dissolution medium, 0.1N HCl with a volume of 900 ml was employed. In the experiment, 10 ml of the formulated solution was introduced into the dissolution medium. At predetermined intervals, 1 ml of the sample was withdrawn from the dissolution medium. To maintain the volume and conditions, the withdrawn sample was immediately replaced by adding 0.1N HCl to the dissolution medium up to the mark. The samples collected at each time point were analyzed using UV spectrophotometry at a wavelength of 281 nm. This specific wavelength was chosen as it likely corresponds to the absorbance maximum of the drug in the samples. The UV spectrophotometer provides insights into the concentration of the drug released over time, allowing for the assessment of drug release kinetics from the formulated solution under specified conditions (Shaik & Rajasekaran, 2021).

2.6.9 Kinetics of drug release

To analyze the *in-vitro* drug release kinetics, data obtained from in-vitro drug release studies were subjected to different kinetic models viz., Zero-order kinetics (The percentage of drug released was plotted against time); First-order kinetics (The logarithm of the percentage of drug retained was plotted against time); Higuchi model (The percentage of drug released was plotted against the square root of time); Korsmeyer-Peppas model (The logarithm of the percentage of drug released was plotted against the logarithm of time). By comparing the coefficient of determination (r^2 values) obtained from these different models, the most appropriate or "best-fit" model was selected. The model with the highest r^2 value indicates the one that best describes the drug release kinetics for the particular formulation under investigation. The chosen model helps in understanding and predicting the underlying mechanisms of drug release from the formulated solution and aids in optimizing the formulation for desired release profiles (Chinthaginjala et al., 2019; Harsha et al., 2020; Hindustan et al., 2010).

3. Results

3.1 Drug Description, and Solubility

Sucralfate is a white-colored solid compound that lacks any distinctive odor. Sucralfate's solubility characteristics indicate that it is practically insoluble in water, meaning it doesn't dissolve to a significant extent in water. However, it is soluble in NaOH, and it is freely soluble in a solution of 0.1N HCl. This solubility behavior can be essential for its pharmaceutical applications, as it might affect how it dissolves and interacts with different physiological conditions, such as those found in the stomach (HCl environment) or other situations where sodium hydroxide might be used for solubilization.

3.2 Melting Point results

When tested, Sucralfate demonstrates a melting point of approximately 220±2.1°C. This specific temperature indicates the point at which the solid Sucralfate transforms from a solid state to a liquid state as a result of

increasing temperature. Melting point information is valuable for understanding the compound's thermal behavior and stability, and it can be crucial for processes involving its formulation, handling, and application.

3.3 Calibration curve

The standard calibration curve of Sucralfate in 0.1N HCl is represented by the equation y = 0.0813x + 0.0177, where "x" is the concentration of Sucralfate and "y" is the corresponding absorbance value. The r^2 associated with this calibration curve is 0.9928 (Fig. 1). This high r^2 value indicates a strong linear correlation between the concentration of Sucralfate and the observed absorbance values, suggesting that the calibration curve is a reliable representation of the relationship between these variables. This calibration curve is instrumental in quantitatively determining the concentration of Sucralfate in samples using the absorbance data obtained from a UV spectrophotometer at the specified wavelength.

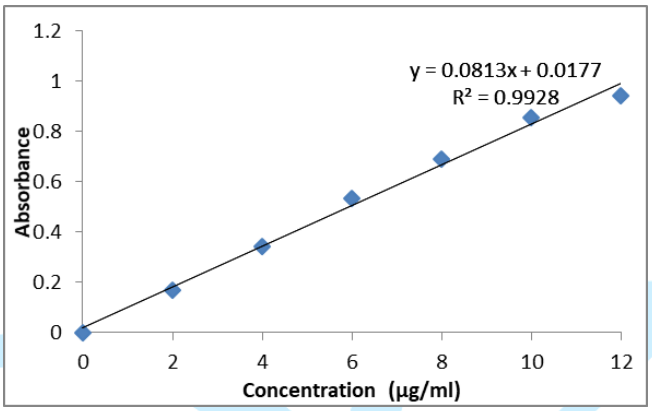

Fig. 1 Standard Calibration Curve of Sucralfate in 0.1N HCl

3.4 Results of FTIR spectra

The distinctive peaks and spectral features of Sucralfate, both individually and in combination with the utilized excipients, were in accordance with the information provided in Table 2 and visually represented in Fig. 2.

Table 2 Interpretation of FTIR Spectral data of Sucralfate

Functional Group	Sucralfate frequency	Sucralfate+Gelrite+HPMC
O-H Stretching Aliphatic	3398	3880
C-O Stretching	1634	1371
C-C Stretching pyran ring	1225	1125
C-C Stretching furan	1053	1243
C-C bending in Mon substituting ring	998	954

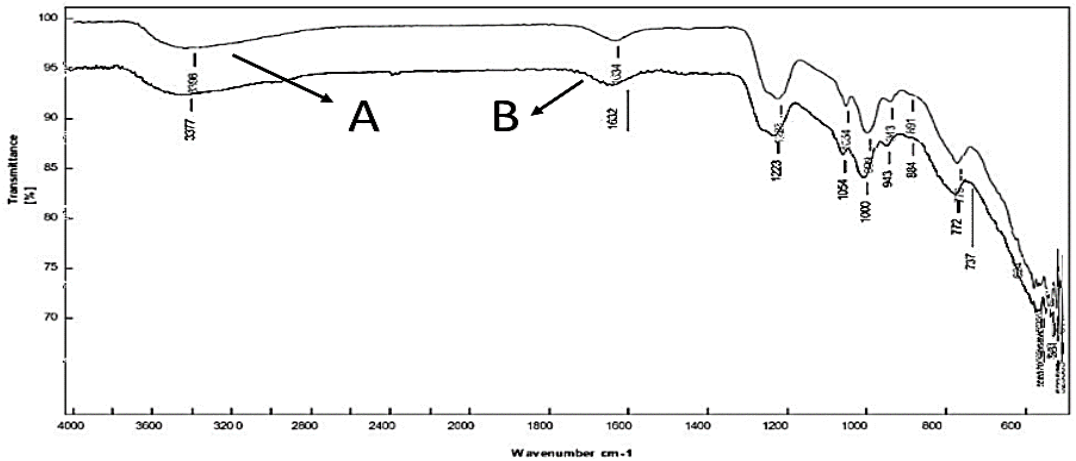

Fig. 2 FTIR overlay spectra of A) Sucralfate; B) Sucralfate with excipients

3.5 Physical Appearance & Clarity

The prepared gels were clear and transparent. This observation suggests that the formulation and combination of ingredients were successful in creating gels with desirable visual characteristics. Clear and transparent gels are often indicative of good homogeneity and uniform dispersion of the components, which can contribute to the overall quality and effectiveness of the final product.

3.6 pH values

It's notable that the pH values of all the prepared gels were found to be near neutral. The pH values ranged from 6.48 ± 0.45 (for F-3) to 7.15 ± 0.05 (for F-6). Maintaining a pH close to neutral is often important for the compatibility of the formulation with the physiological conditions it will encounter, such as the body's internal environment. This pH range is generally well-tolerated and less likely to cause irritation or discomfort when applied or administered. The consistency of the pH values across the formulations suggests careful formulation and appropriate choice of excipients to achieve these desired pH levels.

3.7 Viscosity values

At a shear rate of 0.3 RPM, the viscosity of the formulations showed a range from 8000 cps (F-1) to 20000 cps (F-9). Conversely, at a higher shear rate of 60 RPM, the viscosity of the formulations demonstrated a different spectrum, spanning from 200 cps (F-1) to 260 cps (F-9) (Fig. 3). This suggests that the viscosity of the formulations was influenced by the shear rate, highlighting the shear-thinning behavior typical of many complex fluids. Such variations in viscosity under different shear conditions could have implications for the formulations' behavior during processing and application.

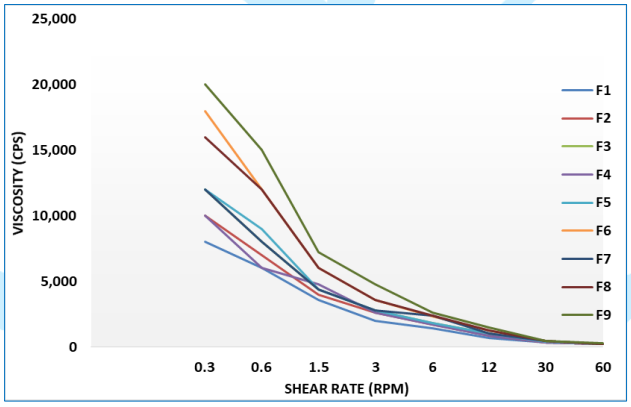

Fig. 3 Viscosity formulation of F1-F9

3.8 Floating behaviour

The formulations, ranging from F1 to F9, demonstrated a noticeable reduction in floating lag time as they progressed. This trend indicated that the time it took for these formulations to start floating decreased gradually from F1 to F9 (Fig. 4A).

Moreover, formulations F7, F8, and F9 exhibited favorable floating times. In these specific formulations, the ability to remain afloat was satisfactory and consistent, implying that they maintained their buoyancy effectively over the designated period (Fig. 4B). This variation in floating behaviors among the formulations underscores their potential differences in terms of floating and dissolution characteristics, which are important factors in certain applications like gastro retentive drug delivery systems.

3.9 Gelling time and in vitro gelling capacity

The gelling capacity of the formulations was assessed, and it was found that certain formulations had different behaviours in terms of their gelation properties. Specifically, formulations F5, F6, F7, F8, and F9 displayed a positive outcome in terms of their gelling capacity (Fig. 4C). These formulations exhibited an immediate

gelation effect that remained consistent for an extended period of time. In contrast, the gelling capacity of formulations F1, F2, F3, and F4 was also evaluated. These formulations demonstrated an initial gelation response that occurred promptly after application. However, this gelation effect was not as enduring as that observed in the first group of formulations. In these cases, the gelation remained effective for only a few hours before gradually losing its strength. Formulations F5, F6, F7, F8, and F9 displayed a desirable and sustained gelling capacity, while formulations F1, F2, F3, and F4 showed an immediate but relatively short-lived gelation effect. This distinction in gelling behaviors among the formulations highlights the potential variations in their practical applications and stability over time

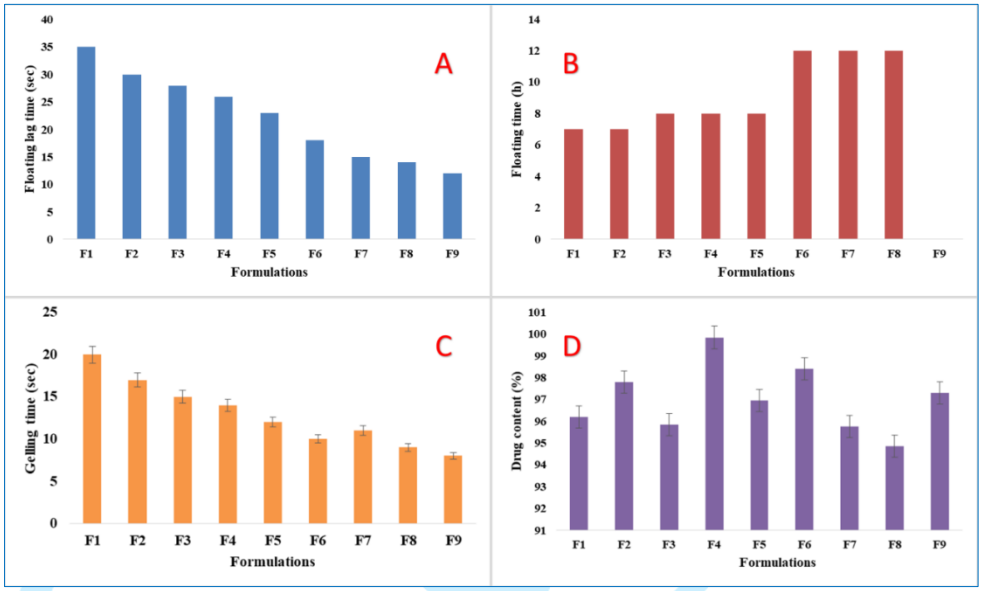

Fig. 4 A) Floating lag time B) Floating time C) Gelling time D) Drug content of in situ gelling formulation (F1-F9)

3.10. In vitro release

The study encompassed formulations labeled as F1 to F9, and these formulations displayed distinct levels of drug release during *in vitro* testing. Specifically, the percentages of drug release were recorded as follows: 71.37%, 68.19%, 66.36%, 81.36%, 71.61%, 50.47%, 79.41%, 69.91%, and 60.61% respectively for F1 through F9. Notably, among the array of formulations, formulation F4 showcased the highest drug release percentage, reaching 81.36%. On the opposite end of the spectrum, formulation F6 exhibited the lowest drug release percentage, which was measured at 50.47%. This variance in drug release levels across the formulations indicates the diversity in their potential effectiveness and performance as drug carriers or delivery systems.

The data concerning the release of sucralfate was additionally examined using kinetic graphs, specifically Zero-order, first-order, Higuchi model, and Korsmeyer-peppas, in order to determine the pattern of sucralfate release from the in situ gel (Table 3).

Table 3 Kinetics Drug Release from sucralfate in situ gels

Formulation	Zero-order	First order	Higuchi model	Korsmeyer-peppas	
				R^2	n
F1	0.9721	0.5893	0.9542	0.9482	0.59
F2	0.8189	0.4079	0.8524	0.8359	0.28
F3	0.7921	0.3844	0.9670	0.9176	0.27
F4	0.7777	0.3657	0.9388	0.8816	0.25
F5	0.8716	0.4433	0.9535	0.9288	0.03
F6	0.8174	0.4185	0.9805	0.9695	0.32
F7	0.7881	0.3733	0.9623	0.9452	0.27
F8	0.6812	0.3325	0.9299	0.8534	0.19
F9	0.7393	0.3619	0.9236	0.889	0.22

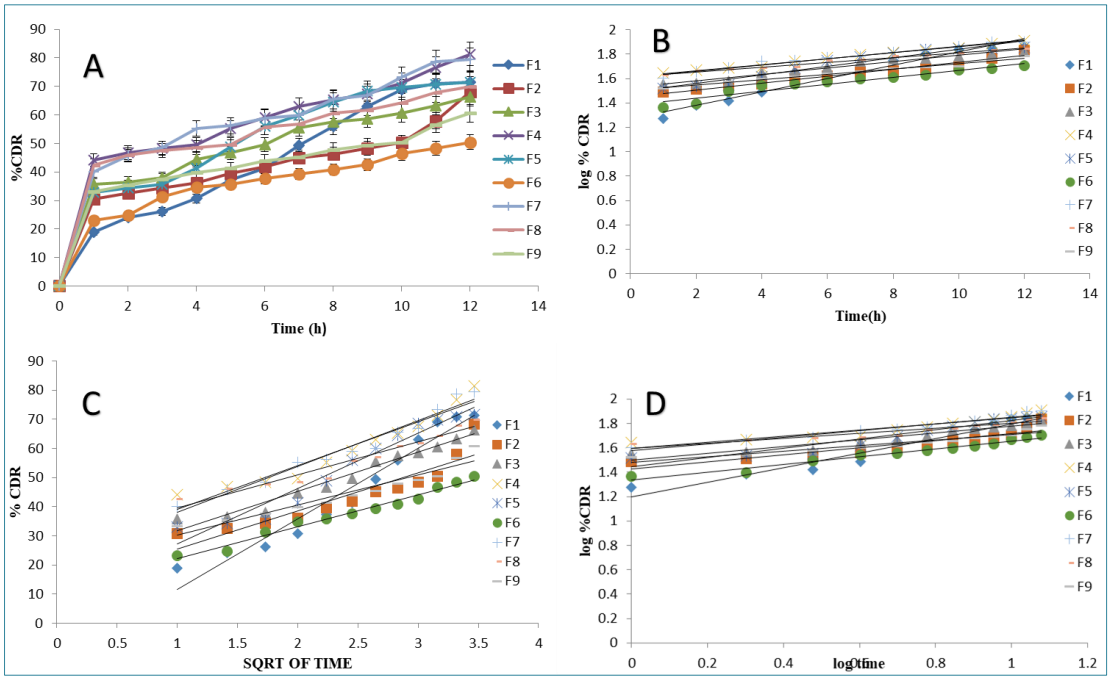

Fig. 5 A) Zero-order; B) First-order; C) Higuchi; D) Korsmeyer-peppas models for the Sucralfate in situ gels

4. Discussion

The evaluation of organoleptic properties is a critical initial step in pharmaceutical analysis. It involves assessing sensory attributes like colour, odour, and overall appearance of a drug. These attributes are compared against predefined specifications provided in literature references. The purpose is to ensure that the drug sample meets the expected sensory characteristics, signifying its quality and conformity. Such study was performed by Bansal et al. (2013) made in situ gel using tamarind seed polysaccharide and observed appreciable organoleptic assets

Solubility analysis is a fundamental test for pharmaceutical substances. It gauges the ability of a drug to dissolve in specific solvents or in the medium used for dissolution testing. For sucralfate, the study revealed its solubility in diluted HCl and NaOH solutions. Nagy et al. (2007) also saw such solubility. This information is crucial as it indicates the drug's behavior in different environments and its potential for effective dissolution in the body.

The melting point is the temperature at which a solid substance transitions to a liquid state. It's an essential parameter that helps verify the purity of a drug sample. In the case of sucralfate, its melting point was found to be 220°C, which falls within an acceptable range. This implies that the procured sucralfate is of high purity and doesn't contain impurities that might affect its melting behavior.

λ_{max} refers to the wavelength at which a substance's absorbance is highest in a spectrophotometric analysis. This analysis is used to determine the optimal wavelength for quantifying the drug's concentration in a solution. In the study, sucralfate's λ_{max} in diluted hydrochloric acid was identified as 281nm. This information aids in designing accurate analytical methods for drug concentration measurement.

Compatibility studies are conducted to assess whether interactions occur between drug and excipient (polymer) components in a formulation. The FTIR technique is commonly used for this purpose. In the case of sucralfate and the chosen polymer, the absence of significant peaks or shifts in the FTIR spectrum indicates that there's no significant interaction between the drug and polymer. This is a positive outcome, as it suggests that the drug and polymer can be used together without compromising their properties.

In-situ gels are formulations that transform from a liquid to a gel state after administration. This transformation can be triggered by factors such as pH, temperature, or ion concentration. The formulations were assessed for their appearance, clarity, and pH to ensure they meet the desired characteristics for oral

administration. The pH measurement is particularly important to prevent any irritation to the throat upon ingestion.

The rheological properties of a formulation, particularly viscosity, are crucial for its intended administration. The viscosity determines how easily the liquid formulation can be swallowed, and it can also impact its ability to transform into a gel after administration. The formulations were analyzed using a Brookfield viscometer at various shear rates. The observed pseudoplastic flow behavior implies that the viscosity decreases as shear rate increases. The order of viscosity among the formulations provides insights into their potential behavior during administration. Such observations were made by Goudoulas & Germann (2019), for gelatin gels and found non-linear flow properties.

Floating behavior is important for oral dosage forms, as it ensures prolonged contact with the gastrointestinal tract, enhancing drug absorption. The formulations were tested for their ability to float in a specific dissolution medium. The floating lag time and duration were measured. The results indicate that higher polymer concentrations lead to quicker floating times and prolonged floating duration due to the entrapment of CO_2 bubbles. Thomas (2014) observed such floating behavier in metronizazole in situ gel.

The in vitro drug release study measures how a drug is released from a formulation over time. The formulations were tested in a simulated stomach environment. The zero-order release kinetics observed indicate a constant rate of drug release, which is desirable for controlled drug delivery. Gupta & Sharma (2009) also seen such findings in clindamycin in-situ gel.

Different mathematical models are used to analyze and interpret in vitro drug release data. These models include zero order, first order, Higuchi, and Korsmeyer-Peppas. The highest regression value for zero order kinetics suggests that the drug release follows a consistent pattern dependent on polymer concentration. The Korsmeyer-Peppas model indicated that the drug release mechanism is Fickian, implying diffusion-controlled release.

Choosing the optimal formulation is crucial for drug delivery systems. It involves considering factors such as viscosity, drug content, and in vitro drug release. Formulation F4 emerged as the preferred choice due to its balanced attributes. It exhibited suitable gelling capacity, viscosity, drug content within USP limits, and efficient drug release behavior.

5. Conclusion

In this study of the development and assessment of an in situ gel formulation designed to address stomach ulcers, the primary objective was to ensure the sustained delivery of the drug within the stomach over an extended duration. Utilizing the ion-activated method, in situ gel containing Sucralfate was successfully formulated. Several formulations (F1-F9) were meticulously crafted, utilizing varying concentrations of Gelrite and HPMC K 100M as essential excipients. Gelrite served as the gelling agent, HPMC K100M played a dual role as a release retardant and viscosity enhancer, calcium chloride facilitated cation-induced gelation, and sodium citrate was incorporated to prevent premature gelation prior to reaching the stomach. The analysis revealed a direct relationship between the polymer concentration and various properties of the developed gelling system. As polymer concentration increased, characteristics like viscosity exhibited a corresponding rise, underscoring the significant influence of polymer levels on formulation properties. After careful evaluation, Formulation F4 emerged as the optimal choice due to its exceptional gelling capacity and optimal viscosity. Importantly, the results obtained from release kinetics highlighted that drug release from the ion-activated in situ gel followed a Fickian mechanism, in alignment with a zero-order kinetic model. This mechanism signifies controlled diffusion-driven drug release, contributing to the effectiveness of the formulated gel as a drug delivery system. This study provides an intricate understanding of the formulation's potential to effectively deliver the drug, addressing stomach ulcers. The comprehensive assessment undertaken sheds light on critical parameters impacting the gel's performance and its potential application in treating gastric ailments.

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Declaration of Conflict

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