EJPMR, 2026, 13(5), 108-115 **Review Article** **Impact Factor: 8.158**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

FORMULATION TECHNIQUES OF FLOATING MICROBEADS IN MANAGEMENT OF HYPERTENSION

Chetan Nagaraj Kayakad*[1], Mrs. Bhavyashree T.[2], A. R. Shabaraya[3]

[1,2,3]Srinivas College of Pharmacy, Valachil, Farangipete, Mangalore – 574143, Karnataka, India.

***Corresponding Author: Chetan Nagaraj Kayakad**

Srinivas College of Pharmacy, Valachil, Farangipete, Mangalore - 574143, Karnataka, India.

DOI: https://doi.org/10.5281/zenodo.19884048

How to cite this Article: Chetan Nagaraj Kayakad[1], Mrs. Bhavyashree T.[2], A. R. Shabaraya[3]. (2026). Formulation Techniques of Floating Microbeads In Management of Hypertension. European Journal of Pharmaceutical and Medical Research, 13(5), 108–115.

Article Received on 30/03/2026 **Article Revised on 20/04/2026** **Article Published on 01/05/2026**

ABSTRACT

Hypertension is a chronic condition requiring continuous drug therapy, but standard drug modes are still mostly limited due to the rapid gastric emptying that causes variable pharmacokinetics. Floating microbeads, multi particulate gastro retentive systems, are drug delivery devices designed to prolong the gastric retention time and hence improve the bioavailability of drugs. They also provide a sustained release of antihypertensive drugs having absorption windows in the upper GI tract. This paper reviews various formulations and evaluations of the systems with the help of different polymers. This review focuses on formulation techniques such as ionotropic gelation, spray drying, formation and key performance parameters. However, great difficulties still exist in clinical translation from animal studies which have shown increased pharmacokinetic profiles. These include physiological variability, inconsistent fed state performance and manufacturing scalability. *In vitro* trials of thorough promise have been met by the analysis with the reality that physiological and regulatory hurdles have to be overcome before floating microbeads in hypertension can be a clinical reality.

KEYWORDS: Hypertension; Gastro retentive drug delivery, Sustained release, Polymeric systems, Ionotropic

INTRODUCTION

The world still faces increasing challenges from hypertension. About 1.3 billion adults around the globe are suffering from hypertension and new advanced therapies are needed for effective long term treatment.[1]

It is true that a wide range of antihypertensive drugs is available. However, the therapeutic effects of such drugs are generally compromised because of the limitations of the conventional dosage forms. Especially the problem of the quick passage through the gastrointestinal tract and hence the unpredictable patterns of drug absorption have been identified as the major limiting factors. Drugs that have a narrow absorption window in the upper small intestine or whose solubility depends on pH frequently result in low bioavailability when administered in traditional dosage forms.[2]

Floating microbeads are a new concept in drug delivery system that have been developed in an attempt to remedy these issues of drugs by gastric retention through the mechanism of buoyancy. These spherical multi particulate systems, usually with a particle size range of 100 µm – 1000 µm, have a density less than that of gastric fluids which allows them to float over the gastric contents and at the same time they are able to release the drugs incorporated gradually.[3] The effectiveness of these systems relies heavily on the proper choosing of polymers to be used, as they not only determine the systems chemical resistance but also the performance of the systems in terms of floatability and drug release.

This review is mainly concerned with the systematic development and thorough investigation of floating microbeads made with different polymeric systems aimed at hypertension therapy. We delve into the correlations between the molecular structure and functional properties of various polymers, their methods of processing, and the resulting physicochemical characteristics that affect the treatment outcomes. By integrating scientific studies, the article offers a critical evaluation of the polymer-focused formulation

approaches and their potential in the design of efficacious antihypertensive floating microbead systems.

Polymeric Systems in Floating Microbead Formulation

The selection of appropriate polymers constitutes the foundation of effective floating microbead formulation, with each polymer imparting distinct physicochemical and biopharmaceutical properties to the final dosage form.

Natural Polymers

Natural polymers, by way of biocompatibility, biodegradability, and in many cases, innate mucosal adhesion properties that can improve gastric retention, are beneficial to drug delivery systems.

Alginate Based Systems: Sodium alginate, a linear anionic polysaccharide extracted from brown algae, is by far the most extensively used polymer for floating microbeads, primarily because it can be gelled ionotropic with divalent cations (Ca^{2+}, Ba^{2+}, Zn^{2+}) to form stable gels. The extent of cross-linking, which is a function of the cation concentration and the time the beads are exposed to the cations, has a direct effect on the mechanical strength of the beads, their ability to swell, and their drug release pattern.[4]

Chitosan Based Systems: A cationic polysaccharide, this is extracted from the deacetylation of crustacean chitin. It imparts mucoadhesive properties and also has permeation enhancing effects. Chitosan can make gels by ionic interactions with polyanions (e.g., tripolyphosphate) or through polyelectrolyte complexation with alginate, resulting in matrices with controlled porosity and adjustable release characteristics.[5]

Plant Derived Polymers: Recently, the focus has been on exploring different plant derived polymers such as gellan gum, pectin, guar gum, and xanthan gum. These are mainly used to increase the viscosity, act as gel forming agents or modify the release in combination with other agents.[6]

Semi Synthetic and Synthetic Polymers

Such polymers give the advantage of enhanced reproducibility, predictable release patterns, and the ability to adjust physicochemical properties to the desired extent.

Cellulose Derivatives: Hydroxypropyl methylcellulose (HPMC) and sodium carboxymethyl cellulose (NaCMC) are amongst the most common swellable matrix formers. The amount and viscosity grade of the polymers basically decide the rate at which they hydrate, the thickness of the gel layer, and the resulting drug release profiles.[7]

Acrylic Polymers: Eudragit polymers, especially RS and RL variants, offer pH-independent controlled release through diffusion mechanisms. They can be used alone or with other polymers as well as for coating purposes to control the release pattern.[8]

Release Retardants: Ethyl cellulose, being a water-insoluble polymer, is an excellent release retardant if used in correct proportions. Frequently, it is mixed with hydrophilic polymers to get the right buoyancy and release features.[9]

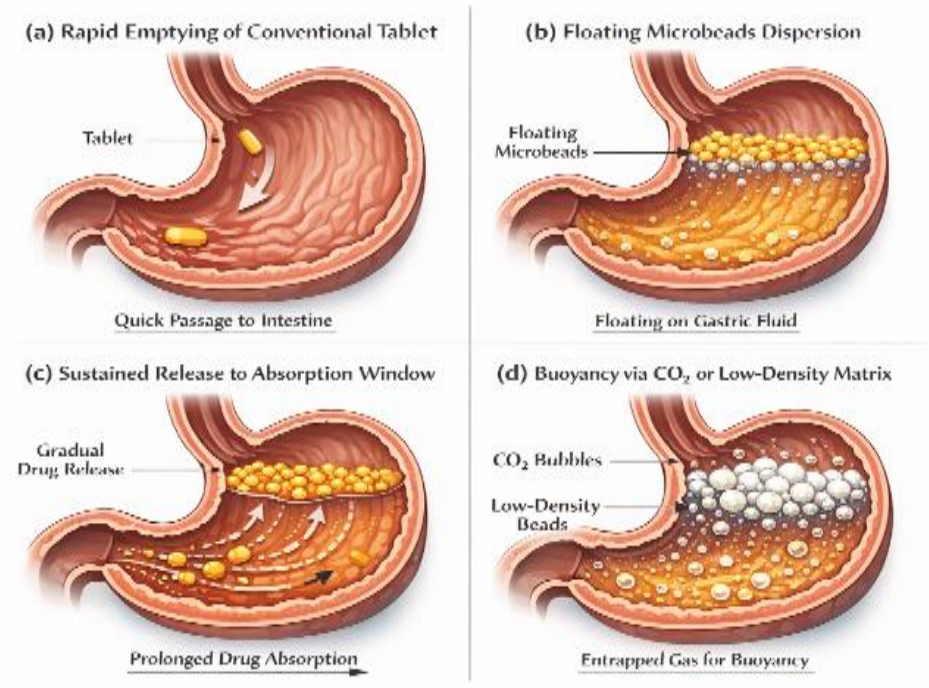

Figure 1: Mechanism of Floating Microbead Action.

Floating microbeads (density <1.004 g/cm³) prolong Gastric Retention Time (GRT) by resisting pyloric propulsion while enabling controlled drug release to the duodenal absorption window.

Polymer Blends and Composites

Nowadays, more and more formulations rely on polymer blends or composites to obtain a synergistic effect of the desired properties. For example, alginate with HPMC blends to get stronger gels, chitosan and alginate polyelectrolyte complexes to increase mucoadhesion, and gellan combined with xanthan to achieve optimal viscosity and controlled release.[10] The extent of compatibility between the polymers, their intermolecular interactions, and the behavior of the phases determine the nature of the final microbeads to a great extent.

Formulation Techniques and Process Parameters

The choice and execution of microbead manufacturing methods have a profound impact on the microbeads' size distribution, morphological features, drug encapsulation, and other functional properties.

Ionotropic Gelation

The ionotropic gelation technique is the most common method for the preparation of hydrophilic ionic polymers such as alginate. A polymer drug solution is forced through a syringe needle and extruded into a vial containing a cation solution usually ($CaCl_2$) under gentle stirring. The following are some of the crucial process parameters:

Polymer Solution Parameters: polymer concentration (1–4% w/v)**,** viscosity low to moderate (≈50–500 cP)**,** and drug loading usually drug: polymer ratio of 1:1 to 1:3.

Extrusion Parameters: needle gauge (18G–22G), dropping height (5–10 cm), flow rate (0.5–2 mL/min)

Cross-linking Parameters: cation concentration (1–5% w/v), temperature (25–40°C), residence time (10–30 minutes)

Post-processing: curing time (20–30 min), washing protocol, drying method (air/oven/freeze drying).[11]

Emulsion-Gelation Method

This method is based on the formation of water-in-oil emulsion which subsequently undergoes gelation. The method is, therefore, perfect for hydrophilic and hydrophobic polymer systems. Basically, the process comprises the following major components:

Emulsion Characteristics**:** Emulsion characteristics involve the selection of an appropriate oil phase, such as light liquid paraffin or sesame oil, along with the type and concentration of emulsifier (Span 80 or Tween 80, typically 0.5–2% w/v). Additionally, the stirring speed (500–2000 rpm) plays a crucial role in controlling droplet size, stability, and uniformity of the microbeads.

Gelation Induction: Gelation induction is achieved by ionic cross-linking using calcium chloride via internal (aqueous phase) or external (oil phase) gelation methods, which influence the structure and drug release properties of microbeads.

Solvent Removal: Several washing stages using organic solvents (n-hexane, petroleum ether).[12]

Spray Drying

This standalone and easily scalable process stage essentially consists of spraying an atomized polymer-drug solution into a hot chamber, thus resulting in the formation of dry, free-flowing microspheres. The parameters of optimization are:

Feed Solution: Solid content (5–20%), solvent composition (aqueous/organic mixtures (water: ethanol 50:50–80:20 v/v; water: methanol 50:50–70:30 v/v), depending on polymer solubility)

Process Conditions: Inlet temperature (100–160°C), outlet temperature (50–80°C), feed rate (3–10 mL/min), atomization pressure (2–4 bar), aspirator setting (70–90%). It is still very difficult to keep the low density (<1 g/cm³) consistent through several production batches mainly due to the variability in the droplet formation and drying kinetics.[13]

Innovative Fabrication Approaches

Some new methods that have been introduced are:

Vibrational Nozzle Systems: Vibrational nozzle systems are based on the application of controlled mechanical vibrations to a liquid jet, leading to its breakup into uniformly sized droplets. The droplet size and frequency can be precisely tuned by adjusting vibration parameters such as frequency and amplitude. This technique significantly improves monodispersity and reproducibility, overcoming limitations of conventional dripping methods.

Electrostatic Droplet Generation: Electrostatic droplet generation employs an external electric field to overcome surface tension and induce droplet formation. The interaction between electric forces and interfacial tension allows precise control over droplet size and formation dynamics. This method enables the production of fine droplets with narrow size distribution, making it highly suitable for controlled drug delivery applications.

Microfluidic Devices: Microfluidic devices utilize microscale channels to manipulate immiscible fluid streams and generate droplets under controlled flow conditions. These systems allow the formation of highly monodisperse droplets with tunable size, morphology, and internal architecture, including core–shell and multicompartment structures. Such precise control enhances reproducibility and encapsulation efficiency, making microfluidics a powerful tool in advanced drug delivery systems.[14]

Evaluation Parameters and Characterization Methods

A detailed evaluation of the product involves various physicochemical, biopharmaceutical, and stability parameters.

Physicochemical Characterization

Particle Size and Distribution: Particle size is typically determined by laser diffraction or dynamic image analysis. Size distribution is represented by the span value [Span = (D90 – D10)/D50]. For gastric retention, the optimum size is generally within 400–800 µm.[15]

Morphology: It is examined by scanning electron microscopy (SEM), which helps to understand the surface features (porosity, smoothness) and the cross-sectional structure.[16]

Density and Porosity: True density is a property of matter and is measured using helium pycnometry. Bulk density, another property of matter, is determined by the method of graduated cylinder. Effective porosity is derived from the porosity and density measurements and it influences the buoyancy and drug release.[17]

Buoyancy Evaluation

The buoyancy behavior of microbeads is commonly evaluated to determine their ability to float in simulated gastric fluid. In this method, a known quantity of microbeads is placed in 0.1 N hydrochloric acid (pH 1.2) containing a small amount of surfactant such as Tween 80 to mimic the surface tension of gastric fluid. The study is generally carried out at 37 ± 0.5 °C using a USP type II dissolution apparatus or a beaker with gentle stirring to simulate gastric motility. The time taken by the beads to rise to the surface of the medium is recorded as the floating lag time. At predetermined time intervals, the floating particles are collected, dried, and weighed to determine the proportion of beads that remain buoyant.

The percentage buoyancy is calculated using the following equation

Buoyancy (%) = (Weight of Floating Particles / Initial Weight of Particles) × 100

Floating Lag Time: The time taken by the beads to reach the surface of the medium in simulated gastric fluid (SGF) of pH 1.2 at 37°C

Total Floating Time**:** The time span beads stay on the top as buoyant (target >8 hours)[18]

Drug Loading and Release Studies

Drug Entrapment Efficiency (DEE) is an important parameter used to determine the amount of drug effectively entrapped in polymeric microbeads. Generally, a predetermined amount of microbeads is precisely weighed and homogenized in a suitable solvent like phosphate buffer solution, hydrochloric acid solution, or methanol to extract the entrapped drug. The suspension is then transferred to a volumetric flask and sonicated to ensure complete extraction of the drug. The solution is then filtered to separate polymeric debris and, if required, diluted. The absorbance of the sample solution is measured at the drug's maximum absorbance wavelength (λmax) using a UV-Visible spectrophotometer. The concentration of the drug is determined using a calibration curve. The Drug Entrapment Efficiency is calculated using the appropriate formula.[19]

Drug Entrapment Efficiency (DEE): DEE (%) = (Actual drug content / Theoretical drug content) × 100

Drug Loading Capacity: Amount of drug per unit weight of beads

In Vitro Dissolution Studies

In vitro drug release experiments are performed to evaluate the dissolution profile of drug-loaded microbeads. Generally, these experiments are performed using a USP apparatus II (paddle) with a dissolution medium of 900 ml of 0.1 N hydrochloric acid (pH 1.2). The system is operated at a temperature of 37 ± 0.5 °C and a paddle speed of 50-100 rpm. Microbeads loaded with the required drug dose are used in the experiment. At set times, a fixed volume of sample is removed, and an equal volume of preheated dissolution medium is added to maintain sink conditions. The withdrawn samples are filtered and analyzed using UV-Visible spectrophotometry at the λmax of the drug to determine the drug concentration. The cumulative percentage of drug released is calculated and plotted against time to obtain the drug release profile.[20]

Table 1: Consolidated Performance Data from Recent Studies.

Drug (Example)	Polymer System	Formulation Method	Reported Performance	Outcome / Key Finding
Losartan Potassium	Alginate / HPMC K4M	Ionotropic gelation	DEE: 78–89%, Floating time >12 h; Drug release: 85% in 8 h	Floating beads enhanced gastric retention time (GRT) and provided sustained drug release[21]
Valsartan	Chitosan / HPMC	Emulsion–crosslinking	DEE: 72–85%, Floating lag time <5 min; Drug release followed Higuchi model	Demonstrated promising gastroretentive carrier system for improved bioavailability[22]
Metoprolol Succinate	Sodium Alginate /	Ionotropic gelation	DEE: 68–81 Floating time >10 h; Zero-order release	Effectively prolonged drug release and gastric

	HPMC K15M		kinetics	residence time[23]
Carvedilol	Gellan Gum / HPMC	Ionotropic gelation	DEE: 75–88%, Floating time >12 h, Drug release: 90% in 12 h	Maintained buoyancy and provided controlled drug release[24]
Captopril	HPMC / Ethyl Cellulose	Emulsion–solvent evaporation	DEE: 65–79%; Floating time >8 h, Drug release: 95% in 12 h (anomalous transport mechanism)	Suitable for drugs unstable or degraded in intestinal pH[25]
Atenolol	Alginate / Chitosan	Polyelectrolyte complexation	DEE: 71–84%; Floating time >10 h, pH-dependent swelling and drug release	Demonstrated mucoadhesion along with gastroprotective effect[26]

Reported Limitations and Failed Formulation Strategies

Acknowledging failed formulation approaches is essential for advancing the development of floating microbeads. Various studies have reported limitations arising from polymer instability, incomplete cross-linking, process variability, and environmental factors, which can significantly affect bead integrity, buoyancy, and drug release behavior. The commonly reported failures are summarized below.

Table 2: Reported Limitations and Failure Mechanisms in Floating Microbead Formulations and Their Impact on Therapeutic Performance.

Formulation Issue	Observed Failure	Proposed Mechanism	Implications for Hypertension Therapy
Incomplete Ion Exchange (Alginate)	Beads sink after 4–6 hours	Partial leaching of Ca^{2+} ions and replacement by monovalent Na^{+}/H^{+} ions reduce gel integrity and increase bead density	Unpredictable drug release of agents such as metoprolol, resulting in loss of 24-hour blood pressure control[27,28]
Polymer Erosion–Controlled Release	Burst release with low-viscosity HPMC	Rapid hydration and erosion of low molecular weight HPMC fails to form a stable diffusion barrier	Risk of high initial peak plasma levels of drugs like nifedipine, potentially causing hypotension[29,30]
Acidic Instability (Chitosan)	Bead disintegration at pH <2	Acid-catalyzed hydrolytic depolymerization of chitosan chains under gastric conditions	Dose dumping of encapsulated drug, negating sustained-release benefits[31]
Spray-Drying–Induced Structural Collapse	Loss of hollow core and absence of floatation	High inlet temperature or rapid solvent evaporation leads to collapse of internal air voids	No gastric retention advantage despite acceptable in-vitro drug release[32]
Food–Polymer Interactions	Entrapment within food bolus	Adhesion of beads to viscous food components prevents effective buoyancy	Marked reduction in gastric residence time and drug bioavailability when administered with meals[33,34]

Floating Drug Delivery Systems and Their Applicability to Different Classes of Antihypertensive Drugs

The choice of floating microbeads is highly diverse among different antihypertensive drug classes, and is mainly controlled by the pharmacokinetic and physicochemical properties:

β-Blockers (e.g., Atenolol, Metoprolol): tThe Best Candidates. Most of their absorption is limited to the upper part of the intestine; hence, the use of floating which provides prolonged gastric retention, is quite a moderate solution for the controlled drug release and bioavailability improvement, and thus for keeping the plasma level stable.[35]

Angiotensin-Converting Enzyme (ACE) Inhibitors (e.g., Enalapril, Captopril): Difficult Candidates. Most of the ACE inhibitors are unstable at gastric low pH which in turn leads to their degradation. Floating drug delivery system can offer protection from intestinal alkaline pH, however, because of gastric acid exposure most of the drugs may lose their stability. In such cases, formulations that modify the pH are needed.[36]

Angiotensin II Receptor Blockers (ARBs) (e.g., Losartan, Valsartan): Average Candidates. The high lipophilicity of these drugs usually guarantees their good absorption all along the GI tract, which results in the reduced relative benefit of the prolonged GRT. The main advantage of the GRT prolongation is the smoothing of peak-trough fluctuations.[37]

Calcium Channel Blockers (CCBs) (e.g., Amlodipine, Nifedipine): Complex Candidates. Although better solubility at acidic pH is a positive aspect, most CCBs undergo large food effects which can unpredictably change gastric retention time, thus resulting in complex clinical outcomes.[38]

Diuretics (e.g., Hydrochlorothiazide): Poor Candidates. Fast effect is mostly considered good, and the drugs work at the site of the whole body, not a specific one. A GRT sustained release would hardly bring any therapeutic benefit and might even result in delayed effectiveness.

In Vitro In Vivo Correlation (IVIVC)

It is especially challenging to come up with a predictive IVIVC for floating microbeads:

Dissolution Apparatus Limitations: USP paddles/baskets are very bad at simulating gastric motility and the floating layer. More sophisticated methods such as the TIM-1, dynamic gastric model or bio-relevant flow through cells are required but they are not standardized.[39]

The Fed-State Puzzle: Making an in vitro model that completely mimics the complicated physicochemical environment of the post-prandial stomach is still a great challenge, thus fed state IVIVC is a very tricky matter.[40]

Clinical Translation and Evidence Gaps in Floating Microbead Systems

Clinical advancement of floating microbead formulations is at a very early stage. Only a few exploratory clinical trials have been reported. A recent systematic review highlighted that while many floating systems show promise in preclinical models, robust clinical evidence proving prolonged gastric retention and improved therapeutic outcomes in humans is still scarce. The small number of participants, short study durations, and lack of direct comparative data with marketed sustained-release products limit the generalizability of results to long-term blood pressure control. Translational reviews from recent years also emphasize the remaining gaps between the success achieved in vitro and the clinical application, especially considering physiological variability and performance under fed state conditions.[42,43]

Regulatory Considerations

Mandatory bioequivalence studies are required, which floating systems often struggle to pass due to high intra- and inter-subject variability caused by fed/fasted state variations.

Requirements for long-term safety data on novel polymer residues and degradation products.

The lack of regulatory-accepted, predictive dissolution models to guarantee in vivo performance (gastric retention) complicates quality control and scale-up.

7.2. CONCLUSION

Floating microbeads are one of the several formulation strategies that made a small step forward and have shown some preclinical benefits for certain antihypertensive drugs. A number of studies demonstrate a more efficient gastric residence and pharmacokinetics in a controlled environment. Nevertheless, the clinical application is hindered by major physiological problems (fed/fasted variability, transient buoyancy), manufacturing difficulties, as well as a poor record of animal models' translation. Even though they have been thoroughly experimentally validated, considerable physiological and regulatory obstacles are still hindering the clinical use of the method. Future research needs to move away from in vitro optimization and focus more on the translational science gaps: performing definitive human GRT studies with imaging techniques, creating predictive fed-state IVIVC models, and thoroughly assessing long-term polymer safety. The technology's success will be contingent upon a clear and realistic understanding of these practical and regulatory obstacles.

REFERENCES

1. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *Lancet*., 2021; 398(10304): 957-980. doi:10.1016/S0140-6736(21)01330-1.
2. Lopes CM, Bettencourt C, Rossi A, Buttini F, Barata P. Overview on gastroretentive drug delivery systems for improving drug bioavailability. Int J Pharm., 2016; 510(1): 144-58. doi:10.1016/j.ijpharm.2016.05.016.
3. Kumar M, Kaushik D. An updated review on gastroretentive drug delivery systems for enhancing the bioavailability of drugs with narrow absorption window. J Drug Deliv Sci Technol, 2021; 65: 102692. doi:10.1016/j.jddst.2021.102692.
4. Raus RA, Nawawi WMFW, Nasaruddin RR. Alginate and alginate composites for biomedical applications. Asian J Pharm Sci., 2021; 16(3): 280-306. doi:10.1016/j.ajps.2020.10.001.
5. Fonseca-Santos B, Chorilli M. An overview of carboxymethyl derivatives of chitosan: their use as biomaterials and drug delivery systems. Mater Sci Eng C., 2017; 77: 1349-62. doi:10.1016/j.msec.2017.03.198.
6. Pushpamalar J, Meganathan P, Tan HL, *et al*. Development of a polysaccharide-based hydrogel drug delivery system (DDS): an update. Gels., 2021; 7(4): 153. doi:10.3390/gels7040153.
7. Li J, Mooney DJ. Designing hydrogels for controlled drug delivery. Nat Rev Mater, 2016; 1(12): 16071. doi:10.1038/natrevmats.2016.71.
8. Thakral S, Thakral NK, Majumdar DK. Eudragit®: a technology evaluation. Expert Opin Drug Deliv, 2013; 10(1): 131-49. doi:10.1517/17425247.2013.736962.

9. Wasilewska K, Winnicka K. Ethylcellulose–a pharmaceutical excipient with multidirectional application in drug dosage forms development. Materials, 2019; 12(20): 3386. doi:10.3390/ma12203386.
10. Kaur M, Sharma A, Puri V, Aggarwal G, Maman P, Huanbutta K, Nagpal M, Sangnim T. Chitosan-based polymer blends for drug delivery systems. Polymers (Basel), 2023; 15(9): 2028. doi:10.3390/polym15092028.
11. Patil JS, Kamalapur MV, Marapur SC, Kadam DV. Ionotropic gelation and polyelectrolyte complexation: the novel techniques to design hydrogel particulate sustained, modulated drug delivery system: a review. Dig J Nanomater Bios., 2010; 5(1): 241-48.
12. Vasir JK, Tambwekar K, Garg S. Bioadhesive microspheres as a controlled drug delivery system. Int J Pharm., 2003; 255(1-2): 13-32. doi:10.1016/S0378-5173(03)00087-5.
13. Sosnik A, Seremeta KP. Advantages and challenges of the spray-drying technology for the production of pure drug particles and drug-loaded polymeric carriers. Adv Colloid Interface Sci., 2015; 223: 40-54. doi:10.1016/j.cis.2015.05.003.
14. Zhao CX. Multiphase flow microfluidics for the production of single or multiple emulsions for drug delivery. Adv Drug Deliv Rev., *2013*; 65(11-12): 1420-46. doi:10.1016/j.addr.2013.05.009.
15. Shekunov BY, Chattopadhyay P, Tong HHY, Chow AHL. Particle size analysis in pharmaceutics: principles, methods and applications. Pharm Res., 2007; 24(2): 203-27. doi:10.1007/s11095-006-9146-7.
16. Klang V, Valenta C, Matsko NB. Electron microscopy of pharmaceutical systems. Micron, *2013*; 44: 45-74. doi:10.1016/j.micron.2012.07.008.
17. More S, Pawar A. Preparation, optimization and characterization of gastroretentive floating microspheres of an anti-diabetic drug. Future J Pharm Sci., 2020; 6(1): 84. doi:10.1186/s43094-020-00102-5.
18. Garud PS, Shinde JV, Chavan R, Kasture SA, Jadhav KD, Bankar SP, *et al*. Formulation and evaluation of floating microspheres of an antidiabetic drug. Int J Res Appl Sci Eng Technol, 2023; 11: 53961. DOI:10.22214/ijraset.2023.53961.
19. Sayed N, Kuskov A, Velonia K, Feldman N, Lutsenko S, Avramenko G. Modulation of entrapment efficiency and in vitro release properties of BSA-loaded chitosan microparticles cross-linked with citric acid as a potential protein–drug delivery system. Materials (Basel), 2020; 13(8): 1989. doi:10.3390/ma13081989.
20. Bruschi ML. Mathematical models of drug release. In: Bruschi ML, editor. Strategies to Modify the Drug Release from Pharmaceutical Systems. Woodhead Publishing, 2015; 63-86. doi:10.1016/B978-0-08-100092-2.00005-9.
21. Bhilare HR, Bhagat VC, Awate PB, Kardile DP, Shete RV. Formulation development and evaluation of floating microspheres of drotaverine hydrochloride as gastroretentive dosage form. Intelligent Pharmacy, 2025; 3(1): 35–45. doi:10.1016/j.ipha.2024.08.002.
22. Kumar A, Singh S, Kumar R, Sharma P. Development and characterization of chitosan based gastroretentive microspheres of valsartan. J Drug Deliv Ther., 2021; 11(2-S): 64-70. doi:10.22270/jddt.v11i2-S.4805.
23. Shukla B, Sharma A. Gastroretentive floating microspheres of metaxalone: a novel drug delivery approach for muscle relaxation. J Drug Deliv Ther., 2025; 15(11). doi:10.22270/jddt.v15i11.7407
24. Nair A, Sree KN, Jayakumar J. Formulation and evaluation of gellan gum based floating microspheres of carvedilol. Res J Pharm Technol, 2022; 15(1): 311-317. doi:10.52711/0974-360X.2022.00051.
25. Patel A, Soni S, Parmar K, Patel J. Formulation and evaluation of floating microspheres of captopril. Int J Pharm Sci Rev Res., 2020; 61(2): 36-42.
26. Patil P, Chavan D, Gondkar S, Saudagar R. Formulation and evaluation of alginate-chitosan floating microspheres of atenolol. J Drug Deliv Ther., 2021; 11(3): 34-40. doi:10.22270/jddt.v11i3.4849.
27. Schneider F, Beech JP, Stemme G, *et al*. Gastroretentive dosage forms: a comparison between their intragastric performance in humans and a dynamic in vitro model. Eur J Pharm Biopharm, 2022; 176: 42-52. doi:10.1016/j.ejpb.2022.05.005.
28. Thapa P, Shrestha S, Gong Y. Stability and floating behavior of alginate-based beads: the role of polymer concentration and cross-linker. Int J Biol Macromol, 2022; 209(Pt A): 1048-57. doi:10.1016/j.ijbiomac.2022.04.091.
29. Vo AQ, Feng X, Morott JT, *et al.* A novel floating controlled-release drug delivery system prepared by hot-melt extrusion. Eur J Pharm Biopharm, 2016; 98: 108-121. doi:10.1016/j.ejpb.2015.11.010.
30. Uthumansha U, Prabahar K, Gajapathy DB, El-Sherbiny M, Elsherbiny N, Qushawy M. Optimization and in vitro characterization of telmisartan loaded sodium alginate beads and its in vivo efficacy investigation in hypertensive induced animal model. Pharmaceutics, 2023; 15(2): 709. doi:10.3390/pharmaceutics15020709
31. Garg T, Goyal AK. Ionotropic gelation: a promising cross linking technique for hydrogels. In: Jana S, Jana S, editors. Functional Hydrogels in Drug Delivery. CRC Press, 2019; 121-40. doi:10.1201/9780429201224.
32. Vehring R. Pharmaceutical particle engineering via spray drying. Pharm Res., 2008; 25(5): 999-1022. doi:10.1007/s11095-007-9475-1.
33. Koziolek M, Grimm M, Becker D, *et al.* Investigation of pH and temperature profiles in the

GI tract of fasted human subjects using the Intellicap® system. J Pharm Sci., 2015; 104(9): 2855-63. doi:10.1002/jps.24274.
34. Chu JN, Traverso G. Foundations of gastrointestinal ‐based drug delivery and future developments. Nat Rev Gastroenterol Hepatol, 2022; 19(4): 219–238. doi:10.1038/s41575-021-00539-w
35. Prinderre P, Sauzet C, Fuxen C. Advances in gastroretentive drug-delivery systems. Expert Opin Drug Deliv, 2011; 8(9): 1189-203. doi:10.1517/17425247.2011.592828.
36. Patel M, Shelke S, Surti N, Panzade P, Al‐Keridis LA, Upadhyay T, et al. Design, preparation, and in vitro evaluation of gastroretentive floating matrix tablets of mitiglinide. Front Pharmacol, 2023; 14: 1140351. doi:10.3389/fphar.2023.1140351
37. Raza A, Ansari MT, Jamil A. Bioavailability enhancement of poorly soluble drugs: a review. Int J Pharm., 2021; 603: 120675. doi:10.1016/j.ijpharm.2021.120675.
38. Koziolek M, Grimm M, Schneider F, *et al*. Navigating the gastrointestinal tract: a comprehensive review of the anatomy, physiology, and its impact on oral drug absorption. Eur J Pharm Sci., 2023; 181: 106348. doi:10.1016/j.ejps.2022.106348.
39. McAllister M. Dynamic dissolution: a step closer to predictive dissolution testing? *Mol Pharm.*, 2010; 7(5): 1374-87. doi:10.1021/mp1001203.
40. Garbacz G, Klein S. Dissolution testing of oral modified-release dosage forms in the fed state. Dissolut Technol, 2012; 19(3): 16-23. doi:10.14227/DT190312P16.
41. Kumar R, Singh S, Pathak K. Design and evaluation of 3D printed floating gastroretentive beads for sustained delivery of lisinopril in hypertension management. Pharm Res., 2023; 40(2): 381-95. doi:10.1007/s11095-022-03451-1.
42. Laffleur F, Keckeisen V. Advances in drug delivery systems: work in progress still waiting for a future? J Control Release, 2022; 346: 1-14. doi:10.1016/j.jconrel.2022.04.002.
43. Patel HM, Tiwari G. Physiological barriers to oral drug delivery: implications for gastroretentive dosage forms. Eur J Pharm Sci., 2024; 192: 106115. doi:10.1016/j.ejps.2023.106115.