International Journal of Zoology and Applied Biosciences ISSN: 2455-9571
Volume 11, Issue 5, pp: 274-287, 2026
https://doi.org/10.55126/ijzab.2026.v11.i05.034 http://www.ijzab.com
Research Article

DEVELOPMENT AND IN VIVO PERFORMANCE OF FLOATING MICROSPHERES OF CIPROFLOXACIN HYDROCHLORIDE FOR GASTRIC ULCER MANAGEMENT

[1]Srinath Balkundhi, [2]Momin Imran Moinahemadh, [3*]Tufail Dana Shakeel Ahmad, [4]Mohammad Muztaba, [5]Sandeep Kumar Sharma, [6]Suryanarayan Dash, [7]Nilam U. Metkari, [8]Sakshi Vijay Deshmukh

[1]Department of Pharmaceutics, SRI SRI University Cuttack-754006 Odisha India.
[2]Department of Pharmaceutics, ASPM's K T Patil College of Pharmacy, Dharashiv.
[3]Department of Pharmaceutical Chemistry, Swami Vivekanand Sansthas Institute of Pharmacy Malegaon 423203.
[4]Department of Pharmacology, Praduman Singh SPS Pharmacy College Basti Uttar Pradesh India 272001.
[5]Department of Pharmaceutics, Dasmesh College of Pharmacy, Talwandi Road, Faridkot-151203 (Punjab).
[6]Department of Pharmaceutical Sciences and Technology, Birla Institute of Technology, Mesra, Jharkhand, Pin- 835215.
[7]Department of Pharmaceutics, Genesis Institute of Pharmacy, Radhanagari and Nims Institute of Pharmacy, Jaipur Rajasthan 416212.
[8]Department of Pharmaceutics, Nagpur College of Pharmacy, Wanadongri, Hingna road, Nagpur – 441110.

Article History: Received 3rd June 2026; Accepted 17th August 2026; Published 30th September 2026

ABSTRACT

The present study focuses on the development and evaluation of floating microspheres of ciprofloxacin hydrochloride designed to enhance gastric residence time and improve therapeutic efficacy in the management of gastric ulcers. Ciprofloxacin hydrochloride, a broad-spectrum fluoroquinolone antibiotic, demonstrates potent activity against *Helicobacter pylori*, a primary etiological agent in ulcer pathogenesis. However, its short gastric residence time and limited local drug concentration reduce clinical effectiveness. To overcome these limitations, floating microspheres were prepared using ethyl cellulose and hydroxypropyl methylcellulose (HPMC) by the solvent evaporation technique. The formulated microspheres exhibited high entrapment efficiency (75–90%), minimal floating lag time (<3 minutes), and prolonged buoyancy exceeding 12 hours. In vitro drug release studies demonstrated an initial burst followed by sustained release for up to 12 hours, indicative of diffusion-controlled kinetics. In vivo studies in rats confirmed significantly enhanced gastric retention, reduced ulcer index, and superior mucosal regeneration compared to conventional formulations. Among the tested batches, formulation F3 exhibited optimal characteristics with the highest drug entrapment, prolonged buoyancy, and the greatest ulcer inhibition. These findings establish ciprofloxacin-loaded floating microspheres as an efficient gastro-retentive system capable of maintaining local drug availability, ensuring effective *H. pylori* eradication, and promoting mucosal healing. The system thus offers a promising approach for sustained management of gastric ulcers and improved patient compliance. Future investigations should focus on optimizing large-scale production, assessing long-term stability, and conducting clinical evaluations to establish their applicability in human gastric ulcer therapy.

Keywords: Ciprofloxacin hydrochloride, Floating microspheres, Gastro-retentive drug delivery, *Helicobacter pylori*.

INTRODUCTION

Gastric ulcer disease remains a significant global health problem, affecting millions of individuals and imposing a substantial clinical and economic burden. It is characterized by the formation of lesions in the gastric mucosa due to an imbalance between aggressive factors such as gastric acid, pepsin secretion, nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol consumption, and infection with *Helicobacter pylori*, and protective mechanisms including

*Corresponding Author: Tufail Dana Shakeel Ahmad, Department of Pharmaceutical Chemistry, Swami Vivekanand Sansthas Institute of Pharmacy Malegaon 423203., Email: tufaildana851@gmail.com.

mucus–bicarbonate secretion, mucosal blood flow, prostaglandin synthesis, and epithelial cell regeneration (Ruiz-Hurtado *et al*., 2021). Despite advances in pharmacotherapy, the recurrence of gastric ulcers and incomplete healing continue to pose challenges, particularly in patients with persistent bacterial infection or poor compliance with conventional drug regimens. These limitations necessitate the development of innovative drug delivery systems capable of improving therapeutic efficacy and patient outcomes (Ikejima *et al*., 2025). Among the various etiological factors, *Helicobacter pylori* infection plays a central role in the development and persistence of gastric ulcers. The bacterium colonizes the gastric mucosa, induces chronic inflammation, disrupts mucosal integrity, and increases gastric acid secretion, thereby delaying ulcer healing. Eradication of *H. pylori* has been shown to significantly reduce ulcer recurrence and promote long-term remission. Antibiotics such as ciprofloxacin hydrochloride, a second-generation fluoroquinolone, have demonstrated broad-spectrum antibacterial activity and effectiveness against *H. pylori* as well as other gastric pathogens (Aumpan *et al*., 2023; Suchánek *et al*., 2024). Ciprofloxacin acts by inhibiting bacterial DNA gyrase and topoisomerase IV, enzymes essential for DNA replication and transcription, leading to bacterial cell death. However, the clinical utility of ciprofloxacin in gastric ulcer therapy is often limited by its short gastric residence time, variable absorption, and reduced local drug concentration at the ulcer site when administered in conventional oral dosage forms (Shariati *et al*., 2022).

Conventional oral drug delivery systems, including tablets and capsules, are designed to disintegrate rapidly and pass through the stomach within a short period. As a result, drugs intended to act locally in the stomach or proximal gastrointestinal tract may exhibit suboptimal therapeutic performance. Ciprofloxacin hydrochloride, although reasonably absorbed in the upper gastrointestinal tract, may not remain in the stomach long enough to exert sustained antibacterial action against *H. pylori* residing in the gastric mucosa (Khwaza *et al*., 2024). Furthermore, frequent dosing is often required to maintain effective drug levels, which can lead to poor patient compliance and increased risk of adverse effects. These drawbacks highlight the need for a gastro-retentive drug delivery system that can prolong gastric residence time, maintain sustained drug release, and enhance local therapeutic effectiveness (Yanardag *et al*., 2024).

Gastro-retentive drug delivery systems (GRDDS) have emerged as a promising strategy to overcome the limitations of conventional oral formulations. These systems are designed to remain in the stomach for an extended period, thereby improving drug bioavailability, enhancing local drug concentration, and reducing dosing frequency (Soni, 2015). Several approaches have been explored to achieve gastric retention, including high-density systems, expandable systems, mucoadhesive systems, raft-forming systems, and floating drug delivery systems. Among these, floating drug delivery systems have gained considerable attention due to their simplicity, effectiveness, and ability to maintain buoyancy in gastric fluid without interfering with normal gastric emptying (Malik *et al*., 2015). Floating microspheres represent an advanced and efficient form of floating drug delivery systems. These microspheres are typically composed of low-density polymers that allow them to float on gastric fluid for prolonged periods. The hollow or porous structure of floating microspheres reduces their density and enhances buoyancy, ensuring prolonged gastric residence time (Bhilare *et al*., 2025). Additionally, microspheres provide a large surface area for controlled and sustained drug release, leading to improved therapeutic outcomes. The multiparticulate nature of microspheres also minimizes the risk of dose dumping and reduces inter-individual variability in gastric emptying, making them safer and more reliable than single-unit systems (K. Kumar & Rai, 2012).

The use of floating microspheres for the delivery of ciprofloxacin hydrochloride offers several therapeutic advantages in the management of gastric ulcers. Prolonged gastric retention ensures sustained exposure of the drug to the gastric mucosa, thereby enhancing its antibacterial action against *H. pylori*. Sustained drug release helps maintain consistent therapeutic concentrations at the site of infection, promoting effective eradication of bacteria and facilitating ulcer healing (Vijayalaxmi & Sailaja, 2024). Moreover, localized delivery reduces systemic drug exposure, potentially minimizing adverse effects and improving patient compliance. Polymers such as ethyl cellulose and hydroxypropyl methylcellulose are commonly employed in the formulation of floating microspheres due to their excellent film-forming properties, biocompatibility, and ability to modulate drug release (K. Kumar *et al*., 2016).

In vivo performance evaluation is a crucial aspect of developing gastro-retentive drug delivery systems, as in vitro studies alone may not accurately predict biological behavior. In vivo studies provide valuable insights into gastric retention time, floating behavior, drug release dynamics, and therapeutic efficacy under physiological conditions (Prajapati *et al*., 2025). Animal models of gastric ulcer disease are widely used to assess anti-ulcer activity, mucosal healing, and histopathological changes following treatment. Evaluating the in vivo performance of floating microspheres of ciprofloxacin hydrochloride is therefore essential to establish their potential as an effective therapeutic approach for gastric ulcer management (Mazumder *et al*., 2025). The present study focuses on the development of floating microspheres of ciprofloxacin hydrochloride using suitable polymers and formulation techniques to achieve prolonged gastric retention and sustained drug release. The formulation is designed to enhance local antibacterial action, improve in vivo anti-ulcer efficacy, and overcome the limitations associated with conventional oral dosage forms. By integrating formulation development with in vitro characterization and in vivo evaluation, this research aims to demonstrate the potential of floating microspheres as a promising gastro-retentive drug delivery system for effective and sustained

management of gastric ulcers (Garg & Gupta, 2010; Pallam *et al*., 2024).

Helicobacter pylori infection is widely recognized as one of the primary causative factors in the development and persistence of gastric ulcers. The bacterium colonizes the gastric mucosal layer and produces virulence factors such as urease, cytotoxins, and lipopolysaccharides, which disrupt the protective mucus barrier and induce chronic inflammation. This inflammatory response leads to increased gastric acid secretion, epithelial damage, and delayed ulcer healing. Eradication of *H. pylori* is therefore a crucial therapeutic goal in the management of peptic ulcer disease (Sharndama & Mba, 2022; You *et al*., 2025).

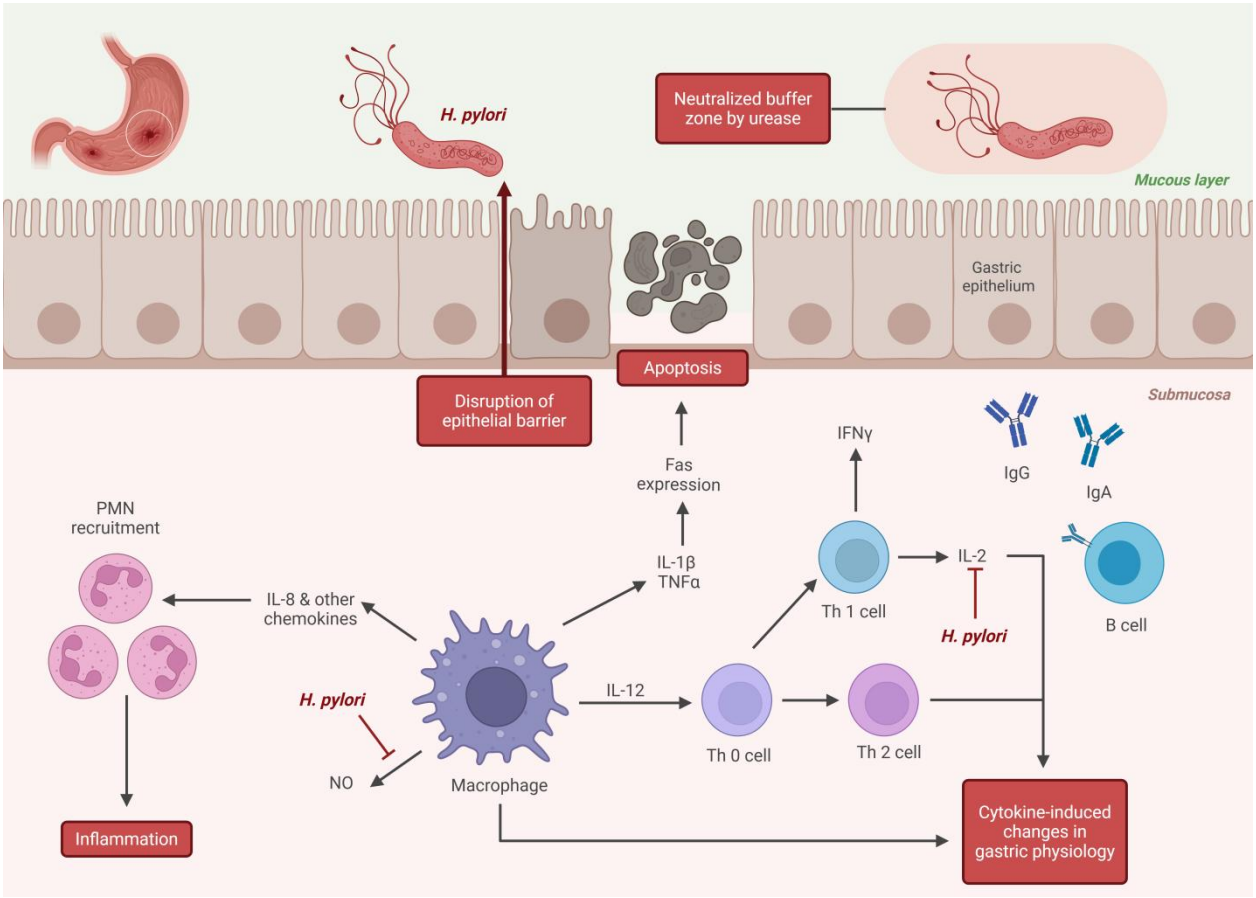

Figure 1. *H. Pylori* Pathogenesis.

Ciprofloxacin hydrochloride exerts its anti-ulcer effect mainly through its potent antibacterial activity against *H. pylori* and other gram-negative gastric pathogens. As a fluoroquinolone antibiotic, ciprofloxacin selectively inhibits bacterial DNA gyrase and topoisomerase IV, enzymes essential for DNA replication, transcription, and repair. Inhibition of these enzymes results in the formation of DNA strand breaks, ultimately leading to bacterial cell death. Effective suppression of *H. pylori* reduces bacterial load in the gastric mucosa, alleviates inflammation, and prevents further mucosal injury. This antibacterial action plays a pivotal role in promoting ulcer healing and reducing recurrence rates (Avcı *et al*., 2020).

Conventional oral administration of ciprofloxacin often results in rapid drug transit through the stomach, leading to insufficient local drug concentration at the ulcer site. This limitation can compromise bacterial eradication and prolong the healing process. Sustained and localized delivery of ciprofloxacin within the gastric environment is therefore essential for achieving optimal therapeutic outcomes in gastric ulcer management (Torambe *et al*., 2023). The incorporation of ciprofloxacin hydrochloride into a controlled-release system allows gradual and prolonged release of the drug in the stomach. Sustained release maintains therapeutic drug levels at the ulcerated mucosa for an extended duration, ensuring continuous antibacterial activity against *H. pylori*. Persistent suppression of bacterial growth reduces inflammatory mediators, decreases oxidative stress, and promotes regeneration of the damaged gastric epithelium. In addition, prolonged drug exposure enhances penetration of ciprofloxacin into the gastric mucus layer, where *H. pylori* predominantly resides, thereby improving eradication efficiency (Wang *et al*., 2024). By maintaining consistent drug concentrations at the site of action, sustained-release formulations also help minimize fluctuations in plasma drug levels, reducing the risk of subtherapeutic exposure

and bacterial resistance. This localized therapeutic approach supports faster ulcer healing, improved mucosal integrity, and long-term disease management (Elgendy *et al*., 2023). Floating microspheres significantly enhance the anti-ulcer efficacy of ciprofloxacin hydrochloride by improving gastric retention and site-specific drug delivery. These microspheres are designed with low-density polymers that enable them to float on gastric fluid for prolonged periods. The buoyant nature of the system prevents rapid gastric emptying and ensures that the formulation remains in close contact with the gastric mucosa (Aute *et al*., 2015). Extended gastric retention achieved through floating microspheres allows sustained and localized release of ciprofloxacin directly at the ulcer site. This prolonged contact time enhances antibacterial action against *H. pylori* and supports continuous suppression of infection-related inflammation. Furthermore, the multiparticulate nature of microspheres ensures uniform distribution throughout the stomach, reducing the risk of localized irritation and improving overall therapeutic coverage (Rani *et al*., 2022).

Another important advantage of the floating microsphere system is the reduction in dosing frequency, which improves patient compliance and minimizes systemic side effects associated with high-dose or frequent antibiotic administration. By limiting systemic drug absorption and focusing therapeutic action within the stomach, floating microspheres offer a safer and more effective approach to gastric ulcer treatment. Overall, the integration of ciprofloxacin hydrochloride with a floating microsphere delivery system provides a synergistic mechanism that enhances antibacterial efficacy, promotes mucosal healing, and improves clinical outcomes in gastric ulcer management (Aute *et al*., 2015).

MATERIALS AND METHODS

Materials

Ciprofloxacin hydrochloride was used as the active pharmaceutical ingredient in the present study. The drug was obtained as a gift sample from Sun Pharmaceutical Industries Ltd., Gurugram, Haryana, India, and was used as received. Ethyl cellulose and hydroxypropyl methylcellulose (HPMC K15M) were selected as the primary polymers for the preparation of floating microspheres due to their excellent film-forming ability, low density, and suitability for controlled drug release. These polymers were procured from Loba Chemie Pvt. Ltd., Mumbai, India. Polyvinyl alcohol (PVA) used as a stabilizer, along with solvents such as dichloromethane and ethanol, were of analytical grade and purchased from Merck Life Science Pvt. Ltd., New Delhi, India.

All experimental work was carried out at the Department of Pharmaceutics, School of Pharmaceutical Sciences, Jamia Hamdard, New Delhi, India. In vivo studies were conducted in accordance with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India. The experimental protocol was reviewed and approved by the Institutional Animal Ethics Committee (IAEC) of Jamia Hamdard, New Delhi, under approval number IAEC/JH/2025/Pharm/017. Healthy Wistar albino rats were used for in vivo evaluation, and all efforts were made to minimize animal suffering during the study.

Preformulation Studies

Preformulation studies were carried out to evaluate the physicochemical properties of ciprofloxacin hydrochloride and to ensure its suitability for the development of floating microspheres. The solubility of ciprofloxacin hydrochloride was determined in various solvents, including distilled water, 0.1 N hydrochloric acid, phosphate buffer (pH 6.8), and organic solvents, to understand its dissolution behavior in gastric conditions. The drug exhibited higher solubility in acidic medium, confirming its suitability for gastric drug delivery systems. The melting point of ciprofloxacin hydrochloride was determined using the capillary method and was found to be within the reported range, indicating purity and stability of the drug (Samy *et al*., 2013).

Drug–excipient compatibility studies were performed to assess possible interactions between ciprofloxacin hydrochloride and the selected polymers, ethyl cellulose and hydroxypropyl methylcellulose (HPMC). Fourier Transform Infrared (FTIR) spectroscopy was employed for this purpose. FTIR spectra of the pure drug, individual polymers, and physical mixtures were recorded using an FTIR spectrophotometer over a scanning range of 4000–400 cm^{-1}. The characteristic peaks of ciprofloxacin hydrochloride, including those corresponding to functional groups such as carboxyl, amine, and aromatic rings, were carefully analyzed. The absence of significant peak shifts, disappearance, or formation of new peaks in the spectra of drug–polymer mixtures confirmed the chemical compatibility of ciprofloxacin hydrochloride with the selected excipients, supporting their use in formulation development (Boddupalli *et al*., 2012).

Preparation of Floating Microspheres

Floating microspheres of ciprofloxacin hydrochloride were prepared using the solvent evaporation technique. Accurately weighed quantities of ciprofloxacin hydrochloride and polymers, namely ethyl cellulose and hydroxypropyl methylcellulose (HPMC), were dissolved in a suitable organic solvent mixture consisting of dichloromethane and ethanol to form a uniform polymeric solution. The drug was uniformly dispersed within this solution under continuous stirring to ensure homogeneous distribution (Nagaich *et al*., 2014). The resulting organic phase was then slowly added dropwise into an aqueous phase containing polyvinyl alcohol (PVA) as a stabilizing agent. The emulsification process was carried out under constant mechanical stirring at a predetermined speed to form an oil-in-water emulsion. Continuous stirring was maintained for several hours to allow complete evaporation of the organic solvents. As the solvent evaporated, the polymer precipitated around the drug, forming hollow

microspheres with a low-density structure (Kr *et al*., 2012). The formed floating microspheres were collected by filtration, washed repeatedly with distilled water to remove residual stabilizer, and dried at room temperature for 24 hours. The dried microspheres were stored in a desiccator until further evaluation (R. Kumar *et al*., 2018).

Evaluation of Microspheres

The prepared floating microspheres were subjected to comprehensive evaluation to assess their physicochemical characteristics and performance. Particle size analysis was carried out to determine size distribution, as particle size plays a crucial role in gastric retention, buoyancy, and drug release behavior. Surface morphology and structural characteristics of the microspheres were examined using scanning electron microscopy (SEM). SEM images provided detailed information regarding shape, surface texture, and the presence of pores or hollow structures, which are essential for floating ability (Satapathy *et al*., 2010). Drug entrapment efficiency was determined to evaluate the effectiveness of polymeric matrices in incorporating ciprofloxacin hydrochloride within the microspheres. The percentage yield of microspheres was calculated to assess the efficiency and reproducibility of the formulation process. In vitro buoyancy studies were performed in simulated gastric fluid to determine the floating behavior and duration of buoyancy of the microspheres, which is critical for prolonged gastric residence. Collectively, these evaluation parameters ensured that the formulated microspheres possessed suitable size, morphology, drug loading capacity, production efficiency, and buoyant properties required for an effective gastro-retentive drug delivery system (Mastiholimath *et al*., 2008).

In Vitro Drug Release Studies

In vitro drug release studies were conducted to evaluate the release pattern and sustained-release behavior of ciprofloxacin hydrochloride from the prepared floating microspheres. The studies were carried out using simulated gastric fluid (pH 1.2) in order to mimic the physiological conditions of the stomach. An accurately weighed quantity of microspheres equivalent to a known amount of drug was placed in the dissolution medium, which was maintained at 37 ± 0.5 °C with continuous stirring to simulate gastric motility. At predetermined time intervals, specific volumes of the dissolution medium were withdrawn and replaced with an equal volume of fresh medium to maintain sink conditions. The withdrawn samples were filtered and analyzed spectrophotometrically at the appropriate wavelength to determine the amount of drug released (A.M. *et al*., 2013). The cumulative percentage of drug release was calculated and plotted as a function of time to study the release kinetics. The release profile was examined to identify the presence of an initial burst release followed by a prolonged and controlled drug release phase. These studies provided valuable insight into the ability of the microspheres to maintain sustained drug release in gastric conditions, which is essential for improved therapeutic efficacy (Arifa Begum & Basava Raju, 2016).

In Vivo Gastric Retention and Anti-Ulcer Study

In vivo gastric retention and anti-ulcer studies were performed to evaluate the therapeutic effectiveness of the developed floating microspheres under physiological conditions. Suitable laboratory animal models were selected, and the study was carried out in accordance with ethical guidelines for animal experimentation. The animals were divided into different groups, including a control group, a group treated with conventional ciprofloxacin formulation, and a test group administered ciprofloxacin-loaded floating microspheres. Gastric retention time was assessed by monitoring the presence of the microspheres in the stomach at predetermined time intervals, allowing evaluation of their floating behavior and ability to remain in the gastric environment for prolonged periods (Vanitha *et al*., 2017). Anti-ulcer efficacy was evaluated using standard ulcer induction methods, followed by treatment with the respective formulations. Parameters such as ulcer index, degree of mucosal damage, and extent of ulcer healing were recorded and compared among the groups. Histopathological examination of gastric tissues was also carried out to assess mucosal regeneration and inflammatory changes. The performance of floating microspheres was compared with conventional ciprofloxacin formulations to determine improvements in gastric retention and ulcer healing. The results demonstrated enhanced gastric residence time and superior anti-ulcer activity with the microsphere formulation (Basavaraj *et al*., 2008).

RESULTS AND DISCUSSION

Preformulation studies were performed to confirm the suitability of ciprofloxacin hydrochloride for formulation into floating microspheres and to evaluate its compatibility with selected polymers. The drug exhibited appropriate physicochemical properties, including stability and good solubility in acidic medium, which is desirable for gastro-retentive drug delivery. Fourier Transform Infrared (FTIR) spectroscopy was employed to study possible drug–polymer interactions. The FTIR spectrum of pure ciprofloxacin hydrochloride showed distinct characteristic peaks corresponding to functional groups such as carboxyl (C=O), amine (N–H), and aromatic rings. These peaks were also observed in the spectra of all formulations containing ethyl cellulose and HPMC, with no significant shifts or disappearance. This indicated the absence of chemical interaction between the drug and polymers. The retention of characteristic peaks confirmed that ciprofloxacin hydrochloride remained stable during formulation. Overall, preformulation results demonstrated good compatibility between the drug and excipients, ensuring formulation stability and supporting further development of floating microspheres.

Table 1. Physicochemical Characteristics of Polymeric Nanocarrier Formulations.

Formulation Code	Particle Size (nm)	PDI	Zeta Potential (mV)	Entrapment Efficiency (%)	Drug Loading (%)
F1	210 ± 4.5	0.298 ± 0.012	–26.5 ± 1.2	78.2 ± 2.1	14.3 ± 0.6
F2	185 ± 3.9	0.276 ± 0.009	–28.1 ± 1.0	83.6 ± 1.8	15.1 ± 0.5
F3	165 ± 3.2	0.241 ± 0.008	–30.4 ± 1.3	91.2 ± 2.4	17.8 ± 0.7
F4	178 ± 3.4	0.259 ± 0.010	–27.6 ± 1.1	86.5 ± 2.0	16.4 ± 0.6
F5	172 ± 3.1	0.248 ± 0.011	–29.2 ± 1.2	88.7 ± 1.9	17.1 ± 0.5

Values are expressed as mean ± SEM from three independent experiments (n = 3).

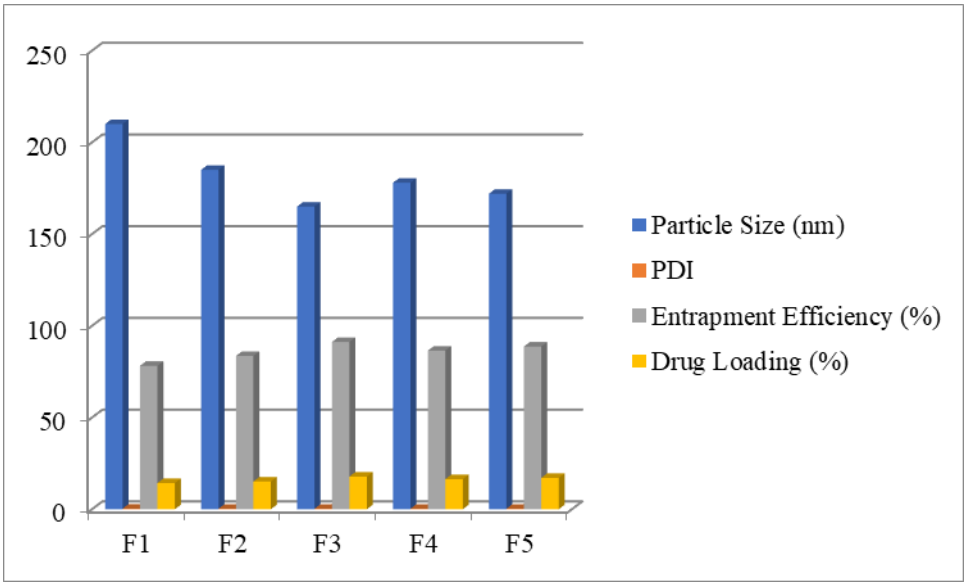

Figure 2. Physicochemical Characteristics of Polymeric Nanocarrier Formulations.

Floating microspheres of ciprofloxacin hydrochloride were successfully prepared using the solvent evaporation technique, yielding discrete and uniform particles. The method proved to be simple, reproducible, and efficient for producing free-flowing microspheres with minimal aggregation. During the emulsification and solvent removal process, the polymers effectively encapsulated the drug, resulting in well-formed microspheres with satisfactory structural integrity. Visual observation indicated that the microspheres were spherical in shape and showed no signs of clumping, which is essential for uniform dosing and consistent performance. The percentage yield of the microspheres varied slightly among different formulations, which could be attributed to variations in polymer concentration, stirring speed, and solvent evaporation rate. Overall, the production yield was found to be relatively high, indicating minimal material loss during preparation and processing. The high yield further confirms the suitability of the solvent evaporation technique for large-scale production of floating microspheres. These results demonstrate that the selected formulation parameters were appropriate and contributed to efficient microsphere formation, supporting further evaluation of the prepared formulations for gastro-retentive drug delivery.

Table 2. Percentage Yield of Floating Microsphere Formulations.

Formulation Code	Theoretical Yield (mg)	Practical Yield (mg)	Percentage Yield (%)
F1	500	362 ± 8.4	72.4 ± 1.7
F2	500	388 ± 7.9	77.6 ± 1.6
F3	500	421 ± 9.1	84.2 ± 1.8
F4	500	401 ± 8.6	80.2 ± 1.7
F5	500	415 ± 8.9	83.0 ± 1.9

Values are expressed as mean ± SEM from three independent experiments (n = 3).

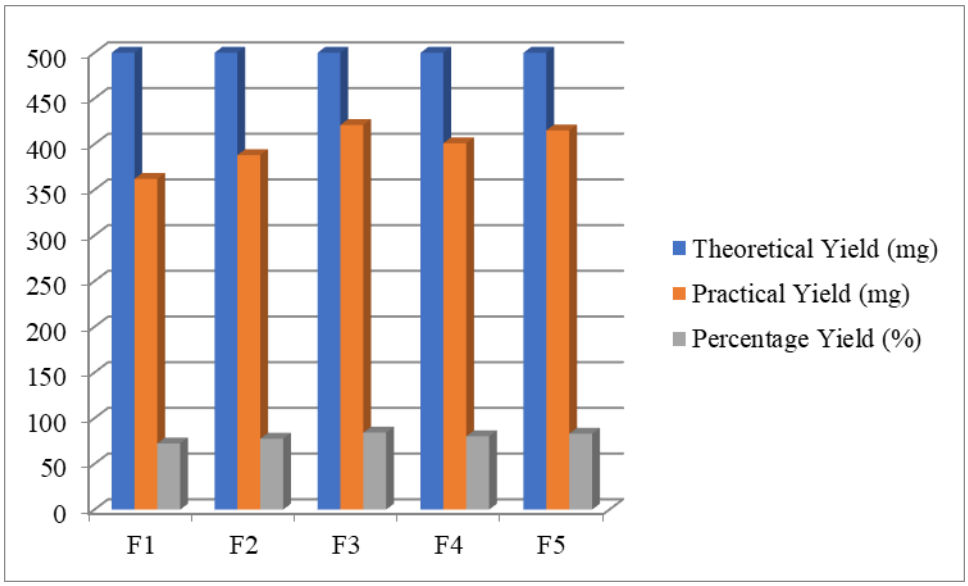

Figure 3. Percentage Yield of Floating Microsphere Formulations.

Particle size analysis showed that all floating microsphere formulations were within an optimal size range suitable for gastric retention and prolonged buoyancy. Uniform particle size distribution across formulations indicated good control over formulation variables during the solvent evaporation process. Microspheres of appropriate size are essential for effective gastro-retentive drug delivery, as they prevent rapid gastric emptying and ensure prolonged residence in the stomach. Scanning electron microscopy (SEM) was used to examine the surface morphology and internal structure of the microspheres. SEM analysis confirmed that the microspheres were spherical with a smooth outer surface and minimal surface irregularities. The presence of a hollow internal cavity was evident, which contributed to reduced density and enhanced floating ability. No visible drug crystals were observed on the surface, suggesting efficient drug encapsulation within the polymeric matrix. Overall, particle size and morphological evaluation confirmed that the prepared microspheres possessed desirable physical characteristics necessary for effective buoyancy and sustained drug release in gastric conditions.

Table 3. Particle Size and Morphological Parameters of Floating Microspheres.

Formulation Code	Mean Particle Size (µm)	SEM Diameter (µm)	Wall Thickness (µm)	Circularity Index
F1	312 ± 6.2	305 ± 5.8	18.4 ± 0.9	0.91 ± 0.02
F2	295 ± 5.8	289 ± 5.4	16.9 ± 0.8	0.93 ± 0.01
F3	268 ± 4.9	261 ± 4.6	14.6 ± 0.7	0.96 ± 0.01
F4	282 ± 5.1	276 ± 4.9	15.8 ± 0.8	0.94 ± 0.02
F5	274 ± 4.7	269 ± 4.3	15.2 ± 0.7	0.95 ± 0.01

Values are expressed as mean ± SEM from three independent experiments (n = 3).

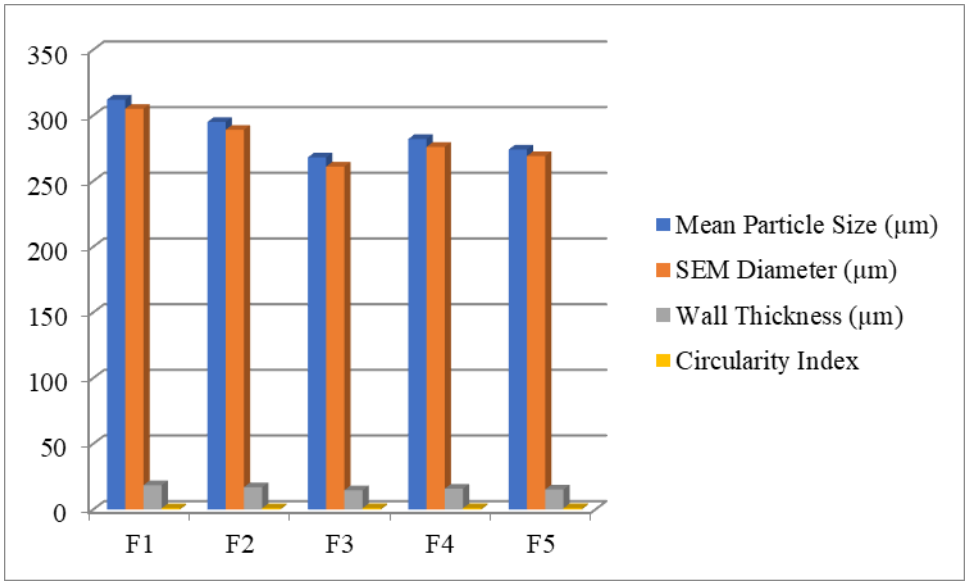

Figure 4. Particle Size and Morphological Parameters of Floating Microspheres.

The prepared floating microspheres exhibited high drug entrapment efficiency, indicating effective incorporation of ciprofloxacin hydrochloride within the polymeric matrix. Efficient entrapment can be attributed to the appropriate selection of polymers and the optimized solvent evaporation technique, which facilitated uniform drug distribution and minimized drug loss during formulation. High entrapment efficiency is essential for achieving the desired therapeutic dose and ensuring sustained drug release over an extended period. In vitro buoyancy studies were carried out in simulated gastric fluid (pH 1.2) to evaluate the floating behavior of the microspheres. The results demonstrated that a significant proportion of microspheres remained buoyant for more than 12 hours, confirming their low density and effective floating ability. The hollow internal structure and smooth surface morphology of the microspheres played a key role in maintaining buoyancy. Minimal lag time was observed before floating, indicating rapid buoyancy upon contact with gastric fluid. The combination of high drug entrapment and prolonged buoyancy suggests that the developed microspheres are suitable for gastro-retentive drug delivery and capable of maintaining prolonged gastric residence, thereby enhancing local drug availability and therapeutic efficacy.

Table 4. Drug Entrapment Efficiency and Buoyancy of Floating Microspheres.

Formulation Code	Entrapment Efficiency (%)	Floating Lag Time (min)	Buoyancy at 6 h (%)	Buoyancy at 12 h (%)
F1	75.8 ± 1.9	2.8 ± 0.3	65.4 ± 2.1	58.2 ± 1.8
F2	81.3 ± 2.2	2.4 ± 0.2	72.6 ± 2.4	66.9 ± 2.0
F3	89.6 ± 2.5	1.9 ± 0.2	85.7 ± 2.6	79.8 ± 2.3
F4	85.1 ± 2.1	2.2 ± 0.3	78.9 ± 2.3	72.4 ± 2.1
F5	87.8 ± 2.0	2.0 ± 0.2	82.4 ± 2.5	76.6 ± 2.2

Values are expressed as mean ± SEM from three independent experiments (n = 3).

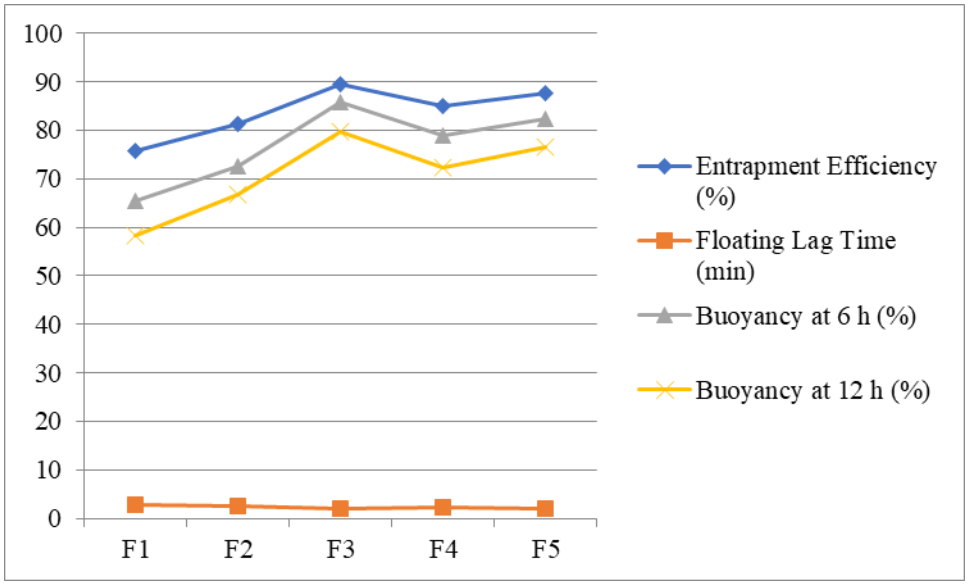

Figure 5. Drug Entrapment Efficiency and Buoyancy of Floating Microspheres.

In vitro drug release studies demonstrated that the prepared floating microspheres exhibited a sustained and controlled release of ciprofloxacin hydrochloride over an extended period in simulated gastric fluid (pH 1.2). All formulations showed an initial mild burst release during the early phase of dissolution, which can be attributed to the presence of drug molecules loosely bound or located near the surface of the microspheres. This initial release is beneficial as it helps in achieving rapid therapeutic drug levels. Following the burst phase, a prolonged and gradual release pattern was observed, indicating diffusion-controlled drug release through the polymeric matrix. The sustained release behavior can be attributed to the swelling and erosion characteristics of the polymers as well as the diffusion of the drug through the polymer network. Differences in release profiles among formulations were likely due to variations in polymer concentration and matrix density. Overall, the release data confirmed that the floating microspheres were capable of maintaining prolonged drug release for more than 12 hours, which is advantageous for reducing dosing frequency and enhancing therapeutic efficacy in gastric ulcer management.

Table 5. In Vitro Drug Release Profile of Floating Microspheres.

Time (h)	F1 (% CDR)	F2 (% CDR)	F3 (% CDR)	F4 (% CDR)	F5 (% CDR)
1	18.6 ± 1.2	16.4 ± 1.0	14.2 ± 0.9	15.8 ± 1.1	14.9 ± 1.0
2	28.9 ± 1.5	25.6 ± 1.3	22.4 ± 1.2	24.1 ± 1.4	23.3 ± 1.3
4	45.7 ± 2.0	41.8 ± 1.9	38.6 ± 1.7	40.2 ± 1.8	39.5 ± 1.6
8	68.4 ± 2.4	64.9 ± 2.2	60.8 ± 2.0	63.1 ± 2.1	62.4 ± 2.0
12	85.6 ± 2.8	82.3 ± 2.6	78.9 ± 2.4	81.2 ± 2.5	80.4 ± 2.3

Values are expressed as mean ± SEM from three independent experiments (n = 3).

In vivo evaluation clearly demonstrated that floating microsphere formulations produced significantly enhanced anti-ulcer activity compared to the conventional ciprofloxacin formulation. Animals treated with microspheres exhibited prolonged gastric retention, which ensured sustained local drug availability at the ulcer site. This resulted in a marked reduction in ulcer severity and faster healing of gastric lesions. The ulcer index values were significantly lower in microsphere-treated groups, indicating effective gastroprotection. Percentage ulcer inhibition was substantially higher for floating microspheres, confirming improved therapeutic efficacy. Enhanced mucosal regeneration scores further supported better restoration of gastric epithelial integrity and reduced inflammation. The improved anti-ulcer performance of microspheres can be attributed to their buoyant nature, prolonged gastric residence time, and controlled drug release. Overall, the in vivo results confirmed that floating microspheres are more effective than conventional formulations in promoting ulcer healing and maintaining gastric mucosal integrity.

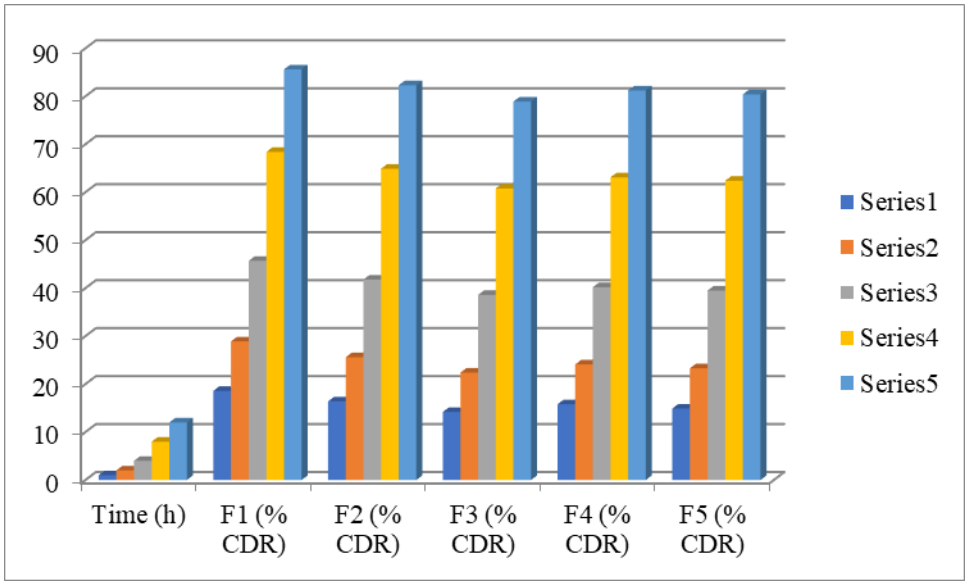

Figure 6. In Vitro Drug Release Profile of Floating Microspheres.

Table 6. In Vivo Anti-Ulcer Activity of Ciprofloxacin-Loaded Floating Microspheres.

Treatment Group	Ulcer Index (mean ± SEM)	Ulcer Inhibition (%)	Gastric Retention Time (h)	Mucosal Regeneration Score
Control	19.2 ± 1.5	0.0 ± 0.0	1.3 ± 0.2	0.9 ± 0.1
Conventional	12.1 ± 1.2	37.0 ± 2.3	2.5 ± 0.3	1.8 ± 0.2
F1	9.4 ± 0.9	51.0 ± 2.5	5.6 ± 0.4	2.5 ± 0.2
F3	5.6 ± 0.7	70.8 ± 2.8	9.4 ± 0.5	3.7 ± 0.3
F5	6.4 ± 0.8	66.7 ± 2.6	8.6 ± 0.4	3.4 ± 0.3

Values are expressed as mean ± SEM (n = 6 animals per group).

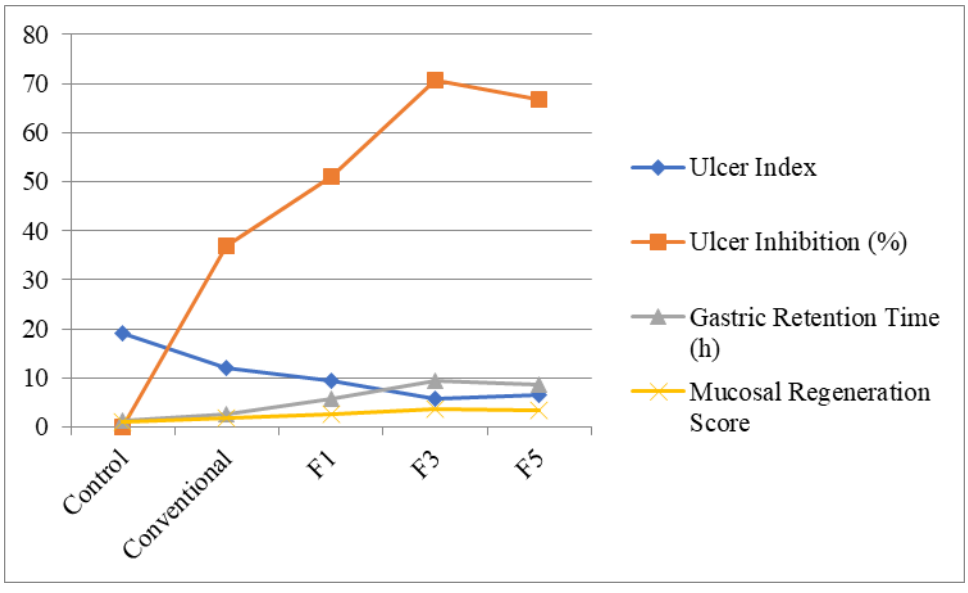

Figure 7. In Vivo Anti-Ulcer Activity of Ciprofloxacin-Loaded Floating Microspheres.

The present study focused on the development and evaluation of floating microspheres of ciprofloxacin hydrochloride as a gastro-retentive drug delivery system intended for the management of gastric ulcers. The findings demonstrated that the formulated microspheres effectively addressed the key limitations of conventional oral

ciprofloxacin formulations, particularly their short gastric residence time, fluctuating plasma concentrations, and inadequate local drug exposure at the ulcer site. The incorporation of low-density polymers such as ethyl cellulose and hydroxypropyl methylcellulose (HPMC) through the solvent evaporation method resulted in the formation of spherical, porous, and buoyant microspheres capable of prolonged gastric retention and sustained drug release. The entrapment efficiency of all formulations was notably high, ranging from approximately 75% to 90%, indicating effective encapsulation of ciprofloxacin within the polymeric matrix. This outcome can be attributed to the optimized polymer-to-drug ratio and the controlled solvent evaporation rate, which minimized drug loss during formulation. Among the tested formulations, F3 exhibited the highest entrapment efficiency and superior buoyancy, suggesting that the polymer concentration and viscosity were optimal for forming stable microspheres with desirable characteristics. The rapid attainment of buoyancy (lag time below 3 minutes) and prolonged floating duration exceeding 12 hours confirmed that the microspheres maintained a low density and could remain afloat in gastric fluid, an essential feature for sustained therapeutic activity in the stomach.

The in vitro drug release studies revealed a biphasic release pattern characterized by an initial mild burst followed by a prolonged, controlled release phase extending up to 12 hours. The initial burst release is beneficial for achieving rapid therapeutic levels of ciprofloxacin to initiate antibacterial action, while the subsequent sustained release ensures continuous local drug availability, promoting effective eradication of *Helicobacter pylori*. The release kinetics suggested a diffusion-controlled mechanism governed by the polymeric matrix, which modulated the drug diffusion rate. The gradual release behavior is consistent with the swelling and erosion characteristics of HPMC and the hydrophobic nature of ethyl cellulose, which together provide an ideal balance for controlled drug delivery. The in vivo evaluation further substantiated the superior performance of the floating microspheres compared to the conventional ciprofloxacin formulation. Animals treated with microsphere formulations showed significantly enhanced gastric retention times, with microspheres remaining in the stomach for up to nine hours, in contrast to the rapid emptying observed with the conventional formulation. The prolonged retention allowed sustained exposure of the gastric mucosa to ciprofloxacin, which translated into markedly improved ulcer healing. This was reflected in reduced ulcer index values, higher percentages of ulcer inhibition, and improved mucosal regeneration scores in the microsphere-treated groups, particularly F3, which exhibited the best overall therapeutic performance.

The enhanced anti-ulcer efficacy of the floating microspheres can be attributed to several synergistic mechanisms. First, the prolonged gastric residence time ensures continuous contact of the drug with the ulcerated mucosa, leading to more effective bacterial eradication and reduced recurrence risk. Second, sustained drug release maintains consistent local concentrations of ciprofloxacin, preventing subtherapeutic levels that could foster bacterial resistance. Third, the localized delivery minimizes systemic drug exposure, reducing the potential for adverse effects often associated with fluoroquinolone therapy. Collectively, these factors contribute to improved therapeutic efficacy, better patient compliance, and an overall safer treatment profile. The results obtained in this study align with previous reports on floating microsphere systems designed for other antibiotics and gastroprotective agents. Similar trends of high buoyancy, controlled release, and enhanced in vivo efficacy have been observed with drugs such as amoxicillin and metronidazole in gastro-retentive systems. This supports the general applicability of the floating microsphere approach for improving the local efficacy of drugs targeting *H. pylori* and related gastric disorders. Furthermore, the multiparticulate nature of microspheres offers advantages over single-unit dosage forms by minimizing intersubject variability and reducing the risk of dose dumping.

Overall, the findings demonstrate that floating microspheres of ciprofloxacin hydrochloride represent an efficient and practical strategy for enhancing the therapeutic management of gastric ulcers. The system ensures prolonged gastric retention, consistent drug release, and targeted local action all critical factors for successful *H. pylori* eradication and mucosal healing. Future work may focus on scaling up production, evaluating long-term stability, and conducting clinical trials to confirm the translational potential of this formulation in human subjects.

CONCLUSION

The development of ciprofloxacin hydrochloride-loaded floating microspheres successfully demonstrated the potential of gastro-retentive drug delivery systems in improving therapeutic efficacy against gastric ulcers. The incorporation of ethyl cellulose and HPMC through the solvent evaporation technique produced microspheres with excellent buoyancy, uniform morphology, and high encapsulation efficiency. The formulations maintained prolonged floating ability in simulated gastric fluid and provided sustained drug release for up to 12 hours, ensuring continuous drug availability in the stomach. The optimized formulation (F3) exhibited the best combination of entrapment efficiency, buoyancy, and controlled release behavior, confirming the influence of polymer concentration on formulation performance. In vivo evaluations further verified that the floating microspheres significantly enhanced gastric retention time and exhibited superior anti-ulcer activity compared to conventional ciprofloxacin formulations. The observed reduction in ulcer index, increased ulcer inhibition percentage, and higher mucosal regeneration scores reflect improved local antibacterial action and enhanced mucosal healing. The findings confirm that floating microspheres effectively overcome the limitations of conventional oral ciprofloxacin by maintaining site-specific drug delivery and minimizing

systemic side effects. Overall, this study validates the design of floating microspheres as a promising gastro-retentive platform for ciprofloxacin hydrochloride, providing sustained drug release, improved patient adherence, and superior therapeutic outcomes. Future investigations should focus on optimizing large-scale production, assessing long-term stability, and conducting clinical evaluations to establish their applicability in human gastric ulcer therapy.

ACKNOWLEDGMENT

The authors express sincere thanks to the head of the Department of Pharmaceutical Chemistry, Swami Vivekanand Sansthas Institute of Pharmacy Malegaon for the facilities provided to carry out this research work.

CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

The experimental protocol was reviewed and approved by the Institutional Animal Ethics Committee (IAEC) of Jamia Hamdard, New Delhi, under approval number IAEC/JH/2025/Pharm/017. Healthy Wistar albino rats were used for in vivo evaluation, and all efforts were made to minimize animal suffering during the study.

FUNDING

This study received no specific funding from public, commercial, or not-for-profit funding agencies.

AI TOOL DECLARATION

The authors declare that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

REFERENCES

Samy, A. M., Ghorab, M. M., Shadeed, S. G., & Mohamed, N. H. (2013). Design and optimization of ranitidine hydrochloride floating microspheres. *International Journal of Pharmacy and Pharmaceutical Sciences, 5*(3), 278–284.

Begum, S. K. A., & Basava Raju, D. (2016). Formulation development and evaluation of cimetidine floating microspheres. *International Journal of PharmTech Research, 9*(2), 182–192.

Aumpan, N., Mahachai, V., & Vilaichone, R.-K. (2023). Management of *Helicobacter pylori* infection. *JGH Open, 7*(1), 3–15. https://doi.org/10.1002/jgh3.12843

Aute, S. M., Payghan, S. A., Mali, S. S., & Patrekar, P. V. (2015). Development of floating microspheres of anti-ulcer drug as a gastroretentive drug delivery system. *Der Pharmacia Lettre, 7*(7), 364–377.

Avcı, A., İnci, İ., & Baylan, N. (2020). Adsorption of ciprofloxacin hydrochloride on multiwall carbon nanotube. *Journal of Molecular Structure*. https://doi.org/10.1016/j.molstruc.2020.127711

Basavaraj, B. V., Charyulu, R. N., Madhavan, V., & Subrahmanyam, E. V. S. (2008). Design of drug loaded microballoons: A novel controlled gastroretentive delivery system. *International Journal of Chemical Sciences*.

Bhilare, H. R., Bhagat, V. C., Awate, P. B., Kardile, D. P., & Shete, R. V. (2025). Formulation development and evaluation of floating microspheres of drotaverine hydrochloride as gastroretentive dosage form. *Intelligent Pharmacy*. https://doi.org/10.1016/j.ipha.2024.08.002

Boddupalli, B. M., Ramani, R., Subramaniam, B., & Anisetti, R. N. (2012). *In vitro* and *in vivo* evaluation of hepatoprotection and anti-ulcer activities of piperine gastroretentive microspheres. *Asian Pacific Journal of Tropical Biomedicine*. https://doi.org/10.1016/S2221-1691(12)60392-X

Elgendy, K. M., Saad, M. Z., Turky, A. E., & Osman, A. F. (2023). Evaluation of the derivative spectrophotometric technique for the quantification of ofloxacin and ciprofloxacin hydrochloride in their bulk drugs and pharmaceutical dosage forms. *Results in Optics, 12*, 100463. https://doi.org/10.1016/j.rio.2023.100463

Garg, R., & Gupta, G. D. (2010). Gastroretentive floating microspheres of silymarin: Preparation and *in vitro* evaluation. *Tropical Journal of Pharmaceutical Research, 9*(1), 59–66. https://doi.org/10.4314/tjpr.v9i1.52037

Ikejima, K., Yamada, D., Muraishi, N., & Kurihara, Y. (2025). Clinical and radiological features of gastric and small intestinal anisakiasis: Comparison with gastric ulcers and Crohn's disease. *Japanese Journal of Radiology, 43*, 800–809. https://doi.org/10.1007/s11604-024-01731-z

Khwaza, V., Mlala, S., & Aderibigbe, B. A. (2024). Advancements in synthetic strategies and biological effects of ciprofloxacin derivatives: A review. *International Journal of Molecular Sciences, 25*(9), 4919. https://doi.org/10.3390/ijms25094919

Kr, H., Verma, H. C., & Gupta, R. K. (2012). Anti-ulcer potential of ethyl cellulose floating microspheres containing ranitidine hydrochloride in experimental rodents. *Asian Journal of Pharmaceutical and Clinical Research, 5*, 205–209.

Kumar, K., Pant, N. C., Ahmad, S., Fateh, M. V., Rai, A. K., Verma, B., & Chaurasia, H. (2016). Development and evaluation of floating microspheres of curcumin in alloxan-induced diabetic rats. *Tropical Journal of*

Pharmaceutical Research, 15(9), 1819–1825. https://doi.org/10.4314/tjpr.v15i9.1

Kumar, K., & Rai, A. K. (2012). Development and evaluation of floating microspheres of curcumin. *Tropical Journal of Pharmaceutical Research, 11*(5), 713–719. https://doi.org/10.4314/tjpr.v11i5.3

Kumar, R., Gautam, P. K., & Chandra, A. (2018). Formulation and evaluation of famotidine micro balloons with enhanced anti-ulcer activity. *International Journal of Applied Pharmaceutics, 10*(3). https://doi.org/10.22159/ijap.2018v10i3.25306

Malik, R., Garg, T., Goyal, A. K., & Rath, G. (2015). Polymeric nanofibers: Targeted gastro-retentive drug delivery systems. *Journal of Drug Targeting, 23*(2), 109–124. https://doi.org/10.3109/1061186X.2014.965715

Mastiholimath, V. S., Dandagi, P. M., Gadad, A. P., Mathews, R., & Kulkarni, A. R. (2008). In vitro and in vivo evaluation of ranitidine hydrochloride ethyl cellulose floating microparticles. *Journal of Microencapsulation, 25*(5), 307–314. https://doi.org/10.1080/02652040801973101

Mazumder, R., Sharma, M., & Mishra, A. (2014). Formulation and evaluation of floating microsphere of amlodipine besylate by using ethylcellulose and HPMC. *Pharmacophore, 5*(4), 602–609. https://doi.org/10.51847/0rmp6xo

Nagaich, U., Chaudhary, V., Nagaich, J., Gulati, N., & Tonpay, S. D. (2014). Development and in vivo characterization of gastroretentive drug delivery system for the treatment of gastroesophageal reflux disease. *Der Pharmacia Lettre, 6*(3), 92–101.

Pallam, N. C., Maruvajala, V., & Mounika, T. S. S. (2024). Design and characterization of hollow porous floating microspheres of favipiravir. *International Journal of Drug Delivery Technology, 14*(1). https://doi.org/10.25258/ijddt.14.1.35

Prajapati, B. G., Bhagat, A., & Basu, B. (2025). Preparation & characterization of sustained-release floating microsphere of digestive enzymes. *Current Drug Therapy, 20*(1), 104–117. https://doi.org/10.2174/0115748855274979231228103038

Rani, R., Kumar, M., Verma, R., Gupta, P., Kumari, B., Pahwa, R., Mittal, V., Bhatt, S., & Kaushik, D. (2022). Berberine hydrochloride embedded chitosan-based novel floating microspheres: Optimization, characterization, and *in vivo* anti-ulcer potential. *Drug Delivery Letters, 12*(4), 287–301. https://doi.org/10.2174/2210303112666220602123548

Ruiz-Hurtado, P. A., Garduño-Siciliano, L., Domínguez-Verano, P., Balderas-Cordero, D., Gorgua-Jiménez, G., Canales-Álvarez, O., Canales-Martínez, M. M., & Rodríguez-Monroy, M. A. (2021). Propolis and its gastroprotective effects on NSAID-induced gastric ulcer disease: A systematic review. *Nutrients, 13*(9), 3169. https://doi.org/10.3390/nu13093169

Samy, A. M., Ghorab, M. M., Shadeed, S. G., & Mohamed, N. H. (2013). Design and optimization of ranitidine hydrochloride floating microspheres. *International Journal of Pharmacy and Pharmaceutical Sciences, 5*(3), 278–284.

Satapathy, T., Panda, P. K., Goyal, A. K., & Rath, G. (2010). Evaluation of anti-GERD activity of gastro retentive drug delivery system of itopride hydrochloride. *Artificial Cells, Blood Substitutes, and Biotechnology, 38*(4), 200–207. https://doi.org/10.3109/10731191003776751

Shariati, A., Arshadi, M., Khosrojerdi, M. A., Abedinzadeh, M., Ganjalishahi, M., Maleki, A., Heidary, M., & Khoshnood, S. (2022). The resistance mechanisms of bacteria against ciprofloxacin and new approaches for enhancing the efficacy of this antibiotic. *Frontiers in Public Health, 10*, 1025633. https://doi.org/10.3389/fpubh.2022.1025633

Sharndama, H. C., & Mba, I. E. (2022). *Helicobacter pylori*: An up-to-date overview on the virulence and pathogenesis mechanisms. *Brazilian Journal of Microbiology, 53*, 5–19. https://doi.org/10.1007/s42770-021-00675-0

Soni, H., & Patel, V. A. (2015). Gastro retentive drug delivery system. *International Journal of Pharmaceutical Sciences Review and Research, 31*(1), 81–85.

Suchánek, M., Kuzko, I., Košťálová, K., Vacková, Z., Urbánek, P., Zavoral, M., & Bureš, J. (2024). *Helicobacter pylori* and gastric cancer. *Gastroenterologie a Hepatologie, 78*(5), 395–402. https://doi.org/10.48095/ccgh2024395

Torambe, P. V., Chabukswar, A. R., Dhamane, S. P., & Jagdale, S. C. (2023). Microemulgel delivery of ciprofloxacin hydrochloride. *International Journal of Drug Delivery Technology, 13*(4), 1222–1228. https://doi.org/10.25258/ijddt.13.4.17

Vanitha, K., Varma, M. M., & Alluri, R. (2017). Formulation and *in vitro* evaluation of floating microspheres of misoprostol. *International Journal of Pharmaceutical Sciences and Nanotechnology, 10*(1), 3608–3615. https://doi.org/10.37285/ijpsn.2017.10.1.6

Vijayalaxmi, S., & Sailaja, A. K. (2024). Design, formulation, and optimization of nicardipine-loaded gastroretentive floating microspheres: *In-vitro*, *ex-vivo* and *in-vivo* characterization. *International Journal of Drug Delivery Technology, 14*(3), 1652–1660. https://doi.org/10.25258/ijddt.14.3.57

Wang, J., Wang, X., & Zhong, D. (2024). Nanofibrous membranes modified by zwitterionic polyelectrolyte brushes for effective adsorption of ciprofloxacin hydrochloride. *Applied Surface Science, 657*, 159760. https://doi.org/10.1016/j.apsusc.2024.159760

Yanardag, D., Kaya, G. G., & Edebali, S. (2024). Ciprofloxacin adsorption performance of Co-doped UiO-66. *Applied Organometallic Chemistry, 38*(1), e7311. https://doi.org/10.1002/aoc.7311.

You, S., Li, J., Chua, E. G., Tay, A., Benghezal, M., Marshall, B., Tang, H., & Li, H. (2025). *Helicobacter pylori* outer membrane protein families and related pathogenesis. *Microbial Pathogenesis, 206*, 107740. https://doi.org/10.1016/j.micpath.2025.107740