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An In-Depth Review on Floating Microspheres for Stomach-Targeted Drug Delivery

Mansi sangari[1] , Disha dutta[2]*, Ramsha aslam[3]
1,2*,3Devsthali Vidyapeeth College of Pharmacy, Rudrapur Uttarakhand, India

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ABSTRACT
Gastroretentive drug delivery systems have gained significant attention as a strategy to enhance the bioavailability of drugs that are mainly absorbed in the upper gastrointestinal tract. Among these systems, floating microspheres stand out due to their ability to combine extended gastric retention with the advantages of multiple-unit dosage forms. Their low-density structure enables them to float on gastric fluids, allowing the drug to be released gradually at the site where it is best absorbed. This review summarizes the fundamental concepts of floating microspheres, including the mechanisms that provide buoyancy, factors affecting gastric retention, and formulation approaches used to develop stable and effective systems. Various preparation methods—such as solvent evaporation, ionotropic gelation, and hot-melt techniques—are examined, along with critical evaluation parameters like particle size, floating ability, drug loading efficiency, and release characteristics. Recent developments in polymer selection, manufacturing processes, and clinical applications have further enhanced the potential of floating microspheres for targeted and sustained drug delivery. Overall, this review emphasizes the important design considerations and future directions of floating microsphere technology for improving oral drug delivery.

1. INTRODUCTION:

The oral route remains the most preferred pathway for drug administration due to its convenience, patient compliance, and cost-effectiveness[1]. However, conventional oral dosage forms face significant limitations when delivering drugs with site-specific absorption windows, particularly those absorbed primarily in the stomach or upper small intestine[2]. The physiological constraints of the gastrointestinal tract, including variable gastric emptying times and regional differences in drug absorption, pose substantial challenges to therapeutic efficacy.gastroretentive drug delivery systems (GRDDS) have been developed to overcome these limitations by prolonging the residence time of dosage forms in the stomach [3]. By maintaining drugs in the gastric environment for extended periods, these systems can maximize absorption for compounds with pH-dependent solubility, narrow absorption windows, or local therapeutic action in the upper gastrointestinal tract [4]. Among the various gastroretentive technologies, floating drug delivery systems have gained considerable attention due to their ability to remain buoyant on gastric contents without affecting gastric emptying rate.floating microspheres represent an advanced iteration of gastroretentive technology, combining the benefits of multiparticulate systems with controlled buoyancy characteristics [5]. Unlike single-unit floating tablets, microspheres offer several advantages including reduced risk of dose dumping, minimized local irritation, predictable gastric retention independent of meal composition, and improved distribution throughout the gastric mucosa [6]. The hollow or porous structure of these microspheres provides density lower than gastric fluids, enabling sustained flotation and controlled drug release.This review provides a comprehensive analysis of floating microsphere technology,

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encompassing fundamental principles, formulation strategies, characterization techniques, and therapeutic applications. Understanding the intricate relationship between formulation variables and system performance is essential for rational design and optimization of these promising drug delivery platforms.

2. Physiological Considerations of the Gastric Environment:

2.1 Gastric Anatomy and Physiology:

The stomach serves as a temporary reservoir for ingested food and initiates the digestive process through mechanical and chemical mechanisms [7]. The gastric environment presents unique physiological characteristics that influence drug delivery system behavior, including acidic pH (1.5-3.5 in fasted state, 3-7 in fed state), pepsin secretion, mucus layer coating, and rhythmic peristaltic contractions[8]. Gastric emptying represents a critical determinant of oral drug bioavailability. The process is regulated by neural and hormonal mechanisms, with the migrating motor complex (MMC) playing a central role during fasted states [9]. The MMC consists of four phases, with Phase III characterized by intense contractions that sweep undigested materials from the stomach into the small intestine, occurring approximately every 90-120 minutes during fasting[10].

2.2 Factors Affecting Gastric Retention:

Multiple physiological and formulation-related factors influence the gastric residence time of drug delivery systems. Physiological variables include fed or fasted state, gastric pH, gender, posture, age, and disease conditions [11]. The presence of food significantly extends gastric retention time, with high-calorie meals, particularly those rich in fats and proteins, promoting prolonged retention compared to fasted conditions [12]. Formulation characteristics affecting retention include particle size, density, shape, and floating capacity. Systems with diameter greater than the pyloric sphincter opening (approximately 12.8 mm) demonstrate enhanced retention, though this advantage is limited during Phase III of the MMC [13]. Floating systems with density less than 1.0 g/cm³ remain buoyant on gastric contents, avoiding the sweeping action of housekeeping waves and achieving prolonged gastric residence [14].

3. Fundamental Principles of Floating Microspheres:

3.1 Mechanism of Floatation:

Floating microspheres are able to remain buoyant in the stomach because their overall density is kept lower than that of gastric fluids, which typically ranges from 1.004 to 1.010 g/cm³. This low density can be achieved in two main ways: either by incorporating lightweight, low-density excipients into the formulation, or by creating hollow or porous microspheres that trap air or gas within their structure [15]. Their ability to float can be explained using Archimedes' principle, which states that the buoyant force (Fb) acting on a microsphere depends on the difference between the density of the surrounding fluid (Df) and the density of the microsphere (Ds), multiplied by gravitational acceleration and the particle's volume [16]. For the microspheres to maintain floatation over an extended period, the buoyant force must consistently remain greater than the gravitational force pulling them downward. This balance ensures prolonged gastric retention, which is essential for effective drug delivery [17].

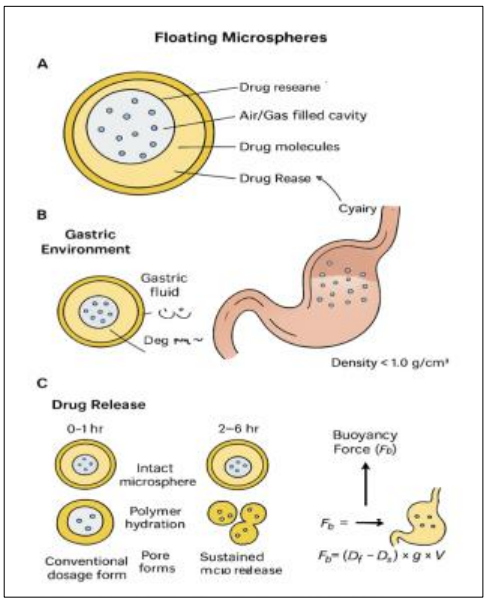

Figure: Schematic Representation of the Mechanism of Floating Microspheres in the Gastric Environment

3.2 Classification of Floating Microspheres

Floating microspheres can be classified based on their structural characteristics and mechanism of buoyancy:

Hollow Microspheres: These microspheres consist of a drug-loaded polymeric shell that surrounds a central hollow cavity filled with air or an inert gas. The presence of this internal cavity significantly reduces the overall density of the particle, allowing it to remain buoyant in gastric fluids for an extended period. Meanwhile, the outer polymer shell plays a crucial role in regulating the release of the drug, ensuring a controlled and sustained delivery profile. By combining buoyancy with controlled release, hollow microspheres provide an

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efficient approach for improving gastric retention and enhancing the therapeutic effectiveness of orally administered drugs [18].

Porous Microspheres: These microspheres feature a continuous porous network distributed throughout the polymer matrix. The interconnected or closed pores trap air within the structure, lowering the overall density so that it becomes lighter than gastric fluids. This trapped air is what allows the microspheres to float for extended periods once they enter the stomach. The porous architecture also influences drug release, as the internal channels can facilitate controlled diffusion of the drug from the matrix. By combining reduced density with a structured release pathway, porous microspheres provide an effective strategy for enhancing gastric retention and improving oral drug delivery performance [19].

Matrix-Type Microspheres: In this approach, the drug is uniformly dispersed within a swellable polymer matrix that also contains fatty excipients or effervescent agents. When the formulation comes into contact with gastric fluid, the polymer begins to hydrate and swell, while the effervescent components release gas—typically carbon dioxide. This generated gas becomes trapped within the swollen matrix, reducing its overall density and enabling the system to float on gastric contents. The combination of swelling, gas entrapment, and gradual drug diffusion supports prolonged gastric retention and controlled drug release, making this design highly effective for gastroretentive delivery [20].

3.3 Advantages of Floating Microsphere Systems:

Floating microspheres offer numerous advantages over conventional dosage forms and single-unit floating systems. The multiparticulate nature provides predictable gastric dispersion and retention, reducing inter- and intra-subject variability [21]. The small particle size (typically 50-1000 μm) enables passage through the pyloric sphincter even during fed states while maintaining gastric residence through flotation[22]. These systems demonstrate enhanced bioavailability for drugs with absorption windows in the upper gastrointestinal tract, reduced frequency of administration, minimized fluctuations in plasma drug concentrations, and improved patient compliance [23]. The gradual drug release from floating microspheres decreases the risk of local tissue irritation and adverse effects associated with high drug concentrations [24].

4. Formulation Components and Selection Criteria:

4.1 Polymeric Materials:

Polymer selection represents a critical determinant of floating microsphere performance, influencing buoyancy characteristics, drug release kinetics, and system stability. Both synthetic and natural polymers have been successfully employed in floating microsphere formulation.

Synthetic Polymers: Cellulose derivatives including hydroxypropyl methylcellulose (HPMC), ethyl cellulose (EC), and cellulose acetate demonstrate excellent film-forming properties and controlled release characteristics [25]. Acrylic polymers such as Eudragit RS, RL, and S100 offer pH-dependent or pH-independent release profiles depending on functional group composition [26]. Chitosan, though natural in origin, has been extensively modified for floating microsphere applications due to its mucoadhesive properties and biodegradability [27].

Natural Polymers: Sodium alginate, gelatin, albumin, and various gums have been investigated for floating microsphere preparation. These materials offer advantages of biocompatibility, biodegradability, and low toxicity, though they may demonstrate inferior mechanical strength and less predictable release characteristics compared to synthetic alternatives [28].

Polymer Properties for Optimal Performance:
An ideal polymer for formulating floating microspheres should possess several key characteristics to ensure effective performance. It should have an appropriate molecular weight that supports the desired drug release kinetics, neither too fast nor too slow. Adequate hydrophobicity is essential to limit rapid water penetration, helping maintain the microsphere's structure and buoyancy. The polymer must also exhibit good film-forming ability to create strong, uniform shells around the microspheres. Chemical stability within the acidic gastric pH range is crucial to prevent degradation during stomach residence. Additionally, the material must be non-toxic, biocompatible, and capable of providing reproducible physicochemical properties to ensure consistent formulation quality.

4.2 Active Pharmaceutical Ingredients

Drug selection significantly influences formulation strategy and system performance. Ideal candidates for floating microsphere delivery include compounds with narrow absorption windows in the upper GIT, pH-dependent solubility (higher solubility in acidic pH), local action in stomach, degradation in alkaline environment, and poor bioavailability from conventional formulations [29].

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Drug properties affecting formulation design include aqueous solubility, partition coefficient, molecular weight, stability in gastric environment, and dose requirements [30]. Highly water-soluble drugs may require additional strategies to prevent rapid release and maintain buoyancy, while poorly soluble compounds may benefit from enhanced dissolution in the gastric environment.

4.3 Plasticizers and Release Modifiers:
Plasticizers enhance polymer flexibility and reduce brittleness of microsphere shells. Common plasticizers include dibutyl phthalate, polyethylene glycol, propylene glycol, and triacetin [31]. The selection and concentration of plasticizer affect mechanical properties, drug permeability, and release rate.Release modifiers such as hydrophobic materials (stearic acid, glycerylmonostearate) retard drug release, while hydrophilic materials (polyvinylpyrrolidone, sodium starch glycolate) enhance dissolution and release [32]. The incorporation of effervescent agents (sodium bicarbonate, citric acid) generates carbon dioxide in acidic medium, creating porous structures that enhance buoyancy and modulate release kinetics[33].

5. Preparation Methods:
5.1 Emulsion Solvent Diffusion Method:
This widely employed technique involves dissolving the polymer and drug in a volatile organic solvent (dichloromethane, ethanol, acetone), which is then emulsified into an aqueous phase containing a surfactant under continuous stirring [34]. The organic solvent diffuses into the aqueous phase and evaporates at the interface, causing polymer precipitation and microsphere formation. The hollow structure develops as the solvent diffuses from the interior, creating internal cavities that impart buoyancy [35].

Process Parameters: The preparation of floating microspheres generally involves optimizing several key formulation parameters, such as maintaining a polymer concentration between 1–5% w/v and adjusting the stirring speed within the range of 500–2000 rpm to control particle size and uniformity. The process is typically conducted at a moderate temperature of 25–40°C to ensure proper solvent evaporation and polymer solidification. A solvent-to-aqueous phase ratio of 1:5 to 1:10 is used to achieve stable emulsification, while the emulsification time is usually maintained between 2–6 hours to allow complete formation and hardening of the microspheres.The method offers advantages of simplicity, room temperature processing, and applicability to thermolabile drugs. However, limitations include residual solvent traces, potential drug loss into aqueous phase, and requirement for solvent removal [36].

5.2 Emulsion Solvent Evaporation Method:
The solvent evaporation method is similar to the solvent diffusion technique but differs in the way the solvent is removed, relying on gradual evaporation rather than rapid diffusion. In this process, the drug–polymer organic solution is emulsified into an aqueous phase and kept under constant stirring while the organic solvent slowly evaporates. As the solvent is removed, the polymer precipitates and solidifies around the drug particles, forming microspheres [37]. Increasing the temperature to 40–60°C or applying reduced pressure can accelerate the solvent evaporation rate, improving process efficiency. Compared to solvent diffusion, this method provides better control over microsphere size distribution, polymer deposition rate, and drug entrapment efficiency. The slow and uniform solidification promotes the formation of smooth, spherical particles with controlled porosity, ensuring improved stability and predictable drug release characteristics [38].

5.3 Ionotropic Gelation Method:
Particularly suitable for natural polymers like alginate and chitosan, this method involves dropwise addition of polymer solution containing drug into a cross-linking agent solution (calcium chloride for alginate, sodium tripolyphosphate for chitosan) [39]. Immediate gelation occurs at the interface, forming microspheres that can be recovered by filtration.For floating properties, gas-forming agents or low-density materials are incorporated into the polymer solution prior to gelation. The method operates under mild conditions without organic solvents, making it suitable for sensitive biological molecules [40].

5.4 Spray Drying Technique
This single-step process involves atomizing a drug-polymer dispersion or solution into a hot drying medium, causing rapid solvent evaporation and particle formation [41]. Spray drying parameters including inlet temperature (100-200°C), feed rate (5-20 mL/min), atomization pressure (2-5 bar), and aspirator rate control microsphere characteristics.The rapid solidification prevents complete particle compaction, creating porous structures with low density. Incorporation of volatile components or foaming agents further enhances porosity and buoyancy [42]. Advantages include scalability, continuous processing, and narrow particle size distribution, though heat-sensitive drugs may undergo degradation.

5.5 Novel and Emerging Techniques Electrospraying:
Electrospraying involves applying a high-voltage electric field to a polymer–drug solution, causing it to break into fine, charged droplets that are rapidly

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atomized. As these droplets travel toward a grounded collector, the solvent evaporates, allowing the polymer to solidify and form uniform microspheres. This technique offers precise control over particle size, morphology, and distribution by adjusting parameters such as voltage, flow rate, needle diameter, and polymer concentration. Because the droplets are formed through electrical forces rather than mechanical stirring, the method produces highly spherical, smooth particles with narrow size ranges, making it ideal for controlled drug delivery applications [43].

Supercritical Fluid Technology: Supercritical fluid technology uses supercritical carbon dioxide either as a solvent or an anti-solvent to precipitate the polymer and drug into fine microspheres. When CO_2 acts as an anti-solvent, it rapidly diffuses into the polymer solution, reducing solubility and causing instantaneous particle formation. In solvent mode, CO_2 dissolves the polymer–drug mixture and then depressurization leads to controlled precipitation. Because the process occurs at relatively low temperatures and avoids the use of organic solvents, it prevents thermal degradation and eliminates solvent residue concerns. The method also allows precise control over particle size, morphology, and purity, making it highly suitable for sensitive drug formulations [44].

3D Printing: Additive manufacturing—particularly 3D printing technologies—is increasingly being explored for designing floating microspheres with highly controlled architecture, porosity, and spatial drug distribution. These techniques allow researchers to tailor the internal structure of microspheres far more precisely than conventional fabrication methods. By adjusting printing parameters, it becomes possible to engineer microspheres with predictable buoyancy, release kinetics, and mechanical strength. However, current 3D printing platforms are generally restricted to producing larger particle sizes, limiting their suitability for true microsphere-scale applications. Despite this limitation, ongoing advancements in micro-scale printing and novel printable biomaterials are expected to broaden the feasibility of additive manufacturing for next-generation floating microsphere systems [45].

Table 1: Comparison of Different Preparation Methods for Floating Microspheres

Method	Principle	Organic Solvent	Size Range (µm)	Advantages	Limitations
Emulsion Solvent Diffusion	Solvent diffusion from dispersed to continuous phase	Required (DCM, ethanol, acetone)	50-500	Simple process, room temperature, good reproducibility	Residual solvent, drug loss to aqueous phase
Emulsion Solvent Evaporation	Evaporation of organic solvent under stirring	Required (DCM, chloroform)	100-800	Better size control, good entrapment	Higher temperature, longer processing time
Ionotropic Gelation	Ionic cross-linking of polymers	Not required	200-1000	Mild conditions, no organic solvents, biocompatible	Limited to specific polymers, lower mechanical strength
Spray Drying	Atomization and rapid drying	Required or aqueous	10-100	Scalable, continuous process, narrow distribution	High temperature, expensive equipment
Electrospraying	Electrostatic atomization	Required	1-50	Precise size control, monodisperse	Low throughput, specialized equipment
Supercritical Fluid	CO_2-based precipitation	Minimal/none	5-100	No residual solvent, mild conditions	High equipment cost, complex process

6. Characterization and Evaluation Parameters:

6.1 Particle Size and Size Distribution:

Particle size significantly influences flotation behavior, drug release kinetics, and gastric retention. Techniques for size determination include optical microscopy, laser diffraction, and dynamic light scattering [46]. The optimal size range for floating microspheres is typically 100-1000 µm, balancing buoyancy capacity with gastric emptying considerations.Size distribution is quantified using parameters such as mean diameter, polydispersity index, and span. Narrow size distributions provide more predictable and reproducible performance characteristics [47].

6.2 Surface Morphology

Scanning electron microscopy (SEM) enables detailed visualization of microsphere surface characteristics, including smoothness, porosity, and structural integrity [48]. Surface morphology influences drug release mechanisms, with porous surfaces facilitating diffusion-controlled release and

smooth surfaces promoting erosion or swelling-controlled release.Atomic force microscopy (AFM) provides additional surface topography information at nanoscale resolution, revealing surface roughness parameters and mechanical properties[49].

6.3 Buoyancy Assessment:
In vitro floating behavior of microspheres is typically evaluated by dispersing them in simulated gastric fluid (pH 1.2) containing 0.02% Tween 20 and maintaining the medium at 37°C. Their buoyancy performance is then monitored at predetermined intervals for 12–24 hours to assess sustained flotation[50]. Important parameters include the floating lag time, which is the time required for microspheres to ascend to the surface; the total floating time, representing how long they remain buoyant; and the buoyancy percentage, indicating the proportion of microspheres that continue to float. The buoyancy percentage is calculated mathematically using the formula: Buoyancy (%) = (Wf / (Wf + Ws)) × 100, where Wf denotes the weight of floating microspheres and Ws represents the weight of settled ones [51].

6.4 Density Determination:
True density is measured using gas pycnometry, while apparent density is determined by liquid displacement method using solvents that do not cause swelling [52]. Bulk density and tapped density provide information on powder flow properties and compaction behavior.Density values below 1.0 g/cm³ are essential for sustained flotation. The relationship between density and flotation capacity enables prediction of gastric retention behavior [53].

6.5 Drug Entrapment Efficiency:
Drug loading and entrapment efficiency are critical parameters that reflect how effectively a drug is incorporated into floating microspheres and ultimately determine the formulation's practical usefulness. To assess these parameters, a measured quantity of microspheres is dissolved or extracted using a suitable solvent, after which the drug content is quantified using analytical methods such as UV spectroscopy, HPLC, or other validated techniques [54]. Entrapment efficiency is then calculated using the equation: Entrapment Efficiency (%) = (Actual drug content / Theoretical drug content) × 100. A high entrapment efficiency, typically above 70%, signifies successful encapsulation of the drug and minimal loss during formulation, highlighting the robustness of the preparation process [55].

6.6 In Vitro Drug Release Studies:
Drug release behavior of floating microspheres is typically evaluated using a USP dissolution apparatus—either Type I (basket) or Type II (paddle)—in simulated gastric fluid maintained at 37 °C and stirred at an appropriate speed [56]. Samples are collected at predefined time intervals, and the drug concentration is quantified using UV spectrophotometry or chromatographic methods. The release data are then fitted to various kinetic models to understand the mechanism of drug release. These include zero-order (constant release), first-order (concentration-dependent), Higuchi (diffusion-controlled), Korsmeyer–Peppas (mechanistic interpretation), and Hixson–Crowell (surface area-dependent release). Key model-fitting parameters such as the correlation coefficient (r^2) and release exponent (n) help identify the dominant release mechanism and evaluate how well the formulation meets desired performance criteria [57].

6.7 Mucoadhesive Properties:
Some floating microsphere formulations are designed with mucoadhesive polymers to further improve gastric retention by enabling the particles to adhere to the gastric mucosal surface. This added adhesion helps the microspheres resist gastric motility and prolongs their residence time, thereby enhancing drug absorption and overall therapeutic efficacy. Mucoadhesive strength is commonly evaluated using texture analyzers or tensile testing instruments, which measure the force required to detach the microspheres from a mucus layer or excised gastric mucosa. These tests mimic physiological conditions and provide quantitative data on adhesive performance. Factors such as polymer type, molecular weight, hydration capacity, and surface characteristics directly influence mucoadhesion. Strong mucoadhesive interactions ensure prolonged localization in the stomach, which is especially beneficial for drugs with narrow absorption windows or those requiring extended gastric exposure. This approach integrates both buoyancy and adhesion to create a robust gastroretentive drug delivery system [58].

7. Factors Influencing Floating Microsphere Performance:
7.1 Formulation Variables:
Several formulation factors play a crucial role in determining the buoyancy, structural integrity, and drug-release performance of floating microspheres. The type and concentration of polymer are particularly important—higher polymer levels increase matrix viscosity and density, which can strengthen the structure but may alter flotation and release patterns. Hydrophobic polymers generally improve buoyancy by reducing water penetration, whereas hydrophilic polymers promote faster drug release but may compromise floatation stability[59]. Drug loading also significantly influences microsphere behavior; as drug content increases, overall density may rise, potentially reducing buoyancy, while the polymer-to-drug ratio strongly affects release kinetics [60]. Plasticizers further modify performance by lowering the glass transition temperature and enhancing polymer flexibility. This improves permeability and mechanical strength, but only when used at

optimized levels to avoid weakening the microsphere shell [61]. Additionally, the choice of organic solvent impacts particle formation, as its volatility, polarity, and miscibility dictate solidification rate, internal porosity, and residual solvent levels, ultimately shaping microsphere quality and functionality [62].

7.2 Process Variables:

Several critical process parameters significantly influence the quality, size, and performance of floating microspheres during their preparation. Stirring speed is one of the most important factors, as it determines the size of emulsion droplets; higher speeds generally yield smaller, more uniform microspheres but can also introduce excessive shear, leading to aggregation or structural distortion [63]. Temperature also plays a key role by controlling solvent evaporation, polymer solubility, and the rate of microsphere solidification. While elevated temperatures can speed up the process, they must be carefully controlled to avoid degradation of heat-sensitive drugs [64]. The concentration of emulsifier helps stabilize the droplet interface, preventing coalescence and ensuring consistent particle size; however, the optimal amount depends on the hydrophobicity of the polymer and target characteristics of the formulation [65]. Additionally, the phase volume ratio—the proportion of dispersed phase to continuous phase—affects particle size, process yield, and reproducibility, making it essential for ensuring consistent batch performance [66].

7.3 Physiological Variables:

Floating microspheres must function effectively within the highly dynamic and variable environment of the stomach, where several physiological factors significantly influence their in vivo performance. **Gastric pH** fluctuates widely, ranging from highly acidic conditions in the fasted state to higher pH levels after food intake. These variations can affect polymer swelling, drug stability, and overall buoyancy. **Gastric motility patterns**, including peristaltic movements and migrating motor complexes, can either support prolonged retention or push the microspheres into the intestine prematurely. Additionally, **mucus secretion** influences how microspheres interact with the gastric lining; increased mucus can enhance retention for formulations with mucoadhesive properties, whereas reduced mucus may diminish adhesion. The **fed or fasted state** also plays a crucial role—food delays gastric emptying and may enhance floating time, while the fasted state accelerates transit, challenging the sustained buoyancy of the system. Therefore, floating microsphere formulations must be robust enough to maintain structural integrity, floatation, and controlled drug release despite these fluctuating gastric conditions, ensuring consistent therapeutic performance throughout the dosing interval [67].

8. Stability Considerations:

Floating microspheres can experience both physical and chemical stability challenges during storage, which may affect their performance and shelf life. Physically, they may undergo aggregation, lose buoyancy, or exhibit changes in porosity and particle structure due to factors like temperature, humidity, and light exposure [68]. To enhance long-term stability, techniques such as freeze-drying or spray-drying are commonly used along with cryoprotectants, while sealed packaging with desiccants helps preserve integrity during storage[69]. Chemically, instability may arise from drug degradation, polymer breakdown, or unfavorable drug–polymer interactions. These issues are typically evaluated through accelerated stability studies conducted under ICH-recommended conditions (40°C/75% RH), which help predict shelf life and identify suitable storage environments [70]. Analytical tools such as HPLC, DSC, FTIR, and XRD are essential for monitoring chemical changes and assessing compatibility throughout the storage period [71].

9. Therapeutic Applications:

Floating microspheres have shown significant potential across various therapeutic areas by improving gastric retention and enhancing drug absorption. In *H. pylori* treatment, microspheres containing antibiotics such as amoxicillin, clarithromycin, and metronidazole prolong gastric residence, increasing drug concentration at the infection site and improving eradication rates, while sustained release helps reduce dosing frequency and systemic side effects [72]. For antihypertensive drugs like propranolol and metoprolol, which have narrow absorption windows in the upper GIT, floating microspheres enhance bioavailability and provide more stable plasma levels through controlled release [73]. Similarly, gastric ulcer medications including ranitidine, famotidine, and omeprazole benefit from prolonged gastric retention, maintaining effective drug levels and supporting faster healing with fewer doses [74]. In diabetes management, metformin-loaded floating microspheres help overcome its limited absorption window, ensuring sustained plasma concentrations, improved glycemic control, and reduced gastrointestinal discomfort [75]. Additionally, floating microspheres have been explored in antiretroviral therapy, where enhanced bioavailability and sustained drug levels may improve patient adherence and overall treatment outcomes in HIV management [76].

10. Recent Advances and Future Perspectives:

Future directions for floating microsphere technology highlight several innovative advancements aimed at improving therapeutic precision and patient outcomes. Combination drug delivery systems are being developed to allow simultaneous release of multiple agents with coordinated kinetics, which is especially valuable in multidrug therapies such as *H. pylori* eradication and complex antihypertensive regimens [77]. Stimuli-responsive floating microspheres—capable of reacting to pH changes, enzymatic activity, or magnetic fields—offer more precise and controlled drug release in response to physiological cues [78]. Targeted floating microspheres functionalized with ligands such as antibodies, peptides, or aptamers further enhance site-specific interactions within the stomach, improving drug localization and therapeutic selectivity [79]. Integration of nanotechnology has also led to hybrid systems that embed nanoparticles within floating microspheres, enabling enhanced cellular uptake and improved delivery of poorly soluble or biological drugs [80]. Additionally, advances in personalized medicine, including 3D printing and on-demand manufacturing, support the customization of floating microsphere formulations tailored to an individual's physiological profile and therapeutic requirements [81].

11. Challenges and Limitations:

Despite their promising therapeutic benefits, floating microspheres still face several important challenges that limit broader clinical and commercial adoption. One major issue is manufacturing scalability, as many preparation methods optimized at the laboratory level do not easily translate to industrial-scale production, requiring significant process refinement and specialized equipment for commercial viability [82]. Regulatory hurdles also arise because these systems demand extensive characterization, strict quality control, and strong in vitro–in vivo correlation data to meet approval standards [83]. Additionally, patient-to-patient variability in gastric physiology, motility, and food intake can influence performance, so formulations must be robust enough to function consistently across diverse populations [84]. Economic considerations further impact their adoption, as floating microspheres often incur higher production costs compared to conventional oral dosage forms, making thorough cost-benefit analyses essential to justify their clinical advantages [85].

12. CONCLUSION:

Floating microspheres represent a sophisticated approach to gastroretentive drug delivery, offering significant advantages in bioavailability enhancement, controlled release, and therapeutic efficacy. The technology has matured considerably, with well-established formulation principles, diverse preparation methods, and comprehensive characterization techniques. Successful translation from laboratory research to clinical applications has been demonstrated for multiple therapeutic categories.Future developments will likely focus on intelligent stimuli-responsive systems, integration with nanotechnology platforms, and personalized medicine applications. Addressing current challenges in manufacturing scalability, regulatory pathways, and cost-effectiveness will accelerate market adoption. As understanding of gastric physiology and polymer science advances, floating microsphere technology will continue evolving to meet the complex demands of modern pharmaceutical therapy.The multidisciplinary nature of this field, spanning pharmaceutics, materials science, physiology, and clinical medicine, ensures continued innovation and refinement. Floating microspheres will remain an important tool in the pharmaceutical scientist's arsenal for optimizing oral drug delivery and improving patient outcomes.

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