Journal of Pharmacology, Genetics and Molecular Biology (JPGMB)
ISSN: 3049-3757 | Vol. 02, Issue-02, March-April, 2026

Gastroretentive Floating Microspheres: A Promising Approach for Site-Specific and Controlled Drug Delivery

Shashank Dhar Tiwari[1*], Surendra Pratap Singh[1]

[1]Faculty of Pharmacy, PK University, Shivpuri, Pin Code- 473665, India

***Corresponding Author E-mail: tshashanadhar@gmail.com**

Abstract:

Gastroretentive drug delivery systems (GRDDS) have drawn a lot of interest as a successful method for increasing the oral bioavailability of medications that act locally in the stomach, have a limited absorption window, or are unstable in the intestinal environment. Among the several GRDDS, gastroretentive floating microspheres are a promising multi-unit system that offers site-specific and controlled drug release while extending the stomach residence period. Because of their low density and ability to float on stomach contents for prolonged periods of time without interfering with gastric emptying, these microspheres enhance patient compliance and therapeutic effectiveness. Polymers, such as natural, semi-synthetic, or synthetic polymers, and gas-forming agents are commonly used in the formulation of floating microspheres utilizing methods such solvent evaporation, emulsion solvent diffusion, spray drying, and ionic gelation. To get the best buoyancy, drug entrapment efficiency, and sustained drug release profiles, it is essential to choose the right polymers and formulation parameters. Micromeritic characteristics, in vitro buoyancy, drug release kinetics, stability tests, and in vivo stomach retention evaluation are all part of the evaluation of floating microspheres.

Keywords: Gastroretentive Drug Delivery, Floating Microspheres, Controlled Drug Release, Site-Specific Delivery, Gastric Retention, Oral Drug Delivery System

Received: Jan. 12, 2026 **Revised: Feb. 28, 2026** **Accepted: March. 12, 2026** **Published: April 22, 2026**

DOI: https://doi.org/10.64062/JPGMB.Vol2.Issue2.7

https://jpgmb.com/1/issue/archive

1. Introduction:

1.1 Overview of Gastroretentive Drug Delivery Systems (GRDDS):

Specialized oral dose forms called gastroretentive drug delivery systems (GRDDS) are intended to extend the duration of medication residence in the stomach and upper gastrointestinal tract. Conventional oral formulations frequently pass through the stomach quickly, which restricts the absorption of medications that need local action in the gastric area,

have a limited absorption window, or are unstable at higher intestinal pH. In order to improve drug bioavailability and therapeutic efficacy, GRDDS employ a number of strategies to postpone gastric emptying and keep the dose form in the stomach for prolonged periods of time [1].

There are several methods used in GRDDS, such as high-density systems that sink to stay in the stomach, expandable and swelling systems that enlarge to prevent passage through the pylorus, mucoadhesive systems that stick to the gastric mucosa, and floating systems that stay buoyant on gastric fluids. These systems frequently include polymers and excipients designed to maximize stomach retention while achieving controlled or prolonged medication release.

Improved bioavailability, fewer doses, and targeted drug delivery to the stomach or upper small intestine are the main benefits of GRDDS. However, physiological variables including pH, stomach motility, and the patient's fed or fasting condition affect how well these systems work. Novel materials and technologies are still being researched to address the physiological and formulation issues of today [2].

1.2 Need for Prolonged Gastric Retention:

In gastroretentive drug delivery systems (GRDDS), prolonged stomach retention is crucial for enhancing the therapeutic efficacy of several oral medications. Especially for medications that are absorbed primarily in the stomach or upper small intestine, are unstable in the higher pH of the intestine, or have a narrow absorption window, conventional oral dosage forms frequently travel quickly from the stomach into the intestine, reducing the amount of time available for drug dissolution and absorption. By extending the gastric residence time, the dosage form can stay in the stomach's acidic environment for a longer period of time, improving drug absorption and solubility and raising total bioavailability [3].

Additionally, longer retention allows for more regulated and sustained release profiles, which lower the frequency of dose and maintain therapeutic drug concentrations for longer periods of time, improving patient compliance and lowering side effects. Additionally, prolonged contact time at the target region greatly improves the localized therapeutic benefits of medications designed for the local treatment of gastrointestinal conditions, such as Helicobacter pylori infections or peptic ulcers. By avoiding an early passage into the colon, where medications may deteriorate or become less soluble, GRDDS can help reduce drug waste. In general, maximizing the clinical efficacy of several medication regimens that cannot be effectively

administered by traditional oral dose forms depends on attaining a longer gastric residence duration [4].

1.3 Limitations of Conventional Oral Drug Delivery:

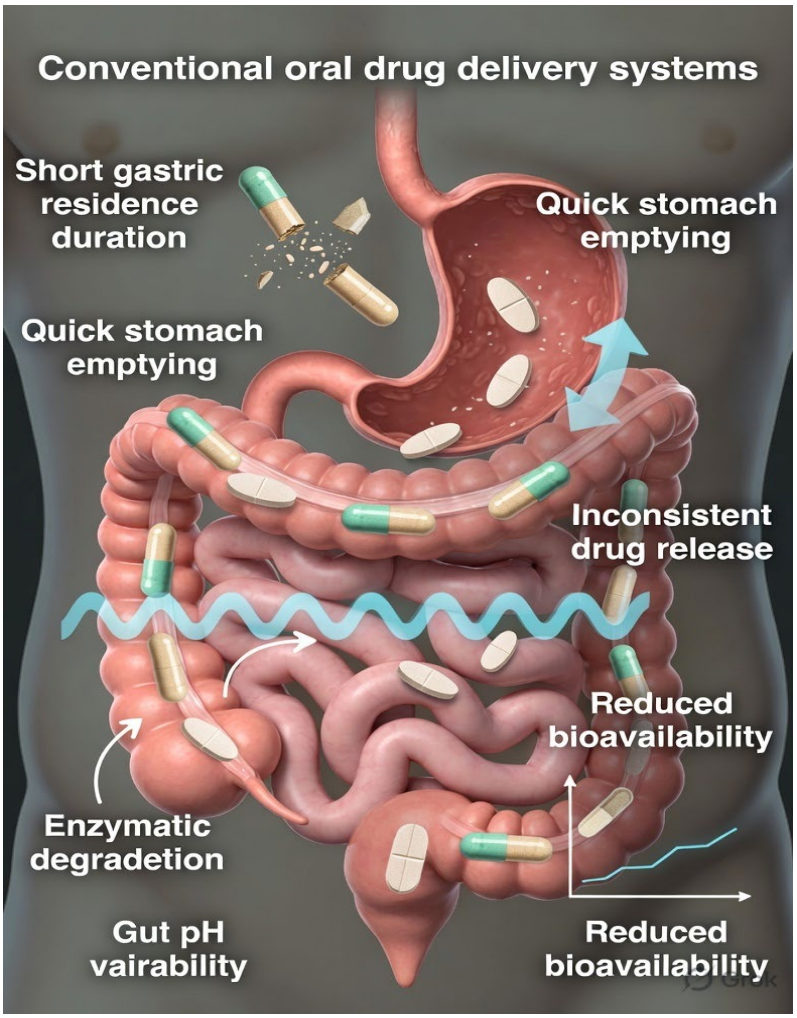


Fig 1 : Conventional Oral Drug Delivery

Due to their cost-effectiveness, ease of administration, and patient comfort, conventional oral medication delivery methods such as regular tablets and capsules remain the most popular. These conventional dose formulations do, however, have a number of significant drawbacks that limit their therapeutic efficacy and clinical performance. One of the main issues is the short and inconsistent gastric residence duration, which causes the dose form to pass quickly from the stomach and into the intestine, especially while fasting. Particularly for medications with limited absorption windows or those that are mostly absorbed in the stomach and upper small intestine, this reduces the amount of time available for drug disintegration and absorption, resulting in inadequate drug absorption and decreased bioavailability shown in fig 1 [5].

Furthermore, the site and rate of drug release cannot be controlled by traditional oral forms, which frequently leads to erratic plasma drug levels and the need for repeated doses to maintain

therapeutic concentrations. This raises the possibility of adverse consequences and reduces patient compliance. Drug stability and absorption are further jeopardized by physiological obstacles such quick stomach emptying, enzymatic degradation, and fluctuating gut pH. Furthermore, conventional oral distribution poses serious absorption problems for medications that are unstable in alkaline conditions or poorly soluble in intestinal fluids. All things considered, these drawbacks underscore the unfulfilled demand for sophisticated delivery methods that may increase site-specific absorption, extend stomach residence duration, and provide controlled drug release for better therapeutic results [6].

1.4 Rationale for Floating Microspheres:

By extending the gastrointestinal residence duration of medications, floating microspheres solve significant drawbacks of traditional oral dose forms, making them a crucial tactic in gastroretentive drug delivery systems (GRDDS). These multiarticulate systems float on stomach fluids for longer periods of time because of their buoyant architecture and low density, which delays transit through the pylorus and guarantees prolonged exposure at the site of absorption. Drugs that are unstable at higher intestinal pH, have limited absorption windows in the stomach or upper small intestine, or need local action in the gastric environment like anti-H. pylori agents benefit most from this extended gastric retention [7].

The capacity of floating microspheres to deliver regulated and prolonged drug release is another justification for their use. This capability aids in preserving constant plasma drug levels, lowering dose frequency, and reducing fluctuations in therapeutic concentration. Compared to traditional formulations, this leads to higher bioavailability, therapeutic effectiveness, and patient compliance. Due to its multiarticulate nature, floating microspheres disperse more evenly in the stomach, minimizing intra- and inter-subject variability in medication absorption and preventing the "all-or-none" gastric emptying that single-unit systems are known for [8].

2. Anatomy and Physiology of the Stomach Relevant to Gastroretention:

2.1 Gastric Anatomy and pH Environment:

The stomach's distinct anatomical shape and very acidic environment make it an essential component of gastroretentive drug delivery systems (GRDDS). The cardia, fundus, body (corpus), and pylorus are the four primary anatomical divisions of the stomach. The antrum and pylorus are engaged in the mixing, grinding, and regulated emptying of stomach contents into the duodenum, whilst the fundus and body serve mainly as storage areas. Because dose forms kept in the fundus and body are less likely to experience fast stomach emptying, this geographical difference is crucial for gastroretention [9].

Another important element affecting medication stability, solubility, and release behavior is the pH environment in the stomach. Because parietal cells continuously secrete hydrochloric acid, the pH of the stomach is very acidic during fasting, usually ranging from 1 to 3. The pH may momentarily rise to 4–6 after eating, but as digestion continues, the pH will eventually revert to an acidic state. Drugs that are weak bases or those that need a low pH for maximum solubility benefit from this acidic environment. Long-term exposure to stomach pH improves

drug dissolution, sustained release, and absorption for medications with pH-dependent solubility or local gastric action in gastroretentive systems such floating microspheres. Therefore, the logical design of efficient gastroretentive formulations requires an understanding of stomach architecture and pH dynamics [10].

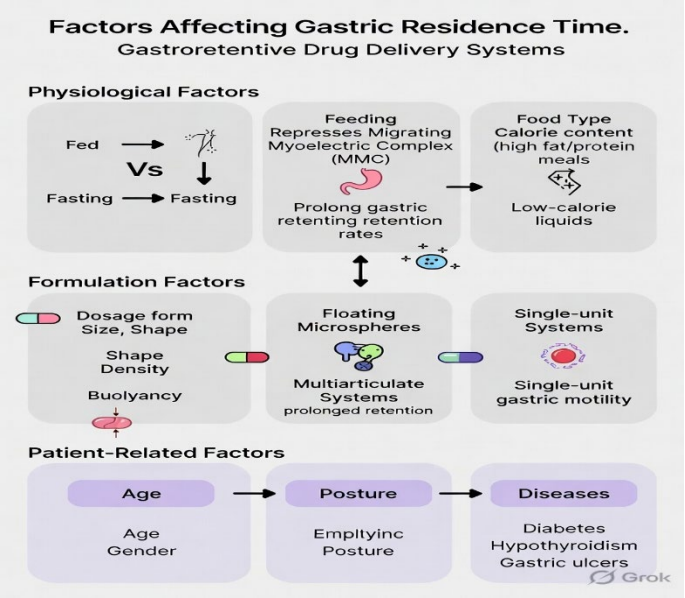
2.2 Gastric Motility and Migrating Myoelectric Complex (MMC):

The efficiency of gastroretentive drug delivery systems (GRDDS) is directly impacted by gastric motility, which is a key factor in determining the stomach residence length of oral dose forms. When the stomach is fed or fasted, it moves in distinct ways. The Migrating Myoelectric Complex (MMC), a cyclic motor activity that acts as a "housekeeping wave" to remove indigestible items and leftover food from the stomach and small intestine, controls gastric motility during a fast [11].

Phase I (quiescent stage) with mild contractions, Phase II with sporadic and irregular contractions, Phase III with strong, regular peristaltic contractions, and Phase IV, a brief transition phase returning to Phase I, are the four phases of the MMC. Because it may evacuate dose forms from the stomach into the intestine regardless of their size or density, phase III is especially crucial in gastroretentive administration. When fasting, the MMC cycle usually happens every 90 to 120 minutes, which causes the stomach to empty traditional oral formulations quickly [12].

2.3 Factors Affecting Gastric Residence Time:

The amount of time a dose form stays in the stomach before moving on to the small intestine is known as the gastric residence time (GRT). It is a crucial factor that affects how well gastroretentive drug delivery systems (GRDDS) work. The efficacy of gastroretentive formulations is determined by a number of physiological, formulation-related, and patient-dependent variables that impact GRT



.

Fig 2: Factors Affecting Gastric Residence Time

The stomach's condition, whether fed or fasting, is one of the most crucial physiological variables. The Migrating Myoelectric Complex (MMC) causes the stomach to empty quickly while fasting, but it is repressed when feeding, which prolongs the stomach's retention. Food type and calorie content are important factors as well; meals heavy in fat and protein slow down the emptying of the stomach more than liquids or meals low in calories shown in fig 2 [13].

GRT is greatly influenced by the size, shape, density, and buoyancy of the dosage form. Low-density methods, including floating microspheres, and larger dose forms last longer in the stomach. Compared to single-unit systems, multiarticulate systems show lower variability and improved retention. Gastric retention is also influenced by the characteristics of the medication and excipient, such as the kind of polymer and swelling behavior. Gastric motility and emptying rates are further influenced by patient-related variables such age, gender, posture, and disease condition. GRT may be prolonged by diseases including diabetes, hypothyroidism, or stomach ulcers. Designing efficient gastroretentive systems with consistent and long-lasting drug release patterns requires an understanding of these elements [14].

2.4 Challenges in Gastric Retention:

Despite the many benefits of gastroretentive drug delivery systems (GRDDS), a number of physiological, formulation-related, and patient-dependent variables make it difficult to achieve consistent and extended stomach retention. The unpredictability of stomach motility, especially during fasting, is one of the main obstacles. No matter the size or shape of the dose form, the presence of the Migrating Myoelectric Complex (MMC), particularly its strong Phase III contractions, might cause it to be expelled from the stomach, resulting in early gastric emptying and decreased therapeutic effectiveness.

Variability in stomach pH and volume is another significant issue that can affect the buoyancy, swelling, and drug release characteristics of gastroretentive systems. Low stomach fluid levels during fasting may impair the ability of floating systems to sustain buoyancy. Predictable stomach retention is further complicated by inter-individual heterogeneity associated with age, gender, posture, and medical disorders including diabetes or gastroparesis [15].

It is challenging to strike the ideal balance between buoyancy, mechanical strength, and controlled drug release from a formulation standpoint. While little swelling or low density may lead to early emptying, excessive edema may irritate the stomach. Furthermore, problems with stability, repeatability, and scale-up present real-world difficulties in the production and marketing phases. The GRDDS's general application is further restricted by patient-related issues such the requirement for meal intake to improve retention and the possibility of dosage dumping. These difficulties show that in order to achieve successful gastroretention, proper formulation design and a thorough grasp of stomach physiology are essential [16].

3. Gastroretentive Drug Delivery Systems: An Overview:

3.1 Floating Drug Delivery Systems:

Among gastroretentive drug delivery systems (GRDDS), floating drug delivery systems (FDDS) are among the most researched and effective strategies. These systems may float on the contents of the stomach for extended periods of time without being quickly discharged into the intestine because they are made to have a lower density than gastric fluids. FDDS extends the gastric residence duration and permits regulated and prolonged medication release in the stomach or upper portion of the small intestine by staying buoyant shown in fig 3.

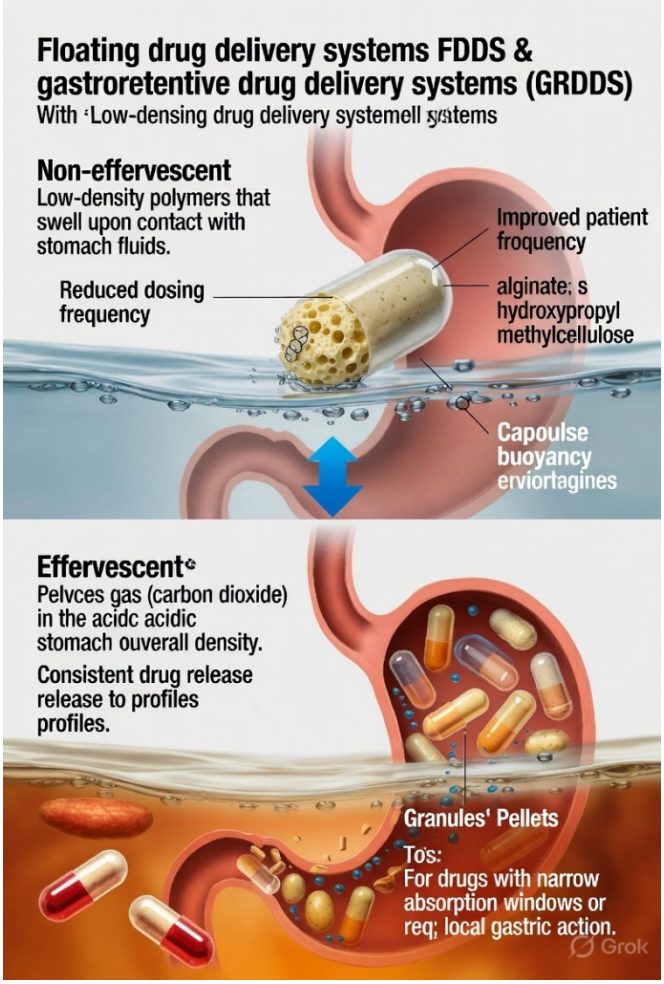


Fig 3: Floating Drug Delivery Systems

The foundation of FDDS is buoyancy, which may be attained by employing low-density polymers that swell when they come into contact with stomach fluids (non-effervescent systems) or by adding gas-forming chemicals (effervescent systems). In the acidic stomach environment, effervescent systems produce carbon dioxide, which becomes trapped in the polymeric matrix and lowers the density of the system. Swellable polymers like alginate or hydroxypropyl methylcellulose are necessary for non-effervescent systems to stay buoyant [17].

Drugs that have limited absorption windows, are poorly soluble at intestinal pH, or are meant to work locally in the stomach like antiulcer or anti-Helicobacter pylori agents benefit greatly from floating drug delivery devices. Furthermore, FDDS lessens the frequency of dose,

enhances patient compliance, and maintains constant plasma drug concentrations. However, stomach fluid volume, pH fluctuations, and fed or fasting circumstances may affect how well they operate [18].

3.2 Mucoadhesive Systems:

In gastroretentive drug delivery systems (GRDDS), mucoadhesive drug delivery systems are a crucial strategy for extending the duration of gastric residency by binding to the mucosal surface of the stomach. Through physical and chemical processes including hydrogen bonding, electrostatic interactions, and polymer chain entanglement, these systems make use of bio adhesive polymers that interact with the mucus layer lining the stomach. Mucoadhesive devices prevent gastric emptying and enable localized, sustained medication release by staying affixed to the stomach mucosa.

The contact step, in which the dosage form makes intimate contact with the mucosal surface, and the consolidation stage, in which polymer chains interpenetrate with mucus glycoproteins to create robust adhesive connections, are the two phases that typically comprise the mucoadhesion process. Because of their superior mucoadhesive qualities and biocompatibility, polymers including chitosan, Carbopol, sodium alginate, hydroxypropyl methylcellulose, and polyacrylic acid are frequently utilized shown in table 1 [19].

Table 1: Common Mucoadhesive Polymers Used in GRDDS

Polymer	Type	Mechanism of Adhesion	Advantages
Chitosan	Natural	Electrostatic interaction	Biodegradable, strong adhesion at low pH
Carbopol	Synthetic	Hydrogen bonding	High mucoadhesive strength
Sodium alginate	Natural	Polymer chain entanglement	Good swelling and gel-forming ability
HPMC	Semi-synthetic	Hydrogen bonding	Biocompatible, controlled release
Polyacrylic acid	Synthetic	Hydrogen bonding	Prolonged adhesion time

Mucoadhesive systems are especially useful for medications that need to be delivered to specific locations in the stomach, have a short half-life, or are poorly absorbed in the digestive tract. However, adhesion time can be shortened by variables such varied mucus thickness, stomach motility, and continuous mucus turnover. Despite these difficulties, compared to

traditional oral dose forms, mucoadhesive systems provide increased therapeutic effectiveness, decreased dosing frequency, and greater absorption shown in table 2 [20].

Table 2: Advantages and Limitations of Mucoadhesive Systems

Advantages	Limitations
Prolonged gastric residence time	Mucus turnover reduces adhesion
Site-specific drug delivery	Adhesion affected by gastric motility
Improved bioavailability	Variable mucus thickness
Reduced dosing frequency	Formulation complexity

3.3 Expandable and Swelling Systems:

A significant family of gastroretentive drug delivery systems (GRDDS) are expandable and swelling systems, which are made to enlarge after oral administration in order to block the pyloric sphincter. By expanding or unfolding to a size greater than the pyloric aperture, which normally has a diameter of 12 to 14 mm, these systems stay in the stomach for extended periods of time. Following the achievement of gastric retention, the dosage form delivers the medication in a regulated fashion before dissolving or shrinking to provide safe gastric emptying [21].

Swellable, biodegradable polymers including hydroxypropyl methylcellulose, polyethylene oxide, Carbopol, and super-porous hydrogels are typically used to create expandable systems. These polymers quickly absorb water when they come into contact with gastrointestinal contents, causing considerable swelling and dimensional expansion. While some expandable systems just use polymer swelling to accomplish retention, others are made as folded or compressed structures that unfold in the stomach [22].

3.4 High-Density Systems:

Instead of floating or sticking to the mucosa, high-density gastroretentive drug delivery devices are made to sink to the bottom of the stomach contents. These systems may withstand peristaltic motions and postpone stomach emptying because of their density, which is substantially higher than that of gastric fluid (usually > 2.5 g/cm³). High-density systems offer regulated medication release at the intended spot and extend gastric residence duration by settling in the lower portion of the stomach [23].

Heavy, inert excipients like titanium dioxide, zinc oxide, barium sulfate, or iron powder are used in the formulation of high-density systems to raise the dosage form's overall density. To

guarantee constant density and medication release, these substances are evenly distributed throughout the polymeric matrix. These systems are especially helpful for medications that benefit from extended stomach exposure and are stable in acidic conditions [24].

3.5 Comparative Advantages of Floating Microspheres:

Because of its outstanding buoyancy, regulated drug release features, and multiarticulate nature, floating microspheres are regarded as one of the most effective gastroretentive drug delivery systems (GRDDS). In contrast to single-unit solutions like expandable devices or floating tablets, floating microspheres disperse evenly across the stomach contents, limiting gastric emptying variability and lowering the possibility of dosage dumping. They may float on stomach juices for extended periods of time because to their low density, which lengthens the gastric residence time and improves medication absorption [25].

The capacity of floating microspheres to carry drugs to the stomach and upper small intestine in a site-specific and sustained manner is one of its main advantages. They work especially well with medications that have a limited window for absorption, a brief half-life, or low solubility at gut pH. Floating microspheres are safer and more patient-friendly than mucoadhesive systems since they are less impacted by mucus turnover and do not require heavy excipients as high-density systems do [26].

4. Floating Microspheres: Concept and Mechanism:

4.1 Definition and Classification:

Multiarticulate gastroretentive drug delivery systems called floating microspheres are made to stay buoyant in the stomach environment for extended periods of time while releasing the medication in a regulated way. Usually made of polymers with a density lower than that of stomach juices, these microspheres are spherical, hollow, or porous particles. Because of their low density, floating microspheres float over the contents of the stomach without obstructing regular gastric emptying, lengthening the duration of gastric residency and improving the bioavailability of drugs. This method works especially well for medications that are meant to function locally in the stomach, have a limited absorption window, a short biological half-life, or are poorly soluble at gut pH shown in table 3 [27].

Table 3: Classification of Floating Microspheres:

Basis of Classification	Type	Description
Structure	Hollow microspheres	Contain internal cavity; high buoyancy
	Solid porous microspheres	Porous matrix; reduced density
Polymer type	Natural polymers	Chitosan, alginate

	Semi-synthetic polymers	HPMC
	Synthetic polymers	Ethyl cellulose, Eudragit
Drug release mechanism	Diffusion-controlled	Drug diffuses through polymer
	Erosion-controlled	Polymer erosion governs release
	Combined mechanism	Diffusion + erosion

4.2 Principle of Buoyancy:

In order for the dosage form to float atop the contents of the stomach for an extended amount of time, the buoyancy principle in floating microspheres is based on keeping a density lower than that of gastric fluid (≈1.004 g/cm³). The polymeric matrix of floating microspheres either holds produced gas or traps air inside internal cavities when they come into touch with stomach fluid, which lowers the density overall. Archimedes' principle states that if the upward buoyant force of the stomach fluid is greater than the downward gravity force acting on the microspheres, the system will float [28].

Both effervescent and non-effervescent methods can produce buoyancy. Low-density polymers expand when hydrated in non-effervescent environments, creating a gel barrier that retains air inside the microsphere structure and permits continuous floating. Gas-forming substances (such sodium bicarbonate) react with stomach acid in effervescent systems to create carbon dioxide, which becomes trapped in the polymer matrix and lowers density. Because of the interior gaps created by solvent diffusion or evaporation, hollow microspheres, also known as micro balloons, are buoyant [29].

4.3 Mechanism of Floating and Drug Release:

Polymer hydration, buoyancy creation, and controlled drug diffusion or erosion combine to regulate the process of floating and drug release from floating microspheres. The outer polymeric shell of floating microspheres hydrates and swells when they come into contact with stomach juice. Solvent diffusion during preparation produces an air-filled interior cavity in hollow microspheres, lowering their density and allowing for instant floating. Gas-forming chemicals react with stomach acid in effervescent microspheres to produce carbon dioxide, which is retained in the polymer matrix and adds buoyancy shown in table 4 [30].

Table 4: Mechanism of Floating and Drug Release in Floating Microspheres

Stage	Process	Description	Outcome
Initial contact	Hydration	Polymer absorbs gastric fluid	Matrix swelling

Buoyancy generation	Air/CO_2 entrapment	Internal cavity or gas formation	Floating achieved
Drug release – I	Diffusion	Drug diffuses through hydrated polymer	Sustained release
Drug release – II	Erosion	Polymer erosion/degradation	Prolonged release
Final stage	Disintegration	Reduction in size/density	Safe gastric emptying

4.4 Single-Unit vs Multi-Unit Floating Systems:

Based on their dosage form design and stomach activity, floating gastroretentive systems may be roughly divided into single-unit and multi-unit systems. Choosing a suitable gastroretentive strategy requires an understanding of the distinctions between these two methods.

A single dose form that stays buoyant in stomach fluid makes up single-unit floating devices, including floating tablets or capsules. Although these devices are very easy to design and produce, stomach motility has a critical role in how well they work. The possibility of dosage dumping in the event that a single-unit system fails to float or disintegrates too soon is a significant drawback. High inter- and intra-subject variability can also result from the unpredictability of stomach emptying of a single unit [31].

Multi-unit floating systems, on the other hand, such pellets or floating microspheres, are made up of many tiny, distinct units that are evenly distributed throughout the stomach. In addition to offering more regular drug release profiles and stomach retention, this distribution lowers the possibility of dosage dumping. Multi-unit systems are safer and more dependable for extended drug administration because they are less impacted by physiological variability and stomach emptying patterns. For regulated and site-specific gastroretentive medication administration, floating microspheres are frequently chosen because of these benefits [32].

5. Polymers and Excipients Used in Floating Microspheres:

5.1 Natural Polymers:

Because of their low toxicity, biocompatibility, biodegradability, and affordability, natural polymers are used extensively in the creation of floating microspheres. For regulated and prolonged drug release, these polymers which come from natural sources like plants, animals, or microbes are frequently chosen in gastroretentive drug delivery systems.

Natural polymers aid in matrix formation, buoyancy, swelling, and drug release regulation in floating microspheres. Their ability to absorb stomach fluid, expand, and form a gel-like barrier due to their hydrophilic nature aids in preserving low density and extended gastric retention. Furthermore, a lot of natural polymers have mucoadhesive qualities, which let them stick to the stomach mucosa and prolong the gastric residency period [33].

5.2 Semi-Synthetic Polymers:

Because they combine the mechanical strength and repeatability of synthetic materials with the safety of natural polymers, semi-synthetic polymers are frequently used in the creation of floating microspheres. These polymers give improved control over swelling behavior, viscosity, drug release rate, and buoyancy since they are chemically modified variants of natural polymers. They are ideal for gastroretentive medication delivery systems due to their reliable quality and regulatory approval [34].

Semi-synthetic polymers mainly serve as matrix formers, release retardants, and buoyancy enhancers in floating microspheres. They hydrate and expand when exposed to stomach fluid, creating a gel barrier that lowers system density and extends the duration of gastric residency. Drug release profiles may be successfully customized from immediate to sustained release by varying polymer grade and concentration.

Hydroxypropyl methylcellulose (HPMC), ethyl cellulose (EC), hydroxypropyl cellulose (HPC), and carboxymethyl cellulose (CMC) are examples of semi-synthetic polymers that are often utilized. Because of its superior swelling, gel-forming, and release-controlling qualities, HPMC is widely employed. Because ethyl cellulose is hydrophobic, it is frequently used with hydrophilic polymers to enhance encapsulation efficiency and regulate drug release. While HPC supports matrix integrity and film formation, CMC increases swelling and viscosity [35].

5.3 Synthetic Polymers:

Compared to natural and semi-synthetic polymers, synthetic polymers provide higher stability, precise control over drug release, high mechanical strength, and remarkable repeatability, which is why they are widely utilized in floating microspheres. These chemically produced polymers are ideal for gastroretentive drug delivery systems because they may be engineered to attain particular physicochemical characteristics including buoyancy, hydrophobicity, permeability, and degradation rate.

Synthetic polymers primarily serve as matrix formers, coating materials, and release-controlling agents in floating microspheres. In the hostile stomach environment, their hydrophobic characteristic aids in preserving the structural integrity of microspheres and slowing down drug diffusion. Furthermore, synthetic polymers provide sustained drug release and prolonged floating behavior when paired with gas-forming agents or low-density excipients [36].

6. Formulation Approaches for Floating Microspheres:

6.1 Solvent Evaporation Technique:

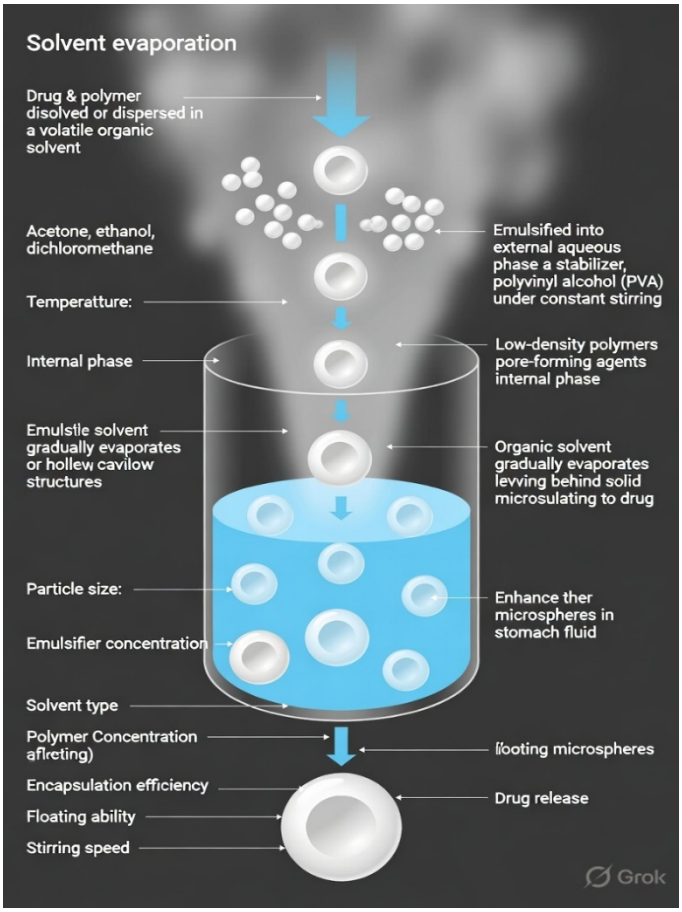


Fig 4: Solvent Evaporation Technique

One of the most widely used and dependable processes for creating floating microspheres is solvent evaporation. Because of its ease of use, scalability, repeatability, and compatibility with both hydrophilic and hydrophobic medications, this method is recommended. When synthetic and semi-synthetic polymers are employed as matrix formers, it is very helpful [37].

This process creates an internal phase by dissolving or dispersing the drug and polymer in a volatile organic solvent (such as acetone, ethanol, dichloromethane, or their mixtures). After that, this phase is emulsified under constant stirring into an external aqueous phase that contains a stabilizer such as polyvinyl alcohol (PVA). The organic solvent eventually evaporates as the stirring process goes on, causing polymer precipitation and the creation of solid microspheres that encapsulate the medication.

Low-density polymers and pore-forming agents are added to floating microspheres in order to lower the system's density. Internal cavities or hollow structures are created as solvent evaporates, and these structures add to the buoyancy of stomach fluid. Particle size, encapsulation efficiency, floating ability, and drug release behavior are all strongly influenced by process variables such temperature, emulsifier concentration, solvent type, polymer concentration, and stirring speed shown in fig 4 [38].

6.2 Emulsion Solvent Diffusion Method:

A popular and efficient approach for creating floating microspheres with a hollow interior structure that greatly increases buoyancy is the emulsion solvent diffusion (ESD) method. This approach, which is regarded as a variation of the solvent evaporation technique, works especially well with hydrophobic polymers and medications that are poorly soluble in water.

This approach involves dissolving the drug and polymer in a mixture of organic solvents that are somewhat water-miscible, usually ethanol and acetone or dichloromethane. Then, under constant stirring, this organic phase is gradually added to an aqueous phase that contains a stabilizer such polyvinyl alcohol. Polymer precipitation occurs at the droplet interface as a result of the organic solvent diffusing outward and water diffusing inward upon contact with the aqueous phase [39].

Hollow or porous microspheres, which have a low density and good buoyancy in stomach fluid, are created as a result of the quick solvent diffusion. Microsphere size, encapsulation efficiency, floating lag time, and drug release behavior are all significantly influenced by variables including temperature, emulsifier content, polymer concentration, solvent ratio, and stirring speed.

High buoyancy, consistent particle size, and enhanced encapsulation efficiency are some benefits of the emulsion solvent diffusion process. To guarantee safety and repeatability, it must be carefully optimized and may entail complicated solvent systems. All things considered; this technique is ideal for creating floating microspheres for applications involving the administration of gastroretentive drugs [40].

6.3 Ionic Gelation Technique:

Using natural and semi-synthetic polymers, the ionic gelation technique also known as ionotropic gelation is a straightforward, gentle, and solvent-free procedure that is frequently employed to create floating microspheres. This method avoids severe processing conditions and organic solvents, making it particularly appropriate for heat-sensitive medications, peptides, and proteins [41].

Ionic gelation is based on the electrostatic interaction of multivalent counter-ions with oppositely charged polymers. An aqueous solution containing divalent or trivalent cations, such as calcium chloride (Ca2+), is usually mixed with an anionic polymer, such as sodium alginate. Instantaneous cross-linking takes place upon contact, resulting in the creation of gelled microspheres. Low-density polymers or gas-forming agents, such as sodium bicarbonate, are added to floating microspheres to improve buoyancy and decrease density.

By varying the polymer content, cross-linker strength, curing duration, and stirring conditions, this method provides good control over drug release, encapsulation efficiency, and particle size. The resultant microspheres exhibit remarkable biocompatibility, regulated medication release, and outstanding stomach retention. Nevertheless, compared to systems made with synthetic polymers, ionically gelled microspheres could show less mechanical strength and quicker drug release [42].

6.4 Spray Drying Method:

A sophisticated and scalable approach for creating floating microspheres for gastroretentive medication administration is spray drying. This technique creates dry solid microspheres by atomizing a drug and polymer solution or suspension into a stream of hot drying gas, typically heated air. This causes the solvent to evaporate quickly. Spray drying is an excellent method for preparing floating systems on an industrial and laboratory scale because it provides uniform morphology, regulated particle size, and quick manufacturing in a single process [43].

Through a nozzle, the feed solution comprising the medication and dissolved polymer is delivered into the spray dryer, producing tiny droplets inside a heated chamber. The solvent immediately evaporates as these droplets pass through the drying chamber, creating solid microspheres with porous or hollow interiors features that help with low density and improved buoyancy. The procedure enables the control of airflow, feed rate, and intake temperature to produce the required particle properties, including size distribution, drug encapsulation effectiveness, and floating behavior [44].

6.5 Novel and Hybrid Preparation Techniques:

Novel and hybrid preparation methods for floating microspheres have been developed as a result of recent developments in gastroretentive medication delivery. These strategies overcome the drawbacks of traditional techniques while including their benefits, especially with regard to scalability, buoyancy control, drug loading efficiency, and release modulation. To satisfy the rising need for patient-friendly and precisely regulated gastroretentive devices, new approaches are being investigated more and more [45].

Hybrid procedures, such as solvent evaporation–ionic gelation, emulsion–spray drying, or solvent diffusion–coacervation, usually combine two or more formulation processes. These combinations allow for the creation of microspheres with improved structural integrity, porous surfaces, and hollow cores, which improve floating behavior and prolong drug release. Ionic gelation and solvent evaporation, for instance, can be used to increase mechanical strength while maintaining the biocompatibility of natural polymers.

Innovative methods include 3D-printed gastroretentive devices, electrospinning-assisted microsphere production, microfluidic procedures, and supercritical fluid technologies are becoming more popular. While supercritical fluid techniques minimize the use of hazardous organic solvents, microfluidic devices provide exact control over particle size and shape. Furthermore, enhanced drug solubility and site-specific administration are made possible by nanotechnology-assisted floating microspheres shown in table 5 [46].

Table 5: Novel and Hybrid Techniques for Floating Microsphere Preparation

Technique	Principle	Key Advantage
Solvent evaporation + ionic gelation	Dual solidification mechanism	Improved strength and buoyancy
Emulsion–spray drying	Emulsification followed by rapid drying	Uniform hollow microspheres
Supercritical fluid technique	Solvent-free particle formation	Eco-friendly, high purity
Microfluidic method	Controlled droplet formation	Narrow size distribution
Nano-assisted microspheres	Drug nanosizing within microspheres	Enhanced solubility and release

7. Optimization and Design Considerations:

7.1 Effect of Polymer Concentration:

A crucial formulation factor that greatly affects the physicochemical properties, floating behavior, and drug release profile of floating microspheres is polymer concentration. Long-term stomach retention, sufficient buoyancy, high drug entrapment efficiency, and regulated drug release all depend on optimizing polymer concentration [47].

Larger microspheres occur during emulsification or droplet formation as a result of increased internal phase viscosity caused by an increase in polymer concentration. Because of their lower density, larger particles increase buoyancy; yet, they may also delay drug dispersion by forming a thicker polymeric matrix. Therefore, a sustained or protracted drug release profile is usually produced by increased polymer levels. The effectiveness of drug entrapment is also directly impacted by polymer concentration. Inadequate polymer content at lower concentrations may produce porous microspheres with reduced medication loading and poor structural integrity. By reducing drug diffusion into the external phase during microsphere formation, on the other hand, ideal polymer levels enhance encapsulation. Reproducibility may be impacted by poor flowability, aggregation, and processing issues brought on by an overly high polymer concentration [48].

7.2 Drug–Polymer Compatibility:

Since drug stability, encapsulation effectiveness, buoyancy, and release behavior are all directly impacted by drug–polymer compatibility, it is a crucial design factor in the creation of

floating microspheres. Throughout formulation, storage, and in-vivo performance, a suitable drug–polymer system guarantees that the drug is chemically stable and evenly distributed inside the polymeric matrix.

Drug degradation, crystallization, decreased entrapment efficiency, or changed release profiles might result from incompatible interactions between the drug and polymer. Additionally, these interactions may weaken the microspheres' structural integrity, which might lead to uneven stomach retention and poor floating capacity. Thus, before choosing polymers for microsphere formation, Preformulation experiments are necessary to verify compatibility [49].

7.3 Particle Size Control:

Because particle size directly affects buoyancy, drug loading, release kinetics, stomach retention, and in-vivo efficacy, it is an important optimization parameter in the design of floating microspheres. In gastroretentive drug delivery systems, consistent and controlled particle size guarantees repeatability and predictable treatment results.

Smaller particles in floating microspheres have a greater surface area, which speeds up medication release. However, because of their increased density and quicker stomach emptying, they may be less buoyant. Larger microspheres, on the other hand, often exhibit better floating ability and longer stomach retention; yet, too big a particle size may lead to poor flow characteristics and irregular drug release. To balance buoyancy and controlled release, an ideal particle size range must be carefully maintained [50].

7.4 Floating Ability vs Drug Release Balance:

A key design factor in floating microspheres is striking the ideal balance between medication release profile and floating ability. Long-term stomach residency is guaranteed by floating ability, and therapeutic levels are maintained over a predetermined time via controlled drug release. Nevertheless, comparable formulation factors may have conflicting effects on these two traits, requiring careful optimization.

The density and structural integrity of microspheres are the main factors influencing floating ability. For long periods of time, low-density systems with hollow cores or trapped gas (from gas-forming chemicals) float easily on stomach fluid. Low-density or very porous matrices, on the other hand, can allow for quicker drug dispersion, leading to a burst release that jeopardizes sustained release goals. On the other hand, early stomach emptying may result from the decreased buoyancy of densified matrices intended for controlled release [51].

7.5 Quality by Design (QbD) Approach:

The Quality by Design (QbD) methodology is a methodical, risk- and science-based technique that is being used more and more in the creation of floating microspheres to guarantee reliable performance and consistent product quality. In contrast to conventional trial-and-error techniques, QbD places a strong emphasis on comprehending formulation and process factors and how they affect important quality attributes over the course of product development.

The Quality Target Product Profile (QTPP), which describes the desired properties of the gastroretentive floating microspheres, including controlled drug release, prolonged gastric retention, acceptable buoyancy duration, and desired particle size, is the first step in the QbD framework's development process. Critical Quality Attributes (CQAs) are determined using the QTPP. Particle size distribution, floating lag time, total floating duration, drug entrapment efficiency, and in-vitro drug release profile are common CQAs for floating microspheres [52].

8. Evaluation Parameters of Floating Microspheres:

8.1 Micromeritic Properties:

Micromeritic qualities, which include the formulation's flow behavior, packing capacity, and particle size characteristics, are crucial assessment criteria for floating microspheres. During large-scale manufacturing, these characteristics have a direct impact on repeatability, dosage homogeneity, capsule filling, and manufacturability. A thorough micromeritic analysis guarantees that floating microspheres have suitable handling properties and reliable performance [53].

Particle size and size distribution, bulk density, tapped density, Carr's compressibility index, Hausner's ratio, and angle of repose are important micromeritic characteristics. Particle size influences drug release behavior, buoyancy, and flow characteristics. For constant floating ability and predictable medication release patterns, a uniform particle size distribution is ideal.

Measurements of bulk and tapping density shed light on how microspheres pack. Carr's index and Hausner's ratio, two measures of powder flowability, are also computed using these values. Microspheres with lower Hausner's ratio (<1.25) and Carr's index (<15%) often have acceptable flow characteristics, making them appropriate for additional processing. Another straightforward yet accurate way to evaluate flow characteristics is the angle of repose; better flow is indicated by smaller angles [54].

8.2 Particle Size and Morphology:

Because they have a significant impact on floating behavior, drug entrapment efficiency, drug release kinetics, and stomach residence period, particle size and surface morphology are essential quality aspects of floating microspheres. The repeatability, stability, and therapeutic efficacy of gastroretentive devices are guaranteed by appropriate regulation of these parameters.

Particle Size:

Drug diffusion, polymer hydration, and microsphere buoyancy are all directly impacted by the surface area-to-volume ratio, which is determined by particle size. bigger particles may enhance floating time and extend drug release, whereas smaller particles often offer quicker drug release because of their bigger surface area. On the other hand, particles that are too big may have uneven gastric distribution and poor flow characteristics.

Optical microscopy, laser diffraction, and dynamic light scattering (for smaller microspheres) are frequently used methods for particle size characterization. Because it guarantees uniform floating performance and predictable medication release patterns, a restricted particle size distribution is preferable [55].

Morphology:

The form, surface roughness, porosity, and structural integrity of floating microspheres may all be inferred from morphological analysis. To improve buoyancy and regulate medication release, microspheres should ideally have spherical, smooth, or slightly porous surfaces.

Scanning electron microscopy (SEM) is commonly used to investigate surface morphology. SEM pictures can be used to detect surface holes, fissures, or drug crystallization that could cause burst release or decreased floating capacity. By decreasing density, highly porous microspheres increase buoyancy, while thick and irregular particles may sink quickly in stomach fluid [56].

8.3 Percentage Yield and Drug Entrapment Efficiency:

Medication entrapment efficiency (DEE) and percentage yield are crucial assessment metrics for floating microspheres because they reveal the efficacy of the formulation process and the polymeric matrix's ability to encapsulate the medication.

Percentage Yield:

By comparing the actual weight of the dried microspheres produced to the total weight of the starting ingredients (drug + polymer), the percentage yield which indicates the effectiveness of the production process is computed. Minimal material loss during processing stages such solvent evaporation, washing, and drying is indicated by a high percentage yield. For manufacturing to be both economical and scalable, consistently high yields are preferred.

Percentage Yield =Total weight of drug + polymer / Actual weight of microspheres recovered × 100 [57]

Drug Entrapment Efficiency (DEE):

The amount of drug effectively encapsulated within the microspheres in relation to the total amount of drug employed in the formulation is measured by drug entrapment efficiency. Achieving the intended therapeutic dose and controlled release patterns requires effective drug incorporation into the polymer matrix, which is indicated by high DEE.

DEE (%) = Initial amount of drug used / Amount of drug present in microspheres × 100

DEE is often measured by dissolving the microspheres in an appropriate solvent to release the medication, then quantifying the drug using HPLC, UV spectrophotometry, or other analytical techniques. Formulation factors including solvent system, drug–polymer ratio, polymer concentration, and processing conditions affect both characteristics [58].

8.4 In-vitro Buoyancy Studies:

Because they measure the formulation's capacity to stay afloat over simulated stomach fluid for an extended amount of time, in-vitro buoyancy tests are essential for assessing the floating behavior of gastroretentive microspheres. Prior to in-vivo testing, buoyancy studies offer vital information on the stomach residence potential of floating microspheres, which is crucial for improving bioavailability and attaining regulated drug release.

Principle:

The floating microspheres are placed in a simulated stomach media (often 0.1 N HCl or pH 1.2 buffer) and gently stirred at 37 ± 0.5 °C to measure buoyancy. When submerged, thick or non-floating particles sink to the bottom of the medium, whereas microspheres with the proper low density and internal gas or hollow structures stay afloat on the surface [59].

Parameters Evaluated:

1. **Floating Lag Time (FLT):**

This is the time interval between the introduction of microspheres into the medium and the moment they begin to float. A shorter FLT indicates rapid onset of floatation, which is desirable for early gastric retention.

2. **Total Floating Duration (TFD):**

This is the total time the microspheres remain buoyant on the surface of the medium. Longer floating duration indicates better gastroretentive potential.

Procedure:

- Place a known quantity of floating microspheres in a beaker containing simulated gastric fluid (pH 1.2) at 37 °C.
- Stir at a controlled speed (e.g., 50–100 rpm) to mimic gastric motility.
- Record the FLT and TFD visually or using video capture.
- Microspheres that remain afloat for > 8 h are generally considered suitable for gastroretentive delivery [60].

8.5 In-vitro Drug Release Studies:

To assess the release behavior, rate, and mechanism of drug diffusion from floating microspheres under simulated stomach circumstances, in vitro drug release investigations are carried out. Predicting in-vivo performance, refining formulation parameters, and guaranteeing repeatable controlled-release profiles for gastroretentive devices all depend on these investigations.

In order to replicate the gastrointestinal environment, the test is often conducted using simulated gastric fluid (0.1 N HCl, pH 1.2) kept at 37 ± 0.5 °C. The USP dissolving apparatus I (basket) or USP apparatus II (paddle) are often used pieces of equipment that rotate at an

appropriate speed, usually between 50 and 100 rpm. The dissolving media is filled with a predetermined number of floating microspheres equal to the necessary medication dosage.

Samples are removed, filtered, and subjected to UV-visible spectrophotometry or HPLC analysis at prearranged intervals. Sink conditions are maintained by substituting new medium for the removed volume. After that, the cumulative percentage of drug release is computed and plotted against time [61].

8.6 Release Kinetic Models:

Because it aids in the description, comparison, and prediction of the process of drug release from floating microspheres, release kinetic modeling is a crucial component of in vitro drug release investigations. To determine whether drug release happens by diffusion, erosion, swelling, or a mix of processes, mathematical models are used to dissolution data. Controlled gastroretentive medication administration and formulation variable optimization depend on this knowledge.

A variety of kinetic models, including zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Hixson–Crowell models, are fitted to the cumulative percentage drug release data acquired from in vitro investigations. The correlation coefficient (R2) is used to determine which model fits the data the best.

1. **Zero-Order Model:**

This model describes drug release at a constant rate independent of concentration, which is ideal for maintaining steady plasma drug levels.

2. **First-Order Model:**

Drug release depends on the concentration of drug remaining in the microspheres.

3. **Higuchi Model:**

This model explains drug release from porous matrices, where release occurs primarily by diffusion.

4. **Korsmeyer–Peppas Model:**

Used to analyze the mechanism of release, especially when more than one process is involved [62].

8.7 Stability Studies:

The physical, chemical, and medicinal stability of floating microspheres over time under certain environmental conditions is assessed by stability studies. These investigations guarantee that the drug content, floating ability, particle integrity, and release profile of the formulation are maintained during the course of its shelf life. A crucial prerequisite for verifying the effectiveness, safety, and quality of gastroretentive medication delivery systems is stability testing.

According to ICH criteria, floating microspheres are often submitted to accelerated and long-term stability assessments (Q1A(R2)). For long-term research, the typical storage settings are

25 ± 2 °C/60 ± 5% RH, while for expedited research, they are 40 ± 2 °C/75 ± 5% RH. To avoid moisture absorption and deterioration, the samples are kept in appropriate, well-sealed containers shown in table 6 [63].

Table 6: Typical Stability Study Conditions for Floating Microspheres

Condition	Temperature	Relative Humidity	Duration
Long-term	25 ± 2 °C	60 ± 5% RH	6–12 months
Accelerated	40 ± 2 °C	75 ± 5% RH	3–6 months

9. In-Vivo Evaluation and Correlation:

9.1 Gastric Retention Studies:

In order to assess gastroretentive floating microspheres in vivo, gastric retention experiments are essential since they verify that the formulation can stay in the stomach for an extended period of time under physiological settings. In-vivo research offers practical insight into the impacts of stomach motility, fed/fasted status, gastric emptying patterns, and physiological variability, whereas in-vitro buoyancy testing only give preliminary data.

Determining the residence time, location, and mobility of floating microspheres within the stomach is the main goal of gastric retention investigations. Depending on the formulation's stage of development and ethical issues, these tests are frequently conducted on human volunteers or animal models (dogs, rats, and rabbits) [64].

9.2 In-Vivo Imaging Techniques:

To see, monitor, and measure the stomach retention behavior of gastroretentive floating microspheres under physiological settings, in-vivo imaging methods are widely employed. These methods enhance in-vitro results and formulation improvement by offering accurate, non-invasive, and real-time proof of the position, mobility, and residence duration of dosage forms in the stomach.

Gamma scintigraphy is regarded as the gold standard among the techniques available for assessing gastroretentive systems. In this technique, floating microspheres are radiolabeled with a suitable gamma-emitting isotope (commonly technetium-99m), and their transit through the gastrointestinal tract is monitored using a gamma camera. Without interfering with regular stomach physiology, this technique enables accurate assessment of gastric residence duration and formulation integrity shown in table 7 [65].

Table 7: Common In-Vivo Imaging Techniques for Gastroretentive Systems

Technique	Principle	Advantages	Limitations
Gamma scintigraphy	Radioisotope tracking	High accuracy, non-invasive	Radiation exposure
X-ray imaging	Radio-opaque markers	Simple, economical	Low soft-tissue contrast
Ultrasonography	Sound wave imaging	No radiation	Operator-dependent
MRI	Magnetic resonance	High resolution	Expensive, limited access

9.3 Pharmacokinetic Studies:

Pharmacokinetic (PK) studies are performed to evaluate the in-vivo drug absorption, distribution, metabolism, and elimination characteristics of gastroretentive floating microspheres. These studies provide quantitative evidence of whether prolonged gastric retention leads to improved bioavailability, sustained plasma drug levels, and reduced dosing frequency compared to conventional oral dosage forms.

Pharmacokinetic evaluation is commonly carried out in suitable animal models (rats, rabbits, dogs) or in human volunteers, following ethical approval. Floating microspheres and reference formulations are administered orally, and blood samples are collected at predetermined time intervals. Plasma drug concentrations are analyzed using validated analytical techniques such as HPLC, LC–MS/MS, or UV spectroscopy [66].

9.4 In-Vitro–In-Vivo Correlation (IVIVC):

A predicted mathematical connection known as "in-vitro–in-vivo correlation" (IVIVC) connects the floating microspheres' in-vitro drug release properties to their in-vivo pharmacokinetic performance. For gastroretentive drug delivery systems, establishing IVIVC is especially crucial since it helps determine whether the extended stomach retention and controlled release shown in vitro transfer into improved bioavailability and sustained plasma drug levels in vivo.

IVIVC is often created by contrasting in-vitro dissolution profiles with in-vivo plasma concentration–time data, which are typically reported as the ratio of drug absorption to drug release. A robust IVIVC facilitates regulatory approval, scale-up, and post-approval

modifications while minimizing the need for lengthy in-vivo investigations during formulation optimization [67].

10. Therapeutic Applications of Floating Microspheres:

10.1 Drugs with Narrow Absorption Window:

The stomach or upper portion of the small intestine (duodenum and proximal jejunum) is where drugs with a narrow absorption window are mostly absorbed. Traditional oral dose forms frequently go through this area quickly, which results in poor bioavailability, inconsistent therapeutic response, and inadequate absorption. By extending the gastrointestinal residency time and keeping the medication in its ideal absorption site for a longer period of time, floating microspheres provide a possible approach.

Long-term drug exposure to the absorption window is ensured by floating microspheres, which stay buoyant in stomach fluid and release the medication in a regulated and sustained way. This strategy is especially helpful for medications that are broken down by colonic bacteria or that are unstable or poorly soluble at gut pH. Floating microspheres lessen oscillations in plasma levels, decrease dosage frequency, and enhance extent of absorption (AUC) via improving stomach retention shown in table 8 [68].

Table 8: Examples of Drugs with Narrow Absorption Window Suitable for Floating Microspheres

Drug	Primary Absorption Site	Therapeutic Benefit of Floating Microspheres
Levodopa	Stomach & duodenum	Improved bioavailability
Riboflavin	Upper small intestine	Enhanced absorption
Furosemide	Stomach	Reduced variability
Metformin	Duodenum & jejunum	Sustained plasma levels
Ciprofloxacin	Upper GIT	Improved therapeutic effect

10.2 Drugs Acting Locally in Stomach:

Long-term interaction with the gastric mucosa is necessary for medications meant to work locally in the stomach to have the best possible therapeutic effect. Traditional oral dose forms frequently have a brief gastrointestinal residence period, which lowers the local drug concentration and leaves treatment unfinished. Because they stay buoyant in stomach juice, floating microspheres are particularly helpful in these situations, guaranteeing prolonged medication retention and sustained local activity.

By releasing the medication gradually in the stomach, floating microspheres allow for site-specific administration and sustain efficient local drug levels for a longer period of time. Helicobacter pylori infections, gastritis, gastric ulcers, and diseases related to stomach acid can all be effectively treated with this method. Floating microspheres diminish systemic adverse effects, lower dosage frequency, and improve medication stability in acidic pH by extending gastrointestinal residency [69].

10.4 Floating Microspheres in Treatment of H. pylori:

One of the main causes of stomach cancer, peptic ulcer disease, and chronic gastritis is Helicobacter pylori infection. Due to quick gastric emptying, short drug residence times in the stomach, and drug breakdown in the intestinal environment, conventional oral antibiotic treatment frequently exhibits unsatisfactory eradication rates. By extending the gastrointestinal residence duration and preserving high local medication concentrations at the infection site, floating microspheres provide a tailored gastroretentive approach to get around these restrictions.

In order to ensure extended interaction with the stomach mucosa where H. pylori lives, floating microspheres stay buoyant in gastric fluid and release antibiotics in a regulated and sustained way. This targeted distribution lowers systemic exposure and dose frequency while improving medication stability in acidic environments and mucus layer penetration. As a result, gastrointestinal side effects are reduced and eradication efficiency is increased [70].

11. Recent Advances and Research Trends:

11.1 Nano floating Microspheres:

Combining the benefits of nanotechnology and floating drug delivery, nano floating microspheres are a novel and recent development in gastroretentive drug delivery systems. These devices, which are typically in the 100–1000 nm nanosized range, are made to stay afloat in stomach fluid while offering better drug loading, controlled drug release, and surface contact.

greater stability, increased surface area, greater penetration into the stomach mucus layer, and closer interaction with the gastrointestinal epithelium are only a few advantages of the smaller particle size of nano floating microspheres. This is especially helpful for medications that need to act specifically in the stomach, such antibiotics for Helicobacter pylori infections and medications with limited absorption windows. Additionally, their nanoscale size reduces dosage dumping and inter-patient variability by promoting uniform distribution throughout the stomach [71].

11.2 Floating Microspheres for Herbal Drugs:

When administered orally, herbal medications frequently encounter difficulties such as poor solubility, gut pH instability, limited absorption, and quick excretion. By extending the gastrointestinal residence duration and facilitating regulated or sustained release at the site of absorption, floating microspheres provide a novel gastroretentive approach to improve the therapeutic effectiveness of herbal bioactive.

Chitosan, alginate, pectin, and HPMC are examples of natural or semi-synthetic polymers used in the formulation of floating microspheres loaded with herbal extracts or phytoconstituents. These polymers provide buoyancy, mucoadhesion, and stability. For herbal medications that target the stomach or upper gastrointestinal tract, such as curcumin, piperine, betel leaf extract, gingerol, and polyphenolic chemicals, these systems are very helpful in boosting both local and systemic therapeutic effects shown in table 9 [72].

Table 9: Examples of Herbal Drugs Formulated as Floating Microspheres

Herbal Drug / Extract	Polymer Used	Therapeutic Benefit of Floating Microspheres
Curcumin	Chitosan, HPMC	Enhanced gastric retention & bioavailability
Piperine	Alginate, HPMC	Sustained release, improved absorption
Betel leaf extract	Chitosan, Sodium alginate	Prolonged gastric contact, controlled release
Gingerol	HPMC, Eudragit®	Gastric protection & anti-inflammatory effect
Green tea polyphenols	Alginate, Pectin	Sustained antioxidant activity

11.3 Dual-Function Gastroretentive Systems:

In order to improve stomach retention, drug release control, and therapeutic efficacy, dual-function gastroretentive systems a next-generation method in floating microsphere technology integrate two complementing processes, such as buoyancy and mucoadhesion or floating and swelling. The shortcomings of traditional single-mechanism microspheres, including irregular drug release or early stomach emptying, are intended to be addressed by these systems.

In dual-function systems, one portion imparts mucoadhesion or expansion, guaranteeing a solid attachment to the stomach mucosa, while another gives buoyancy, enabling microspheres to float on gastric fluid. This combination improves bioavailability, residence duration, and site-specific drug distribution, especially for medications with pH-sensitive stability, local action in the stomach, or limited absorption windows [73].

12. Limitations and Challenges:

12.1 Formulation Challenges

Designing floating microspheres with consistent buoyancy, drug loading, and controlled release is complex. Key formulation challenges include:

- **Polymer selection:** Choosing polymers that provide adequate buoyancy, controlled release, and stability can be difficult. Natural polymers may have batch-to-batch variability, whereas synthetic polymers may increase cost.
- **Drug–polymer compatibility:** Incompatibility may cause drug degradation or altered release kinetics.
- **Buoyancy optimization:** Achieving sustained floating without premature sinking is critical; improper gas-forming agents or density imbalance can lead to failure.
- **Drug solubility:** Poorly water-soluble drugs may show incomplete release, while highly soluble drugs may cause burst release.

12.2 Scale-Up and Manufacturing Issues:

Translating lab-scale formulations to commercial-scale production presents several hurdles:

- Maintaining uniform particle size and morphology during large-scale preparation.
- Ensuring reproducible drug entrapment efficiency and release profiles across batches.
- Handling solvent evaporation or gelation techniques at scale safely and efficiently.
- High cost of polymers and advanced manufacturing techniques like spray drying or nano-emulsion methods.

12.3 Patient-Related Factors:

Patient physiology can significantly impact the performance of floating microspheres:

- Gastric motility and emptying rates vary with fed or fasted states, age, and health conditions.
- pH variations in the stomach may affect polymer swelling and drug release.
- Gastrointestinal disorders like gastroparesis or hyperacidity can compromise floating behavior.

12.4 Regulatory Concerns:

Regulatory approval for floating microspheres faces specific challenges:

- In-vitro–in-vivo correlation (IVIVC) must be demonstrated to ensure predictability of drug release and therapeutic efficacy.
- Stability and safety studies need to meet stringent ICH guidelines.
- Complex manufacturing processes and novel excipients require extensive validation.
- Lack of standardized protocols for buoyancy testing and gastric retention evaluation may delay approval [74].

13. Future Perspectives:

1. Smart and Stimuli-Responsive Floating Microspheres:

The integration of stimuli-responsive polymers enables microspheres to respond to pH, temperature, or enzymes, providing site-specific and on-demand drug release. Such smart

systems can adapt to physiological changes in the stomach, ensuring precise and controlled delivery for drugs with narrow absorption windows or unstable intestinal behavior.

2. Nanotechnology Integration:

Nano floating microspheres combine nanoscale advantages with gastroretentive properties. These systems offer higher surface area, enhanced mucus penetration, uniform gastric distribution, and improved bioavailability, making them ideal for drugs with poor solubility, low stability, or local gastric action. Targeted ligand-functionalized nanocarriers may allow precision delivery to specific gastric tissues or pathogens, such as H. pylori.

3. 3 D-Printed and Customized Gastroretentive Systems:

3D printing technologies enable the fabrication of floating microspheres with precise geometry, controlled porosity, and tailored buoyancy, facilitating personalized therapy. Customized designs allow optimization for individual patient gastric physiology, drug properties, and release kinetics.

4. Herbal and Combination Therapy Applications:

Floating microspheres for herbal drugs or combination formulations provide opportunities for enhanced bioavailability, prolonged gastric contact, and synergistic therapy, bridging traditional medicine with advanced drug delivery technologies.

5. Regulatory and Clinical Translation:

Future research aims to standardize in-vitro–in-vivo correlation (IVIVC), buoyancy testing, and stability protocols, supporting smoother regulatory approval and commercialization. Advanced in-vivo imaging and predictive modeling will facilitate translation from laboratory to clinic [75].

14. Conclusion:

Floating microspheres represent a versatile and promising platform for gastroretentive drug delivery, offering prolonged gastric retention, controlled drug release, and improved bioavailability. They are particularly beneficial for drugs with narrow absorption windows, local gastric action, pH-sensitive stability, or poor solubility in intestinal fluids. The mechanism of buoyancy, combined with strategic polymer selection and formulation optimization, allows floating microspheres to maintain sustained drug release, enhance therapeutic efficacy, and reduce dosing frequency. Advances such as dual-function systems, nano floating microspheres, stimuli-responsive polymers, and 3D-printed formulations have expanded their potential, making them suitable for both synthetic and herbal drugs.

Notwithstanding these benefits, there are still issues with patient variability, scale-up, formulation, and regulatory compliance. Successful clinical translation and commercialization depend on addressing these constraints using novel polymers, reliable manufacturing processes, in-vitro–in vivo correlation studies, and predictive modeling. Floating microspheres have the potential to develop into next-generation gastroretentive drug delivery systems that provide effective, individualized, and targeted treatment. Their combination with smart polymers, nanotechnology, and sophisticated manufacturing methods will probably improve patient compliance, improve treatment results, and increase the range of medications that can be delivered gastroretentively.

References:

1. Tafish AM, Ebraheem AS, El Naggar EE, Elfar N, Yasser M. Gastroretentive Drug Delivery Systems: A Summarized Overview. Octahedron Drug Res. 2023;3(1):40–56. doi:10.21608/odr.2023.209174.1027
2. Sharma H, Sharma A, Bansal D, Gupta DRK. A Review on Techniques and Applications of Gastroretentive Drug Delivery System. Int J Med Biomed Stud. 2022;6(12). doi:10.32553/ijmbs.v6i12.2632
3. Maurya VB. A review on gastroretentive drug delivery systems. Int J Pharm Pharm Sci. 2025;7(1):375-380. doi:10.33545/26647222.2025.v7.i1e.192
4. Martin S, Soma Sundaram I. Gastro retentive drug delivery systems (GRDDS)-Comprehensive review. J Neonatal Surg. 2024; Volume n/a. (Review discusses need for prolonged gastric retention.)
5. Mahale S, et al. Limitations of conventional oral drug delivery systems and need for gastroretentive systems. Asian J Pharm Res Dev. 2025;13(4):106-116.
6. Introduction to oral drug delivery systems and physiological challenges. Int J Trend Sci Res Dev. 2025; eISSN:2456-6470.
7. Birajdar AA, Deshmukh MT, Shete RV. A Review on Gastro-Retentive Floating Microspheres. J Drug Delivery Ther. 2021;11(1-s):131-138. doi:10.22270/jddt.v11i1-s.4518.
8. Krishna K, Kumar A, Srivastava R. In Vitro In Vivo Studies on Floating Microspheres for Gastroretentive Drug Delivery System: A Review. Asian J Pharm Clin Res. 2021;14(1):13-26. doi:10.22159/ajpcr.2021.v14i1.39183.
9. Tripathi J, Thapa P, Maharjan R, Jeong SH. Current state and future perspectives on gastroretentive drug delivery systems. Pharmaceutics. 2019;11(4):193. doi:10.3390/pharmaceutics11040193
10. Omidian H, Park K. Gastroretentive drug delivery systems: past, present and future. J Control Release. 2014;190:3–15. doi:10.1016/j.jconrel.2014.03.042
11. Tripathi J, Thapa P, Maharjan R, Jeong SH. Current state and future perspectives on gastroretentive drug delivery systems. Pharmaceutics. 2019;11(4):193. doi:10.3390/pharmaceutics11040193
12. Khosla R, Feely LC, Davis SS. Gastrointestinal transit of pharmaceutical dosage forms in humans. Int J Pharm. 1989;53(2):107–117. doi:10.1016/0378-5173(89)90324-4

13. Mojaverian P, Vlasses PH, Kellner PE, Rocci ML. Effects of gender, posture, and age on gastric residence time of an indigestible solid. Pharm Res. 1988;5(10):639–644. doi:10.1023/A:1015971108419
14. Khosla R, Feely LC, Davis SS. Gastrointestinal transit of pharmaceutical dosage forms in humans. Int J Pharm. 1989;53(2):107–117. doi:10.1016/0378-5173(89)90324-4
15. Klausner EA, Lavy E, Friedman M, Hoffman A. Expandable gastroretentive dosage forms. J Control Release. 2003;90(2):143–162. doi:10.1016/S0168-3659(03)00203-5
16. Rouge N, Buri P, Doelker E. Drug absorption sites in the gastrointestinal tract and dosage forms for site-specific delivery. Int J Pharm. 1996;136(1–2):117–139. doi:10.1016/0378-5173(96)04506-1
17. Deshpande AA, Shah NH, Rhodes CT, Malick AW. Development of a novel controlled-release system for gastric retention. Pharm Res. 1997;14(6):815–819. doi:10.1023/A:1012127008626
18. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: A review. AAPS PharmSciTech. 2005;6(3):E372–E390. doi:10.1208/pt060347
19. Smart JD. The basics and underlying mechanisms of mucoadhesion. Adv Drug Deliv Rev. 2005;57(11):1556–1568. doi:10.1016/j.addr.2005.07.001
20. Andrews GP, Laverty TP, Jones DS. Mucoadhesive polymeric platforms for controlled drug delivery. Eur J Pharm Biopharm. 2009;71(3):505–518. doi:10.1016/j.ejpb.2008.09.028
21. Klausner EA, Friedman M, Lavy E, Hoffman A. Expandable gastroretentive dosage forms. J Control Release. 2003;90(2):143–162. doi:10.1016/S0168-3659(03)00203-5
22. Chen J, Blevins WE, Park H, Park K. Gastroretentive drug delivery systems: recent advances. Pharm Res. 2000;17(6):703–712. doi:10.1023/A:1007571907770
23. Rouge N, Buri P, Doelker E. Drug absorption sites in the gastrointestinal tract and dosage forms for site-specific delivery. Int J Pharm. 1996;136(1–2):117–139. doi:10.1016/0378-5173(96)04506-1
24. 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. doi:10.1016/S0168-3659(99)00204-7
25. Streubel A, Siepmann J, Bodmeier R. Floating microparticles based on low density foam powder. Int J Pharm. 2002;241(2):279–292. doi:10.1016/S0378-5173(02)00233-6
26. Soppimath KS, Kulkarni AR, Rudzinski WE, Aminabhavi TM. Microspheres as floating drug delivery systems to increase gastric retention of drugs. Drug Metab Rev. 2001;33(2):149–160. doi:10.1081/DMR-100104402
27. Soppimath KS, Kulkarni AR, Rudzinski WE, Aminabhavi TM. Microspheres as floating drug delivery systems to increase gastric retention of drugs. Drug Metab Rev. 2001;33(2):149–160. doi:10.1081/DMR-100104402
28. Timmermans J, Moës AJ. Factors controlling the buoyancy and gastric retention capabilities of floating matrix capsules. J Pharm Sci. 1990;79(1):76–79. doi:10.1002/jps.2600790113

29. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y. Hollow microspheres for use as a floating controlled drug delivery system in the stomach. J Pharm Sci. 1992;81(2):135–140. doi:10.1002/jps.2600810207
30. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y. Preparation of multiple unit hollow microspheres (microballoons) with acrylic resins containing tranilast and their drug release characteristics. J Control Release. 1991;16(3):279–290. doi:10.1016/0168-3659(91)90018-9
31. Davis SS. Formulation strategies for absorption windows. Drug Discov Today. 2005;10(4):249–257. doi:10.1016/S1359-6446(04)03351-3
32. Fell JT, Whitehead L. Prolonged gastric retention using floating dosage forms. Pharm Technol Int. 1996;8:47–53.
33. George M, Abraham TE. Polyionic hydrocolloids for the intestinal delivery of protein drugs: Alginate and chitosan A review. J Control Release. 2006;114(1):1–14. doi:10.1016/j.jconrel.2006.04.017
34. George M, Abraham TE. Polyionic hydrocolloids for the intestinal delivery of protein drugs: Alginate and chitosan—A review. J Control Release. 2006;114(1):1–14. doi:10.1016/j.jconrel.2006.04.017
35. Anal AK, Stevens WF, Remuñán-López C. Ionotropic cross-linked chitosan microspheres for controlled release of ampicillin. Int J Pharm. 2006;312(1–2):166–173. doi:10.1016/j.ijpharm.2006.01.028
36. Bodmeier R, Chen H. Preparation and characterization of microspheres containing the anti-inflammatory agents, indomethacin, ibuprofen, and ketoprofen. J Control Release. 1990;10(2):167–175. doi:10.1016/0168-3659(89)90087-8
37. Bodmeier R, McGinity JW. Solvent selection in the preparation of poly(D,L-lactide) microspheres prepared by the solvent evaporation method. Int J Pharm. 1987;43(1–2):179–186. doi:10.1016/0378-5173(87)90229-0
38. Freiberg S, Zhu XX. Polymer microspheres for controlled drug release. Int J Pharm. 2004;282(1–2):1–18. doi:10.1016/j.ijpharm.2004.04.013
39. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y. Hollow microspheres for floating controlled drug delivery. J Pharm Sci. 1992;81(2):135–140. doi:10.1002/jps.2600810211
40. Kawashima Y, Yamamoto H, Takeuchi H, Kuno Y. Mucoadhesive hollow microspheres for gastric retention. J Control Release. 2000;68(3):305–318. doi:10.1016/S0168-3659(00)00283-2
41. Anal AK, Stevens WF, Remuñán-López C. Ionotropic cross-linked chitosan microspheres for controlled release of ampicillin. Int J Pharm. 2006;312(1–2):166–173. doi:10.1016/j.ijpharm.2006.01.028
42. George M, Abraham TE. Polyionic hydrocolloids for the intestinal delivery of protein drugs: Alginate and chitosan—A review. J Control Release. 2006;114(1):1–14. doi:10.1016/j.jconrel.2006.04.017
43. Nataren-Rodríguez F, et al. Spray-Dried Polymeric Microspheres for Lipophilic Drugs: Formulation Design, Physicochemical Characterization, and In Vitro Release Evaluation. Pharmaceuticals. 2025;18(7):1020. doi:10.3390/ph18071020

44. Saini S, et al. A REVIEW ON APPROACH OF USING FLOATING … (Discusses spray drying in microsphere preparation). IJCRT. 2023; (Article).
45. Sosnik A, Seremeta KP. Advances in the design of gastroretentive drug delivery systems. Adv Drug Deliv Rev. 2015;85:1–16. doi:10.1016/j.addr.2014.10.006
46. Choi DH, Park CH, Kim IH, Chun HJ, Park K, Han DK. Gastric floating drug delivery systems: Current status and future perspectives. Pharmaceutics. 2019;11(7):1–21. doi:10.3390/pharmaceutics11070394
47. Streubel A, Siepmann J, Bodmeier R. Floating microparticles based on low-density foam powder: Effects of formulation and processing parameters on drug release. Int J Pharm. 2002;241(2):279–292. doi:10.1016/S0378-5173(02)00233-6
48. Jain SK, Awasthi AM, Jain NK, Agrawal GP. Calcium silicate-based microspheres of repaglinide for gastroretentive floating drug delivery. J Control Release. 2005;107(2):300–309. doi:10.1016/j.jconrel.2005.06.012
49. Crowley MM, Schroeder B, Fredersdorf A, Obara S, Talarico M, Kucera S, et al. Physicochemical properties and mechanism of drug release from ethyl cellulose matrix tablets. Drug Dev Ind Pharm. 2004;30(6):593–606. doi:10.1081/DDC-120037497
50. Freiberg S, Zhu XX. Polymer microspheres for controlled drug release. Int J Pharm. 2004;282(1–2):1–18. doi:10.1016/j.ijpharm.2004.04.013
51. Savjani KT, Gajjar AK, Savjani JK. Drug release models in controlled drug delivery systems: A review. Int J Pharm Investig. 2012;2(1):34-40. doi:10.4103/2230-973X.96920
52. Yu LX, Amidon G, Khan MA, Hoag SW, Polli J, Raju GK, Woodcock J. Understanding pharmaceutical quality by design. AAPS J. 2014;16(4):771–783. doi:10.1208/s12248-014-9598-3
53. Aulton ME, Taylor KMG. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 5th ed. London: Elsevier; 2018. doi:10.1016/C2016-0-04453-0
54. Staniforth JN, Aulton ME. Powder flow. In: Aulton ME, editor. Pharmaceutics: The Science of Dosage Form Design. London: Churchill Livingstone; 2002. p. 197–210. doi:10.1016/B978-0-7020-1769-8.50014-6
55. 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
56. Badewale MS, Tegeli VS. Formulation, designing and evaluation of gastro-retentive floating microspheres using silymarin, curcumin and piperine for hepatoprotection. J Appl Pharm Res. 2025;13(4):1167. doi:10.69857/joapr.v13i4.1167
57. Bhilare HR, Bhagat VC, Awate PB, Kardile DP, Shete RV. Formulation development and evaluation of floating microspheres of drotaverine hydrochloride as a gastroretentive dosage form: Yield and entrapment studies. Intelligent Pharmacy. 2025;3(1):35–45. doi:10.1016/j.ipha.2024.08.002
58. Badewale MS, Tegeli VS. Formulation, designing, and evaluation of gastro-retentive floating microspheres using silymarin, curcumin, and piperine for hepatoprotection. J Appl Pharm Res. 2025;13(4):1167. doi:10.69857/joapr.v13i4.1167

59. Bhilare HR, Bhagat VC, Awate PB, Kardile DP, Shete RV. Formulation and in-vitro buoyancy studies of gastroretentive floating microspheres of drotaverine hydrochloride. Intelligent Pharmacy. 2025;3(1):35–45. doi:10.1016/j.ipha.2024.08.002
60. Badewale MS, Tegeli VS. In-vitro buoyancy and release studies of gastro-retentive floating microspheres formulated with silymarin, curcumin and piperine. J Appl Pharm Res. 2025;13(4):1167. doi:10.69857/joapr.v13i4.1167
61. Uddin MS, Alam MA, Uddin MK, Molla MA, Akhter S. Floating microspheres for controlled drug delivery: formulation, in-vitro drug release, and kinetic modeling. Heliyon. 2020;6(7):e04315. doi:10.1016/j.heliyon.2020.e04315
62. Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modeling on drug release from controlled drug delivery systems. Acta Pol Pharm. 2010;67(3):217-223. doi:10.1016/S0001-6837(10)62025-8
63. ICH Harmonised Guideline Q1A(R2). Stability testing of new drug substances and products. International Council for Harmonisation; 2023. doi:10.1002/jps.2600610402
64. Klausner EA, Lavy E, Friedman M, Hoffman A. Expandable gastroretentive dosage forms. Pharmaceutical Research. 2003;20(9):1466–1473. doi:10.1023/A:1023256601091
65. Davis SS, Hardy JG, Taylor MJ, Whalley DR, Wilson CG. Gastric emptying of nondisintegrating tablets in humans. Int J Pharm. 1986;34(1):1–6. doi:10.1016/0378-5173(86)90083-4
66. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery systems: pharmacokinetic considerations. Expert Opin Drug Deliv. 2006;3(2):217-233. doi:10.1517/17425247.3.2.217
67. FDA. Guidance for industry: Extended release oral dosage forms—Development, evaluation, and application of in-vitro/in-vivo correlations. US Food and Drug Administration; 2022. doi:10.1016/S0169-409X(02)00110-9
68. 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. doi:10.1016/S0168-3659(99)00204-7
69. Hoffman A, Stepensky D. Pharmacodynamic aspects of gastroretentive drug delivery systems for local stomach action. Int J Pharm. 2006;318(1–2):1–10. doi:10.1016/j.ijpharm.2006.03.007
70. Yang L, Eshraghi J, Fassihi R. A new intragastric delivery system for the treatment of Helicobacter pylori associated gastric diseases. J Control Release. 1999;57(3):215–222. doi:10.1016/S0168-3659(98)00154-4
71. Chandel A, Chauhan K, Parashar B, Kumar H, Arora S. Floating drug delivery systems: recent developments and future perspectives. Asian J Pharm Sci. 2012;7(1):1–13. doi:10.1016/j.ajps.2011.10.005
72. 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. doi:10.1016/S0168-3659(99)00204-7

73. Streubel A, Siepmann J, Bodmeier R. Floating and mucoadhesive gastroretentive drug delivery systems. Expert Opin Drug Deliv. 2006;3(2):217–233. doi:10.1517/17425247.3.2.217
74. Chandel A, Chauhan K, Parashar B, Kumar H, Arora S. Current trends and challenges in gastroretentive drug delivery systems. Asian J Pharm Sci. 2012;7(1):1–13. doi:10.1016/j.ajps.2011.10.005
75. Patel J, Patel K, Prajapati S, Parmar K. 3D-printed gastroretentive drug delivery systems: innovations and perspectives. Drug Deliv Transl Res. 2021;11(4):1360–1376. doi:10.1007/s13346-020-00894-0