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DESIGN AND EVALUATION OF PANTOPRAZOLE-LOADED FLOATING MUCOADHESIVE MICROSPHERES FOR PROLONGED GASTRIC RETENTION

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ABSTRACT

Objective: The present study aimed to design and evaluate pantoprazole-loaded floating mucoadhesive microspheres to overcome the challenges associated with conventional pantoprazole delivery, namely its acid-lability and narrow absorption window in the proximal small intestine, by achieving prolonged gastric retention and sustained drug release. **Methods:** Floating mucoadhesive microspheres were prepared using the ionotropic gelation technique with sodium alginate as the polymer matrix and calcium chloride as the cross-linking agent. Calcium carbonate was incorporated as a gas-forming agent to impart buoyancy. A 3^2 factorial design was employed to systematically evaluate the influence of polymer concentration (2-4% w/v) and cross-linker concentration (5-15% w/v) on critical formulation attributes. The prepared microspheres were characterized for micromeritic properties, surface morphology using Scanning Electron Microscopy (SEM), drug-excipient compatibility by FTIR and DSC, percentage yield, drug entrapment efficiency, in-vitro buoyancy, ex-vivo mucoadhesive strength, in-vitro drug release in simulated gastric fluid (pH 1.2), and drug release kinetics. **Results:** All formulations produced discrete, spherical microspheres with good flow properties (Carr's index 12.4-18.7%). Mean particle size ranged from 425 ± 12.5 µm to 680 ± 18.3 µm, showing a direct correlation with polymer concentration. FTIR studies confirmed the absence of drug-polymer interactions, while DSC analysis indicated amorphous dispersion of pantoprazole within the polymer matrix. Percentage yield ranged from 72.5% to 89.6%, and drug entrapment efficiency varied from 58.3% to 87.2%, with both parameters significantly influenced by polymer and cross-linker concentrations. All formulations exhibited excellent buoyancy with floating lag times of 2-8 minutes and total floating time exceeding 12 hours. Ex-vivo mucoadhesive strength ranged from 8.5 ± 0.8 g to 15.2 ± 1.2 g, increasing with higher polymer concentration. In-vitro drug release studies revealed a biphasic pattern with initial burst release (18-32%) followed by sustained release over 12 hours. Drug release kinetics followed the Higuchi model ($R^2 > 0.96$) with anomalous (non-Fickian) transport mechanism (n = 0.512-0.651), indicating diffusion coupled with polymer relaxation. Formulation F5 (3% sodium alginate, 10% calcium chloride) was identified as the optimized formulation, exhibiting highest entrapment efficiency (87.2%), minimal floating lag time (2 minutes), maximum mucoadhesive strength (15.2 g), and optimal sustained release (86.3% in 12 hours) with anomalous transport kinetics. **Conclusion:** The developed floating mucoadhesive microspheres successfully addressed the biopharmaceutical limitations of conventional pantoprazole delivery by combining buoyancy and mucoadhesion to achieve prolonged gastric retention. The optimized formulation (F5) demonstrated superior performance characteristics, offering a promising gastroretentive drug delivery system capable of enhancing the oral bioavailability and therapeutic efficacy of pantoprazole through sustained release at its absorption site, potentially enabling once-daily dosing and improved patient compliance in the management of acid-related disorders.

KEYWORDS: Pantoprazole; Gastroretentive Drug Delivery System (GRDDS); Floating Microspheres; Mucoadhesive.

INTRODUCTION

While this protective strategy ensures the drug reaches the small intestine, its site of absorption is largely confined to the proximal segment, creating a narrow absorption window that limits the timeframe for optimal systemic uptake. Furthermore, conventional immediate or even extended-release formulations are subject to the vagaries of gastrointestinal transit, particularly the variable process of gastric emptying. This physiological reality means that even a protected drug has a finite residence time in the stomach and its primary absorption site, after which the remaining unreleased or unabsorbed drug is propelled along the intestine, potentially leading to incomplete absorption and suboptimal bioavailability. The short plasma half-life of pantoprazole, common to all PPIs, exacerbates this issue, often requiring frequent dosing to maintain therapeutic effect and manage conditions like gastroesophageal reflux disease or gastric ulcers effectively. In response to these biopharmaceutical hurdles, Gastroretentive Drug Delivery Systems (GRDDS) have emerged as a sophisticated strategy to revolutionize the oral delivery of drugs with a narrow absorption window, such as pantoprazole. The fundamental rationale underpinning GRDDS is the deliberate and prolonged retention of the dosage form in the stomach, independent of the natural gastric emptying process. By resisting premature expulsion through the pyloric sphincter, these systems ensure that the drug remains at or above its primary absorption site for an extended duration. This controlled gastric residence confers multiple therapeutic advantages: it maximizes the time available for drug dissolution and subsequent absorption, enhances the overall bioavailability of drugs like pantoprazole that are absorbed from the upper gastrointestinal tract, and allows for the sustained release of the active pharmaceutical ingredient over many hours . Consequently, GRDDS can transform a drug with a short absorption window into a candidate for once-daily or less frequent dosing, thereby improving patient compliance and reducing the fluctuations in plasma drug concentrations that can lead to breakthrough symptoms or adverse effects . This approach is particularly valuable for achieving local drug delivery within the stomach, such as for the eradication of *Helicobacter pylori* in peptic ulcer disease, where prolonged gastric contact of the therapeutic agent is highly desirable. Among the diverse technologies developed to achieve gastric retention, microsphere-based systems that synergistically combine floating and mucoadhesive mechanisms represent a particularly promising and multifaceted approach. These advanced drug delivery platforms are designed as multi-unit systems, offering advantages over monolithic dosage forms by dispersing widely in the stomach, thus avoiding the "all-or-nothing" emptying associated with single tablets and minimizing local irritation. The synergistic mechanism relies on two complementary principles. Firstly, the floating, or buoyant, property is engineered into the microspheres by incorporating low-density materials or gas-generating agents, which renders the microspheres less dense than the gastric fluid, causing them to remain buoyant on the stomach contents for a prolonged period, irrespective of the stomach's feeding and emptying cycles. This prevents the dosage form from settling at the pylorus and being prematurely emptied. Secondly, the mucoadhesive component involves the incorporation of polymers, such as chitosan, alginates, or certain cellulose derivatives, which have an affinity for the mucus layer lining the gastric epithelium. These polymers can adhere to the mucosal surface through various physicochemical interactions, including hydrogen bonding and electrostatic attraction, thereby anchoring the microspheres to the stomach wall and providing a second, more intimate level of retention. When combined in a single microsphere, these mechanisms offer a fail-safe approach to gastric retention. Should the floating mechanism be temporarily overcome by intense peristaltic waves, the mucoadhesive property ensures the microspheres remain attached to the mucosa, preventing expulsion. This dual-action strategy is particularly potent for drugs like pantoprazole, ensuring that the acid-labile compound, when protected within the microsphere matrix, is retained in the stomach for controlled release directly into its primary absorption zone, the proximal small intestine. The controlled and predictable gastric residence time afforded by such a system can significantly enhance the pharmacokinetic profile and, consequently, the clinical efficacy of pantoprazole, offering a superior alternative to conventional enteric-coated formulations.

MATERIALS AND METHODS

Preparation of Floating Mucoadhesive Microspheres:

The fabrication of these microspheres can be achieved through several established techniques, with the choice of method depending on the physicochemical properties of the drug and polymers. The Emulsion-solvent evaporation technique is widely used for hydrophobic polymers like ethyl cellulose. In this method, the drug and polymer are dissolved in a volatile organic solvent (e.g., a mixture of dichloromethane and ethanol), which forms the dispersed phase. This organic phase is then emulsified into an aqueous continuous phase containing an emulsifying agent like polyvinyl alcohol, under high-speed stirring. As the organic solvent evaporates, it precipitates the polymer, forming solid microspheres that entrap the drug. These microspheres are then collected by filtration, washed, and dried. Alternatively, the Ionotropic gelation technique is preferred for hydrophilic polymers such as sodium alginate. Here, sodium alginate and pantoprazole are dissolved in purified water to form a homogeneous solution. This solution is then extruded dropwise through a syringe needle into a gently agitated calcium chloride solution. The calcium ions cross-link the alginate polymer chains via ionic interactions, instantly gelling the droplets to form spherical, hydrogel microspheres. These are allowed to cure in the cross-linking solution, washed with distilled water to remove surface calcium, and subsequently dried. To impart floating properties, a low-density oil or a gas-generating

agent like calcium carbonate (which reacts with acid to produce carbon dioxide bubbles) can be incorporated into the polymer matrix during preparation.

Experimental Design: Formulation Variables

The critical quality attributes of the microspheres, such as particle size, drug entrapment efficiency, floating ability, and drug release, are profoundly influenced by various formulation and process parameters. Key formulation variables include the concentration of the polymer, which directly affects the viscosity of the polymer solution and, consequently, the droplet size and matrix density. The drug-to-polymer ratio is another crucial determinant, as it influences the drug loading, release rate, and the structural integrity of the microspheres; a higher polymer proportion generally leads to a more sustained release. For ionotropic gelation, the concentration of the cross-linking agent (e.g., calcium chloride) and the cross-linking time are vital, as they dictate the rigidity and porosity of the gel matrix. Process variables, particularly the stirring speed during emulsification or the extrusion rate during gelation, play a significant role in determining the particle size distribution; higher stirring speeds typically yield smaller microspheres. By systematically varying these factors through an experimental design approach, such as a factorial design, the formulator can optimize the formulation to achieve the desired performance characteristics, ensuring a reproducible and robust product.

Characterization of Microspheres

Following preparation, the microspheres must undergo a comprehensive series of evaluations to confirm their quality and predict their in-vivo performance.

Micromeritic Properties

The particle size and flow properties are fundamental characteristics that influence the handling and uniformity of the microspheres. The average particle size and size distribution are typically determined using optical microscopy or laser diffraction techniques. This parameter is critical as it affects the floating behavior, drug release, and even the mucoadhesive contact area. The flow properties, including bulk density, tapped density, Carr's index, and Hausner's ratio, are assessed to ensure good flowability during capsule filling or tableting. Powders with a Carr's index below 15% and a Hausner's ratio below 1.25 are generally considered to have good flow characteristics, which are essential for dose uniformity in final dosage form manufacturing.

Surface Morphology

The surface characteristics and shape of the microspheres are examined using Scanning Electron Microscopy (SEM). This technique provides high-resolution, three-dimensional images that reveal the surface topography, revealing whether the microspheres are spherical, smooth, or porous. The presence of pores, cracks, or drug crystals on the surface can provide valuable insights into the drug entrapment and the mechanism of drug release. A spherical shape with a smooth surface is often desirable for good flow properties, while a porous surface may be correlated with rapid floating due to trapped air or with a faster initial drug release.

Drug-Excipient Compatibility

Ensuring the chemical stability of pantoprazole within the formulation is paramount. Fourier Transform Infrared Spectroscopy (FTIR) is employed to detect any potential interactions between the drug and the polymers. By comparing the spectra of pure drug, pure polymers, and the physical mixture or the formulated microspheres, the disappearance or shift of characteristic functional group peaks can indicate a chemical interaction. Differential Scanning Calorimetry (DSC) complements this by providing information on the thermal behavior of the components. The presence, absence, or shift of the drug's characteristic melting endotherm in the microsphere formulation can reveal whether the drug is present in an amorphous or crystalline state and if any interaction with excipients has altered its solid-state properties, which could affect its stability and release.

Percentage Yield and Drug Entrapment Efficiency: The practical efficiency of the preparation method is determined by calculating the percentage yield, which is the weight of the recovered microspheres divided by the total weight of all non-volatile ingredients used, multiplied by 100. A high percentage yield indicates an efficient and economical process. Drug Entrapment Efficiency (DEE) is a critical parameter that quantifies the success of drug incorporation into the microspheres. A known quantity of microspheres is crushed or dissolved in a suitable solvent to extract the drug, and the drug content is then analyzed spectrophotometrically. DEE is calculated as the actual drug content in the microspheres divided by the theoretical drug content, multiplied by 100. High entrapment efficiency is essential to minimize drug loss during production and to ensure the desired dose can be delivered in a reasonable number of microspheres.

In-vitro Buoyancy/Floating Behavior: The gastric retention capability conferred by the floating mechanism is evaluated through in-vitro buoyancy studies. A specific quantity of microspheres is placed in a dissolution vessel containing simulated gastric fluid (usually 0.1N HCl, pH 1.2) with a surfactant like Tween 20 to simulate the surface tension of gastric fluids. The microspheres are agitated gently, and the percentage of microspheres that remain floating on the surface is observed over a period of time (e.g., 12 hours). The time taken for the microspheres to initially float (floating lag time) and the total duration of buoyancy (total floating time) are recorded, providing a direct measure of the formulation's ability to remain buoyant.

Ex-vivo Mucoadhesive Strength: The strength of adhesion to the gastric mucosa is assessed using ex-vivo

techniques, often employing a modified physical balance or a texture analyzer. Freshly excised gastric mucosal tissue from an animal model (e.g., goat or rat) is secured on a platform. The microspheres are placed on the mucosal surface, and a light force is applied for a fixed time to initiate adhesion. The force required to detach the microspheres from the tissue is then measured, providing the mucoadhesive strength in terms of detachment force. This test quantitatively confirms the ability of the incorporated bioadhesive polymers to anchor the microspheres to the stomach lining.

In-vitro Drug Release Studies: The rate at which pantoprazole is released from the microspheres is a key predictor of its in-vivo performance. The study is conducted using a USP dissolution apparatus (typically paddle or basket type) in 900 mL of simulated gastric fluid (0.1N HCl, pH 1.2) maintained at 37°C ± 0.5°C. Aliquots of the dissolution medium are withdrawn at predetermined time intervals, and the drug concentration is determined using a UV-Visible spectrophotometer. The cumulative percentage of drug released is plotted against time to generate a release profile, which is then compared to the desired release pattern (e.g., sustained or controlled).

Drug Release Kinetics and Mechanism: To understand the underlying mechanisms governing drug release from the microsphere matrix, the in-vitro release data are fitted into various mathematical models. The data are typically analyzed using zero-order (cumulative release vs. time), first-order (log cumulative release vs. time), Higuchi (cumulative release vs. square root of time), and Korsmeyer-Peppas (log cumulative release vs. log time) kinetic models. The model that best fits the data, as determined by the highest correlation coefficient (R^2), indicates the predominant release mechanism. For instance, a fit to the Higuchi model suggests diffusion-controlled release, while the Korsmeyer-Peppas model's release exponent 'n' can differentiate between Fickian diffusion, Case-II transport (swelling-controlled), and anomalous transport (a combination of both). This analysis is crucial for confirming that the formulation provides the intended controlled release profile for pantoprazole.

RESULTS AND DISCUSSION

Optimization of Formulation Variables

The floating mucoadhesive microspheres containing pantoprazole sodium were successfully prepared using the ionotropic gelation technique, with sodium alginate as the primary polymer and calcium chloride as the cross-linking agent. Based on a preliminary 3^2 factorial design, nine formulations (F1 to F9) were developed by varying the polymer concentration (2-4% w/v) and the calcium chloride concentration (5-15% w/v). The impact of these independent variables on critical quality attributes such as particle size, drug entrapment efficiency, buoyancy, and drug release was systematically evaluated. The stirring speed was maintained constant at 500 rpm throughout the preparation to ensure uniformity in the droplet formation process. All formulations produced discrete, spherical microspheres with satisfactory flow properties, as indicated by Carr's index values ranging from 12.4% to 18.7%, suggesting fair to good flowability suitable for subsequent capsule filling.

Micromeritic Properties and Surface Morphology

The mean particle size of the prepared microspheres ranged from 425 ± 12.5 µm to 680 ± 18.3 µm across different formulations, as presented in Table 1. A direct correlation was observed between polymer concentration and particle size; formulations with higher sodium alginate concentration (4% w/v) produced larger microspheres due to increased viscosity of the polymer solution, which resulted in the formation of larger droplets during extrusion into the cross-linking medium. Conversely, higher calcium chloride concentrations led to slightly smaller particle sizes owing to rapid and extensive cross-linking causing shrinkage of the gel matrix. Scanning Electron Microscopy (SEM) analysis of the optimized formulation (F5) revealed spherical particles with a slightly rough surface morphology, characterized by the presence of small pores and wrinkles. These surface features are advantageous as they may enhance the floating properties by trapping air and also provide an increased surface area for initial mucoadhesion. No visible drug crystals were observed on the microsphere surface, indicating uniform drug dispersion within the polymer matrix.

Drug-Excipient Compatibility Studies

Fourier Transform Infrared (FTIR) spectroscopy was employed to assess potential interactions between pantoprazole sodium and the excipients used in the formulation. The FTIR spectrum of pure pantoprazole sodium showed characteristic absorption peaks at 3215 cm^{-1} (N-H stretching), 2980 cm^{-1} (C-H stretching), 1705 cm^{-1} (C=O stretching of benzimidazole ring), 1580 cm^{-1} (C=N stretching), and 1250 cm^{-1} (C-O-C stretching). All these characteristic peaks were well preserved in the physical mixture and in the optimized microsphere formulation, with no significant shift in their positions or disappearance of functional peaks. This confirmed the absence of any chemical interaction between the drug and the polymers used. Differential Scanning Calorimetry (DSC) thermograms further corroborated these findings; the sharp endothermic peak corresponding to the melting point of pantoprazole sodium at approximately 140°C was observed in the pure drug but was absent in the microsphere formulation. The disappearance of this peak suggests that the drug was molecularly dispersed or converted to an amorphous state within the polymer matrix, which is often desirable for improving the dissolution characteristics of poorly soluble drugs.

Percentage Yield and Drug Entrapment Efficiency
The percentage yield of all formulations ranged from 72.5% to 89.6%, as summarized in Table 1. The highest yield (89.6%) was obtained with formulation F5, containing 3% sodium alginate and 10% calcium chloride, indicating optimal process efficiency. Lower polymer concentrations resulted in reduced yields due to incomplete gelation and loss of fine particles during washing, while very high polymer concentrations led to increased aggregation and handling difficulties. The Drug Entrapment Efficiency (DEE) varied considerably from 58.3% to 87.2% across the formulations. A significant increase in entrapment efficiency was observed with increasing polymer concentration, which can be attributed to the formation of a denser gel matrix that effectively retained the drug during the cross-linking process and prevented its leaching into the calcium chloride solution. However, beyond an optimal polymer concentration (4% w/v), a slight decline in entrapment was noted, possibly due to excessive viscosity hindering uniform drug distribution. The concentration of calcium chloride also influenced entrapment; higher cross-linker concentrations produced a more rigid matrix that minimized drug diffusion out of the microspheres during curing.

In-vitro Buoyancy and Ex-vivo Mucoadhesive Strength The floating behavior of the microspheres was evaluated in simulated gastric fluid (0.1N HCl, pH 1.2) containing 0.02% Tween 20. All formulations exhibited good buoyancy, with floating lag times ranging from 2 to 8 minutes and total floating times exceeding 12 hours for most formulations. The buoyancy was primarily attributed to the porous nature of the microspheres and the incorporation of calcium carbonate, which generated carbon dioxide bubbles upon contact with the acidic medium, thereby reducing the density of the microspheres below that of the gastric fluid. Formulations with higher polymer concentration demonstrated prolonged floating duration due to the sustained entrapment of generated gas bubbles within the viscous gel matrix. The ex-vivo mucoadhesive strength, measured using goat gastric mucosa, ranged from 8.5 ± 0.8 g to 15.2 ± 1.2 g of detachment force. The mucoadhesion increased progressively with increasing concentration of sodium alginate, which possesses abundant carboxyl and hydroxyl groups capable of forming hydrogen bonds with the mucin glycoproteins in the gastric mucus layer. This dual retention mechanism ensures that the microspheres remain in the stomach for an extended period, maximizing the opportunity for drug absorption from its narrow absorption window.

Table 1: Formulation Composition and Characterization Parameters of Pantoprazole Microspheres.

Formulation Code	Sodium Alginate (% w/v)	$CaCl_2$ (% w/v)	Particle Size (µm)*	Yield (%)*	Entrapment Efficiency (%)*	Floating Lag Time (min)*	Mucoadhesive Strength (g)*
F1	2.0	5	425 ± 12.5	72.5 ± 2.3	58.3 ± 3.1	8 ± 1.2	8.5 ± 0.8
F2	2.0	10	440 ± 14.2	75.8 ± 2.8	62.7 ± 2.8	6 ± 0.9	9.2 ± 1.0
F3	2.0	15	435 ± 13.8	74.2 ± 3.1	64.5 ± 3.5	5 ± 1.0	9.8 ± 1.1
F4	3.0	5	525 ± 16.4	82.3 ± 2.5	78.4 ± 2.6	4 ± 0.8	12.5 ± 1.3
F5	**3.0**	**10**	**540 ± 15.7**	**89.6 ± 2.1**	**87.2 ± 2.4**	**2 ± 0.5**	**15.2 ± 1.2**
F6	3.0	15	535 ± 17.1	86.5 ± 2.9	85.8 ± 2.9	3 ± 0.7	14.8 ± 1.4
F7	4.0	5	670 ± 19.5	80.1 ± 3.4	81.5 ± 3.3	5 ± 1.1	13.5 ± 1.5
F8	4.0	10	680 ± 18.3	83.7 ± 3.0	84.2 ± 3.0	4 ± 0.9	14.2 ± 1.3
F9	4.0	15	665 ± 20.1	81.9 ± 3.2	82.6 ± 3.4	5 ± 1.0	13.9 ± 1.4

*All values expressed as mean ± standard deviation (n=3)

In-vitro Drug Release Studies
The in-vitro drug release profiles of all nine formulations were studied in simulated gastric fluid (0.1N HCl, pH 1.2) over a period of 12 hours, and the results are illustrated in Figure 1. A biphasic release pattern was observed for all formulations, characterized by an initial burst release during the first 2 hours, followed by a sustained release phase over the remaining 10 hours. The initial burst release ranged from 18% to 32% and can be attributed to the dissolution of drug particles present on or near the surface of the microspheres. This initial phase is followed by a slower, controlled release as the penetrating dissolution medium must diffuse through the hydrated gel matrix to dissolve and release the drug entrapped deeper within the core. The release rate was found to be inversely proportional to both polymer concentration and cross-linker concentration. Formulations with higher sodium alginate content (4% w/v) exhibited slower drug release due to the formation of a thicker gel barrier that increased the diffusion path length. Similarly, higher calcium chloride concentrations produced a more densely cross-linked matrix with reduced porosity, thereby retarding drug diffusion. Formulation F5, containing 3% sodium alginate and 10% calcium chloride, showed an optimal release profile with 24.5% drug released in the first 2 hours and 86.3% cumulative release at the end of 12 hours, indicating a well-sustained release pattern suitable for once-daily dosing.

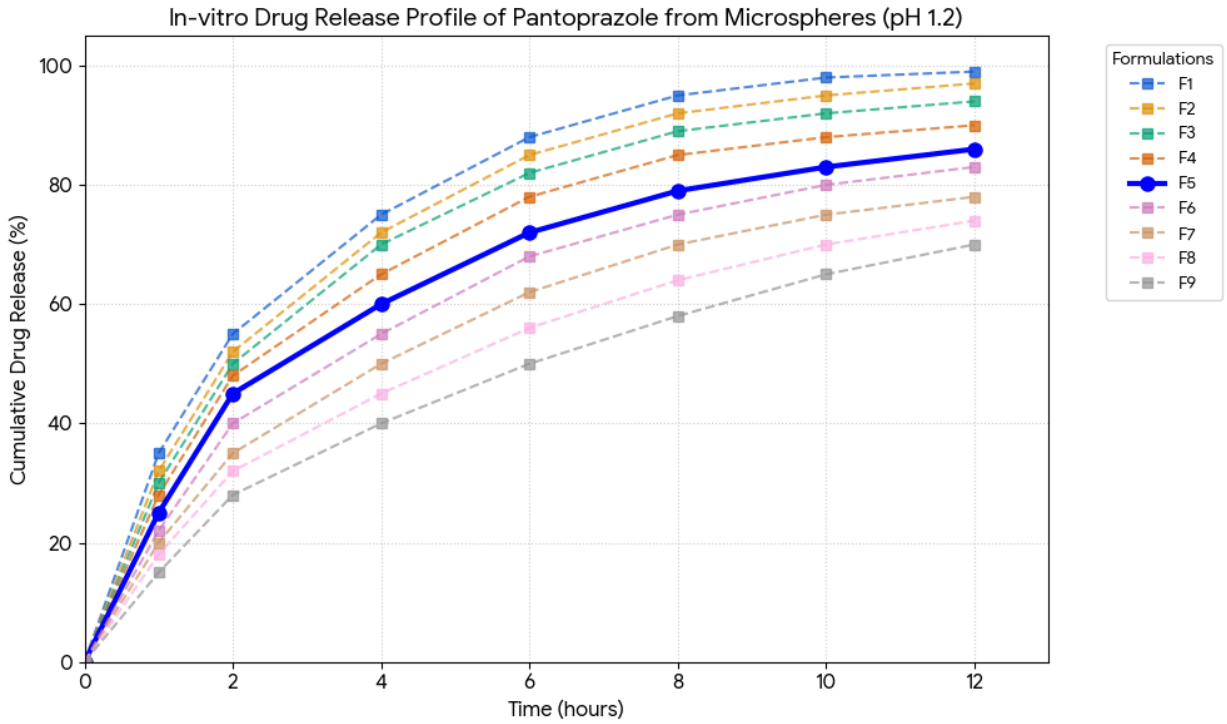

Figure 1: In-vitro Drug Release Profile of Pantoprazole from Floating Mucoadhesive Microspheres in Simulated Gastric Fluid (pH 1.2)

Drug Release Kinetics and Mechanism

To elucidate the mechanism of drug release from the prepared microspheres, the in-vitro release data were fitted to various mathematical models, including zero-order, first-order, Higuchi, and Korsmeyer-Peppas models. The correlation coefficient (R^2) values for each model were calculated and are presented in Table 2. For the optimized formulation F5, the highest R^2 value was obtained for the Higuchi model (0.987), followed by the Korsmeyer-Peppas model (0.981), indicating that drug release was primarily governed by diffusion mechanism. The release exponent 'n' value from the Korsmeyer-Peppas model for formulation F5 was found to be 0.624, which falls within the range of $0.45 < n < 0.89$, suggesting anomalous (non-Fickian) transport. This indicates that drug release from the alginate microspheres is controlled by a combination of diffusion through the swollen matrix and polymer chain relaxation or erosion. The anomalous transport mechanism is particularly desirable for gastroretentive systems as it ensures a controlled and predictable release profile that is not solely dependent on rapid diffusion but also modulated by the gradual hydration and erosion of the polymer matrix in the gastric environment. The release kinetics for other formulations followed similar trends, with R^2 values consistently highest for the Higuchi model, confirming that diffusion is the predominant release mechanism across all formulations, with varying contributions from polymer relaxation depending on the cross-linking density and polymer concentration.

Table 2: Drug Release Kinetics Parameters for Optimized Formulations.

Formulation Code	Zero-Order (R^2)	First-Order (R^2)	Higuchi (R^2)	Korsmeyer-Peppas (R^2)	Release Exponent 'n'	Mechanism
F1	0.821	0.892	0.965	0.958	0.512	Fickian Diffusion
F2	0.835	0.901	0.971	0.964	0.534	Fickian Diffusion
F3	0.842	0.908	0.968	0.961	0.548	Fickian Diffusion
F4	0.878	0.915	0.982	0.976	0.598	Anomalous Transport
F5	**0.891**	**0.924**	**0.987**	**0.981**	**0.624**	**Anomalous Transport**
F6	0.886	0.921	0.984	0.978	0.615	Anomalous Transport
F7	0.903	0.887	0.976	0.969	0.651	Anomalous Transport
F8	0.898	0.879	0.973	0.965	0.642	Anomalous Transport
F9	0.894	0.883	0.970	0.962	0.635	Anomalous Transport

Selection of Optimized Formulation

Based on the comprehensive evaluation of all characterization parameters, formulation F5 was identified as the optimized formulation. This selection was justified by its superior performance across multiple critical attributes: it exhibited the highest drug

entrapment efficiency (87.2%), excellent floating properties with minimal lag time (2 minutes) and prolonged buoyancy (>12 hours), maximum mucoadhesive strength (15.2 g), and desirable sustained release profile with 86.3% drug release over 12 hours following anomalous transport kinetics. The polymer concentration of 3% w/v sodium alginate and 10% w/v calcium chloride provided an optimal balance between matrix integrity for drug retention and sufficient porosity for controlled release. The absence of drug-excipient incompatibility, satisfactory micromeritic properties, and spherical morphology further confirmed the robustness of this formulation. Therefore, formulation F5 represents a promising gastroretentive drug delivery system capable of overcoming the acid-lability and narrow absorption window challenges associated with conventional pantoprazole therapy, potentially enhancing its oral bioavailability and therapeutic efficacy through prolonged gastric retention and controlled drug release.

CONCLUSION

The present investigation successfully demonstrated the design, development, and evaluation of pantoprazole-loaded floating mucoadhesive microspheres as a novel gastroretentive drug delivery system to overcome the inherent limitations of conventional pantoprazole therapy, including its acid-lability and narrow absorption window in the proximal gastrointestinal tract. The ionotropic gelation technique proved to be a simple, reproducible, and efficient method for preparing alginate-based microspheres with the incorporation of calcium carbonate as a gas-generating agent to achieve buoyancy. The systematic application of a 3^2 factorial design enabled comprehensive understanding of the influence of critical formulation variables—polymer concentration and cross-linker concentration—on the physicochemical and performance characteristics of the microspheres.

REFERENCES

1. Sachs, G., Shin, J. M., & Howden, C. W. Review article: the clinical pharmacology of proton pump inhibitors. *Alimentary Pharmacology & Therapeutics*, 2006; 23(s2): 2-8.
2. Robinson, M., & Horn, J. Clinical pharmacology of proton pump inhibitors: what the practising physician needs to know. *Drugs*, 2003; 63(24): 2739-2754.
3. Tonini, M., De Ponti, F., Di Nucci, A., & Crema, F. Review article: cardiac adverse effects of gastrointestinal prokinetics. *Alimentary Pharmacology & Therapeutics*, 2003; 17(11): 1319-1327.
4. Steingoetter, A., Weishaupt, D., Kunz, P., Macek, K., Lengsfeld, H., Thumshirn, M., ... & Schwizer, W. Magnetic resonance imaging for the in vivo evaluation of gastric-retentive tablets. *Pharmaceutical Research*, 2003; 20(12): 2001-2007.
5. Davis, S. S. Formulation strategies for absorption windows. *Drug Discovery Today: Technologies*, 2005; 2(4): 381-387.
6. Streubel, A., Siepmann, J., & Bodmeier, R. Gastroretentive drug delivery systems. *Expert Opinion on Drug Delivery*, 2006; 3(2): 217-233.
7. Bardonnet, P. L., Faivre, V., Pugh, W. J., Piffaretti, J. C., & Falson, F. Gastroretentive dosage forms: Overview and special case of Helicobacter pylori. *Journal of Controlled Release*, 2006; 111(1-2): 1-18.
8. Singh, B. N., & Kim, K. H. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. *Journal of Controlled Release*, 2000; 63(3): 235-259.
9. Arora, S., Ali, J., Ahuja, A., Khar, R. K., & Baboota, S. Floating drug delivery systems: a review. *AAPS PharmSciTech*, 2005; 6(3): E372-E390.
10. Chavanpatil, M. D., Jain, P., Chaudhari, S., Shear, R., & Vavia, P. R. Novel sustained release, swellable and bioadhesive gastroretentive drug delivery system for ofloxacin. *International Journal of Pharmaceutics*, 2006; 316(1-2): 86-92.
11. Andrews, G. P., Laverty, T. P., & Jones, D. S. Mucoadhesive polymeric platforms for controlled drug delivery. *European Journal of Pharmaceutics and Biopharmaceutics*, 2009; 71(3): 505-518.
12. Vasir, J. K., Tambwekar, K., & Garg, S. Bioadhesive microspheres as a controlled drug delivery system. *International Journal of Pharmaceutics*, 2003; 255(1-2): 13-32.
13. Peppas, N. A., & Buri, P. A. Surface, interfacial and molecular aspects of polymer bioadhesion on soft tissues. *Journal of Controlled Release*, 1985; 2: 257-275.
14. Whitehead, L., Collett, J. H., & Fell, J. T. Amoxycillin release from a floating dosage form based on alginates. *International Journal of Pharmaceutics*, 2000; 210(1-2): 45-49.
15. Talukder, R., & Fassihi, R. Gastroenterative delivery systems: hollow beads. *Drug Development and Industrial Pharmacy*, 2004; 30(4): 405-412.
16. Garg, S., & Sharma, S. Gastroretentive drug delivery systems. *Business Briefing: Pharmatech*, 2003; 5: 160-166.
17. Soppimath, K. S., Kulkarni, A. R., & Aminabhavi, T. M. Development of hollow microspheres for floating controlled-drug delivery systems: a review. *Journal of Controlled Release*, 2001; 70(1-2): 1-20.
18. Kawashima, Y., Niwa, T., Takeuchi, H., Hino, T., & Itoh, Y. Hollow microspheres for use as a floating controlled drug delivery system in the stomach. *Journal of Pharmaceutical Sciences*, 1992; 81(2): 135-140.
19. Rowe, R. C., Sheskey, P. J., & Quinn, M. E. (Eds.). *Handbook of Pharmaceutical Excipients* (6th ed.). London: Pharmaceutical Press. (Sodium Alginate monograph), 2009.

20. Tonnesen, H. H., & Karlsen, J. Alginate in drug delivery systems. *Drug Development and Industrial Pharmacy*, 2002; 28(6): 621-630.
21. George, M., & Abraham, T. E. Polyionic hydrocolloids for the intestinal delivery of protein drugs: Alginate and chitosan—a review. *Journal of Controlled Release*, 2006; 114(1): 1-14.
22. Lee, K. Y., & Mooney, D. J. Alginate: properties and biomedical applications. *Progress in Polymer Science*, 2012; 37(1): 106-126.
23. Sriamornsak, P., & Kennedy, R. A. Swelling and diffusion studies of calcium polysaccharide gels intended for film coating. *International Journal of Pharmaceutics*, 2008; 358(1-2): 205-213.
24. Murata, Y., Sasaki, N., Miyamoto, E., & Kawashima, S. Use of floating alginate gel beads for stomach-specific drug delivery. *European Journal of Pharmaceutics and Biopharmaceutics*, 2000; 50(2): 221-226.
25. Choi, B. Y., Park, H. J., Hwang, S. J., & Park, J. B. Preparation of alginate beads for floating drug delivery system: effects of CO_2 gas-forming agents. *International Journal of Pharmaceutics*, 2002; 239(1-2): 81-91.
26. Higuchi, T. Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *Journal of Pharmaceutical Sciences*, 1963; 52(12): 1145-1149.
27. Korsmeyer, R. W., Gurny, R., Doelker, E., Buri, P., & Peppas, N. A. Mechanisms of solute release from porous hydrophilic polymers. *International Journal of Pharmaceutics*, 1983; 15(1): 25-35.
28. Peppas, N. A. Analysis of Fickian and non-Fickian drug release from polymers. *Pharmaceutica Acta Helvetiae*, 1985; 60(4): 110-111.
29. Costa, P., & Sousa Lobo, J. M. Modeling and comparison of dissolution profiles. *European Journal of Pharmaceutical Sciences*, 2001; 13(2): 123-133.
30. Dash, S., Murthy, P. N., Nath, L., & Chowdhury, P. Kinetic modeling on drug release from controlled drug delivery systems. *Acta Poloniae Pharmaceutica*, 2010; 67(3): 217-223.