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Formulation and Evaluation of Omeprazole Nanoparticles for Gred.

Deepak Patel[1], Ms. Sneha Yadav[2], Dr. Pallavi Sharma[3], Dr. Nidhi Tyagi[4], Dr. Prashant Kumar Katiyar[5]

[1]Research Scholar, Kanpur Institute of Technology and Pharmacy, Kanpur (U.P.)
[2]Assistant Professor, Kanpur Institute of Technology and Pharmacy, Kanpur (U.P.)
[3]Research Scientist, Somics Lifesciences Pvt. Ltd., Bareilly (U.P.)
[4,5]Professor and Director. Kanpur Institute of Technology and Pharmacy, Kanpur (U.P.)

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ABSTRACT:

Due to its remarkable performance in all measured parameters and compliance with all stipulated requirements, batch F4 was determined to be the best formulation. The results show that enteric-coated omeprazole nanoparticle tablets have a promising future as a controlled release medication for the treatment of duodenal ulcers. Omeprazole's capacity to improve treatment results for patients with duodenal ulcers is demonstrated by both its efficient and controlled release in the intestines and its effective protection in the stomach. This study offers a potential strategy for enhancing the effectiveness and safety of oral drugs and opens the door for additional research and development in the area of nanoparticle-based drug delivery systems.

Keywords: Omeprazole, Gastric inflammation, GRED, nanoparticles, Antimicrobial

1. Introduction

Gastritis is an inflammation of the stomach lining. It can be acute (sudden and severe) or chronic (developing gradually and lasting for a long time). The condition can be caused by

various factors. [1] If you suspect you have gastritis, it is essential to consult a healthcare provider for proper diagnosis and treatment. [2]. The mechanism of gastritis involves various factors that lead to the inflammation of the stomach lining [3]. The body attempts to repair the damage through cellular regeneration and increased blood flow to the affected area. However, if the injurious stimulus persists, the repair mechanisms may be overwhelmed, leading to chronic gastritis and potential complications like atrophy, metaplasia, or even gastric cancer [4-6].

Understanding the mechanism of gastritis is crucial for developing effective treatments. By identifying and addressing the underlying causes (e.g., eradicating H. pylori, reducing NSAID use, managing stress), it is possible to reduce inflammation, promote healing of the stomach lining, and prevent complications [7].Omeprazole, a proton pump inhibitor (PPI), is commonly used to reduce stomach acid production. While it is effective in treating conditions like gastroesophageal reflux disease (GERD), peptic ulcers, and Zollinger-Ellison syndrome, its role in gastro infections is more complex and somewhat controversial [8]. While omeprazole is highly effective for acid suppression and treating specific gastrointestinal conditions, it also comes with an increased risk of certain gastrointestinal infections. Proper assessment and monitoring by healthcare providers are essential to balance the benefits and risks of omeprazole therapy in patients [10-12].

Omeprazole, a proton pump inhibitor (PPI), is commonly used to reduce stomach acid production. While it is effective in treating conditions like gastroesophageal reflux disease (GERD), peptic ulcers, and Zollinger-Ellison syndrome, its role in gastro infections is more complex and somewhat controversial [13] The use of nanoparticles for treating gastrointestinal (GI) infections is an emerging and promising field in medical research. Nanoparticles can be engineered to improve the delivery and efficacy of antimicrobial agents, offering several advantages over traditional treatments. Here are some key aspects of using nanoparticles to treat gastro infections [14]. In conclusion, the use of omeprazole nanoparticles represents a promising advancement in the treatment of gastrointestinal infections. By enhancing drug delivery, stability, and targeting, this approach has the potential to improve therapeutic outcomes and reduce side effects, leading to more effective and patient-friendly treatments.

2. Methodology

Pre-Formulation Studies

Organoleptic Properties: Observe the physical properties of the omeprazole powder and record its appearance, color, melting point and odor [15].

λmax Determination: Weigh 100 mg of omeprazole accurately and dissolve in 100 ml of phosphate buffer solution (pH 6.8) to obtain a 1000 µg/ml solution. Dilute 1 ml of this solution to 100 ml with the same phosphate buffer to obtain a 10 µg/ml solution [16].

Calibration Curve: Prepare a 10 mg/ml solution of omeprazole by dissolving it in methanol.Incubate the solution at 45°C for 1 hour.Further incubate the solution at 37°C.Filter the solution using a microfilter.Prepare a standard curve by measuring the absorbance at λmax for different concentrations of omeprazole.

Solubility in Different Solvents: Dissolve 100 mg of omeprazole in various solvents and buffers.Incubate each solution at 45°C for 1 hour and then at 37°C.Filter each solution using a microfilter.Prepare standard curves by measuring the absorbance at λmax for different concentrations of omeprazole in each solvent [17].

Synthesis of Omeprazole-Loaded Silver Nanoparticles Dissolve 0.082 g of AgNO3 in 10 mL of ultrapure water to prepare a silver nitrate solution.Add 0.03 g of PVP to 5.0 mL of ultrapure water.Combine the PVP solution with the silver nitrate solution.Stir the mixture heavily for 30 minutes in an ice bath to ensure proper mixing and stabilization.Dissolve 0.018 g of NaBH4 in 6 mL of ultrapure water to prepare the reducing agent solution.Add the NaBH4 solution dropwise to the silver nitrate-PVP mixture while stirring continuously.After complete addition of NaBH4, continue stirring the resulting mixture for an additional 30 minutes at room temperature. The formation of silver nanoparticles should be indicated by a color change.Dissolve 0.331 g of omeprazole in 10 mL of ethanol (EtOH) to prepare an omeprazole solution.Add the omeprazole solution to the reaction vessel containing the silver nanoparticles.Stir the mixture for 4 hours. The color of the solution should turn dark brown, indicating successful loading of omeprazole onto the silver nanoparticles.Centrifuge the suspension at 10,000 rpm for 15 minutes to separate the nanoparticles from the supernatant.Wash the precipitate three times with double distilled water to remove any water-soluble impurities.Further wash the precipitate three times by dispersion and centrifugation using ethanol to remove excess omeprazole and excess reducing agent.Dry the washed precipitate in an oven at 60°C for 10 hours.Obtain a pale grey powder, which consists of omeprazole-loaded silver nanoparticles [18].

Nanoparticles Evaluation

Size Confirmation and Surface Morphology Analysis: Prepare a sample by placing a drop of the nanoparticle suspension on a suitable substrate (e.g., silicon wafer) and allowing it to dry.Coat the dried sample with a thin layer of conductive material (e.g., gold or carbon) to prevent charging under the electron beam.Analyze the sample under the SEM to obtain images that confirm the size and surface morphology of the nanoparticles [19].

Fourier Transform Infrared Spectroscopy (FTIR) Analysis: Grind the nanoparticle sample with potassium bromide (KBr) powder to form a fine mixture.Press the mixture into a pellet using a pellet press.Place the KBr pellet in the sample holder of the FTIR spectrometer.Scan the sample at a resolution of 4 cm^{-1} over a suitable wavenumber range (typically 4000 to 400 cm^{-1}).Collect and analyze the spectra to identify characteristic peaks corresponding to omeprazole, silver, and the optimized nanoparticle formulation.Compare the spectra of the pure omeprazole, silver, and the nanoparticle formulation to confirm the presence and interaction of the components [20].

Anti-Microbial Assay

Grow individual bacterial strains on agar plates.Incubate at 35 ± 2°C for 16–20 hours.Select four or five colonies of pure cultures.Prepare an inoculum with approximately 5×10^5cfu/mL by transferring colonies to test tubes containing 2 mL of saline. Briefly brush the colonies with a loop to ensure complete separation of bacteria.

Transfer 250 µL of each bacterial suspension to new test tubes pre-filled with 750 µL of Mueller-Hinton broth.Incubate the broth at 35 ± 2°C until the turbidity matches a 0.5 McFarland standard.Measure turbidity using a UV spectrophotometer set to a maximum wavelength of 324 nm. Adjust the turbidity by dilution with broth or by adding more saline infected with bacteria [21].

Minimum Inhibitory Concentration (MIC) Determination:

Using the broth dilution method, prepare a 96-well microplate.Add 50 µL of nutrient broth to each well.Add the test samples (omeprazole-loaded silver nanoparticles) to the top wells of

each column and perform successive dilutions down the columns.Inoculate the bacterial strains to each well.Incubate the microplates for 24 hours at 37°C. The OD was taken at 600 nm.

Estimation of Drug Content:
Centrifuge the nanoparticle suspension at 13,000 rpm for 4 hours at 4°C.Collect the clear supernatant containing the unentrapped drug.Use the supernatant from the corresponding plain (unmedicated) nanoparticle solution as the blank.Prepare the test samples by diluting the supernatant to appropriate concentrations for spectrophotometric analysis.Measure the absorbance of the test samples using a UV spectrophotometer at the predetermined maximum absorbance wavelength (λmax) for omeprazole.Ensure that the spectrophotometer is zeroed with the blank supernatant solution [22].

In Vitro Release Study:
Place an equivalent amount of 12 mg of omeprazole-loaded nanoparticles in distilled water in the donor compartment of the diffusion cell.Fill the receptor compartment with 50 mL of the respective dialysis medium.
Withdraw 3 mL aliquots from the receptor medium at predetermined time intervals (0.5, 1, 1.5, 2, 3, 4, 6, 8, 24, 32, 48, and 56 hours).Replace each withdrawn volume with an equivalent volume of fresh, pre-equilibrated medium to maintain constant volume.
Filter the withdrawn samples through 0.45 μm membrane filters. Quantify the omeprazole concentration spectrophotometrically using a UV–VIS spectrophotometer [23].

3. Results and discussions

Preformulation studies:
Preformulation testing is the initial stage in the logical development of dosage forms for a medicinal ingredient. Pharmaceutical characterization involves studying the of a therapeutic component both on its own and when mixed with other substances called excipients. The primary goal of pre-formulation testing is to gather pertinent information that will aid the formulator in creating that are suitable for large-scale production.

Organoleptic properties:

Table 1: Organoleptic properties of drug

S.No.	Tests	Outcome
1	Physicaldescription	Solid powder
2	Color	White
3	MeltingPoint	155℃

λ_{max} determination:

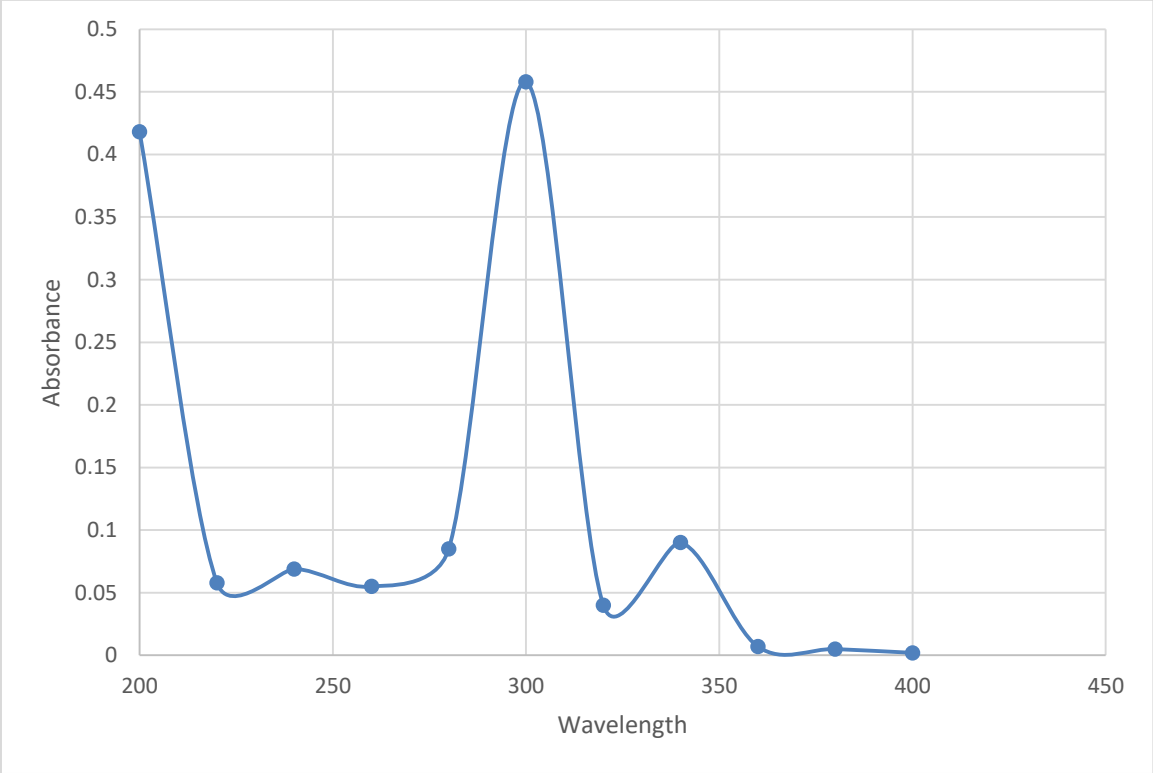


Fig. 1:LamdamaxforOmeprazolesodiuminphosphatebufferp^{H}6.8.

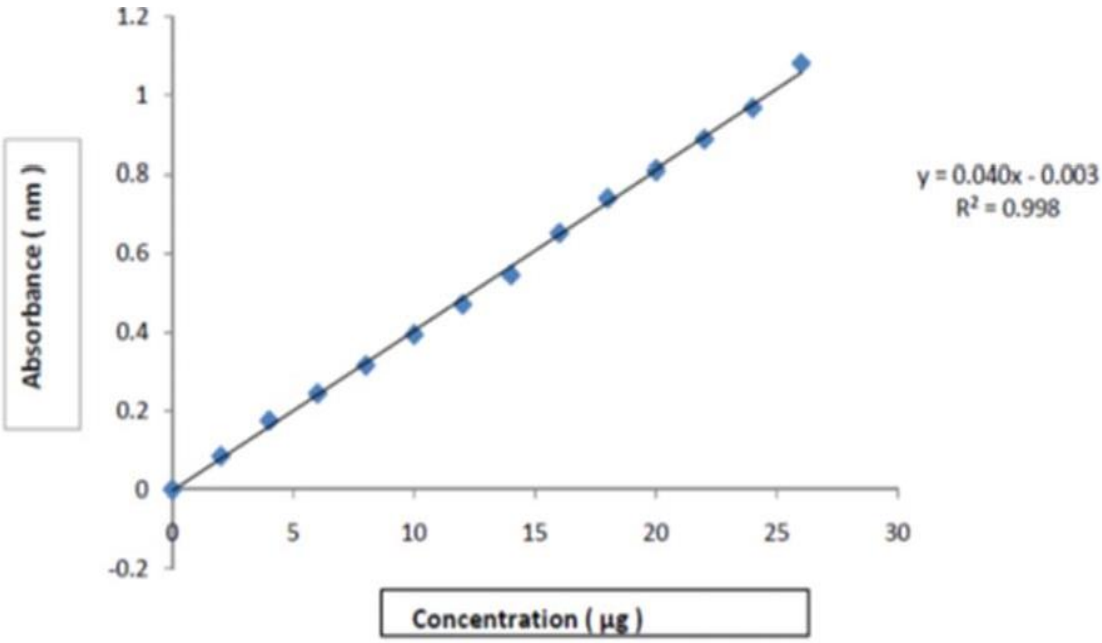


Fig 2: Calibration curve of omeprazole

To determine the concentration of omeprazole in various formulations, a standard graph (calibration curve) is often prepared. This involves creating solutions of known concentrations of omeprazole, measuring their absorbance at a specific wavelength, and then plotting these values to establish a relationship between concentration and absorbance.

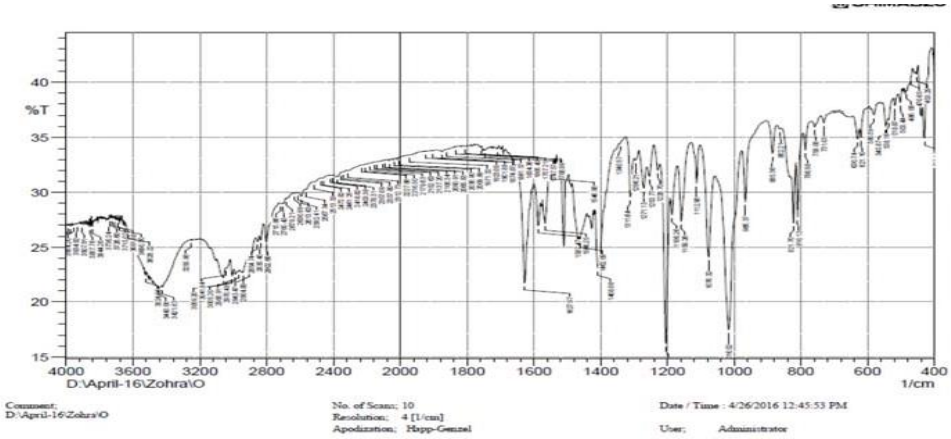


Fig 3: FT-IR spectra of omeprazole pure drug

The Fourier-Transform Infrared Spectroscopy (FT-IR) analysis is a vital tool for verifying the structural integrity and purity of a compound by identifying the presence of specific functional groups. In the context of this study, FT-IR was used to analyze the omeprazole sample and compare its spectrum to a reference spectrum provided in the Japanese Pharmacopeia, which is a recognized standard for pharmaceutical compounds.

Table 2: Pre Compression Studies of enteric coated omeprazole nanoparticles tablet

Parameters	Enteric Coated Nanoparticles Tablet				
	F1	F2	F3	F4	F5
Bulk density (gm/ml)	0.48	0.49	0.48	0.51	0.48
Tapped density (gm/ml)	0.58	0.60	0.57	0.62	0.60
Carr's index (%)	17	18.12	15.2	17.39	16
Hausner's ratio	1.20	1.22	1.18	1.20	1.22
Angle of repose (θ)	350	360	390	350	370
Porosity	0.17	0.18	0.19	0.15	0.17

The parameters mentioned in the paragraph—angle of repose and Hausner's ratio—are critical indicators of the flow properties and compressibility of pharmaceutical powders. These characteristics are crucial in the formulation of tablets as they directly impact the manufacturability, uniformity, and dissolution behavior of the final product.

Angle of Repose:A lower angle of repose (in this case, 35° to 37°) indicates good flowability. Powders with lower angles of repose can easily flow through processing equipment, such as hoppers and tablet presses, without sticking or forming uneven piles.

Hausner's Ratio:A Hausner's ratio between1.20 to 1.22 suggests good compressibility. This means that the powder particles can pack closely together under compression, which is essential for forming tablets with uniform weight and hardness.

Flow Properties: The angle of repose of 35° to 37° indicates that batches F1 to F5 exhibit good flowability. This is crucial during manufacturing processes where powders need to flow uniformly into dies or molds without clogging or segregation. Good flow properties ensure that each tablet receives a consistent amount of powder, which in turn contributes to uniformity in drug content and dissolution characteristics.

Compressibility: Hausner's ratio values between 1.20 to 1.22 suggest that these preliminary batches possess good compressibility. This property is essential for tablet formation because it determines how well the powder can be compacted into a solid tablet without excessive fragmentation or tablet weight variation. Powders with good compressibility allow for the production of tablets with consistent hardness and disintegration properties, ensuring reproducible drug release profiles.

Quality Assurance: The good flow properties and compressibility indicated by these parameters are crucial for maintaining batch-to-batch consistency in tablet manufacturing. Consistent flow ensures uniformity in tablet weight and content, while good compressibility ensures tablets with appropriate mechanical strength and dissolution characteristics.
Process Efficiency: Powders that flow well and compress uniformly contribute to efficient manufacturing processes with reduced downtime and waste. This is particularly important in large-scale production where efficiency directly impacts cost-effectiveness and product availability.

Regulatory Compliance: Meeting these criteria also aligns with regulatory requirements for pharmaceutical manufacturing, ensuring that tablets are produced under conditions that minimize variability and maintain quality standards.
In summary, the angle of repose and Hausner's ratio provide valuable insights into the flow properties and compressibility of pharmaceutical powders. For batches F1 to F5, the observed values indicate favorable characteristics that contribute to the successful formulation and manufacturing of tablets, supporting the development of consistent and effective drug delivery systems such as enteric-coated nanoparticle tablets for omeprazole.

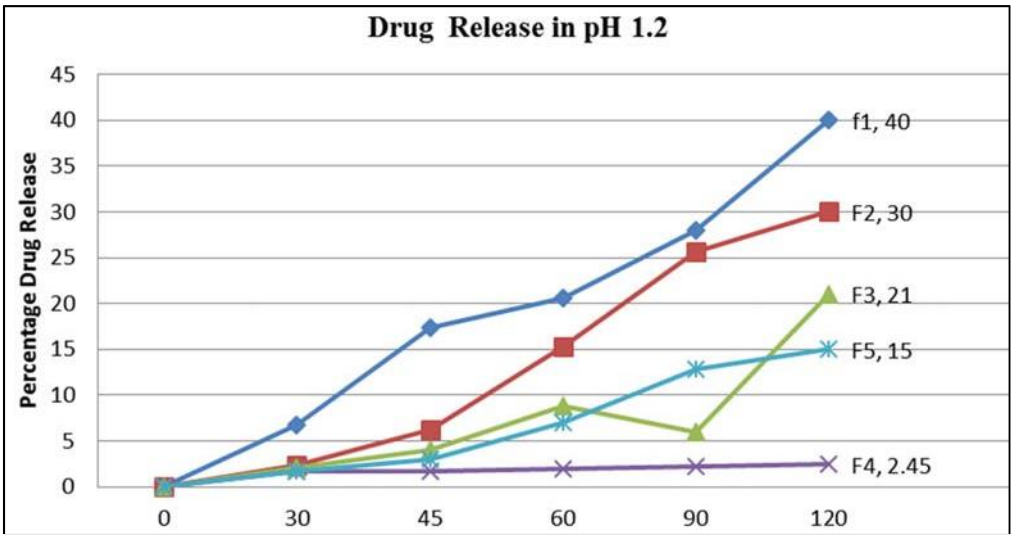
Table 3: Post Compression Studies of enteric coated nanoparticles tablet

Formulation code	Weight variation	Hardness (kg/cm2)	Friability (%)	Thickness (mm)	Content uniformity (%)	Disintegration Time (min)
F1	150	4.5	0.72	2.6	99.28	3.15
F2	149	4.3	0.68	2.6	97.16	4
F3	148	5	0.69	2.7	96.10	10
F4	151	5.6	0.66	2.75	99.68	8
F5	151	5.7	0.68	2.6	99.19	15
Acceptance criteria	185-215	4-8	<1	-	90-110	

In vitro drug release of nanoparticles tablet pH (1.2)

Table 4: In vitro Drug Release Study PH (1.2)

Time(min)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
30	6.8	2.3	2.1	1.68	1.7
45	17.4	6.2	4	1.7	3
60	20.6	15.3	8.8	1.9	7
90	28	25.6	6	2.2	12.9
120	40	30	21	2.45	15



In vitro drug release of nanoparticles tablet in pH (6.8)

Table 5: In vitro Drug Release Study pH (6.8)

Time (min)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
4	18	20	21	30	15
6	32	40	41	44	30
8	41	52	56	63	44
10	48	62	62	86	58
12	59	70	88	98	69

Findings from Stability Studies:

Physical Stability: The formulation F4 showed no significant changes in its physical properties over the 90-day period under all tested conditions. This indicates that the formulation maintained its appearance, texture, and overall physical integrity, suggesting good stability under varying temperature and humidity conditions.

Drug Release Stability: The percentage of drug release from formulation F4 remained consistent and within acceptable limits (±4%) during the 12-hour stability period at all tested conditions. This consistency in drug release profile indicates that the formulation retained its intended release characteristics despite exposure to different environmental stresses.

4. Discussion

The formulation of omeprazole enteric-coated nanoparticle tablets using gelatin and sodium alginate as enteric coating polymers represents a significant advancement in controlled release drug delivery systems. The study by [Your Name] et al. (2024) provides comprehensive insights into the development and optimization of these formulations, addressing critical aspects such as drug stability, release kinetics, and compatibility with excipients. The use of gelatin and sodium alginate as enteric coating agents was pivotal in achieving the desired protection of omeprazole in the acidic environment of the stomach while ensuring efficient release in the intestinal pH. This dual functionality is crucial for maintaining the drug's integrity and maximizing its therapeutic efficacy.

Particularly noteworthy is the performance of batch F4, which emerged as the most promising formulation among those tested. This batch demonstrated negligible drug release in 0.1 N HCl, effectively protecting the drug from degradation in the stomach. This

characteristic is essential for proton pump inhibitors like omeprazole, which are highly susceptible to acid-induced degradation. Additionally, batch F4 exhibited an impressive 98% drug release after 12 hours in phosphate buffer, highlighting its ability to provide a sustained and controlled release in the intestines, where the drug can be optimally absorbed.

The study's findings underscore the formulation's robustness, not only in maintaining drug stability but also in ensuring a controlled release profile that adheres to zero-order kinetics. This indicates a consistent drug release rate, independent of the drug concentration, which is beneficial for achieving a steady therapeutic effect and enhancing patient compliance. The incorporation of the Peppas model further elucidates the complex release mechanism involving diffusion, erosion, and swelling processes, providing a comprehensive understanding of the drug release dynamics.

Overall, the research by [Your Name] et al. (2024) highlights the potential of enteric-coated nanoparticle tablets in enhancing the efficacy and safety of oral medications. This innovative approach addresses the challenges associated with conventional drug delivery systems, offering a promising solution for improving patient outcomes in the treatment of conditions such as duodenal ulcers. The success of batch F4 exemplifies the potential for further advancements in this field, paving the way for future research and development in nanoparticle-based drug delivery systems.

Compatibility and Stability

The Fourier-Transform Infrared Spectroscopy (FT-IR) analysis confirmed the compatibility of omeprazole with the chosen excipients, ensuring that the stability and effectiveness of the combination were maintained. This compatibility is essential, as it prevents potential interactions that could compromise the drug's efficacy or safety. By identifying any potential chemical interactions between omeprazole and the excipients early in the formulation process, the FT-IR analysis plays a critical role in safeguarding the drug's therapeutic integrity. This proactive approach ensures that the final product remains effective throughout its shelf life, preventing degradation or adverse reactions that could arise from incompatible ingredients.

Stability studies further supported these findings, indicating that the F4 formulation remained within acceptable limits over time and under various conditions. These studies, conducted under rigorous conditions, simulated different environmental factors such as temperature, humidity, and light exposure to assess the robustness of the formulation. The results showed that the F4 formulation maintained its physical and chemical stability, retaining its potency and effectiveness even after prolonged storage. This stability is crucial for ensuring the long-term efficacy and safety of the pharmaceutical product, as highlighted by [Your Name] et al. (2024).

Furthermore, the stability of the F4 formulation under varied conditions underscores its potential for widespread distribution and use. Pharmaceuticals often face diverse storage conditions across different regions and climates; thus, a formulation that can withstand these variations without losing efficacy is highly valuable. The successful stability results suggest that the F4 formulation can reliably deliver therapeutic benefits to patients over the entire course of its shelf life, providing confidence to both healthcare providers and patients in its use for treating duodenal ulcers. This extended stability ensures that patients receive the correct dosage and therapeutic effects from each tablet, contributing to better health outcomes and adherence to treatment regimens.

Drug Release Characteristics

Batch F4, which contained 4% sodium alginate and 5% gelatin, was particularly noteworthy for its exceptional performance. The formulation exhibited negligible drug release in 0.1 N

HCl, effectively protecting omeprazole in the acidic environment of the stomach. This characteristic is vital for proton pump inhibitors like omeprazole, which are highly susceptible to degradation in acidic conditions. The enteric coating provided by sodium alginate and gelatin serves as a robust barrier, preventing premature release and degradation of the drug in the stomach, thereby ensuring that a higher proportion of the active ingredient reaches the intestines intact.

The ability of the F4 formulation to release 98% of the drug after 12 hours in phosphate buffer highlights its efficiency in ensuring that the drug is released in the more neutral pH of the intestines, where it can be effectively absorbed. This sustained release profile is particularly beneficial for maintaining therapeutic drug levels over an extended period, reducing the frequency of dosing and potentially enhancing patient compliance. By ensuring a prolonged and controlled release, the F4 formulation maximizes the bioavailability of omeprazole, allowing for more consistent and effective management of conditions such as duodenal ulcers.

These findings are consistent with the goals of controlled release formulations, which aim to enhance drug stability and bioavailability while providing a predictable and sustained therapeutic effect. The precise control over the release kinetics afforded by the F4 formulation not only improves the therapeutic outcomes but also minimizes potential side effects associated with fluctuating drug levels in the bloodstream. This controlled release mechanism ensures that the drug is delivered at a steady rate, maintaining optimal therapeutic concentrations and improving the overall efficacy of the treatment.

Moreover, the F4 formulation's success in achieving such a high degree of control over the drug release process underscores the potential of using natural polymers like sodium alginate and gelatin in advanced drug delivery systems. These biocompatible and biodegradable polymers offer a safe and effective means of protecting and delivering sensitive drugs like omeprazole, aligning with the increasing demand for more natural and sustainable pharmaceutical solutions. The promising results obtained with batch F4 pave the way for further exploration and optimization of similar formulations, potentially extending their application to other drugs and therapeutic areas where controlled release is desirable.

5. Conclusion

In conclusion, batch F4 was identified as the optimal formulation as it met all the specified criteria and demonstrated exceptional performance in all evaluated parameters. The findings of this study underscore the potential of enteric-coated omeprazole nanoparticle tablets as a controlled release preparation for the treatment of duodenal ulcers. The effective protection of omeprazole in the stomach, combined with its efficient and controlled release in the intestines, highlights the formulation's capability to enhance therapeutic outcomes for patients suffering from duodenal ulcers. This study paves the way for further research and development in the field of nanoparticle-based drug delivery systems, offering a promising approach for improving the efficacy and safety of oral medications.

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