

Novel Approaches in Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery: A Review of Recent Advances and Future Perspectives

Veeraganti Alekhya¹, Nampelly Karnakar^{2*}, A. Jithan³, L. Matsyagiri⁴

¹PhD Research Scholar, Department of Pharmaceutics, Malla Reddy Institute of Pharmaceutical Sciences, Malla Reddy Vishwavidyapeeth (Deemed to be University), Maisammaguda, Secunderabad, 500100, Telangana, India.

^{2*}Department of Pharmaceutics, Malla Reddy Institute of Pharmaceutical Sciences, Malla Reddy Vishwavidyapeeth (Deemed to be University), Maisammaguda, Secunderabad, 500100, Telangana, India.

³Department of Pharmaceutics, Omega College of Pharmacy, Edulabad, Ghatkesar, Medchal-501301, Telangana India.

⁴Department of Pharmaceutics, Omega College of Pharmacy, Edulabad, Ghatkesar, Medchal-501301, Telangana India.

*E Mail ID: karnakar.nampelly@mrvv.edu.in

*ORCID- <https://orcid.org/0000-0003-2471-6831>

Corresponding Author*

Dr. N. Karnakar

Professor, Department of Pharmaceutics.

Malla Reddy Institute of Pharmaceutical Sciences,

Malla Reddy Vishwavidyapeeth (Deemed to be University),

Maisammaguda, Secunderabad-500100, Telangana, India.

E Mail: karnakar.nampelly@mrvv.edu.in.

Abstract

Gastroretentive floating microballoons have emerged as a promising oral drug delivery system for improving the therapeutic performance of drugs with a narrow absorption window, poor aqueous solubility, short biological half-life, or local action in the stomach. These hollow, low-density multiparticulate systems remain buoyant in gastric fluid for prolonged periods, thereby extending gastric residence time, enhancing drug dissolution, and providing sustained and site-specific drug release. Compared with conventional dosage forms, floating microballoons minimize fluctuations in plasma drug concentration, improve bioavailability, reduce dosing frequency, and enhance patient compliance. Recent advances in formulation science have focused on the incorporation of natural biodegradable polymers, mucoadhesive materials, pH-responsive polymers, and multifunctional polymeric blends to improve gastric retention and achieve controlled drug release. In addition, the application of Quality by Design (QbD) principles and Design of Experiments (DoE) has enabled systematic optimization of formulation variables, resulting in robust, reproducible, and scalable microballoon formulations with predefined quality attributes. This review provides a concise overview of the fundamental principles, formulation strategies, preparation techniques, characterization methods, and therapeutic applications of gastroretentive floating microballoons. Furthermore, recent developments in natural polymer-based systems, mucoadhesive floating microballoons, and QbD-driven formulation approaches are critically discussed, along with a chronological summary of significant research contributions in the field. Current challenges, research gaps, and future perspectives, including multifunctional gastroretentive systems, personalized drug delivery, and integration of advanced formulation technologies, are also highlighted. Overall, gastroretentive floating microballoons represent a versatile and effective platform for enhancing oral drug delivery and continue to offer significant opportunities for the development of next-generation controlled-release pharmaceutical formulations.

Keywords: Gastroretentive drug delivery system (GRDDS), Floating microballoons, Sustained drug release, Bioavailability enhancement, Natural polymers, Mucoadhesive drug delivery and Quality by Design (QbD)

How to cite this article: Alekhya V, Karnakar N, Jithan A, Matsyagiri L. Novel approaches in gastroretentive floating microballoons for enhanced oral drug delivery: a review of recent advances and future perspectives. *Int J Drug Deliv Technol.* 2026;16(73s): 1462-1472. DOI: 10.25258/ijddt.16.73s.155

1. Introduction

Oral drug delivery remains the most preferred route of drug administration because of its convenience, non-invasive nature, cost-effectiveness, and high patient compliance. However, the therapeutic efficacy of many orally administered drugs is often limited by physiological factors such as rapid gastric

emptying, variable gastrointestinal transit time, poor aqueous solubility, enzymatic degradation, and a narrow absorption window in the upper gastrointestinal tract. These limitations frequently result in reduced bioavailability, fluctuating plasma drug concentrations, and the need for frequent

Novel Approaches in Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery: A Review of Recent Advances and Future Perspectives

dosing, ultimately affecting treatment outcomes and patient adherence [1,2].

To address these challenges, gastroretentive drug delivery systems (GRDDS) have been developed to prolong the residence time of dosage forms within the stomach, thereby enhancing drug absorption and therapeutic efficacy. GRDDS are particularly beneficial for drugs that exhibit pH-dependent solubility, are primarily absorbed from the stomach or proximal small intestine, have a short biological half-life, or exert local therapeutic effects in the gastric mucosa. Various gastroretentive strategies have been explored, including floating systems, high-density systems, expandable systems, swellable matrices, bioadhesive systems, magnetic systems, and superporous hydrogels. Among these approaches, floating drug delivery systems have gained significant attention due to their simplicity, effectiveness, and ability to maintain prolonged gastric residence without interfering with normal gastric physiology [3,4].

Floating microballoons, also referred to as hollow microspheres, represent an advanced multiparticulate gastroretentive drug delivery system designed to remain buoyant in gastric fluid for extended periods. Their hollow internal cavity and low bulk density enable them to float on gastric contents, thereby reducing the risk of premature gastric emptying. As a result, the encapsulated drug is released in a controlled manner over an extended duration, improving dissolution, absorption, and systemic bioavailability while minimizing fluctuations in plasma drug concentration. Compared with single-unit floating dosage forms, multiparticulate microballoons provide more uniform distribution within the stomach, lower the risk of dose dumping, and offer improved reproducibility of drug release [5,6].

Recent advances in pharmaceutical formulation have expanded the potential of floating microballoons through the incorporation of biodegradable natural polymers, mucoadhesive materials, pH-responsive polymers, and multifunctional polymeric blends. Additionally, the adoption of Quality by Design (QbD) principles has enabled systematic optimization of formulation variables using risk assessment and statistical experimental designs, resulting in robust and reproducible formulations with predefined critical quality attributes [7].

The increasing application of gastroretentive floating microballoons in the delivery of anti-ulcer agents, antibiotics, antihypertensive drugs, antidiabetic drugs, nonsteroidal anti-inflammatory drugs, and other therapeutic agents underscores their growing importance in modern oral drug delivery.

2. Gastroretentive Floating Microballoons: Principles and Mechanism

Gastroretentive floating microballoons are low-density, hollow polymeric microspheres designed to

remain buoyant in gastric fluid for prolonged periods while providing sustained drug release. Their prolonged gastric residence enhances the bioavailability of drugs with a narrow absorption window, pH-dependent solubility, poor intestinal permeability, or those intended for local action in the stomach [2,5].

The floating mechanism is based on buoyancy, achieved by the hollow internal cavity that lowers the density of the microballoons below that of gastric fluid (approximately 1.004 g/cm³). After oral administration, the microballoons float on gastric contents, delaying gastric emptying and enabling controlled drug release through diffusion, polymer swelling, erosion, or a combination of these mechanisms [6-8].

Following gastric administration, gastric fluid penetrates the polymeric shell while the trapped air within the hollow cavity maintains buoyancy. Simultaneously, hydration of the polymer matrix facilitates controlled drug diffusion, whereas gradual polymer swelling or erosion contributes to sustained release. This prolonged gastric residence enhances drug dissolution, absorption, and therapeutic efficacy while reducing fluctuations in plasma drug concentrations [8]. The Mechanism of Floating Microballoons is displayed in Figure 1.

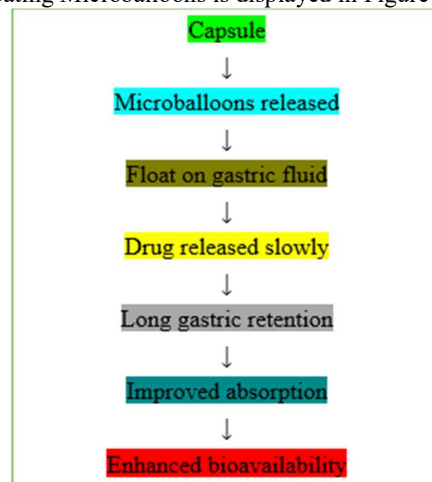


Figure 1: Mechanism of Floating Microballoons

Despite these advantages, the performance of floating microballoons may be influenced by gastric motility, food intake, and gastric pH. Moreover, acid-labile drugs and drugs primarily absorbed in the distal intestine are generally unsuitable for gastroretentive delivery. Nevertheless, advances in natural polymers, multifunctional formulations, pH-responsive systems, and Quality by Design (QbD) continue to improve the clinical potential of floating microballoons [9].

3. Formulation Components of Gastroretentive Floating Microballoons

The performance of gastroretentive floating microballoons is largely determined by the selection of polymers, solvents, and pharmaceutical

Novel Approaches in Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery: A Review of Recent Advances and Future Perspectives

excipients. These components influence particle morphology, buoyancy, encapsulation efficiency, drug release, and overall formulation stability [10].

3.1 Polymers

Polymers form the structural matrix of floating microballoons and govern their floating behaviour, mechanical strength, and drug release characteristics. Synthetic polymers are widely employed because of their excellent film-forming properties and controlled permeability. Among these, ethyl cellulose is the most commonly used polymer owing to its ability to produce hollow, low-density microballoons with prolonged buoyancy. Increasing attention has also been given to natural polymers including chitosan, sodium alginate, xanthan gum, guar gum, and pectin because of their biodegradability, biocompatibility, and mucoadhesive properties [10]. Common Polymers Used in Floating Microballoons along with its function & advantages are reported in Table 1.

Table 1: Common Polymers Used in Floating Microballoons

Polym er	Type	Function	Advantages
Ethyl cellulose	Synthetic	Matrix former	Excellent buoyancy
HPMC	Semi-synthetic	Release retardant	Swelling property
Eudragit RS100	Synthetic	Controlled release	Sustained diffusion
Eudragit RL100	Synthetic	Permeability modifier	Faster release
Chitosan	Natural	Mucoadhesion	Biodegradable
Sodium alginate	Natural	Gel formation	Biocompatible
Xanthan gum	Natural	Release retardant	High viscosity
Guar gum	Natural	Matrix former	Cost-effective
Pectin	Natural	Controlled release	Biodegradable

3.2 Solvents

Organic solvents facilitate polymer dissolution and hollow microballoon formation during solvent evaporation and emulsion solvent diffusion techniques. Commonly used solvents include dichloromethane, ethanol, acetone, ethyl acetate, and methanol, either alone or in combination. [11,12].

3.3 Excipients

Various pharmaceutical excipients are incorporated to improve formulation performance. Tween 80 and

Span 80 act as surfactants to stabilize emulsions, while polyvinyl alcohol serves as a stabilizer to prevent particle aggregation. Plasticizers such as polyethylene glycol (PEG) and triethyl citrate improve polymer flexibility and minimize shell brittleness. In some formulations, pore-forming or gas-generating agents are incorporated to enhance buoyancy and sustain drug release. Careful optimization of these components is essential for obtaining floating microballoons with high encapsulation efficiency, prolonged gastric retention, and controlled drug release [13]. The Preparation of Floating Microballoons is depicted in Figure 2 and comparison of preparation techniques are reported in table 2.

Figure 2: Preparation of Floating Microballoons

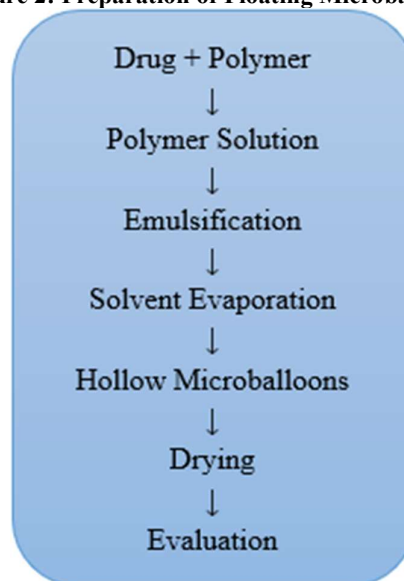


Table 2. Comparison of Preparation Techniques

Technique	Principle	Advantages	Limitations
Solvent evaporation	Polymer precipitation	High entrapment	Organic solvents
Emulsion solvent diffusion	Solvent diffusion	Uniform particles	Process optimization needed
Spray drying	Rapid solvent evaporation	Scale-up possible	High equipment cost
Ionotropic gelation	Ionic crosslinking	Mild conditions	Limited polymers
Phase separation	Polymer precipitation	High loading	Complex process

4. Novel Approaches in Gastroretentive Floating Microballoons

Recent advances in pharmaceutical technology have significantly expanded the scope of gastroretentive

Novel Approaches in Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery: A Review of Recent Advances and Future Perspectives

floating microballoons beyond conventional sustained-release formulations. Modern research focuses on multifunctional systems capable of simultaneously improving gastric retention, drug absorption, formulation robustness, and patient outcomes.

4.1 Natural Polymer-Based Floating Microballoons

Natural polymers have emerged as attractive alternatives to synthetic materials because of their excellent biocompatibility, biodegradability, renewability, and low toxicity. Polymers such as chitosan, sodium alginate, xanthan gum, guar gum, pectin, carrageenan, and gellan gum have been extensively investigated for floating microballoon formulations. [13, 14]

These polymers exhibit excellent swelling properties and can form hydrogel matrices capable of sustaining drug release while maintaining prolonged buoyancy. Chitosan additionally provides inherent mucoadhesive properties, whereas alginate readily undergoes ionic gelation to produce mechanically stable microspheres. Xanthan gum and guar gum effectively retard drug release by forming highly viscous gel networks.

Natural polymer-based formulations offer several advantages, including improved patient safety, reduced environmental impact, lower production costs, and compatibility with biodegradable pharmaceutical systems. Nevertheless, challenges such as batch-to-batch variability, microbial contamination, limited mechanical strength, and sensitivity to environmental conditions remain important considerations.

4.2 Mucoadhesive Floating Microballoons

Mucoadhesive floating microballoons combine buoyancy with bioadhesion to further prolong gastric residence time. In these systems, mucoadhesive polymers establish intermolecular interactions with gastric mucus while the hollow microballoons remain floating on gastric fluid.

Commonly investigated mucoadhesive polymers include chitosan, carbopol, sodium carboxymethyl cellulose, polycarbophil, HPMC, sodium alginate, and pectin. The combination of floating and mucoadhesive mechanisms reduces the probability of premature gastric emptying and promotes localized drug delivery.

Mucoadhesive floating systems have demonstrated considerable potential in the treatment of peptic ulcer disease, *Helicobacter pylori* infection, gastric carcinoma, and other disorders requiring prolonged gastric drug exposure. Their ability to increase contact time with the gastric mucosa may improve local drug concentration while reducing systemic adverse effects.[15]

4.3 pH-Responsive Floating Microballoons

The incorporation of pH-responsive polymers has enabled the development of intelligent

gastroretentive systems capable of modulating drug release according to changes in gastrointestinal pH. Polymers belonging to the Eudragit® family, particularly Eudragit S100, RL100, and RS100, are widely employed because they exhibit controlled permeability and pH-dependent solubility. These formulations maintain buoyancy within the acidic gastric environment while regulating drug diffusion through the polymer matrix.

pH-responsive floating microballoons are particularly advantageous for drugs exhibiting pH-dependent solubility or requiring targeted gastric release. They also contribute to improved formulation stability and reduced burst release.

4.4 Quality by Design (QbD)-Based Formulation Optimization

Quality by Design (QbD) has emerged as a systematic pharmaceutical development strategy that emphasizes product quality through scientific understanding and risk-based optimization rather than end-product testing alone.

The QbD framework begins with defining the Quality Target Product Profile (QTPP), followed by identification of Critical Quality Attributes (CQAs), Critical Material Attributes (CMAs), and Critical Process Parameters (CPPs). Risk assessment tools such as Failure Mode and Effects Analysis (FMEA) are commonly employed to identify variables that significantly influence formulation quality.

Design of Experiments (DoE), including factorial designs, Box–Behnken design, central composite design, and response surface methodology, enables simultaneous optimization of multiple formulation variables while reducing the number of experimental trials. Statistical modelling facilitates prediction of optimal formulation conditions with enhanced reproducibility and robustness.

Application of QbD to floating microballoon development has improved encapsulation efficiency, particle size distribution, buoyancy, drug release profiles, manufacturing consistency, and scale-up capability. Consequently, QbD has become an increasingly important regulatory expectation and a valuable tool for industrial translation of gastroretentive drug delivery systems [16]. The emerging technologies in Floating Microballoons are reported in Table 3.

Table 3: Emerging Technologies in Floating Microballoons

Technology	Current Status	Advantages	Future Potential
Natural polymers	Commercial research	Sustainable	High
Mucoadhesive systems	Advanced	Dual retention	High
pH-responsive systems	Emerging	Site-specific release	Very High

Novel Approaches in Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery: A Review of Recent Advances and Future Perspectives

QbD	Regulatory preferred	Robust formulation	Excellent
AI optimization	Emerging	Prediction	Very High
3D Printing	Experimental	Personalized dosage	Excellent
Machine Learning	Research stage	Process optimization	High

5. Characterization and Evaluation of Gastroretentive Floating Microballoons

Comprehensive characterization of gastroretentive floating microballoons is essential to ensure formulation quality, reproducibility, and therapeutic performance. Evaluation parameters are designed to assess the physicochemical properties, floating behaviour, drug loading capacity, release characteristics, and stability of the developed system. The following parameters are to be evaluated-

- Particle Size and Morphology
- Production Yield, Drug Loading, and Entrapment Efficiency
- Floating Properties
- In Vitro Drug Release Studies
- Compatibility and Thermal Characterization
- Flow Properties and Stability Studies
- In Vivo Evaluation

Table 4: Characterization Parameters

Parameter	Technique	Importance
Particle size	Optical microscopy/SEM	Drug release
Surface morphology	SEM	Hollow structure
Drug entrapment	UV/HPLC	Loading efficiency
Floating percentage	USP dissolution	Gastric retention
Buoyancy time	In vitro test	Floating ability
Swelling index	Gravimetric	Polymer hydration
Drug release	USP II apparatus	Release kinetics
Stability	ICH guidelines	Shelf life

6. Chronological Literature Review [17-37]

Table 5: Chronological overview of Recent Research to earliest existed methods on Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery

Authors	Drug/Approach	Major Pol	Preparation	Major Findings	Significance
---------	---------------	-----------	-------------	----------------	--------------

(Year)		Yme r(s)	n Met hod		
Prakash M. et al. (2026)	Levofloxacin (QbD-assisted floating microballoons)	Eudragit RS100, Ethyl Cellulose	Modified Emulsion Solvent Diffusion	QbD optimization significantly improved entrapment efficiency, particle size uniformity, buoyancy, and sustained drug release.	Demonstrated the usefulness of QbD for robust and scalable gastroretentive formulations.
K.V. Ratnamala et al. (2026)	Febuxostat	Ethyl Cellulose, HP MC K4 M	Solvent Diffusion-Evaporation	High entrapment efficiency, excellent buoyancy (>12 h), sustained drug release	Improved dissolution and oral bioavailability of poorly soluble drugs
Atul Raj et al. (2025)	Clarithromycin	Ethyl Cellulose, HP MC	Solvent Evaporation	Enhanced floating ability with prolonged drug release	Improved gastric targeting against <i>Helicobacter pylori</i> .
Yadav et al. (2026)	Natural gum-based floating	Xanthan gum, Guar	Solvent evaporation, Emulsion	Natural polymers exhibited	Highlighted biodegradable poly

Novel Approaches in Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery: A Review of Recent Advances and Future Perspectives

	microballoons (Review)	gum, Sodium alginate, Chitosan	Ision diffusion, Spray drying	excellent biocompatibility, prolonged gastric retention, and sustained drug release.	mers as promising alternatives to synthetic polymers.
Mat syagiri L. et al. (2025)	Diace rein	Ethyl Cellulose, HP MC	Solvent Evaporation	High drug entrapment with sustained release	Improved management of osteoarthritis through prolonged release
Gyati Shilakari Asthana et al. (2025)	Antitubercular drug	Eudragit S100	Solvent Diffusion	Stable floating microballoons with sustained release	Improved gastric retention of antitubercular drugs
P. Raga vi et al. (2025)	Metformin HCl	Ethyl Cellulose	Solvent Evaporation	Controlled release and prolonged buoyancy	Enhanced oral bioavailability and reduced dosing frequency
Bhila re H.R. et al. (2025)	Drotaverine Hydrochloride	Ethyl Cellulose, HP MC	Emulsion Solvent Diffusion	High encapsulation efficiency and sustained	Enhanced oral bioavailability and

				ed release.	patient compliance.
Manivasakam Prakash et al. (2025)	Levofloxacin	Eudragit polymers	Solvent Evaporation	pH-responsive floating microballoons achieved prolonged gastric retention and targeted drug release.	Advanced pH-sensitive gastroretentive drug delivery.
Archana S. Patil et al. (2025)	Olmesartan Medoxomil	Ethyl Cellulose	Solvent Diffusion	Improved in vitro and in vivo bioavailability	Demonstrated effectiveness of gastroretentive delivery
Biswas S. et al. (2025)	Aceclofenac	Eudragit, HP MC	Solvent Evaporation	Controlled release with prolonged floating time.	Demonstrated suitability for sustained anti-inflammatory therapy.
Rakhi Thareja et al. (2025)	Famotidine	Ethyl Cellulose, HP MC	Solvent Evaporation	Prolonged floating and controlled drug release	Improved anti-ulcer therapy

Novel Approaches in Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery: A Review of Recent Advances and Future Perspectives

Patel A. & Jain D. (2024)	Lafutidine	Ethyl Cellulose, HP MC	Solvent Diffusion	Low-density optimized microballoons with sustained release	Enhanced treatment of peptic ulcer disease
Matsuyagiri Lenkalpal et al. (2024)	Imidapril HCl	Ethyl Cellulose	Solvent Evaporation	Excellent buoyancy and high entrapment efficiency	Improved oral bioavailability
Bindumol K.C. et al. (2023)	Anti-ulcer drug	Ethyl Cellulose, HP MC	Solvent Evaporation	Controlled release with prolonged gastric retention	Effective gastroretentive anti-ulcer delivery
Prachi Gohil et al. (2023)	Allopurinol	Ethyl Cellulose	Solvent Evaporation	Excellent buoyancy and prolonged drug release	Enhanced oral bioavailability and reduced dosing frequency.
Yagvendra Singh et al. (2022)	Amiodarone	Xanthan Gum	Solvent Evaporation	Polymer-controlled release with prolonged action	Demonstrated utility of natural polymers
Pandey C.P. et al. (2022)	Esomeprazole	Chitosan, Carbopol	Solvent Evaporation	Combined floating and mucosal adhesion	Demonstrated dual gastroretentive strategy
					cantly prolonged gastric Combined floating and mucosal adhesion significantly prolonged gastric residence.
Sasidhar R. Lankapalli et al. (2022)	Captopril	Ethyl Cellulose	Emulsion Solvent Diffusion	Controlled release over prolonged duration	Improved antihypertensive therapy
Patil A.S. et al. (2022)	Olmesartan Medoxomil	Ethyl Cellulose	Solvent Diffusion	Improved in vitro and in vivo bioavailability through prolonged gastric retention.	Confirmed pharmacokinetic advantages of floating microballoons.
Ganesh Kumar Y. et al. (2021)	Acebutolol Hydrochloride	Ethyl Cellulose	Solvent Evaporation	High entrapment efficiency and sustained drug release	Demonstrated suitability for controlled cardiovascular drug delivery.
Pranitha P. Hajar et al.	Repaglinide	Ethyl Cellulose	Solvent Diffusion	Excellent floating ability	Improved antidiabetic

Novel Approaches in Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery: A Review of Recent Advances and Future Perspectives

(2021)				and controlled drug release	therapy
Matsuyagiri Lenkalapally et al. (2021)	Pirentanide	Ethyl Cellulose	Solvent Evaporation	Improved in vivo gastric retention and sustained release	Enhanced therapeutic efficacy
Seelam Ramya Krishna et al. (2021)	Dipyridamol & Clopidogrel	Ethyl Cellulose, HP MC	Solvent Diffusion-Evaporation	Pharmacokinetic studies demonstrated significant improvement in oral bioavailability.	Validated the in vivo effectiveness of gastroretentive microballoons.
Sivakumar R. et al. (2021)	Ibuprofen	Ethyl Cellulose, HP MC	Emulsion Solvent Diffusion	Sustained drug release with prolonged gastric residence.	Reduced dosing frequency and gastrointestinal irritation.
Ganesh S. Bangale et al. (2019)	Antihypertensive drug	Ethyl Cellulose	Solvent Evaporation	Extended-release gastroretentive formulation	Improved long-term hypertension management
Daphisha Marbangan et al. (2019)	<i>Clerodendrum colebrookianum</i> Extract	Ethyl Cellulose with natural poly	Solvent Evaporation	Sustained antihypertensive activity with prolonged	Demonstrated potential of herbal floating micro

		mers		gastric retention	balloons
Patlavath Babu (2019)	Imidapril HCl	Ethyl Cellulose	Solvent Evaporation	Excellent floating ability, high drug loading and sustained release	Confirmed suitability of gastroretentive floating microballoons for antihypertensive therapy

Pie Chart: Distribution of Therapeutic Applications

This chart shows the major therapeutic applications of gastroretentive floating microballoons investigated in the reviewed studies.

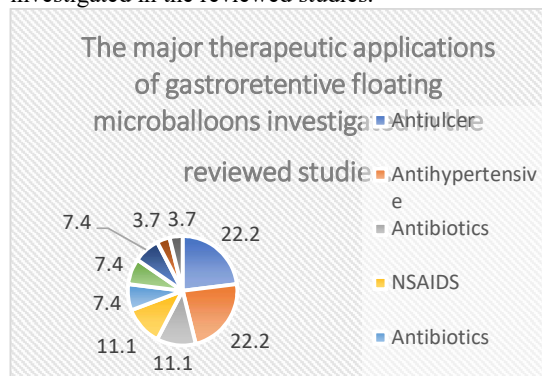


Figure 3: Distribution of therapeutic categories represented in the reviewed studies (n=27)

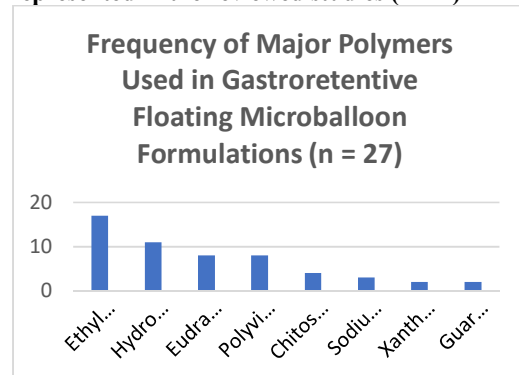


Figure 4: Frequency of Major Polymers used in Gastroretentive Floating Microballoon Formulations (n = 27)

7. Research Gaps

Novel Approaches in Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery: A Review of Recent Advances and Future Perspectives

Although gastroretentive floating microballoons have demonstrated significant potential for enhancing oral drug delivery, several challenges remain to be addressed. Most studies emphasize formulation development and *in vitro* evaluation, whereas relatively few have investigated *in vivo* performance, pharmacokinetics, pharmacodynamics, and clinical efficacy. Consequently, the correlation between *in vitro* and *in vivo* performance remains inadequately established.

The majority of reported formulations utilize synthetic polymers such as ethyl cellulose, HPMC, and Eudragit. Although these polymers provide excellent mechanical strength and controlled drug release, greater emphasis is needed on biodegradable and sustainable natural polymers with improved reproducibility. Furthermore, most formulations rely solely on buoyancy for gastric retention, while comparatively fewer studies have explored multifunctional systems integrating floating, mucoadhesion, pH responsiveness, or enzyme-triggered drug release.

Another important limitation is the limited application of Quality by Design (QbD), artificial intelligence (AI), and machine learning (ML) for formulation optimization. Scale-up studies, process validation, long-term stability studies, and regulatory considerations have also received limited attention. Addressing these research gaps will facilitate the successful translation of gastroretentive floating microballoons from laboratory research to clinical and commercial applications. The Research Gaps and Future Perspectives are summarized in Table 6.

Table 6: Research Gaps and Future Perspectives

Current Limitation	Research Gap	Future Direction
Limited <i>in vivo</i> studies	Clinical translation	Human studies
Synthetic polymers	Sustainability	Natural polymers
Conventional optimization	Process variability	AI + QbD
Single drug delivery	Limited versatility	Combination therapy
Conventional manufacturing	Batch variation	Continuous manufacturing

8. Future Perspectives

Future research on gastroretentive floating microballoons is expected to focus on the development of intelligent, multifunctional, and patient-centric drug delivery systems. Natural biodegradable polymers such as chitosan, sodium alginate, xanthan gum, pectin, and guar gum are likely to gain increasing importance owing to their excellent biocompatibility and environmental sustainability. Hybrid polymeric systems combining natural and synthetic polymers may further improve

formulation stability and drug release characteristics.

The integration of floating behaviour with mucoadhesion, pH-responsive polymers, and stimuli-responsive drug delivery offers promising opportunities for enhancing gastric retention and therapeutic efficacy. The adoption of QbD, Design of Experiments (DoE), AI-assisted formulation design, and machine learning-based predictive modelling is expected to improve formulation robustness and manufacturing efficiency. Emerging technologies such as microfluidics, 3D printing, continuous manufacturing, and personalized medicine may further accelerate the development of next-generation gastroretentive systems. Future investigations should prioritize comprehensive *in vitro*–*in vivo* correlation, multi-centre clinical studies, and regulatory compliance to support commercialization.

A complete Graphical representation of Floating Microballoons for enhanced Oral Drug Delivery is depicted in the figure 5.

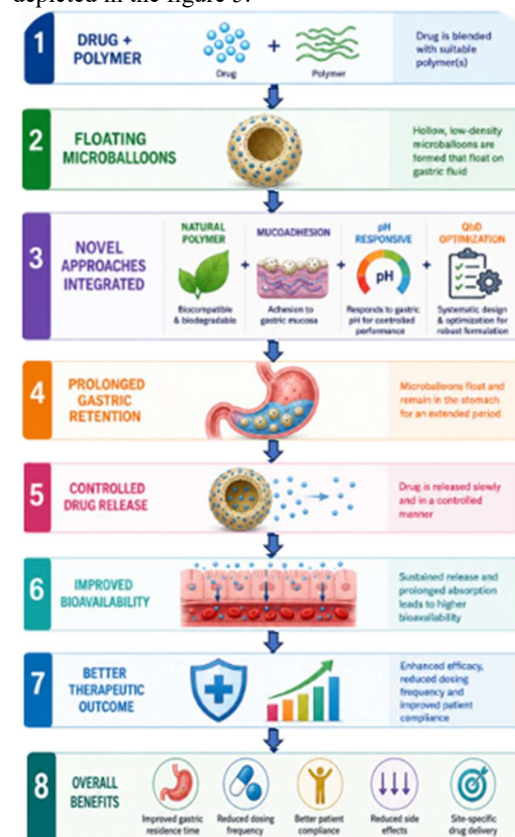


Figure 5: Graphical representation of Floating Microballoons for enhanced Oral Drug delivery

CONCLUSION

Gastroretentive floating microballoons have emerged as an advanced multiparticulate drug delivery system capable of overcoming several limitations associated with conventional oral dosage forms. Their ability to prolong gastric residence, provide sustained drug release, and enhance the

Novel Approaches in Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery: A Review of Recent Advances and Future Perspectives

bioavailability of drugs with narrow absorption windows or pH-dependent solubility has been demonstrated across a wide range of therapeutic applications, including anti-ulcer, antihypertensive, antidiabetic, anti-inflammatory, and antimicrobial therapies.

Recent advances involving natural polymers, mucoadhesive systems, pH-responsive formulations, and QbD-based optimization have significantly expanded the scope of floating microballoon technology. Nevertheless, further research is required to improve large-scale manufacturing, long-term stability, clinical validation, and regulatory acceptance. With continued innovation in pharmaceutical materials, formulation strategies, and digital technologies, gastroretentive floating microballoons are expected to play a pivotal role in the development of next-generation oral controlled drug delivery systems, ultimately improving therapeutic outcomes and patient quality of life.

Author Contributions:

Veeraganti Alekhya, designed the study, and written the original manuscript. The remaining authors analysed, reviewed, supervised and edited the manuscript. All the authors have read and approved the manuscript.

Conflict of Interest:

The authors declare that there is no conflict of interest.

Funding Sources:

The authors received no financial support from any funding agency for this review article.

REFERENCES

1. Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled-release system for gastric retention. *Pharm Res.* 1997;14(6):815–819.
2. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery systems. *Expert Opin Drug Deliv.* 2006;3(2):217–233.
3. Singh BN, Kim KH. Floating drug delivery systems: An approach to oral controlled drug delivery via gastric retention. *J Control Release.* 2000;63(3):235–259.
4. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: A review. *AAPS Pharm Sci Tech.* 2005;6(3): E372–E390.
5. Kawashima Y, Niwa T, Takeuchi H, Hino T, Ito Y. Hollow microspheres for use as a floating controlled drug delivery system in the stomach. *J Pharm Sci.* 1992;81(2):135–140.
6. Jain SK, Agrawal GP, Jain NK. Evaluation of porous carrier-based floating microspheres for gastric delivery. *AAPS Pharm Sci Tech.* 2006;7(4): E90.
7. Yu LX. Pharmaceutical quality by design: Product and process development, understanding, and control. *Pharm Res.* 2008;25(4):781–791.
8. Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modelling on drug release from controlled drug delivery systems. *Acta Pol Pharm.* 2010;67(3):217–223.
9. Prakash M, Nallasamy V, Venkatachalam S, Raman N. Quality-by-Design assisted development and evaluation of a microballoon-based gastroretentive drug delivery system. *Int J Appl Pharm.* 2026;18(2):345–353. doi:10.22159/ijap.2026v18i2.56652.
10. Ratnamala KV, Pole V, Chowdary S. Formulation and evaluation of febuxostat loaded polymeric microballoons as a gastroretentive drug delivery system. *Int J Drug Deliv Technol.* 2026;16(57 Suppl):881–886.
11. Prabha RU, Akilandeswari, Sahala K, Sai Sravan P, Korgaonkar S, Sangeetha R, Tejashwini N, Varshitha A. Microballoons in peptic ulcer therapy: a gastroretentive novel approach. *Int J Drug Deliv Technol.* 2026;16(10 Suppl):323–332. doi:10.25258/ijddt.16.10s.44.
12. Raj A, Kumar A. Development and in-vitro assessment of clarithromycin-encapsulated floating microballoons for targeted gastric drug delivery. *Int J Trend Sci Res Dev.* 2025;9(6).
13. Lenkalapally M, Satyanarayana L, Narendra B, Swetha P. Development and characterization of floating microballoons of diacerein. *Acta Sci Pharm Sci.* 2025;9(11).
14. Asthana GS, Asthana KTKS, Asthana A, Satti SRB, Poldasari S. Eudragit S100-based floating microballoons of antitubercular drug: design, preparation, and in vitro characterization. *FABAD J Pharm Sci.* 2025;50(3):635–654.
15. Ragavi P, Jegath Ratchagan A, Deepika G, Manikandan R, Steins Silvanus Raj N, Chandra. Microballoons based on floating drug delivery system in metformin HCl. *Int J Prog Res Eng Manag Sci.* 2025;5(8):399–409.
16. Bhilare HR, Bhagat VC, Awate PB, Kardile DP, Shete RV. Formulation development and evaluation of floating microspheres of drotaverine hydrochloride as gastroretentive dosage form. *Intell Pharm.* 2025; 3:35–45.
17. Prakash M, Nallasamy V, Venkatachalam S. Fabrication of levofloxacin-loaded pH-sensitive Eudragit polymeric floating microballoon biomaterial for gastroretentive drug delivery. *J Appl Pharm Res.* 2025;13(1):170–178. doi:10.69857/joapr.sv13i1.829.
18. Patil AS, Alosi S, Gaude Y, Masareddy RS. Gastroretentive microballoons of olmesartan medoxomil: formulation and in vitro-in vivo evaluation. *Ther Deliv.* 2025;16(3):227–236. doi:10.1080/20415990.2025.2466418.
19. Biswas S, Sengupta S, Pegu P, Dey N, Sen A, Debnath B, et al. Design and characterization of aceclofenac-loaded microballoons using

Novel Approaches in Gastroretentive Floating Microballoons for Enhanced Oral Drug Delivery: A Review of Recent Advances and Future Perspectives

- Eudragit with hydroxypropyl methylcellulose. *J Drug Deliv Ther.* 2025;15(1):130-141.
20. Thareja R, Tiwari Y, Kothari LP, Somasundaram J, Srivastav Y, Borkar DP, et al. Development and characterization of gastroretentive floating drug famotidine. *J Neonatal Surg.* 2025;14(32 Suppl).
 21. Patel A, Jain D. Design and optimization of low-density gastroretentive polymeric microballoons for the supply of lafutidine in the management of peptic ulcer. *Pharma Sci Anal Res J.* 2024;6(2):180049.
 22. Lenkalapally M, Lagisetty R, Valluri NS. Development and in vitro evaluation of gastroretentive floating microballoons of imidapril HCl. *Int J All Res Educ Sci Methods.* 2024;12(10).
 23. Bindumol KC, Mathew F, Sunil S, Jose A. Formulation and evaluation of floating controlled drug delivery of anti-ulcer drug loaded microballoons. *J Innov Appl Pharm Sci.* 2023;8(3 Suppl):95-100.
 24. Gohil P, Seth M, Kumari S, Jain H, Meshram DB. Formulation and evaluation of floating microballoons of allopurinol. *IJNRD.* 2023;8(2).
 25. Singh Y, Dhangar R, Sharma R. Formulation and evaluation of amiodarone microballoons using xanthan gum as release retardant. *Int J Adv Pharm Sci.* 2022;9(10):254-261.
 26. Pandey CP, Archana. Development and evaluation of gastroretentive mucoadhesive microballoons of esomeprazole to treat peptic ulcer. *J Drug Deliv Ther.* 2022;12(4 Suppl):128-139.
 27. Lankapalli SR, Suryadevara V, Battula SL, Anne R. Development and evaluation of captopril-controlled release floating microballoons. *Indian Drugs.* 2022;59(8):31-38. doi:10.53879/id.59.08.11130.
 28. Ganesh Kumar Y, Pulla RP, Anusha V, Swapna D. Formulation and in vitro evaluation of acebutolol hydrochloride microballoons for sustained drug delivery. *Int J Adv Res Med Pharm Sci.* 2021;6(6).
 29. Lakkakula P, Duddagi S, Tota J, Jogi P, Doma ARS. Formulation and in vitro evaluation of gastroretentive non-effervescent floating matrix tablets of cefaclor. *Biochem Cell Arch.* 2025;25(1):787-793.
 30. Hajare PP, Rachh PR. Formulation and development of novel gastroretentive microballoons of repaglinide. *J Adv Sci Res.* 2021;12(4 Suppl 1):193-204.
 31. Lenkalapally M, Kethavath M. Development and in vivo evaluation of gastroretentive floating microballoons of pirentanide. *J Pharm Sci Res.* 2021;28(2):616-626.
 32. Krishna SR, Ramu A, Vidyadhara S, Prameela Rani A. Bioavailability enhancement by floating microballoons of dipyridamole and clopidogrel: in vivo pharmacokinetic study. *Int J Appl Pharm.* 2021;13(6).
 33. Sivakumar R, Sathish Kumar T, Ubaidulla U, Sinha P, Rathnam G. Formulation development and evaluation of gastroretentive microballoons of ibuprofen for an approach to oral controlled delivery system. *Int J Pharm Ind Res.* 2021;11(3):254-260.
 34. Pradhan S, Tiwari SP, Prasad J, Sanday L. Formulation and in vitro evaluation of floating microballoons of ramipril. *J Cardiovasc Dis Res.* 2021;12(4).
 35. Bangale GS, Shinde GV, Rajesh KS. Development and evaluation of microballoons based extended release drug delivery system for hypertension therapy. *Glob J Pharm Pharm Sci.* 2019;7(4):555718. doi:10.19080/GJPPS.2019.07.555718.
 36. Marbaniang D, Das RJ, Pal P, Saikia A, Pathak MP, Mandal S, et al. Extended release floating microballoons containing *Clerodendrum colebrookianum* extract: in vitro and in vivo evaluation. *Indian J Pharm Educ Res.* 2019;53(3 Suppl 2): S246-S254.
 37. Babu P. Formulation and evaluation of gastroretentive floating microballoons of Imidapril HCl. *J Emerg Technol Innov Res.* 2019;6(3):257-263.