RESEARCH PAPER

Formulation and Characterization of Misoprostol Floating Mucoadhesive Microspheres for Long-Term Ulcer Management

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ABSTRACT

Peptic ulcer disease remains a significant gastrointestinal disorder requiring prolonged pharmacotherapy to ensure mucosal healing and prevent recurrence. The present study aimed to develop and characterize floating mucoadhesive microspheres of misoprostol for sustained gastric retention and controlled drug release in long-term ulcer management. Misoprostol, a prostaglandin E1 analogue with potent cytoprotective activity, exhibits a short half-life and requires frequent dosing, which may reduce patient compliance. To overcome these limitations, floating mucoadhesive microspheres were prepared using an emulsion–solvent evaporation technique with polymers such as hydroxypropyl methylcellulose (HPMC), carbopol, and ethyl cellulose. The formulated microspheres were evaluated for particle size, surface morphology, percentage yield, drug entrapment efficiency, buoyancy, swelling behavior, mucoadhesive strength, and in vitro drug release profile. Microscopic examination revealed spherical particles with a smooth surface. The optimized formulation demonstrated satisfactory buoyancy for more than 12 hours and strong mucoadhesive properties, ensuring prolonged gastric residence. Entrapment efficiency ranged between 68–85%, indicating effective drug incorporation. In vitro release studies showed sustained drug release up to 12–24 hours following non-Fickian diffusion kinetics. The results suggest that floating mucoadhesive microspheres of misoprostol could enhance gastric retention time, reduce dosing frequency, and improve therapeutic efficacy in chronic ulcer management. This delivery system presents a promising approach for site-specific and sustained drug delivery in gastric disorders.

Keywords: Misoprostol, Floating microspheres, Mucoadhesive delivery, Peptic ulcer, Sustained release, Gastric retention system.

How to cite this article: Mahanti K, Nandi S, Santra H, Maity A, Pathak B, Kar B, Parya H. Formulation and Characterization of Misoprostol Floating Mucoadhesive Microspheres for Long-Term Ulcer Management. Int J Drug Deliv Technol. 2026;16(23s): 1063-1067. DOI: 10.25258/ijddt.16.23s.116

Source of support: Nil.

Conflict of interest: None

Introduction

Peptic ulcer disease (PUD) is a common gastrointestinal disorder characterized by erosion of the gastric or duodenal mucosa due to an imbalance between aggressive factors such as gastric acid, pepsin, *Helicobacter pylori* infection, and protective mechanisms including mucus secretion and prostaglandin synthesis. Despite the availability of proton pump inhibitors and H_2-receptor antagonists, recurrence and long-term complications remain a clinical challenge, particularly in patients requiring chronic non-steroidal anti-inflammatory drug (NSAID) therapy.

Therefore, development of gastroprotective and site-specific drug delivery systems is essential for effective long-term ulcer management.[2]

Misoprostol, a synthetic prostaglandin E_1 analogue, exhibits potent cytoprotective and antisecretory effects by enhancing mucus and bicarbonate secretion while reducing gastric acid production. It is widely used for the prevention of NSAID-induced gastric ulcers. However, misoprostol possesses a short biological half-life and requires multiple daily dosing, which may lead to poor patient compliance and dose-related adverse effects. Moreover, rapid gastric emptying can reduce its local therapeutic action in the stomach. These limitations necessitate the development of a sustained-release gastroretentive drug delivery system.[3]

Gastroretentive systems such as floating drug delivery systems have gained considerable attention due to their ability to prolong gastric residence time. Floating microspheres remain buoyant in gastric fluid for extended periods, thereby enhancing local drug concentration in the stomach. Incorporation of mucoadhesive polymers further improves gastric retention by promoting adhesion to the gastric mucosa. The combined floating and mucoadhesive approach offers dual mechanisms for prolonged drug residence, sustained release, and improved therapeutic efficacy.

Microspheres prepared using biodegradable polymers such as hydroxypropyl methylcellulose (HPMC), carbopol, and ethyl cellulose provide controlled drug release and enhanced stability. The emulsion–solvent evaporation technique is widely employed for preparing polymeric microspheres due to its simplicity, reproducibility, and ability to produce uniform spherical particles.

In view of the above considerations, the present study was designed to formulate and characterize misoprostol-loaded floating mucoadhesive microspheres for prolonged gastric retention and sustained drug release. The objective was to enhance therapeutic efficacy, reduce dosing frequency, and provide an effective delivery system for long-term ulcer management.

Materials and Methods

1. Materials

Misoprostol was obtained as a gift sample from a reputed pharmaceutical manufacturer. Hydroxypropyl methylcellulose (HPMC K100M), Carbopol 934P, and Ethyl cellulose were used as polymers for floating and mucoadhesive properties. Polyvinyl alcohol (PVA) served as an emulsifying agent. Dichloromethane and ethanol were used as organic solvents. Liquid paraffin was used as the external oil phase. All other reagents and chemicals were of analytical grade and used without further purification.[4]

2. Preparation of Floating Mucoadhesive Microspheres

Floating mucoadhesive microspheres of misoprostol were prepared by the emulsion–solvent evaporation technique.

Misoprostol and selected polymers (HPMC, Carbopol, and Ethyl cellulose in varying ratios) were dissolved in a mixture of dichloromethane and ethanol to form the internal organic phase. This phase was slowly introduced into liquid paraffin containing 0.5–1% w/v PVA under continuous mechanical stirring (800–1000 rpm) to form an oil-in-oil emulsion.

The system was stirred for 2–3 hours to allow complete evaporation of the solvent and formation of solid microspheres. The formed microspheres were filtered, washed repeatedly with n-hexane to remove residual oil, and dried at room temperature for 24 hours. Dried microspheres were stored in a desiccator until further evaluation.[5]

3. Evaluation of Microspheres

3.1 Percentage Yield

The dried microspheres were weighed and percentage yield was calculated using:

$$\text{Percentage Yield} = \frac{\text{Practical Yield}}{\text{Theoretical Yield}} \times 100$$

3.2 Particle Size Analysis

Particle size was determined using optical microscopy with a calibrated ocular micrometer. The average diameter was calculated by measuring at least 100 microspheres.[6]

3.3 Surface Morphology

Surface characteristics were examined using scanning electron microscopy (SEM). Samples were gold-coated under vacuum before imaging.

3.4 Drug Entrapment Efficiency

A known quantity of microspheres was crushed and dissolved in phosphate buffer (pH 1.2). The solution was filtered and analyzedspectrophotometrically at the predetermined λmax of misoprostol.[7]

\text{Entrapment Efficiency (\%)} = \frac{\text{Actual Drug Content}}{\text{Theoretical Drug Content}} \times 100

3.5 In Vitro Buoyancy Study

Microspheres were dispersed in 900 mL of 0.1N HCl (pH 1.2) at 37 ± 0.5°C using a USP dissolution apparatus II at 100 rpm. After 12 hours, floating and settled microspheres were separated, dried, and weighed.[8]

\text{Buoyancy (\%)} = \frac{\text{Weight of Floating Microspheres}}{\text{Total Weight of Microspheres}} \times 100

3.6 Swelling Index

Microspheres were placed in simulated gastric fluid (pH 1.2) and weighed at predetermined intervals. Swelling index was calculated as:

\text{Swelling Index} = \frac{W_t - W_0}{W_0}

Where is the weight at time t and is the initial weight.

3.7 Mucoadhesive Strength

An in vitro wash-off method was used to evaluate mucoadhesion. Freshly excised goat gastric mucosa was mounted on a glass slide. Microspheres were spread over the mucosal surface and subjected to slow up-and-down movements in 0.1N HCl at 37°C. The percentage of adhered microspheres was determined over time.[9]

3.8 In Vitro Drug Release Study

Drug release was studied using USP dissolution apparatus II in 900 mL of 0.1N HCl (pH 1.2) at 37 ± 0.5°C and 100 rpm. Samples were withdrawn at predetermined intervals and replaced with fresh medium. Drug concentration was measured spectrophotometrically. Release kinetics were analyzed using zero-order, first-order, Higuchi, and Korsmeyer–Peppas models.

4. Statistical Analysis

All experiments were performed in triplicate, and results were expressed as mean ± standard deviation. Statistical analysis was carried out using one-way ANOVA, and $p < 0.05$ was considered statistically significant.[10]

Results

All formulations (F1–F6) were evaluated for physicochemical characteristics, buoyancy, mucoadhesion, and drug release behavior. Data are expressed as Mean ± SD (n = 3). Statistical analysis was performed using one-way ANOVA, and $p < 0.05$ was considered statistically significant.

Table 1. Percentage Yield and Drug Entrapment Efficiency

Formulation	Percentage Yield (%)	Entrapment Efficiency (%)
F1	71.25 ± 1.42	68.40 ± 1.15
F2	74.80 ± 1.36	72.65 ± 1.28
F3	78.45 ± 1.22	79.30 ± 1.34
F4	82.10 ± 1.18	85.12 ± 1.21
F5	80.35 ± 1.40	82.76 ± 1.19
F6	76.90 ± 1.27	77.54 ± 1.33

Statistical Analysis (ANOVA):

Significant difference observed among formulations for entrapment efficiency ($p < 0.05$). F4 showed significantly higher drug entrapment compared to F1 and F2.

Table 2. Particle Size and Surface Morphology

Formulation	Mean Particle Size (µm)	Surface Characteristics
F1	212.5 ± 5.6	Slightly rough
F2	228.3 ± 4.8	Smooth
F3	245.7 ± 6.2	Smooth, spherical
F4	268.4 ± 5.1	Uniform, spherical
F5	259.6 ± 4.9	Smooth
F6	238.2 ± 5.4	Slightly porous

Increase in polymer concentration resulted in significant increase in particle size ($p < 0.05$).

Table3. In-Vitro Buoyancy Study (12 Hours)

Formulation	Floating Percentage (%)
F1	65.20 ± 1.15
F2	72.45 ± 1.32
F3	81.30 ± 1.18
F4	92.65 ± 1.10
F5	88.40 ± 1.24
F6	79.75 ± 1.29

F4 exhibited maximum buoyancy (> 90%) for 12 hours. Statistical analysis showed significant improvement in buoyancy with increasing ethyl cellulose concentration ($p < 0.05$).

Table 4. Swelling Index

Formulation	Swelling Index (6 hr)

F1	0.62 ± 0.03
F2	0.75 ± 0.04
F3	0.88 ± 0.05
F4	1.02 ± 0.04
F5	0.95 ± 0.03
F6	0.82 ± 0.04

Higher HPMC and Carbopol concentration significantly increased swelling capacity ($p < 0.05$).

Table 5. Mucoadhesive Strength (Wash-Off Test)

Formulation	% Drug Adhered After 8 hr
F1	58.40 ± 1.22
F2	65.75 ± 1.35
F3	73.80 ± 1.18
F4	89.25 ± 1.12
F5	84.60 ± 1.30
F6	70.45 ± 1.27

F4 showed significantly higher mucoadhesive strength ($p < 0.05$), attributed to optimal Carbopol concentration.

Table 6. In-Vitro Drug Release Profile

Formulation	% Drug Release at 12 hr	% Drug Release at 24 hr	Release Kinetics (Best Fit Model)
F1	92.30 ± 1.18	—	First Order
F2	88.45 ± 1.25	—	Higuchi
F3	76.60 ± 1.30	94.25 ± 1.22	Korsmeyer-Peppas
F4	68.75 ± 1.15	91.80 ± 1.18	Korsmeyer-Peppas
F5	72.40 ± 1.28	93.15 ± 1.26	Higuchi
F6	80.25 ± 1.35	95.40 ± 1.20	First Order

The optimized formulation (F4) demonstrated sustained drug release up to 24 hours with non-Fickian diffusion (n value between 0.5–0.89).

ANOVA confirmed statistically significant differences in cumulative drug release among formulations ($p < 0.05$).

Optimized Formulation

Based on percentage yield, entrapment efficiency, buoyancy, mucoadhesion, and sustained drug release, **Formulation F4** was considered optimized for long-term ulcer management.

Conclusion

The present study successfully formulated and evaluated floating mucoadhesive microspheres of misoprostol for prolonged gastric retention and sustained drug release. The emulsion–solvent evaporation method produced spherical microspheres with satisfactory percentage yield and high drug entrapment efficiency. The optimized formulation (F4) demonstrated excellent buoyancy for more than 12 hours, strong mucoadhesive strength, and controlled drug release extending up to 24 hours.

The combination of floating and mucoadhesive mechanisms significantly enhanced gastric residence time, which is essential for effective local therapy in peptic ulcer management. In vitro release kinetics indicated non-Fickian diffusion, suggesting a combined mechanism of drug diffusion and polymer relaxation.

Overall, the developed gastroretentive delivery system has the potential to reduce dosing frequency, improve patient compliance, and enhance therapeutic efficacy of misoprostol in long-term ulcer treatment. Further in vivo studies are recommended to confirm clinical performance and safety of the optimized formulation.

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