

Design And In-Situ Performance, Evaluation Of A Floating Gel Loaded GRDDS Of *Centella Asiatica* Leaf Extract

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ABSTRACT

The allopathic healthcare system provides several conventional ways of treatment for ulcer but they have some limitations. As a result, turning to an herb-induced formulation that is safe, effective, and proven would be a better choice. The present investigation focused on the development of a sustained-release gastric floating system incorporating *Centella asiatica* extract to improve its anti-ulcer efficacy and gastric retention. The floating in-situ gel of *Centella asiatica* provides extended drug availability in the stomach, thereby reducing the need for frequent dosing, improving patient compliance, and minimizing potential side effects. *Centella asiatica* leaf extract, rich in asiaticoside and madecassoside, for anti-ulcer effects. It is extracted via hot maceration. The extract was formulated into gels (F1-F3) using sodium alginate, HPMC K100, sodium bicarbonate for buoyancy, and calcium carbonate/sodium citrate for ionic cross-linking. Formulations were characterized for pH, gelling capacity, buoyancy, floating lag time, drug content, viscosity, gel strength, density, and swelling index. F2 showed superior performance with 30s lag time, 12hr floating, and 88.6% drug release over 8hr in 0.1N HCl (pH 1.2), confirmed compatible by FTIR. Results validate F2 as an optimized GRDDS enhancing gastric retention, patient compliance, and therapeutic efficacy of herbal extracts over conventional forms.

Keywords: Floating system, In-situ gel, low density, Sodium alginate, gastric retention, sustained release.

INTRODUCTION

Oral drug administration is the most convenient and preferred route of drug delivery due to its ease of administration, improved patient compliance, and flexibility in formulation design. Despite these advantages, conventional oral dosage forms often suffer from limitations such as short gastric residence time, rapid gastric emptying, and inconsistent drug absorption, which can result in reduced therapeutic efficacy. To overcome these limitations, the gastroretentive drug delivery system has emerged as a highly promising strategy. The primary objective of GRDDS is to retain the drug formulation within the stomach for an extended time period and facilitate the sustained release of the drug. Numerous studies have explored different methodologies to enhance the duration of gastric residence and controlled drug concentration level in the bloodstream. Among these approaches, the development of a floating in-situ gel

system has received considerable attention, mainly because of the advantages shown by this system.

Floating in-situ gel drug delivery systems have been used to deliver many drugs, which are used either systemically or for their local effects in the stomach. In-situ-forming polymeric formulations remain in a sol state before administration and undergo gelation in situ under physiological conditions to form a gel. Floating in situ gels are capable of remaining buoyant in the stomach so as to maintain gastric residence time and allow controlled drug release. Polymers play a major role in floating drug delivery systems. The selection of polymers is important to determine the gelation behaviour, floating ability, mechanical strength, and drug release characteristics of the formulation. Sodium alginate and HPMC k100 are polymers that are responsible for the formation of a stable gel, sodium bicarbonate ensures effective floating, and calcium carbonate and sodium citrate are

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responsible for cross-linking and controlling gelation, respectively.

A disruption of the balance between mucosal defensive factors like mucus, bicarbonate, prostaglandins, and blood flow and aggressive factors like acid, pepsin, *Helicobacter pylori* infection, and non-steroidal anti-inflammatory drugs (NSAIDs) causes a gastric ulcer, a localized defect in the gastric mucosa that penetrates the muscularis mucosae. The mucosal barrier is weakened by oxidative stress and persistent inflammation, resulting in chronic ulceration that can worsen and cause upper gastrointestinal bleeding, perforation, obstruction of the gastric outlet, and an elevated risk of gastric cancer. Therefore, despite advancements in acid suppression and *H. pylori* eradication therapy, peptic ulcer disease, especially stomach ulcers, continues to be a major global health concern.

In recent years, there has been growing interest in the use of herbal drugs for the management of gastric ulcers due to their safety, biocompatibility, and reduced side effects compared to synthetic drugs. Some studies have shown the protective and healing effect of the *Centella asiatica* (CA) extract and its active pentacyclic triterpenoid compounds, especially asiaticoside (AS) and madecassoside (MS), on gastric ulcers. Oral administration of CA extract significantly inhibits gastric lesion formation in rats (induced by ethanol) by decreasing mucosal damage and improving the integrity of the gastric mucosal lining in *ex vivo* models. The anti-inflammatory effect of both AS and MS has been reported in the model of collagen-induced arthritis in mice. Their mechanism of action might be related to the reduction of COX-2 expression and inflammatory cytokines or the inhibition of lymphocyte proliferation. The creation of a floating in situ gel system presents a promising platform to boost local action, extend drug residence time, and guarantee the drug's sustained release within

the stomach, given the therapeutic significance of CA and the requirement for extended gastric retention. Ionic cross-linking, temperature modulation, pH changes, and other stimuli can all cause in situ gel formation. Ionic cross-linking is the foundation of our in-situ gel work. In situ gels are therefore supplied via ocular, rectal, vaginal, injectable, and intraperitoneal methods in addition to the oral route. Due to their different types of mechanisms. The extraction process is crucial in producing the active phytoconstituents, which directly affect the formulation and whose behaviour is mostly dictated by the extraction method. In order to promote gastric retention and prolonged medication release in the treatment of gastric ulcers, our study intends to generate a CA extract using the maceration process in order to acquire a high content of phytoconstituents. The extract will then be incorporated into a floating in situ gel formulation.

MATERIALS AND METHODS

MATERIALS

Sodium alginate was purchased from Isochem Laboratories, Kerala. Sodium bicarbonate and calcium carbonate were bought from Nice Chemicals Private Limited, Ernakulam, Kerala, India. Sodium citrate, HPMC K100, and preservatives were purchased from BRM chemicals Chennai, Tamilnadu. Ethanol was bought from Changshu Hongsheng Fine Chemical Co., Ltd. Distilled water was bought from a local chemical shop, Kanchipuram. All materials were stored at room temperature ($25^{\circ}\text{C} \pm 2^{\circ}\text{C}$) and $60\% \pm 5\%$ relative humidity before use.

PLANT COLLECTION

Fresh leaves of *Centella asiatica* were harvested from the natural source, Kanchipuram. The botanical identity was confirmed by the Siddha Central Research Institute at Arumbakkam, Chennai.



**Fig. 1: Centella asiatica****Fig. 2: Fine powder process****Fig. 3: #60 mesh sieve**

EXTRACTION

Hot maceration

The harvested plant material was washed with distilled water to remove surface contaminants; shade dried at room temperature (22–25°C) for [10-14 days]

until constant weight was achieved. The dried material was then ground into fine powder using a mechanical grinder and passed through a No. #60 mesh sieve to obtain uniformly sized particles. The powder was stored in airtight containers at 4°C,



protected from light, until further use. Accurately weigh the 15g of *C. asiatica* powder into the iodine flask containing 75 ml of solvent (ethanol) in a 1:5 ratio. Place the iodine flask on the heating mantle at 60°C for 120 minutes with continuous shaking. After

the extraction process filtrate was collected and the marc was re-extracted for 2 times with the same solvent volume. The collected filtrates were subjected to a rotary evaporator.



Fig. 4: Hot maceration



Fig. 5: Extraction of centella asiatica

PREPARATION METHOD

Sodium alginate solution was prepared in distilled water containing sodium citrate and heated at 60°C with continuous stirring after cooling down to 40°C, dissolve HPMC k100 by using distilled water, and added to the above solution. Stir well by using a magnetic stirrer until a homogenous solution is obtained and free from any visible particles.

Add Calcium carbonate and sodium bicarbonate to the above solution. Finally, powdered drug (CA), along with preservatives, was added to make the in-situ gel.

Table. 1: Formulation table

INGREDIENTS	F1	F2	F3
Powdered CA extract	1%	1%	1%
Sodium alginate	2%	4%	5%
HPMC k100	0.5%	0.5%	----
Sodium bicarbonate	1.5%	1.5%	1.5%
Calcium carbonate	0.750%	1%	2%
Sodium citrate	0.25%	0.25%	0.25%

Methyl paraben	0.18%	0.18%	0.18%
Propyl paraben	0.02%	0.02%	0.02%
Deionised water	Up to 100ml	Up to 100ml	Up to 100ml

EVALUATION OF FLOATING IN-SITU GEL

1. FTIR (FOURIER TRANSFORM INFRARED)

The compatibility of the drug with the polymer was assessed using Fourier Transform Infrared (FTIR) spectroscopy to investigate possible interactions between *Centella asiatica* extract and the excipients used in the in-situ gel formulation. FTIR spectra were obtained with an FTIR spectrophotometer employing the potassium bromide (KBr) pellet method.

The pure extract and the optimized formulation were separately combined with KBr in a 1:10 ratio and compressed to create transparent pellets. These pellets were examined over a spectral range of 400–4000 cm^{-1} . The spectra obtained from both the extract and the formulation were analyzed and compared to identify any alterations such as peak shifts, loss of peaks, or the emergence of new absorption bands.

2. PHYSICAL APPEARANCE

The physical appearances of all the prepared floating in-situ gel were observed for color, transparency before and after gelation.

3. pH MEASUREMENT

The pH of the in-situ gel was measured by using a previously calibrated digital pH meter at room temperature by taking an adequate amount of floating in-situ gel in a 50 ml beaker.

4. IN-VITRO GELLING CAPACITY

In-vitro gelling capacity can be evaluated visually. It was measured by placing 10 ml of the gelation solution (0.1N HCl, pH 1.2) in a borosilicate glass test tube and maintaining it at $37 \pm 1^\circ\text{C}$ temperature. One milliliter of the formulation solution was added to the test tube containing 10 ml of gelation solution with the help of a pipette.

The prepared formulation was transferred in such a way that it placed the pipette at the surface of the fluid in a test tube, and the formulation was slowly released from the pipette. As the solution comes in contact with the gelation solution, a sol-gel transition occurs.

The gelling capacity of the formulation was evaluated based on the stiffness of the formed gel and the time period for which the gel remains as such.

The in-vitro gelation capacity was graded into 3 categories based on gelation time and the time period for which the gel retained its properties.

(+) gels dispersed rapidly after a few minutes.

(++) immediate gelation, which remains for 12 hrs.

(+++ immediate gelation and remains for more than 12 hrs.

5. IN-VITRO BUOYANCY STUDY

This study was conducted using a Type II USP Dissolution apparatus with 900 ml of simulated gastric fluid (SGF) at pH 1.2 as the dissolution medium, maintained at $37 \pm 0.5^\circ\text{C}$. Ten milliliters of the formulation were transferred to the 500 ml/900 ml SGF using a syringe.

Floating behavior was evaluated based on the time taken for the in-situ gel to float in medium (floating lag time), and the period of time formulation floats on the surface of the medium (duration of floating) was noted by visual observation.

6. DETERMINATION OF DRUG CONTENT

A 100 ml volumetric flask containing 0.1N HCl was filled with 10 ml of the formulated floating in-situ gel, and it was agitated with a magnetic stirrer for an hour.



A UV-visible spectrophotometer was used to measure the absorbance at 278 nm against an appropriate blank solution after the solution had been filtered and appropriately diluted with 0.1N HCl, pH 1.2 medium.

7. IN-VITRO DRUG RELEASE

A USP Type II Dissolution test apparatus with a paddle stirrer rotating at 50 rpm was used to conduct in vitro drug release. Ten millilitres of the gelling solution were added to a Petri dish and placed in a dissolving vessel with 900 millilitres of 0.1N HCl (pH-1.2) at $37 \pm 0.5^\circ\text{C}$ temperature as a release medium without turbulence. At each of the following time intervals (0.5, 1, 2, 3, 4, 6, 7 hours), an aliquot of 5 millilitres was taken out of the dissolution medium (halfway between the paddle and the vessel wall), and the volume was maintained by replacing the removed volume with an equivalent volume of fresh 0.1N HCl (37°C). Immediately after collection, the samples were filtered through a $0.45\mu\text{m}$ membrane filter and appropriately diluted with 0.1N HCl.

8. GEL STRENGTH

A 30 g sample of the formed gel was taken in a 50 ml beaker, and a 50 g weight was carefully placed at the centre of the gel surface. The time required for the weight to penetrate 5 cm through the gel was recorded to evaluate gel strength. The procedure was repeated six times for each fresh formulation, and the average time of penetration was calculated.

9. VISCOSITY

The viscosity of the prepared formulation was determined by using a Brookfield programmable viscometer KL VM-208 with spindle number #2, which was rotated at 60 rpm for 50 sec at the ambient temperature of each formulation. This was done in triplicate.

10. GEL DENSITY

10ml of prepared in-situ gel solution was poured into a beaker containing 50ml of 0.1N HCl (PH 1.2). The converted gel was weighed and taken in a measuring cylinder, and the volume occupied by the gel was calculated using the gel density, following the equation

$$\text{DENSITY} = \text{MASS} / \text{VOLUME}$$

11. SWELLING INDEX

A precisely weighed 100g of formed gel (W1) was placed in a Petri dish containing 50ml of 0.1N HCl and allowed to stand undisturbed for 24 hours. After the specified period, the gel was weighed (W2), and the swelling index was determined using the following equation.

$$\text{SWELLING INDEX} = \frac{W2 - W1}{W1} \times 100$$

RESULT AND DISCUSSION

1. FTIR (FOURIER TRANSFORM INFRA RED)

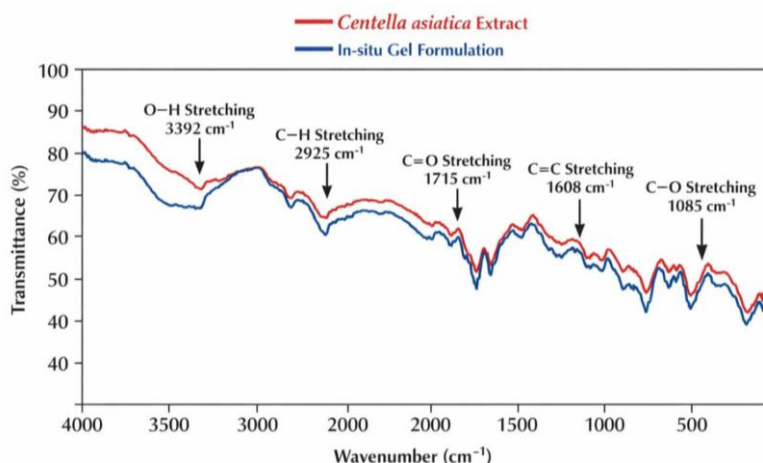


Fig. 6: FTIR of Centella asiatica formulation

Table. 2: FTIR Peak

S.NO	FUNCTIONAL GROUP	VIBRATION	PURE EXTRACT (cm ⁻¹)	FORMULATION (cm ⁻¹)	INTERPRETATION
1.	O-H	stretching	3392	3385	No interaction (hydrogen bond only)
2.	C-H	stretching	2925	2920	Aliphatic C-H
3.	C=O	stretching	1715	1712	Carbonyl compound retained
4.	C=C	Stretching	1608	1605	Aromatic / alkene group
5.	C-C	stretching	1085	1085	Alcohol/ester linkage

The FTIR spectra of pure CA extract and the in-situ formulation are shown in the table.2

The presence of major functional groups such as O-H, C-H, C=O, C=C, and C-C Stretching Vibrations in both spectra confirms the retention of the chemical structure of the extract after formulation.

The absence of new peaks and retention of all major functional groups confirms that there was no chemical interaction between the extract and formulation excipients.

2. PHYSICAL APPEARANCE

All the formulations appear as an off-white to pale colour and are free from turbidity or visible particulate matter before and after gelation.

It appears as a free-flowing solution and does not exhibit gelation at room temperature, but it becomes a stiff gel matrix upon contact with the gastric environment.

**Fig. 7: Physical appearance**

3. pH MEASUREMENT

They had a pH in the range of 7.25-8.13, which is acceptable for the orally administered formulation.

4. IN-VITRO GELLING CAPACITY

In-vitro gelling capacity of various floating in situ gel formulations is reported in the table.3

All the formulations demonstrated immediate gelation with a stiff gel matrix. Among the three formulations, F2 exhibited successful gelation for more than 12 hours when compared to F1 and F3.

This characteristic is advantageous for an in-situ gelling system as it enables prolonged gastric



retention time and sustained release of the drug over time.

Table. 3: In-vitro gelling capacity of floating in-situ gel formulation.

FORMULATION CODE	F1	F2	F3
Gelling capacity	++	+++	++

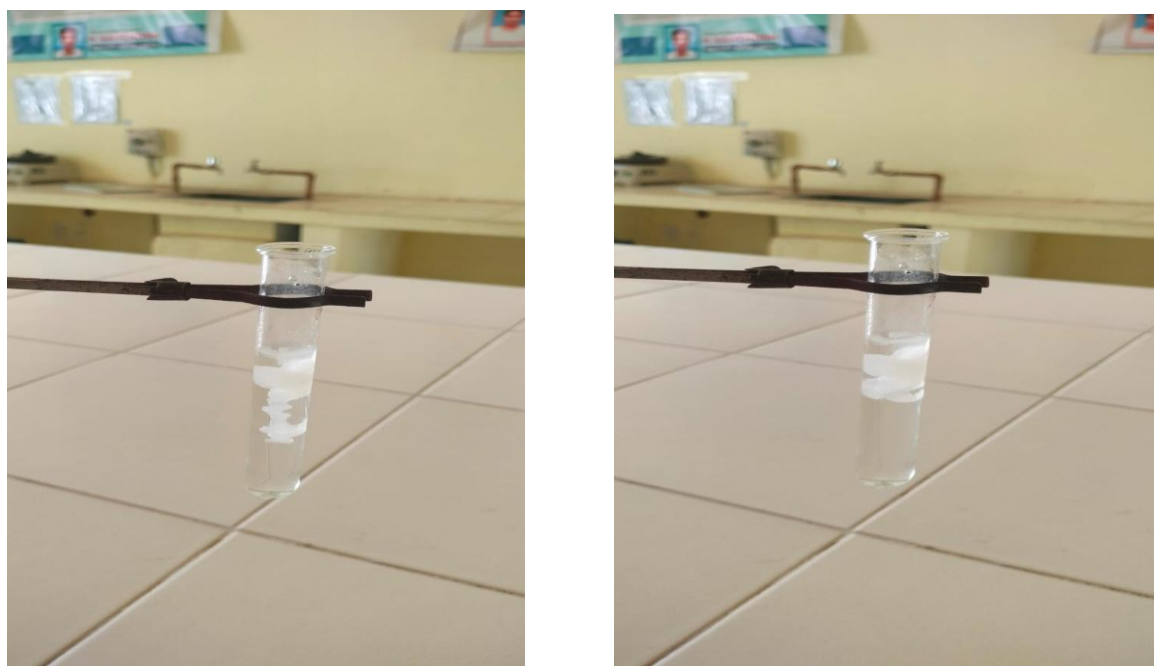


Fig. 8: In-vitro gelling capacity

5. IN-VITRO BUOYANCY STUDY

The buoyancy lag time varied with the formulation variables. The results obtained from the table. 4. It depicts that all the formulations F1 to F3 showed in vitro floating lag time between 30 seconds and 90 secs.

Formulation F2 exhibited the least buoyancy lag time (30 seconds) with a floating duration > 12 hours. While the other formulations, F1 and F3, exhibited the highest lag time of 60 secs and 90 secs respectively, with a floating duration of > 12 hours.

The decrease in the buoyancy lag time of an F2 formulation can be attributed to the increased bioavailability of calcium carbonate, being entrapped in the formed gel to give rapid buoyancy.

Based on the findings, F2 can be considered the best formulation for their immediate gel formulation and extended floating duration. These formulations can potentially provide sustained drug release and improved therapeutic outcomes.

Table. 4: In-vitro buoyancy study of floating in-situ gel formulation.

FORMULATION CODE	F1	F2	F3
Floating lag time (sec)	60	30	90
Floating time (hr)	≥ 12	≥ 12	≥ 12

**Fig. 9: In-vitro buoyancy study**

6. DETERMINATION OF DRUG CONTENT

Table 5 depicts the percentage of drug content for all formulations, which were in the range of 78 ± 0.03 to

74 ± 0.31 . The formulation F2 was found to have a maximum drug content of, indicating homogeneous drug distribution throughout the gel.

Table. 5: Drug content present in various formulations.

FORMULATION CODE	F1	F2	F3
Drug content (%)	78 ± 0.03	81.45 ± 0.03	74 ± 0.31

7. IN-VITRO DRUG RELEASE

A drug release study was conducted for 8 hours using 0.1N HCl (pH 1.2) at $37 \pm 0.5^\circ\text{C}$ temperature as a dissolution medium, and the report shown in Table 6.

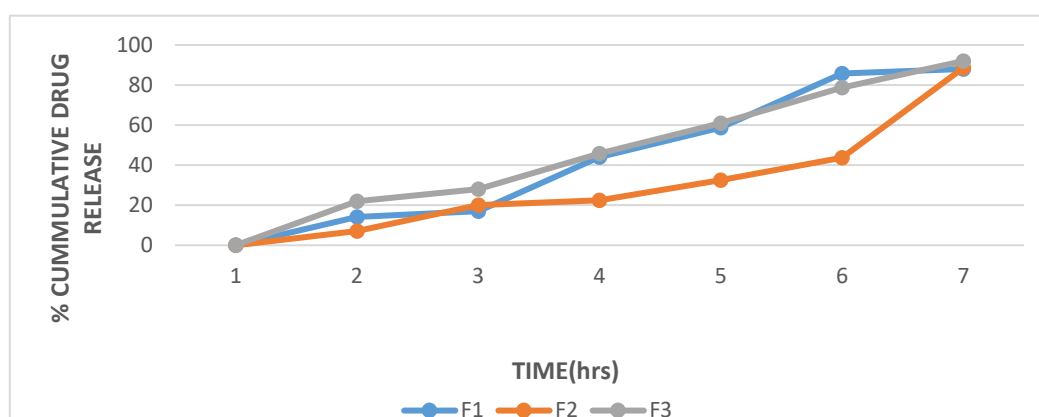
The optimized gel showed an initial burst of approximately 10-20% Centella asiatica within the first hour, attributed to the drug near the gel surface.

It was further followed by a sustained release phase, i.e., 70-80% of the drug release after 8 hours, consistent with prolonged gastric delivery, which is responsible for the ulcer therapy.



Table. 6: In-vitro drug release of a floating in-situ gel.

FORMULATION CODE	0	1	2	3	4	6	8
F1	0	14.10	17.03	44	54.4	62.56	76.66
F2	0	7.09	20.05	22.43	32.45	43.65	69.04
F3	0	22.04	28	45.76	58	70.32	81.76

**Fig. 10: In-vitro drug release**

8. GEL STRENGTH

Gel strength is an important parameter that indicates the ability of a gelled mass to withstand peristaltic movements in vivo and reflects the strength and integrity of the gel structure. In the present study, all formulations exhibited good gel strength, with values ranging from 46.43 ± 0.51 s for formulation F3 to 79.45 ± 0.42 s for formulation F1, as shown in the table. 7.

The higher gel strength observed in F1 and F2 can be attributed to the higher concentrations of sodium alginate and HPMC K100M, which enhance cross-linking and promote the formation of a stronger gel network. The good gel strength of F1 and F2 indicates their ability to resist peristaltic movements within the gastrointestinal tract, maintaining gel integrity during transit. This characteristic is vital for gastroretentive drug delivery systems (GRDDS), as it ensures prolonged retention and sustained drug release.

Table. 7: Gel strength of the floating in-situ gel formulation

FORMULATION CODE	F1	F2	F3
Gel strength	72.75 ± 0.31	79.45 ± 0.42	46.43 ± 0.51



9. VISCOSITY

Determination of viscosity of all the formulations showed that there is a significant change in viscosity of the prepared different concentrations of sodium alginate and HPMC K100 (release retardant) polymer.

The formulation F2 revealed that there is a significant rise in viscosity of the floating in-situ gel solution due to the higher polymer concentration. The formulation viscosities are shown in the table. 8

Table. 8: Viscosity of formulation

FORMULATION CODE	F1	F2	F3
Viscosity (cP)	424.24±0.961	563.37±0.412	326.47±1.236

10. GEL DENSITY

For a system to float, its density must be lower than that of gastric fluid, which is about 1.004 g/cm³. In the present study, the densities of all formulations were measured to be below 1g/cm³, confirming that they

can remain buoyant in gastric conditions. This results in floating for a prolonged period of time. The density of formulation and weight of the gel gradually increased due to the increase in the absorption of water as the concentration of the polymer increased.

Table. 9: Gel density of formulation

FORMULATION CODE	F1	F2	F3
Gel density (g/cm ³)	0.772±0.028	0.839±0.026	0.747±0.024

11. SWELLING INDEX

The in-situ gel formulated with the synthetic polymer HPMC K100M exhibited a higher swelling index over 24 hours than the in-situ gels containing the natural polymers. The maximum water uptake observed for formulation F2 may be attributed to the greater swelling

Capacity of the gum used in the formulation.

Table. 10: Swelling index of the formulation

FORMULATION CODE	F1	F2	F3
Swelling index	44.03±1.69	73.09±1.69	56.19±1.59



CONCLUSION:

To get around the problems with traditional drug delivery methods, we concentrated on creating an in-situ gelling system. The development and assessment of *Centella asiatica*-loaded floating in-situ gel utilizing different polymer concentrations is the focus of our study.

When this solution is introduced into the stomach, it reacts with HCl to generate a floating in-situ gel, which has multiple benefits. First of all, it promotes sustained drug release, prolonged gastric retention, and improved absorption. Patient compliance is improved by the longer residence time in the stomach, which also lowers the frequency of doses and increases therapeutic efficacy. Additionally, the gel matrix maintains the drug's stability and potency by acting as a barrier.

The drug content, viscosity, and sustained drug release of the in-situ formulations were all good. According to this study, oral administration of an aqueous solution comprising sodium alginate and HPMC k100 causes a floating in-situ gel to develop. The concentrations of polymers and other excipients were varied to create three formulations (F1, F2, and F3) while maintaining a constant drug concentration. Out of these three formulations, F2 exhibits exceptional qualities in terms of quick gelation, extended floating time, superior drug content homogeneity, and ideal gel strength.

According to this study, the formulations with the greater concentrations of sodium alginate and HPMC k100 in F2 showed better gelling capability and a higher degree of prolonged drug release, while the right amount of sodium bicarbonate guaranteed excellent floating ability. Sodium citrate and calcium carbonate helped to regulate the polymer matrix's cross-linking and gelation.

The formulation F2 revealed a sustained drug release with stable gel formation and prolonged floating behaviour for more than 12 hours, according to the in-vitro drug release study. Whereas F1 showed faster drug release due to lower polymer concentration, and F3 formed a weak gel matrix because of the lack of HPMC k100 with reduced floating time.

In conclusion, our results highlight the enhanced drug delivery capabilities, sustained release, and improved gastric retention offered by this innovative drug delivery system.

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