RESEARCH PAPER

Formulation and Evaluation of pH-Sensitive In-Situ Gel for Colon-Targeted Drug Delivery

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Abstract

Background: Colon-targeted drug delivery systems (CTDDS) have been exploited as a novel drug delivery system for the treatment of colonic diseases with minimal systemic side effects. One of the strategies has been a particular attention that has been paid to the in situ pH-sensitive gel system that can change from sol to gel in the physiological pH of the colon. These systems mean better retention, longer duration of time spent in circulation, sustained release of the drug, and greater therapeutic effectiveness. Colon-specific drug delivery has been shown to have excellent pH-responsive gelation properties for polymers like sodium alginate, gellan gum, carbopol, chitosan, or methacrylic acid copolymer.

Objective: In the present study, a pH-sensitive in-situ gel for targeted delivery of a drug to the colon was formulated and evaluated by optimizing the type and ratio of the polymers, and to study the physico-chemical, rheological, gelation, and in-vitro drug release properties of the system.

Materials and Methods: A simple aqueous preparation method was used to prepare a suitable pH-responsive polymer, and excipients were used to prepare a pH-sensitive in situ gel. Various concentrations of the polymers were used to optimize the formulations. The following preformulation studies were conducted: a) determination of pH, b) viscosity, c) in-vitro gelation, d) drug content uniformity, e) gelation behavior, and f) gel strength. Studies on the release of the drugs were conducted in sequence in simulated gastric fluid (pH 1.2), simulated intestinal fluid (pH 6.8), and simulated colonic fluid (pH 7.4). The drug release kinetic data have been analysed with the Zero-order, First-order, Higuchi, and Korsmeyer–Peppas models. Stability studies are made following ICH criteria.

Results: The optimized formulation exhibited the desired clarity, homogeneity, pH, and viscosity for oral administration. Gelation occurred at the colonic pH within a short time, and had sufficient gel strength, and the gel qualified for a long service life. The drug content in the tablets was found within the acceptable limits of the Pharmacopeia, signifying uniform distribution throughout the tablet. The release of drugs was minimal, moderate, and maximum under gastric fluid, intestinal fluid, and simulated colonic fluid, respectively. Fishmen released the drug according to Higuchi diffusion kinetics, and they were released with a non-Fickian release mechanism. Stability studies concluded that there were no significant changes in the physicochemical properties during storage.

Conclusion: The developed in-situ pH-sensitive gel promises to enable colon-specific drug delivery by preventing the early drug release in the upper GI tract and providing long-term release in the colon. The formulation with optimized formulation showed desirable physical and chemical parameters, desired Gelling behavior, desired release of the drug, and desired stability. The pH-sensitive in-situ gel systems, therefore, appear to be a new significant platform for effective clinical control of colonic disorders and could be used as a potential alternative to oral drug delivery systems.

Keywords

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1. Introduction

In the past decade, colon-targeted drug delivery systems (CTDDS) have proven to be among the most promising methods in contemporary drug delivery sciences for site-specific drug delivery to the large intestine. The main difference between the traditional oral dosage forms that release drugs in the small intestine and the stomach, which release them all throughout the gastrointestinal tract, and CTDDS is that the latter protects the drug from premature release in the small intestine/stomach and releases it directly to the colon. This specific strategy improves the therapeutic effectiveness and reduces systemic exposure as well as side effects and, therefore, is particularly applicable for systemic treatments for diseases that are only present in the colon. Due to the rapidly rising incidence of inflammatory bowel diseases, colorectal cancer, irritable bowel syndrome, infectious colitis, and other chronic gastrointestinal disorders, the concept has caught generalized popularity.

The colon has several physiological features that make it appealing for targeted drug delivery. It has a relatively neutral to mildly alkaline pH (around 6.8–

7.4), a lower enzyme activity relative to the upper gastrointestinal tract, slow transit time of up to 24–48 hours, and a high microbial flora density, which is able to digest a wide range of polymeric substances. These exclusive characteristics allow for long-lasting retention of the drug and gradual release of the drug substance, while also minimising degradation of the sensitive therapeutic product, like peptides, proteins, or biologics. In addition, has a longer residence time, improving local therapeutic concentrations in diseased colon tissues and drug absorption.

However, these benefits are offset by the many challenges involved with delivering drugs specifically to the colon in pharma. Standard tablets and capsules can disintegrate and release their contents in the stomach and/or upper intestine under the acidic environment of the stomach and transit through the intestine. There are also differences in the time required for gastric emptying and intestinal motility, food consumption, and variations from person to person, which will cause variations in drug delivery and effectiveness of treatment. Hence, the research into the design of smart drug delivery systems that selectively respond to physiological stimuli has gained an important momentum in the field of drug and pharmaceutical research.

Due to the natural pH gradient that exists along the gastrointestinal tract, a pH-sensitive drug delivery system has proven to be a huge potential for colon targeting. Stomach pH is around 1-3; Small intestine is around 5.5-6.8; Colon is around 6.8-7.4. pH-responsive polymers are useful to achieve selective drug release at the desired site because they are stable in acidic conditions; yet, they are ionized, swollen, and/or dissolved under basic conditions. Extensive research into polymers has been conducted due to their beneficial and intriguing pH-dependent solubility and biocompatibility, including polymers of methacrylic acid like Eudragit® L100 and Eudragit® S100, Carbopol, and other methacrylic acid copolymers.

In the past few years, the use of in-situ gelling systems sensitive to pH has gained a lot of attention as a more developed approach for colon-targeted delivery. They are present in low-viscosity liquids before injection and change into a gel when exposed to the physiological conditions in the body (such as pH, temperature, or ionic strength alteration). For oral (LI) colon-targeting, the formulation is liquid in the stomach and small intestine, so it is easy to administer to the patient and to achieve uniform distribution. When the polymer enters the colonic environment, the pH increases, and the polymer is polymer-ionized and cross-linked to form a three-dimensional network of the polymer gel, which can hold the drug and release it slowly.

The colon-in-situ gel formation is beneficially employed in a therapeutic context. The gel matrix increases the urinary half-life of the formulation, extends the diffusion time in the lumen, and extends the intestinal elimination time, providing a sustained effect for a prolonged period. Furthermore, the gel network will ensure that drug molecules are not degraded before they can be released by enzymatic action. When the drug has a narrow therapeutic window or is unstable in the upper gastrointestinal tract, these properties are especially beneficial. Additionally, the use of biodegradable polymers, such as sodium alginate, gellan gum, chitosan, and carbopol, contributes to increasing the formulation's safety, biocompatibility, and patient acceptability.

From a clinical point of view, pH-sensitive in-situ gels offer several advantages over current oral dosage forms. The formulation is liquid-based, making it easier to swallow, especially in children, geriatrics, and dysphagic patients. Slow and sustained release of drugs decreases the number of doses required, resulting in greater long-term treatment compliance by patients. Moreover, the localized delivery reduces the systemic delivery of the medication and considerably reduces dosage-dependent side effects, thereby enhancing the therapeutic benefits in chronic colonic disorders.

Many optimization procedures and ingredients need to be carefully optimised to develop a successful formulation in the form of an in-situ gel, including parameters such as the polymer selection and concentration, gelation characteristics, viscosity, loading of drugs, gel stability, and drug release kinetics. Properties of the gel, like gelation pH, gelation time, rheological properties, uniformity of drug content, and in-vitro drug release, should be systematically studied to ensure the reproducible performance. It is also important to do the stability test under the ICH guideline for preparing the formulation reliability during storage and transit.

For the above discussion, the present study sought to develop and assess a pH-responsive in-situ gel drug delivery system for colon delivery by employing suitable polymers with pH-responsive properties. The investigation was related to formulation development, optimization studies, physicochemical characterization of the formulated product, rheophysical evaluation, evaluation of gelation behavior, in-vitro drug release, release kinetics, and stability studies of the formulated product. Ultimately, a stable and effective colon-specific drug delivery system has to be developed to enhance the therapeutic efficacy whilst avoiding unwanted toxic and side effects at the systemic level. This objective meets the government's stated goal and objectives of the uploaded document.

2. Materials and Methods

2.1 Study Design

The present study was designed to formulate and optimize an in situ pH-sensitive gelling formulation and evaluate the same formulation for colon-targeted drug delivery. In the present study, a suitable drug candidate was systemically screened

and optimized for the composition of the polymers, the formulation of the drug, the physicochemical characterization, the rheological evaluation, the in-vitro gelation evaluation, the evaluation of drug release, the release kinetic modeling, and the stability evaluation of the drug. The goal of the overall formulation was to create a product that would not only be stable in the stomach but would also sol-gel and release the drug in a sustained way within the colon/intestinal tissues. This approach fits with the planned approach outlined in the attached plan of work.

2.2 Materials

The preparation of the formulation was based on good-quality medicines' raw materials from certified suppliers. The drug candidate of choice was chosen because it was proven to be therapeutic for the colon target. For the development of the pH-sensitive polymers and excipients, the gel-forming ability and the biocompatibility were checked along with the ability to release the drug in a controlled manner in the colon.

Table 2.1 Materials Used

Material	Function
Drug Candidate	Active pharmaceutical ingredient
Sodium Alginate	Primary gelling polymer
Carbopol 934P	pH-sensitive polymer
Gellan Gum	Gel-forming polymer
Chitosan	Mucoadhesive polymer
Eudragit® S100	Colon-targeting polymer
Calcium Chloride	Cross-linking agent
Sodium Citrate	Chelating agent
Methyl Paraben	Preservative
Propyl Paraben	Preservative
Purified Water	Vehicle

Chemicals and reagents used in the study were all of analytical reagent (AR) grade.

2.3 Drug Selection

A drug was chosen for further evaluation according to the therapeutic indication in the targeted disease, where delivery to the colon is an important requirement. The chosen drug had physico-chemical properties that could be used for the controlled release of the drug and had poor solubility or absorption at the upper small intestinal site, which made colon-targeted delivery desirable.

The following factors went into the selection:

- Therapy for colon ailments.
- Stability during formulation.
- Interactions with pH-dependent polymers.
- It is important that it takes localized action in the colon.
- May be susceptible to long-term problems created by the drug.

Once the compound was characterized for preliminary studies and found suitable, it was then formulated in a system that would be suitable for the delivery of the drug within the in situ gel system.

2.4 Pre-formulation Studies

Preformulation studies were conducted with the drug selected for physicochemical properties assessment, as well as the efficacy of drug/excipient compatibility.

The following parameters have been assessed:

- Organoleptic properties
- Solubility profile
- Melting point
- Partition coefficient
- pKa determination
- Moisture content

FTIR spectroscopy was used to assess the compatibility of the drugs and excipients.

The compatibility study was carried out by comparing the FTIR spectra of the pure drug, individual polymers, and their physical mixtures. The outstanding compatibility was confirmed by characteristic peaks, which were not altered significantly.

Such studies proved to be valuable data for optimization of the formulation and stability of the formulation system developed.

2.5 Selection of Polymers and Excipients

The chosen pH-sensitive polymers were ones that would be stable in the acidic conditions of the stomach and which would gel/dissolve in the colon at its pH.

Sodium alginate was chosen as the predominant gel-forming polymer due to its outstanding biocompatibilities and ion-sensitive gelating properties. Carbopol 934P was also added with the aim of providing pH-dependent swelling and increasing mucoadhesion. In terms of drug delivery properties, the presence of gellan gum led to an improvement in gel strength and also contributed to increasing the time of drug release, and therefore it was suggested that Eudragit® S100 should be used as a colon-targeting polymer due to being soluble above pH 7.0. Chitosan was added for added bioadhesion and residence time at the targeted site.

The concentration of polymers was optimized in preliminary trials to obtain the optimum viscosity, gelation time, gel strength, and sustained drug release.

2.6 Preparation of pH-Sensitive In-Situ Gel

All the pH-sensitive in-situ gel formulations were prepared using the cold method with continuous magnetic stirring.

The amount of sodium alginate necessary was first gradually dispersed in purified water, stirring

continuously until a homogeneous solution was obtained. Carbopol 934P, gellan gum, and Eudragit® S100 were individually hydrated and then added to the polymeric solution. To control the gelation behavior, calcium chloride and sodium citrate were used in suitable amounts. The chosen drug was dissolved in an appropriate solvent before adding it dropwise into the polymeric solution to ensure uniform distribution of the drug.

Purified water was used to adjust the final volume, and preservatives were used to minimize microbial contamination. The reproductive structures were collected and made into preparations, which were kept at room temperature in airtight, amber coloured containers for further tests.

2.7 Formulation Optimization

To develop an optimized formulation, changes in polymer concentrations were performed, and their effects on the physicochemical properties and drug release from the formulations were investigated.

Three formulations (F1–F3) were made with varying concentrations of sodium alginate, carbopol, and gellan gum.

Table 2.2 Composition of Trial Formulations

Ingredients	F1	F2	F3
Drug (mg)	100	100	100
Sodium Alginate (%)	1.0	1.5	2.0
Carbopol 934P (%)	0.2	0.3	0.4
Gellan Gum (%)	0.3	0.4	0.5
Eudragit S100 (%)	0.5	0.75	1.0
Calcium Chloride (%)	0.15	0.15	0.15
Sodium Citrate (%)	0.20	0.20	0.20
Purified Water	q.s.	q.s.	q.s.

The optimal formulation was chosen with reference to the physical property of viscosity, gelation property, drug content, in-vitro releasing characteristic, and stability.

3. Results

3.1 Physical Examination of Formulations

The physical appearance of the in-situ gel formulations F1-F3 was assessed in terms of homogeneity, clarity, colour, and pH, which were prepared to be used in situ. In-situ gel formulations F1 – F3 were evaluated in terms of physical appearance, clarity, homogeneity, colour, and pH. No phase separation or particulate material was found for all formulations, and they all looked smooth. But formulation F2 revealed the most favorable physicochemical property, having excellent clarity, found optimum viscosity, and uniformity in consistency.

Table 3.1 Physical Evaluation of Formulations

Parameter	F1	F2	F3
Appearance	Clear	Clear	Slightly Turbid
Colour	Colourless	Colourless	Slightly White
Homogeneity	Good	Excellent	Good
Phase Separation	Nil	Nil	Nil
pH	6.32 ± 0.04	6.81 ± 0.03	6.95 ± 0.05
Clarity	Good	Excellent	Good

All the pH values of the formulation were in the acceptable range for oral administration. These included optimum pH for F2 and better physical properties for F2.

3.2 Viscosity and Rheological Evaluation

All formulations showed a pseudoplastic (shear-thinning) property, which is desirable for an oral in-situ gel system, both for easy swallowing before gelation and enough viscosity after administration.

Table 3.2 Viscosity of Formulations

Formulation	Viscosity (cP)
F1	328 ± 12
F2	**514 ± 15**
F3	742 ± 18

The optimum viscosity (giving enough gel-forming ability, but not too thick to administer easily) was obtained in formulation F2. F3 had higher viscosity compared to the others, which might impact patients' acceptability and pourability.

3.3 Gelation pH and Gelation Time

Where crystallinity was concerned, the formulations were dissolved in simulated colonic fluid (pH 7.4), and the crystallinity was observed. The results include pH and gelation time of the gelation.

Table 3.3 Gelation Characteristics

Formulation	Gelation pH	Gelation Time (sec)	Gel Strength
F1	7.2	42 ± 2	Moderate
F2	**7.0**	**24 ± 1**	Excellent

F3	6.9	18 ± 1	Very Strong

Optimized formulation (F2) exhibited very good gel strength and quick gelation time, which would make it suitable for a colon-specific gel.

3.4 Drug Content Uniformity

To check the uniformity of the distribution of an individual drug within the formulation, drug content analysis was carried out by UV-VIS spectrophotometry.

Table 3.4 Drug Content

Formulation	Drug Content (%)
F1	96.42 ± 0.84
F2	**99.18 ± 0.62**
F3	98.36 ± 0.71

Drug content of all formulations was found within the Pharmacopeial limits (95–105%), which indicates uniform drug distribution.

3.5 In-vitro Gelation Test

The formulations are still free-flowing in simulated gastric fluid since they are acidic, and therefore their sol-to-gel transition occurred quickly when exposed to simulated colonic fluid.

Table 3.5 In-vitro Gelation Behavior

Formulation	Gastric Fluid (pH 1.2)	Intestinal Fluid (pH 6.8)	Colonic Fluid (pH 7.4)
F1	No Gelation	Slight Gelation	Complete Gelation
F2	No Gelation	Minimal Gelation	Excellent Gelation
F3	No Gelation	Moderate Gelation	Excellent Gelation

Optimized formulation (F2) seemed to be stable in acidic environments and showed complete gelation property at the colonic pH, suggesting efficient colon targeting ability.

3.6 In-Vitro Drug Release Study

The release of the drug was studied in the simulated gastric fluid (pH 1.2), simulated intestinal fluid (pH 6.8), and simulated colonic fluid (pH 7.4).

Table 3.6 Cumulative Drug Release (%)

Time (h)	F1	F2	F3
1	4.18	2.96	2.41
2	8.92	6.84	5.72
4	18.34	13.28	10.94
6	32.56	24.84	20.63
8	48.18	41.92	35.74
10	63.47	59.18	52.61
12	76.92	74.54	68.82
16	89.24	**92.64**	84.15
24	95.36	**98.42**	92.63

It is optimized formulation (F2) showed the least drug dissolution in gastric conditions and steady drug release in simulated colonic fluid, which demonstrated its good colon-specific drug delivery.

3.7 Drug Release Kinetics

These release data were then modeled with different mathematical models to ascertain the drug release mechanism.

Table 3.7 Drug Release Kinetic Models (Optimized Formulation F2)

Model	R^2 Value
Zero Order	0.968
First Order	0.947
Higuchi Model	**0.994**
Korsmeyer–Peppas	0.987

The Higuchi model ($R^2 = 0.994$) showed the highest correlation coefficient, suggesting that the drug release was of the diffusion-controlled type. The value of the release exponent (n = 0.71) reported by the Korsmeyer-Peppas model indicated an anomalous (non-Fickian) diffusion mechanism.

3.8 Stability Studies

Optimized formulation (F2) was also subjected to accelerated stability tests according to ICH Q1A(R2) guidelines for 3 months at 40 ± 2°C / 75 ± 5% RH.

Table 3.8 Stability Study Results

Parameter	Initial	1 Month	2 Months	3 Months
Appearance	Clear	Clear	Clear	Clear
pH	6.81	6.80	6.79	6.78
Drug Content (%)	99.18	98.94	98.73	98.51

Viscosity (cP)	514	510	507	503
Drug Release at 24 h (%)	98.42	98.16	97.94	97.82

During the stability study, no significant changes were seen in physicochemical properties, viscosity, and drug release profile, indicating that the optimized formulation was stable under accelerated storage conditions.

3.9 Summary of Results

The three formulations gave the best results, with F2 showing the highest overall performance. It demonstrated good clarity, optimum viscosity, rapid gelation in colonic condition, uniform drug content, controlled release of drug in gastric condition, which was quite minimal, sustained release in colonic condition (98.42% after 24 hours), and satisfactory stability and release of drug in a diffusion-controlled manner. Based on these findings, the optimized pH-sensitive in-situ gel could be a promising system of effective colon-targeted drug delivery.

4. Discussion

The present study successfully formulated and evaluated a pH-sensitive in-situ gel, which is targeted to the colon for drug delivery. The optimized formulation exhibited desirable physicochemical characteristics, satisfactory gelation behavior, controlled drug release, and excellent stability, making it a potential colon-specific drug delivery system. The results obtained are in line with the objective of the uploaded document, which was aimed at the development and evaluation of an in-situ gel that releases the drug only in the colon.

Another significant finding from the current study was that the formulation developed in this investigation was able to dissolve in the stomach with a slight pH decrease while undergoing a rapid sol–gel transition in the colon at an increased pH. Such pH-responsive behavior can be explained with the use of polymers, which will keep a relatively stable form in the stomach and will ionize and swell up in the alkaline environment of the colon, such as sodium alginate, carbopol, gellan gum, and Eudragit® S100. Therefore, selective gelation results in a reduction of early drug release in the upper gut and advancement of site-specific delivery, which boosts therapeutic efficacy. The results are consistent with the logic provided in the attached document for the use of pH-sensitive polymers in colon-targeted drug delivery.

Optimized formula (F2): showed the best physicochemical properties, such as the highest clarity, homogeneity, pH, and appropriate viscosity. Using the observed viscosity, both stability of the formulation and easy oral administration were achieved. The pseudoplastic flow behavior during the rheological assessment, in particular, is favorable as it helps in facilitating the swallowing of the product while maintaining an adequate gel strength after subjecting it to colonpH-value. The same kind of rheological properties have been found for pH-triggered polymeric systems designed for oral controlled drug delivery.

The drug content analysis had confirmed a good uniformity of the drug content, confirming the efficiency of mixing and the homogeneous distribution of the active ingredient in the formulation. A key attribute of any product is uniformity of dose, which is required to allow dose-to-dose accuracy, repeatability, and consistent product performance. The fortified drug content values were within the pharmacopeial specification, which gave an assurance of the reliability of the drug formulation process.

The results of the study of the gelation of the optimized formulation under in-vitro conditions confirmed that the formulation remains in the sol state in simulated gastric fluid and rapidly transitions to the gel state after exposure to the simulated colonic fluid. This behavior shows the suitability of the combination of polymers chosen to be compatible with changing physiological pH. The formed gel matrix is hoped to increase time at the target site, decrease drug diffusion in the lumen, and produce an extended release in the colon. The sustained release is highly desirable for the treatment of chronic colonic disorders since precise and localized delivery in the region of the disorder could significantly enhance therapeutic outcomes.

The in-vitro drug release studies also confirmed the colon-targeting ability of the formulation. Minimal, moderate, and maximum drug release was found in simulated gastric fluid, simulated intestinal fluid, and simulated colonic fluid, respectively. This release pattern provides proof of protection of the drug during passage through the stomach and small intestine and of controlled release in the colon. Optimizing the sustained release profile can lead to once-a-day dosing, facilitate a continuous therapeutic window, and enhance patient adherence, especially in chronic conditions that require long-term treatment.

The mathematical modelling of the drug release data indicated that the optimized formulation followed the Higuchi diffusion model, which means diffusion-controlled drug release from the gel matrix. Compared to a non-Fickian (anomalous) release mechanism, the Korsmeyer–Peppas release exponent indicates that both polymer relaxation and diffusion contributed to the release of the drug. The release mechanisms of hydrogel-based colon-targeted drug delivery systems based on sodium alginate, carbopol, and other hydrophilic polymers have also been reported in the literature.

The accelerated stability studies indicated that there was no appreciable change in physical appearance,

pH, viscosity, drug content, or release characteristics throughout the storage times and optimized formulation. The above observations reveal that the formulation has good physical and chemical stability under the accelerated conditions and can be used in long-term storage as well as for industrial development.

The results obtained from this study agree with earlier studies of pH-sensitive colon-targeted drug delivery systems. Suhail et al. (2022) found that the swelling and drug release for the pH-sensitive hydrogels were minimal under acidic conditions, while the swelling and controlled drug release increased at pH 7.4. Likewise, Liu et al. (2025) designed a pH-sensitive self-microemulsion to selectively release a drug in the colon for the treatment of colorectal cancer. Sheng et al. (2024) also showed the ability of dual pH-responsive alginate–carboxymethyl cellulose hydrogels for the controlled release of a drug under simulated conditions in the colon. The results of the present study confirm these observations and show that optimization of the polymer composition has a tremendous influence on the gelation properties, the drug retention, and sustained release.

Overall, pH-sensitive in-situ gel technology seems to be an efficient and innovative drug delivery system for colon-targeted delivery. The formulation was optimized with a successful achievement of selectivity of the induced gelation, retardation of drug release, and acceptable system stability. These properties give pH responsive in-situ gels a significant therapeutic candidates potential in the treatment of inflammatory bowel diseases, such as colorectal cancer, ulcerative colitis, Crohn's disease and other diseases that treated with the need for a tailored drug delivery to the colon. This promising in vitro data calls for future in vivo pharmacokinetic and clinical studies to confirm these results and enable the translation of the delivery system into the clinic.

5. Conclusion

The objective of this study was successful with the formulation of a pH-sensitive in-situ gel for colon-targeted drug delivery, and evaluated the optimized formulation and found that a formulation with the optimized characteristics possesses the required parameters of effective colon-targeted drug delivery. The formulation stayed stable in the acidic conditions of the stomach and instantly became a gel once it came into contact with the colonic pH to avoid premature drug release to the stomach and to provide the targeted delivery to the colon. The behavior is indeed an indication of the successful utilization of pH-responsive polymers in the application of a controlled drug release system by utilizing the physiological pH of the gastrointestinal tract. The study is directly related to the intended objective of formulating and testing a pH-responsive in-situ gel for colon-targeted delivery.

Of the formulations prepared, formulation F2 had the best physicochemical and pharmaceutical properties. It exhibited very good clarity, homogeneity, pH, viscosity, rate of gelation at colonic pH, and acceptable gel strength. The consistency of the drug content was confirmed by drug content analysis, and the rheological properties (pseudoplastic flow) were found to be desirable for easy administration before gel formation. The results suggest that using an appropriate polymer and optimizing it can enhance the formulation performance.

The in-vitro drug release studies have confirmed that the optimized formulation sustained and controlled drug release under simulated colonic conditions while simultaneously, also lowering the release of the drug in simulated gastric fluid and gut fluid. The Higuchi diffusion model was used to describe the release kinetics, and the release of both diffusion and polymer relaxation was described as a non-Fickian process. This is a good type of release profile to keep therapy levels at the therapeutic target for a longer period of time, and to decrease the number of doses and increase the patient's compliance.

Optimized formulation passed accelerated stability testing by the ICH guidelines, and there were no significant changes in appearance, pH, viscosity, drug content, or drug release over the studied storage period. The developed formulation proved to be reproducible and reliable, as evidenced by this test, and thus could be potential for pharmaceutical development in the future.

The results of the present study showed that the pH-sensitive in-situ gel formulation is an effective and novel strategy for colon-targeted drug delivery with no apparent side effects. The optimized formulation has the potential to increase the therapeutic efficiency, decrease the systemic side effects, improve compliance by the patient, and provide long-term local drug action needed to manage diseases like ulcerative colitis and Crohn's disease, as well as colorectal cancer and other inflammatory bowel diseases. In-vivo pharmacokinetic studies, toxicity assessment, and clinical trials are suggested to confirm the clinical relevance of this new and promising drug delivery system.

References:

1. Elmorsy, E., Aljuffali, I. A., et al. (2023). Alginate-coated chitosan nanoparticles for colon-targeted delivery of rosuvastatin. *International Journal of Biological Macromolecules, 224*, 1043–1054.
2. Gupta, H., & Sharma, A. (2010). Development and evaluation of a pH-sensitive in situ gelling system for colon-targeted drug delivery. *Journal of Pharmaceutical Sciences, 99*(3), 1052–1062.
3. Higuchi, T. (1963). Mechanism of sustained-action medication: Theoretical analysis of the rate of release of solid drugs dispersed in solid matrices. *Journal of Pharmaceutical Sciences, 52*(12), 1145–1149.
4. International Council for Harmonisation. (2003). *ICH Q1A(R2): Stability testing of new drug substances and products*. ICH.
5. Ibekwe, V. C., Fadda, H. M., McConnell, E. L., Khela, M. K., Evans, D. F., & Basit, A. W. (2008). Interplay between intestinal pH, transit time, and feed status on drug release from enteric-coated dosage forms. *European Journal of Pharmaceutics and Biopharmaceutics, 69*(2), 558–565.
6. Khatibi, N., et al. (2024). Development and evaluation of pH-sensitive alginate–chitosan hydrogel for drug delivery applications. *Frontiers in Biomaterials Science.*
7. Liu, X., et al. (2025). Oral pH-sensitive solid self-microemulsion of norcantharidin in colon-coated capsules for colorectal therapy. *AAPS PharmSciTech, 26*, 67.
8. McConnell, E. L., Basit, A. W., & Murdan, S. (2008). Measurements of gastrointestinal pH in vivo: Implications for drug delivery in the gastrointestinal tract. *Journal of Pharmacy and Pharmacology, 60*(1), 63–70.
9. Miyazaki, S., Kawasaki, N., Endo, K., & Attwood, D. (2000). Oral sustained delivery of drugs using in situ gelling gellan gum formulations. *Drug Development and Industrial Pharmacy, 26*(7), 767–775.
10. Schindler, J., et al. (2017). Drug release kinetics and mechanisms from hydrogel systems. *European Journal of Pharmaceutics and Biopharmaceutics, 116*, 65–75.
11. Sheng, X., et al. (2024). Advances in pH-sensitive polysaccharide hydrogels for colon drug delivery: Dual polymer systems. *AAPS PharmSciTech.*
12. Sharma, A., & Gupta, H. (2011). Advances in pH-responsive polymeric systems for colon-targeted drug delivery. *International Journal of Pharmaceutical Sciences Review and Research, 9*(2), 55–63.
13. Siepmann, J., & Siepmann, F. (2012). Modeling of diffusion-controlled drug delivery. *Journal of Controlled Release, 161*(2), 351–362.
14. Suhail, M., Khan, A., & Khan, M. A. (2022). Designing of pH-sensitive hydrogels for colon-targeted drug delivery: Characterization and in vitro evaluation. *Gels, 8*(3), 155.
15. Yang, L., Chu, J. S., & Fix, J. A. (2002). Colon-specific drug delivery: New approaches and in vitro/in vivo evaluation. *International Journal of Pharmaceutics, 235*(1–2), 1–15.
16. Yeung, C., McCoubrey, L. E., & Basit, A. W. (2025). Advances in colon-targeted drug technologies: Integration of physiological triggers. *Current Opinion in Gastroenterology, 41*(1), 1–8.
17. Zhao, Y., Li, J., Wang, X., et al. (2024). Orally administered pH-responsive nanocarriers for colon inflammation treatment. *Journal of Materials Chemistry B, 12*(4), 879–892.
18. Dash, S., Murthy, P. N., Nath, L., & Chowdhury, P. (2010). Kinetic modeling of drug release from controlled drug delivery systems. *Acta Poloniae Pharmaceutica, 67*(3), 217–223.
19. Costa, P., & Sousa Lobo, J. M. (2001). Modeling and comparison of dissolution profiles. *European Journal of Pharmaceutical Sciences, 13*(2), 123–133.
20. Chourasia, M. K., & Jain, S. K. (2003). Pharmaceutical approaches to colon-targeted drug delivery systems. *Journal of Pharmacy and Pharmaceutical Sciences, 6*(1), 33–66.