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# A COMPREHENSIVE REVIEW ON GASTRORETENTIVE FLOATING DRUG DELIVERY SYSTEMS: MECHANISMS, FORMULATION APPROACHES, EVALUATION, AND RECENT ADVANCEMENTS

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## ABSTRACT

Floating drug delivery systems are among the most extensively studied strategies for prolonging the gastric residence of orally administered formulations. Their value rests on a simple physical premise: a dosage form whose bulk density remains lower than that of gastric fluid will stay buoyant on the stomach contents, releasing drug at a controlled rate within the gastric milieu and the upper small intestine, where the absorption windows for many therapeutic agents are concentrated. The present review examines the rationale, classification, and design principles of floating gastroretentive systems, with attention to both effervescent and non-effervescent formulations. Polymers commonly used in floating systems, including hypromellose grades, sodium alginate, Carbopol, polyethylene oxide and Eudragit polymers, are discussed alongside gas-generating agents and low-density excipients. Manufacturing methods covered include direct compression, wet granulation, solvent evaporation for hollow microspheres, and ionotropic gelation for floating beads. Standard in vitro evaluations such as floating lag time, buoyancy duration, swelling, and dissolution under simulated gastric conditions, together with in vivo techniques such as gamma scintigraphy, are reviewed. Marketed products with established clinical use are tabulated. Recent advances covered include three-dimensional printing of personalised floating dosage forms, floating in situ gels, raft-forming nanocomposite systems, and the application of artificial neural networks to formulation screening.

## Keywords

Gastroretention; Floating drug delivery system; Effervescent systems; Residence time.

## 1. Introduction

Conventional oral controlled-release formulations have transformed therapy for chronic conditions, yet they share a common vulnerability: once they leave the stomach, their interaction with the absorption window in the upper gastrointestinal tract becomes a race against intestinal transit. For drugs whose absorption is concentrated in the duodenum and proximal jejunum, or for compounds that degrade in the alkaline environment of the lower small intestine and colon, this short window often translates into incomplete bioavailability and erratic plasma concentrations[1-3].

Riboflavin, levodopa, ciprofloxacin, captopril and metformin all exhibit site-restricted absorption with poor or absent uptake beyond the proximal small bowel[2,4,5]. Acid-labile drugs such as ranitidine remain susceptible to inactivation if released after the stomach has been bypassed. Locally acting agents present a different but related challenge. Eradication of *Helicobacter pylori*, for instance, demands sustained luminal concentrations of antimicrobials at the gastric mucosa, which conventional immediate-release tablets cannot reliably provide because of rapid emptying[6-8].

Gastroretentive drug delivery systems (GRDDS) were developed to extend the dwell time of a dosage form in the stomach and thereby improve drug uptake, reduce dosing frequency, and stabilise plasma levels[1,2,9]. Several distinct physical strategies have been pursued to keep formulations in the stomach beyond the usual one to two hours of fasted-state emptying. These include increasing buoyancy so that the dosage form floats on gastric contents, increasing density so that it sinks into the antral folds, expanding to a size greater than the relaxed pyloric diameter, adhering to the gastric mucosa, or applying external magnetic fields to anchor magnetised cores[1-3].

Of these, floating drug delivery systems (FDDS) have attracted the greatest commercial and academic attention. The reasons are practical. Floating tablets and capsules can be manufactured using standard pharmaceutical equipment, polymers such as hypromellose used in conventional matrix tablets are well characterised, and the underlying principle, a bulk density below approximately 1.004 g $mL^{-1}$ relative to gastric contents, is straightforward to engineer[10-12]. While buoyant, the unit hovers on the gastric fluid and releases drug at a controlled rate; the dissolved or dispersed drug is then emptied into the duodenum, where it is presented to absorptive epithelium for an extended period[2,9].

Two large families are recognised within FDDS. Effervescent systems incorporate carbonate or bicarbonate salts that release carbon dioxide on contact with gastric acid; the gas is entrapped within a swollen polymer matrix, lowering the apparent density of the unit until it rises to the surface[10,13,14]. Non-effervescent systems achieve buoyancy through different routes, including hydrodynamically balanced capsules in which gel-forming hydrocolloids hydrate to form a low-density gel layer, hollow microspheres or microballoons that contain entrapped air, and

porous matrices loaded with low-density excipients[9,10,15].

They require an adequate volume of gastric fluid for buoyancy to manifest, perform less consistently under fasted conditions when gastric volume is minimal, and may behave unpredictably in patients with achlorhydria, severe gastric motility disorders or after partial gastrectomy[1,7,9]. Posture and meal pattern also strongly influence performance, and clinical work has shown that gastric retention is most prolonged when the dosage form is administered with or immediately after a meal[7,16].

## 2. Anatomy and Physiology of the Stomach Relevant to GRDDS

The stomach is divided into four anatomical regions: the cardia at the oesophagogastric junction, the fundus that arches above and to the left of the cardia, the body which constitutes the major reservoir and secretory zone, and the pyloric region comprising the antrum and pyloric canal that opens through the pyloric sphincter into the duodenum[17].

Two motor states govern gastric behaviour. In the fasted state, the migrating motor complex (MMC) cycles through four phases with a total duration of about 90 to 120 minutes[18,19]. Phase I is a period of quiescence lasting 40 to 60 minutes, Phase II is characterised by irregular contractions, Phase III consists of intense rhythmic contractions lasting 5 to 10 minutes that sweep undigested material including non-disintegrating dosage forms out of the stomach, and Phase IV is a brief transitional period before the next cycle begins[18].

Feeding interrupts the MMC and replaces it with a fed-state motor pattern of continuous, lower-amplitude contractions that lasts as long as caloric content remains in the stomach[18,20]. Gastric emptying of liquids and small particles is rapid; 240 mL of water typically empties within 15 to 45 minutes in healthy volunteers[21]. Solids empty more slowly, with larger meals delaying gastric transit by several hours and providing the most favourable conditions for the performance of floating systems[16,20].

Gastric pH varies considerably between the fasted and fed states. Fasted median pH is approximately 1.7, with a range of 1.3 to 2.8[22-24]. After a meal, intragastric pH rises rapidly to between 6.2 and 6.7 because of the buffering capacity of food, returning towards baseline over about two hours[23,24]. Gastric volume also fluctuates substantially.

Several patient-related factors modify gastric residence. Age, sex, posture, body mass index, smoking status and concurrent disease states such as diabetes mellitus, gastroparesis, peptic ulceration and Zollinger-Ellison syndrome can each alter motility, pH or volume[16,22]. Drug-related effects, including opioid-induced delay of gastric emptying or prokinetic-induced acceleration, further influence outcomes.

## 3. Classification of Gastroretentive Drug Delivery Systems

Several mechanistic categories are recognised within the broader family of gastroretentive

systems, each exploiting a different physical or biological feature of the upper gastrointestinal tract.

Floating systems achieve buoyancy by maintaining a bulk density lower than that of gastric fluid, typically below 1.004 g $mL^{-1}$[11]. These are subdivided into effervescent and non-effervescent designs, considered in detail in the sections that follow.

Bioadhesive or mucoadhesive systems anchor the dosage form to the gastric mucosa through interactions between adhesive polymers such as chitosan, Carbopol, polycarbophil and lectins, and the mucin layer or epithelial surface[3,4]. They offer prolonged contact, but performance is limited by the continuous turnover of the mucus layer, which is shed every four to six hours.

Swelling and expanding systems absorb gastric fluid and increase in size beyond the relaxed pyloric diameter, which is reported to range between 12 and 15 mm in adults[9,25]. Once expanded, the unit cannot pass through the pylorus and is retained until it degrades or contracts; technologies such as the AcuForm platform exemplify this principle in marketed products[25,26].

High-density (sedimenting) systems incorporate dense excipients such as barium sulphate, zinc oxide or iron powder to produce dosage forms with bulk densities of about 2.5 g $mL^{-1}$ or greater. These are intended to settle into the rugae of the antral region rather than float, although clinical translation has been limited because of difficulties in maintaining position[2,9].

Magnetic systems contain a magnetised component, typically magnetite, and are held in the stomach by an externally applied magnet. While experimentally interesting, the requirement for an external device restricts practical use[2].

Raft-forming systems produce a viscous, low-density gel layer that floats on gastric contents, commonly using sodium alginate together with bicarbonate. They are particularly effective for management of gastro-oesophageal reflux, where the raft acts as a physical barrier at the gastric cardia[27].

Superporous hydrogels swell rapidly to many times their dry volume because of an interconnected pore network. Once fully expanded, they cannot be emptied through the pylorus, achieving retention through size rather than density[4].

## 4. Floating Drug Delivery Systems: Principles and Classification

A floating drug delivery system is, in essence, a dosage form engineered so that its bulk density remains lower than that of gastric contents (approximately 1.004 g $mL^{-1}$) for a duration sufficient to deliver its therapeutic payload[10,11]. While buoyant, the unit hovers on top of the gastric fluid, releasing drug at a controlled rate that is dictated by the polymer matrix, the geometry of the dosage form and the surrounding fluid environment. Drug molecules so released are subsequently emptied with gastric fluid into the duodenum, where they encounter absorptive

epithelium at the upper end of the small intestine[2].

Two architectural choices are commonly made when designing floating systems. Single-unit systems include monolithic tablets, capsules and hydrodynamically balanced systems. They are simpler to manufacture but suffer from an all-or-nothing risk: if the single unit fails to float or is prematurely emptied, the entire dose is lost from its intended residence site[9,10,12]. Multiple-unit systems such as floating microspheres, microballoons, beads and granules distribute the dose across many smaller particles. These spread across the gastric mucosa, reduce the variability arising from individual unit behaviour, and minimise the risk of dose dumping if one fraction is emptied prematurely[13-15].

### *4.1 Effervescent floating systems*

In effervescent designs, the dosage form contains a gas-generating component, usually sodium bicarbonate alone or in combination with citric or tartaric acid. On contact with gastric acid, carbon dioxide is evolved and becomes entrapped within the swollen hydrophilic polymer matrix, lowering the apparent density of the unit until it rises to the surface[10,13,14,28]. Bilayer and multilayer tablets can be engineered to separate the gas-generating layer from the drug-release layer, allowing independent control of buoyancy and release[13].

Two further effervescent variants exist. Gas-generating systems use chemical reaction with gastric acid, as described above. Volatile liquid-containing systems incorporate a low-boiling liquid such as ether or cyclopentane sealed within an inflatable compartment that vapourises at body temperature, conferring buoyancy without acid dependence[9]. The latter approach has not progressed substantially beyond proof of concept because of safety and stability concerns.

### *4.2 Non-effervescent floating systems*

Non-effervescent systems achieve buoyancy without chemical gas evolution. Hydrodynamically balanced systems (HBS), introduced by Sheth and Tossounian, comprise a capsule filled with a mixture of drug and one or more hydrocolloid polymers such as hypromellose or sodium carboxymethylcellulose. On contact with gastric fluid, the outer layer hydrates to form a viscous, low-density gel barrier that maintains buoyancy while the drug is released by diffusion and erosion[9,29]. Madopar HBS and Valrelease are marketed examples of this technology.

Gel-forming or hydrocolloid matrix tablets follow a similar principle in tablet form. Microporous compartment systems use a drug reservoir enclosed within a microporous, low-density polymer wall that allows gastric fluid to enter, dissolve the drug and release it through the pores while the entrapped air maintains buoyancy[9].

Hollow microspheres, also called microballoons, represent one of the most studied multiple-unit non-effervescent designs. They are typically prepared by an emulsion solvent diffusion or solvent evaporation method using polymers such as ethyl cellulose, Eudragit RS or HPMC. The

solvent evaporates leaving a hollow core that confers low density and prolonged buoyancy[15]. Alginate beads prepared by ionotropic gelation in calcium chloride solution can also be engineered to float by including bicarbonate or oil entrapment during gelation, with the additional benefit of mucoadhesion through the negatively charged alginate matrix[16,27].

## 5. Mechanism of Floatation

Buoyancy of a floating dosage form is governed by Archimedes' principle: the unit floats if the weight of the gastric fluid it displaces equals or exceeds its own weight. Translated into formulation language, the bulk density of the dosage form must remain below approximately 1.004 g $mL^{-1}$, which is the typical density of gastric contents[10-12].

In effervescent systems, the mechanism is driven by gas generation. When sodium bicarbonate or calcium carbonate within the tablet contacts gastric hydrochloric acid, carbon dioxide is liberated according to the well-known acid-base reaction:

$$NaHCO_3 + HCl \rightarrow NaCl + H_2O + CO_2$$

The hydrophilic polymer matrix, typically hypromellose or a combination of cellulose ethers, hydrates simultaneously and forms a gel layer that traps the evolving carbon dioxide within its network. As the gas accumulates, the apparent density of the swollen matrix falls below that of gastric fluid and the unit rises to the surface[13,14,28]. Citric acid or tartaric acid are sometimes added to ensure adequate gas generation even when gastric acidity is reduced, such as in patients receiving proton pump inhibitors[28]. The time taken for the unit to rise to the surface is termed the floating lag time and is a critical performance attribute, often required to be below one minute for clinical acceptance[9,13].

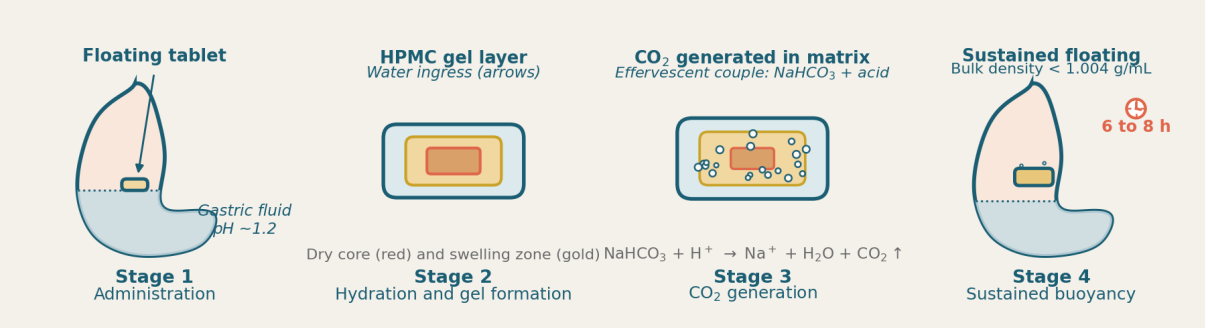


***Figure 1. Mechanism of buoyancy in an effervescent floating tablet, showing sequential hydration, gas generation, gel layer expansion, and sustained floating within the gastric environment.***

For non-effervescent hydrodynamically balanced systems, the mechanism is purely physical. On exposure to gastric fluid, the hydrocolloid blend at the surface of the capsule contents hydrates and swells, producing a hydrated gel layer of low specific gravity that surrounds an unhydrated drug core. The capsule shell dissolves, but the gel layer holds together and remains buoyant for several hours, releasing drug by diffusion across the gel and by gradual erosion[9,29]. The balance

between hydration rate, gel strength and erosion is governed by polymer viscosity grade, polymer concentration and the presence of fillers such as lactose or microcrystalline cellulose.

Hollow microspheres rely on a different mechanism. During preparation by solvent evaporation, a volatile organic solvent escapes from the polymer droplet, leaving behind a hollow internal cavity filled with air or solvent vapour. The trapped air maintains low overall density throughout the residence period, and drug release occurs by diffusion through the polymer shell or by gradual shell erosion[15].

## 6. Polymers and Excipients Used in Floating Systems

Polymers serve multiple functions simultaneously: they form the hydrating gel that traps evolved carbon dioxide, control drug release rate by diffusion and erosion, contribute mucoadhesive properties where required, and influence the mechanical integrity of the dosage form during gastric residence[4,12,30].

Hypromellose (HPMC) remains the most widely used hydrophilic matrix former. Grades K4M, K15M and K100M, with approximate viscosities of 4,000, 15,000 and 100,000 cP respectively in 2% aqueous solution, are routinely selected for floating tablets[12,30]. Lower viscosity grades hydrate more quickly and tend to produce shorter floating lag times, while higher viscosity grades sustain release over longer durations because of slower erosion of the gel layer[13,30].

Carbopol grades, particularly 934P, 940, 971P and 974P, are weakly acidic crosslinked polyacrylic acid polymers used to confer mucoadhesion and to retard release. They are commonly combined with HPMC at concentrations of 5 to 30 percent w/w; higher Carbopol content increases bioadhesive strength but can prolong floating lag time because of slower hydration in acidic media[3,4,12].

Sodium alginate, a natural polysaccharide extracted from brown algae, plays a central role in raft-forming systems. In acidic gastric fluid the sodium form is converted to insoluble alginic acid, which together with calcium ions released from calcium carbonate forms a crosslinked gel raft of low density, an architecture exploited by Liquid Gaviscon and similar antireflux preparations[27].

Other hydrocolloids used as matrix formers include xanthan gum and guar gum, often in synergistic blends because their combined viscosity exceeds that of either individually; chitosan, a cationic mucoadhesive polysaccharide useful both as a matrix and as a coating; and sodium carboxymethylcellulose, commonly used in hydrodynamically balanced capsules in combination with HPMC[3,4,12].

Polyethylene oxide (PEO), particularly the high molecular weight grade WSR 303, swells rapidly to form a durable gel layer and has been used with HPMC and sodium bicarbonate to produce sustained-release floating tablets of ranitidine and other acid-labile drugs[30]. Ethyl cellulose, a water-insoluble polymer, is the principal matrix for hollow microspheres because it permits formation of a stable shell during solvent evaporation; Eudragit RS, RL and RSPO grades

serve similar roles for floating microballoons and provide pH-independent release[15].

Gas-generating agents include sodium bicarbonate (typically 10 to 30 percent w/w), calcium carbonate, citric acid and tartaric acid. The choice and ratio of acid to carbonate determine the rate and quantity of carbon dioxide generation; insufficient acid in the formulation can leave the system reliant on endogenous gastric acid, which is unreliable in achlorhydric or treated patients[13,28,50]. A summary is given in Table 1.

***Table 1. Common polymers and excipients used in floating drug delivery systems.***

| Polymer or excipient | Principal function | Typical concentration (% w/w) | Notes |
|---|---|---|---|
| HPMC K4M | Hydrophilic matrix former, gel-layer formation | 20–60 | Lower viscosity grade, shorter lag time |
| HPMC K100M | Matrix former, prolonged release | 20–50 | High viscosity grade |
| Carbopol 934P / 971P / 974P | Mucoadhesion, release retardant | 5–30 | Often combined with HPMC |
| Sodium alginate | Raft former, gel-forming polymer | 1–5 (liquids); 10–20 (beads) | Crosslinks with $Ca^{2+}$ |
| Ethyl cellulose | Hollow microsphere matrix | 30–70 | Solvent evaporation method |
| Xanthan gum or guar gum | Matrix former, viscosity modifier | 10–30 | Often used as a synergistic blend |
| Chitosan | Mucoadhesive matrix or coat | 1–20 | Cationic polysaccharide |

## 7. Formulation Approaches and Manufacturing Techniques

Direct compression remains the most widely used method for single-unit floating tablets. The active ingredient, hydrophilic polymer (typically HPMC), gas-generating agent and diluent are blended and lubricated, then compressed using a conventional rotary tablet press. Direct compression is preferred when the polymer and drug exhibit good flow and compressibility, and is suitable for drugs sensitive to heat and moisture[13,14]. Tablet hardness is selected to balance two competing requirements: the unit must be mechanically sound enough to survive packaging and handling, but loose enough to allow rapid hydration and gas entrapment.

Wet granulation is used when direct compression is not feasible because of poor flow, low bulk density or low drug content. A granulating fluid such as water, ethanol or a hydroalcoholic binder solution containing polyvinylpyrrolidone is added to the powder blend; granules are then dried in a tray or fluid-bed drier, sieved, lubricated and compressed. Wet granulation must be applied carefully to formulations containing sodium bicarbonate to avoid premature reaction and loss of gas-generating capacity[13].

Melt granulation, in which a low-melting binder such as polyethylene glycol or stearyl alcohol is melted onto the powder mass, has been used to produce floating tablets in which the binder also serves as a release-modifying excipient[31]. Hot-melt extrusion combines mixing, melting and shaping in a single continuous process and has

been employed to manufacture floating pulsatile systems and to produce filaments for fused deposition modelling 3D printing[31-33].

Floating microspheres and microballoons are typically produced by emulsion solvent diffusion or solvent evaporation. The polymer (ethyl cellulose, HPMC, Eudragit RS or a combination) is dissolved in a volatile organic solvent, often dichloromethane with ethanol, together with the drug. The solution is emulsified into an external aqueous phase containing a surfactant such as polyvinyl alcohol. As the organic solvent evaporates or diffuses into the aqueous phase, the polymer precipitates and a hollow cavity is formed within each droplet. The resulting microspheres exhibit densities below 1 g $mL^{-1}$ and float readily on gastric fluid[15].

Ionotropic gelation is the method of choice for floating alginate beads. A solution of sodium alginate containing the drug, and frequently sodium bicarbonate or calcium carbonate, is added dropwise into a calcium chloride bath. Calcium ions crosslink the alginate chains, forming spherical beads; the entrapped bicarbonate reacts during the curing step to evolve carbon dioxide, leaving porous, low-density beads with inherent buoyancy[16,27]. The method is mild, aqueous and suitable for thermolabile and biological drugs.

Lyophilisation has been used to produce porous floating tablets and orodispersible floating systems in which the porous architecture, created by sublimation of ice from frozen aqueous solutions, contributes intrinsic low density and rapid hydration[31].

## 8. Factors Affecting Performance of Floating Drug Delivery Systems

The performance of a floating system in vivo is shaped by both physiological and formulation variables, and the interaction between them often determines clinical success.

Physiologically, the most influential factor is the state of feeding. In the fasted state, gastric volume is small, gastric acidity is at its lowest pH and the migrating motor complex periodically expels solid contents. Floating systems administered to fasted patients consequently exhibit shorter and more variable residence times[9,16]. Administration with a moderately caloric meal increases gastric volume, raises pH transiently, interrupts the MMC and prolongs residence to four to ten hours in most reported studies[11,16]. Body posture also matters: prolonged residence has been documented in upright posture, while supine posture flattens the gastric pool and may allow the floating unit to drift towards the pylorus[9,16]. Age, sex and disease states such as diabetic gastroparesis, partial gastrectomy, Zollinger-Ellison syndrome and chronic use of motility-modifying drugs further alter outcomes[16,20].

Formulation factors are at least as important. Polymer choice and viscosity grade govern both buoyancy and release kinetics. Higher viscosity HPMC grades produce more durable gel layers and longer release durations but can prolong the floating lag time; lower viscosity grades hydrate quickly but may erode rapidly, shortening floating duration[12,30]. The concentration and identity of the gas-generating agent set the

magnitude and timing of carbon dioxide evolution. Insufficient gas leaves the dosage form on the bottom of the stomach, while excessive gas evolution can rupture the gel layer[13,14]. Density, geometry and surface area of the dosage form influence both the lag time before flotation and the integrity of the buoyant unit; small, dense tablets may struggle to float regardless of gas evolution[9,11].

Drug-related factors include solubility (highly soluble drugs may be released too rapidly to benefit from prolonged retention), stability in acidic medium, and the possibility of mucosal irritation. Inclusion of co-excipients such as effervescent acids, hydrophobic lubricants and water-insoluble fillers further modulates hydration rate, gel strength and release. Optimal performance is achieved by matching formulation characteristics to the intended administration scenario; formulations to be administered with food can be designed for longer floating durations and slower release, while those intended for fasted populations require special attention to lag time and resistance to MMC clearance.

## 9. In Vitro and In Vivo Evaluation Parameters

Comprehensive evaluation of a floating dosage form combines in vitro and in vivo studies to characterise both physical buoyancy and pharmaceutical performance.

### *9.1 In vitro evaluation*

Buoyancy and floating behaviour are usually assessed in a USP Type II dissolution apparatus filled with 0.1 N hydrochloric acid or simulated gastric fluid at pH 1.2, maintained at 37 ± 0.5 °C and stirred at 50 to 100 rpm[10,13]. Two parameters are recorded. Floating lag time, the interval between immersion of the dosage form and its rise to the surface of the medium, is generally expected to be less than one minute for an acceptable design[9,13]. Total floating duration, the period during which the unit remains buoyant, should normally be at least eight to twelve hours to provide a clinically meaningful extension of gastric residence[10,30].

Swelling index, determined by measuring the weight gain of a tablet at predetermined intervals after immersion in dissolution medium, provides insight into hydration rate and gel layer development. Drug content uniformity is established by extracting drug from a defined number of tablets and assaying by a validated method, typically high-performance liquid chromatography. Hardness, friability, thickness and weight variation are evaluated using pharmacopoeial methods.

In vitro drug release is determined using the same dissolution apparatus, with aliquots withdrawn at intervals and analysed for drug content. Cumulative release curves are then analysed using a panel of mathematical models to deduce the dominant release mechanism. The zero-order and first-order models describe release that is independent of and proportional to remaining concentration respectively. The Higuchi model relates released fraction to the square root of time and describes diffusion-controlled release from a matrix[34,35]. The

Korsmeyer-Peppas power-law model, applicable to fractional release below 60 percent, distinguishes Fickian diffusion (release exponent $n \leq 0.45$) from anomalous transport and case II relaxational release (n approaching or exceeding 0.89)[36,37]. Comparison of correlation coefficients identifies the model that best fits experimental data.

### *9.2 In vivo evaluation*

In vivo retention is most reliably demonstrated by imaging. Gamma scintigraphy is the gold standard, in which a small quantity of a gamma-emitting radionuclide, typically technetium-99m as the diethylenetriaminepentaacetic acid complex, is incorporated into the dosage form. A gamma camera then records the position and integrity of the unit over time in human volunteers[11,38]. X-ray imaging using barium sulphate as a radio-opaque marker offers a less expensive alternative, although the radiation burden restricts its use in large studies[9].

Pharmacokinetic studies measure plasma drug concentrations after oral administration of the floating system and compare them with an immediate-release reference. Prolongation of the mean residence time, attenuation of peak concentration and extension of the absorption phase indicate gastric retention with sustained release[3,16]. Gastroscopy can directly visualise the dosage form in the stomach and may be used selectively, particularly during early-phase clinical development[9].

## 10. Marketed Formulations

Madopar HBS, introduced by Roche, was the first hydrodynamically balanced system for clinical use; it combines levodopa with the peripheral decarboxylase inhibitor benserazide and provides extended levodopa delivery for Parkinson's disease patients prone to motor fluctuations[29]. Valrelease, also developed by Hoffmann-La Roche, employed the same HBS principle for sustained release of diazepam.

Several effervescent floating tablets are marketed for indications requiring prolonged gastric exposure or extended absorption. Cifran OD, a once-daily ciprofloxacin formulation from Ranbaxy Laboratories, combines effervescent floating technology with sustained release and was developed primarily for urinary tract and respiratory infections that require sustained plasma concentrations[10]. Conviron, an iron formulation also originating from Ranbaxy, is described in review literature as a colloidal gel-forming floating system[1].

For local action in the stomach, alginate-based raft-forming preparations are the most successful gastroretentive concept commercially. Liquid Gaviscon (Reckitt Benckiser) and Topalkan (Pierre Fabre) provide rapid relief of gastro-oesophageal reflux by forming a buoyant raft over the stomach contents[16,27]. Almagate Flot-Coat (Almirall) is an antacid suspension designed for prolonged gastric residence[39].

Swelling-based gastroretentive products include Glumetza, a once-daily metformin formulation, and Gralise, a gabapentin formulation; both

employ AcuForm polymer technology in which the tablet swells in the stomach to a size that resists pyloric passage[25,26].

## 11. Recent Advancements

Three-dimensional printing has emerged as a particularly active area. Fused deposition modelling, in which thermoplastic filaments containing drug are extruded layer by layer, has been used to fabricate floating tablets of propranolol, dipyridamole and other narrow-window drugs with tailored geometry and infill density that permit precise control of buoyancy and release[32,33,40,41]. Semi-solid extrusion has produced floating famotidine tablets with porous internal structures based on hypromellose[42]. The melting solidification printing process has been used to deliver niclosamide nanocrystals through 3D-printed floating tablets, combining gastric retention with nanoparticle-mediated solubility enhancement[43]. A recent review by Mora-Castaño and colleagues provides a thorough account of these developments and the challenges of regulatory translation[40].

Floating in situ gels for oral delivery have advanced as well. Liquid formulations of sodium alginate, gellan gum or pectin combined with carbonate salts are dosed as solutions or suspensions and gel rapidly on contact with gastric acid, yielding a buoyant matrix that releases drug over several hours. Gastroretentive in situ gel formulations of metformin hydrochloride have demonstrated extended in vivo residence and improved glycaemic control in preclinical models[44,45].

Combination strategies have also gained traction. Personalised 3D-printed mucoadhesive matrices that combine flotation with bioadhesion to gastric mucosa have been developed for trospium chloride in the management of overactive bladder, illustrating how gastroretention can extend beyond classical narrow-window drugs[46]. Floating pulsatile systems, in which an initial lag is followed by a programmed burst of release, have been produced by combining hot-melt extrusion with fused deposition modelling and are of interest for chronotherapy[31].

Nanoparticle-loaded floating systems represent another expanding area. Hollow mesoporous silica nanoparticles loaded with anti-ulcer drugs and embedded within a sodium alginate raft have shown enhanced therapeutic effect against gastric ulcers in animal models[47]. Targeted nanoparticles delivered through gastroretentive carriers are also under investigation for eradication of *Helicobacter pylori*, where prolonged local residence at the gastric mucosa is essential for therapeutic success[7,8].

Computational and data-driven methods are beginning to influence formulation development. Artificial neural networks coupled with visual imaging have been applied to predict floating behaviour from tablet attributes, offering a route to faster screening of candidate formulations[48].

## 12. Applications and Therapeutic Relevance

Therapeutic situations that benefit from prolonged gastric residence fall into three broad categories. The first comprises drugs with

narrow absorption windows in the upper gastrointestinal tract. Levodopa, captopril, ciprofloxacin, riboflavin and metformin are absorbed predominantly in the duodenum and proximal jejunum; floating delivery extends the period over which these drugs are presented to the absorptive epithelium, increasing both extent and consistency of absorption[2,3,29]. Antihypertensives such as verapamil and atenolol fall into the same category[9,11].

The second category includes drugs acting locally within the stomach. Triple and quadruple therapy regimens for *Helicobacter pylori* eradication, combining amoxicillin or clarithromycin with metronidazole and a proton pump inhibitor, require sustained luminal antimicrobial concentrations; floating and raft-forming formulations have been investigated to maintain these concentrations beyond the limits of conventional dosage forms[7,8,16]. Antacid suspensions such as Topalkan and Almagate Flot-Coat exploit prolonged retention to provide extended neutralisation of gastric acid[27,39].

The third category covers acid-stable drugs that are unstable or poorly absorbed in the intestinal pH range, such as ranitidine and certain peptides; gastric release reduces exposure of the molecule to less favourable downstream conditions[30]. Sustained-release floating formulations of poorly soluble weak bases including itraconazole and dipyridamole exploit the higher solubility of these compounds in acidic gastric fluid[9,32].

## 13. Limitations and Challenges

Floating drug delivery is not appropriate for every drug or every patient. The principal limitation is the dependence on an adequate volume of gastric fluid; under fasted conditions the resting gastric volume is only about 25 mL, which is insufficient to support consistent flotation[9,21]. Patients are usually instructed to take floating dosage forms with a glass of water and after a meal, which restricts flexibility of administration and complicates compliance for patients on multiple medications.

A second limitation concerns drug properties. Compounds that irritate or damage gastric mucosa, such as non-steroidal anti-inflammatory drugs at high local concentrations and certain cytotoxic agents, are poor candidates because prolonged gastric residence amplifies local exposure[9]. Drugs that are unstable in acidic medium, undergo extensive degradation in gastric fluid, or have low solubility in acid relative to intestinal fluid generally derive no benefit from gastric retention. Highly soluble drugs may release too rapidly from a floating matrix to gain advantage from prolonged residence.

Patient-related limitations include altered gastric physiology in disease and at the extremes of age. Achlorhydria, atrophic gastritis, severe gastroparesis, partial gastrectomy and Zollinger-Ellison syndrome can each compromise the function of effervescent and non-effervescent systems alike[16,22]. Concurrent administration of proton pump inhibitors, antacids or prokinetic agents further modifies performance.

Regulatory and bioequivalence challenges remain considerable. Demonstrating consistent floating behaviour across patients of different ages, body habitus and feeding states requires extensive clinical pharmacokinetic and scintigraphic work, and variability in gastric retention can complicate dose adjustment and product comparison[16,49].

## 14. Future Perspectives

Several trajectories appear likely to shape the next phase of gastroretentive research. Personalised dosage forms produced on demand by 3D printing offer the prospect of tailoring buoyancy, drug load and release profile to individual patient characteristics, including age, comorbidity and concomitant medication[33,40].

Integration of biosensors with gastroretentive carriers may enable feedback-controlled drug release. Devices that sense gastric pH, temperature or biochemical markers and respond by altering release kinetics could provide adaptive therapy for conditions such as diabetes, refractory reflux and inflammatory disease[40].

Computational tools, including machine learning and quantitative structure-property modelling, are beginning to accelerate formulation development[33,48]. Artificial neural networks have been used to predict floating lag time and release profile from formulation composition, reducing the number of experimental batches required for optimisation. Coupling these approaches with high-throughput characterisation may shorten development times substantially.

Nanotechnology-enabled floating systems are likely to mature further. Hybrid platforms in which nanoparticles are embedded within floating microspheres or raft matrices combine local gastric residence with intracellular drug delivery, with particular promise for *Helicobacter pylori* eradication and adjunctive therapy of gastric cancer[7,8,47,50].

## 15. Conclusion

Floating drug delivery represents one of the most thoroughly investigated approaches to prolong the gastric residence of orally administered medicines. Clinical translation has been most successful where the therapeutic rationale is unambiguous: extended absorption of drugs with narrow upper gastrointestinal windows, prolonged local action of antacids and antireflux agents, and management of *Helicobacter pylori*. Current research is broadening both the formulation toolkit and the patient populations that floating delivery might serve. Three-dimensional printing, floating in situ gels, raft-forming nanocomposites, hybrid mucoadhesive-floating constructs and computational formulation methods all stand to reduce the empirical effort involved in development.

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## Declarations

**AI usage:** AI tool has been used to improve the readability of content.

## References


1. 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.
2. Rathor M, Garg A. Gastroretentive drug delivery system: An Overview. Research Journal of Pharmaceutical Dosage Forms and Technology. 2024;16(1):91-7.
3. Garg A, Rathor M. Tablet Evolution: Exploring Cutting-edge Technologies in Formulation and Development. Asian Journal of Pharmacy and Technology. 2024 Dec 21;14(4):373-8.
4. Vinchurkar K, Sainy J, Khan MA, Mane S, Mishra DK, Dixit P. Features and facts of a gastroretentive drug delivery system: a review. Turk J Pharm Sci. 2022;19(4):476-487. doi:10.4274/tjps.galenos.2021.44959.
5. Saini M, Sharma K, Chaudhary G. A COMPREHENSIVE INSIGHT ON GASTRO RETENTIVE DRUG DELIVERY SYSTEM. Journal of Advanced Pharmaceutical Sciences and Natural Products. 2026 Jan 19;1(1).
6. Mandal UK, Chatterjee B, Senjoti FG. Gastro-retentive drug delivery systems and their in vivo success: a recent update. Asian J Pharm Sci. 2016;11(5):575-584. doi:10.1016/j.ajps.2016.04.007.
7. Rajput A, Himani K, Verma A, Singh MK, Kumar B. ORODISPERSIBLE TABLETS AS MODERN ORAL SOLID DOSAGE FORMS. Journal of Advanced Pharmaceutical Sciences and Natural Products. 2026 Jan 19;1(1).
8. Chitas R, Fonseca DR, Parreira P, Martins MCL. Targeted nanotherapeutics for the treatment of Helicobacter pylori infection. J Biomed Sci. 2024;31(1):78. doi:10.1186/s12929-024-01068-9.
9. 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.
10. 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.
11. Timmermans J, Moës AJ. Factors controlling the buoyancy and gastric retention capabilities of floating matrix capsules: new data for reconsidering the controversy. J Pharm Sci. 1994;83(1):18-24. doi:10.1002/jps.2600830106.
12. Blynskaya EV, Tishkov SV, Vinogradov VP, Alekseev KV, Marakhova AI, Vetcher AA. Polymeric excipients in the technology of floating drug delivery systems. Pharmaceutics. 2022;14(12):2779. doi:10.3390/pharmaceutics14122779.
13. Sungthongjeen S, Sriamornsak P, Puttipipatkhachorn S. Design and evaluation of floating multi-layer coated tablets based on gas formation. Eur J Pharm Biopharm.

2008;69(1):255-263. doi:10.1016/j.ejpb.2007.09.013.

14. Sungthongjeen S, Paeratakul O, Limmatvapirat S, Puttipipatkhachorn S. Preparation and in vitro evaluation of a multiple-unit floating drug delivery system based on gas formation technique. Int J Pharm. 2006;324(2):136-143. doi:10.1016/j.ijpharm.2006.06.002.

15. Sato Y, Kawashima Y, Takeuchi H, Yamamoto H. In vivo evaluation of riboflavin-containing microballoons for floating controlled drug delivery system in healthy human volunteers. J Control Release. 2003;93(1):39-47. doi:10.1016/j.jconrel.2003.08.001.

16. Bardonnet PL, Faivre V, Pugh WJ, Piffaretti JC, Falson F. Gastroretentive dosage forms: overview and special case of Helicobacter pylori. J Control Release. 2006;111(1-2):1-18. doi:10.1016/j.jconrel.2005.10.031.

17. Di Natale MR, Athavale ON, Wang X, Du P, Cheng LK, Liu Z, et al. Functional and anatomical gastric regions and their relations to motility control. Neurogastroenterol Motil. 2023;35(7):e14560. doi:10.1111/nmo.14560.

18. Deloose E, Janssen P, Depoortere I, Tack J. The migrating motor complex: control mechanisms and its role in health and disease. Nat Rev Gastroenterol Hepatol. 2012;9(5):271-285. doi:10.1038/nrgastro.2012.57.

19. Vantrappen G, Janssens J, Hellemans J, Ghoos Y. The interdigestive motor complex of normal subjects and patients with bacterial overgrowth of the small intestine. J Clin Invest. 1977;59(6):1158-1166. doi:10.1172/JCI108740.

20. Hellström PM, Grybäck P, Jacobsson H. The physiology of gastric emptying. Best Pract Res Clin Anaesthesiol. 2006;20(3):397-407. doi:10.1016/j.bpa.2006.02.002.

21. Mudie DM, Murray K, Hoad CL, Pritchard SE, Garnett MC, Amidon GL, et al. Quantification of gastrointestinal liquid volumes and distribution following a 240 mL dose of water in the fasted state. Mol Pharm. 2014;11(9):3039-3047. doi:10.1021/mp500210c.

22. Koziolek M, Grimm M, Becker D, Iordanov V, Zou H, Shimizu J, et al. Investigation of pH and temperature profiles in the GI tract of fasted human subjects using the Intellicap system. J Pharm Sci. 2015;104(9):2855-2863. doi:10.1002/jps.24274.

23. Dressman JB, Berardi RR, Dermentzoglou LC, Russell TL, Schmaltz SP, Barnett JL, et al. Upper gastrointestinal (GI) pH in young, healthy men and women. Pharm Res. 1990;7(7):756-761. doi:10.1023/A:1015827908309.

24. Russell TL, Berardi RR, Barnett JL, Dermentzoglou LC, Jarvenpaa KM, Schmaltz SP, et al. Upper gastrointestinal pH in seventy-nine healthy, elderly, North American men and women. Pharm Res.

1993;10(2):187-196. doi:10.1023/A:1018970323716.

25. Berner B, Cowles VE. Case studies in swelling polymeric gastric retentive tablets. Expert Opin Drug Deliv. 2006;3(4):541-548. doi:10.1517/17425247.3.4.541.

26. Gordi T, Hou E, Kasichayanula S, Berner B. Pharmacokinetics of gabapentin after a single day and at steady state following the administration of gastric-retentive extended-release and immediate-release tablets: a randomized, open-label, multiple-dose, three-way crossover, exploratory study in healthy subjects. Clin Ther. 2008;30(5):909-916. doi:10.1016/j.clinthera.2008.05.008.

27. Hampson FC, Farndale A, Strugala V, Sykes J, Jolliffe IG, Dettmar PW. Alginate rafts and their characterisation. Int J Pharm. 2005;294(1-2):137-147. doi:10.1016/j.ijpharm.2005.01.036.

28. Patel A, Modasiya M, Shah D, Patel V. Development and in vivo floating behavior of verapamil HCl intragastric floating tablets. AAPS PharmSciTech. 2009;10(1):310-315. doi:10.1208/s12249-009-9210-9.

29. Erni W, Held K. The hydrodynamically balanced system: a novel principle of controlled drug release. Eur Neurol. 1987;27(Suppl 1):21-27. doi:10.1159/000116170.

30. Dey S, Mahanti B, Mazumder B, Malgope A, Dasgupta S. Formulation and in vitro evaluation of floating tablets of HPMC and PEO using ranitidine hydrochloride as a model drug. J Young Pharm. 2012;4(4):209-215. doi:10.4103/0975-1483.104363.

31. Kotreka UK, Davis VL, Adeyeye MC. Novel gastroretentive floating pulsatile drug delivery system produced via hot-melt extrusion and fused deposition modeling 3D printing. Pharmaceutics. 2020;12(1):75. doi:10.3390/pharmaceutics12010075.

32. Oladeji S, Dadou SM, Zhao M, Li S, Jones DS, Andrews GP. The development and optimisation of gastro-retentive floating tablets using fused deposition modelling 3D printing. J Pharm Pharmacol. 2022;74(10):1450-1466. doi:10.1093/jpp/rgab176.

33. Turac IR, Porfire A, Iurian S, Crișan AG, Casian T, Iovanov R, et al. Expanding the manufacturing approaches for gastroretentive drug delivery systems with 3D printing technology. Pharmaceutics. 2024;16(6):790. doi:10.3390/pharmaceutics16060790.

34. Higuchi T. Rate of release of medicaments from ointment bases containing drugs in suspension. J Pharm Sci. 1961;50(10):874-875. doi:10.1002/jps.2600501018.

35. Higuchi T. Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci. 1963;52(12):1145-1149. doi:10.1002/jps.2600521210.

36. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. Int J

Pharm. 1983;15(1):25-35. doi:10.1016/0378-5173(83)90064-9.

37. Costa P, Sousa Lobo JM. Modeling and comparison of dissolution profiles. Eur J Pharm Sci. 2001;13(2):123-133. doi:10.1016/S0928-0987(01)00095-1.

38. Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled-release system for gastric retention. Pharm Res. 1997;14(6):815-819. doi:10.1023/A:1012171010492.

39. Fabregas JL, Claramunt J, Cucala J, Pous R, Siles A. “In-vitro” testing of an antacid formulation with prolonged gastric residence time (Almagate Flot-Coat). Drug Dev Ind Pharm. 1994;20(7):1199-1212. doi:10.3109/03639049409038361.

40. Mora-Castaño G, Domínguez-Robles J, Himawan A, Millán-Jiménez M, Caraballo I. Current trends in 3D printed gastroretentive floating drug delivery systems: a comprehensive review. Int J Pharm. 2024;663:124543. doi:10.1016/j.ijpharm.2024.124543.

41. Alqahtani AA, Mohammed AA, Fatima F, Ahmed MM. Fused deposition modelling 3D-printed gastro-retentive floating device for propranolol HCl tablets. Polymers (Basel). 2023;15(17):3554. doi:10.3390/polym15173554.

42. Yang HS, Kim DW. Fabrication of gastro-floating famotidine tablets: hydroxypropyl methylcellulose-based semisolid extrusion 3D printing. Pharmaceutics. 2023;15(2):316. doi:10.3390/pharmaceutics15020316.

43. Real JP, Real DA, Lopez-Vidal L, Barrientos BA, Bolaños K, Tinti MG, et al. 3D-printed gastroretentive tablets loaded with niclosamide nanocrystals by the melting solidification printing process (MESO-PP). Pharmaceutics. 2023;15(5):1387. doi:10.3390/pharmaceutics15051387.

44. Kim JH, Song SH, Joo SH, Park GH, Weon KY. Formulation of a gastroretentive in situ oral gel containing metformin HCl based on DoE. Pharmaceutics. 2022;14(9):1777. doi:10.3390/pharmaceutics14091777.

45. Eldeeb AE, Salah S, Mabrouk M, Amer MS, Elkasabgy NA. The development of an in-situ biopolymer-based floating gel for the oral delivery of metformin hydrochloride. Heliyon. 2023;9(4):e14796. doi:10.1016/j.heliyon.2023.e14796.

46. Khizer Z, Akram MR, Tahir MA, Liu W, Lou S, Conway BR, et al. Personalised 3D-printed mucoadhesive gastroretentive hydrophilic matrices for managing overactive bladder (OAB). Pharmaceuticals (Basel). 2023;16(3):372. doi:10.3390/ph16030372.

47. Chen H, Pan L, Zhang C, Liu L, Tu B, Liu E, et al. Gastroretentive raft forming system for enhancing therapeutic effect of drug-loaded hollow mesoporous silica on gastric ulcers. Adv Healthc Mater. 2024;13(22):e2400566. doi:10.1002/adhm.202400566.

48. Kakuk M, Mészáros LA, Farkas D, Tonka-Nagy P, Tóth B, Nagy ZK, et al. Evaluation of floatability characteristics of gastroretentive tablets using VIS imaging with artificial neural networks. Eur J Pharm Biopharm. 2024;204:114493. doi:10.1016/j.ejpb.2024.114493.

49. Vrettos NN, Roberts CJ, Zhu Z. Gastroretentive technologies in tandem with controlled-release strategies: a potent answer to oral drug bioavailability and patient compliance implications. Pharmaceutics. 2021;13(10):1591. doi:10.3390/pharmaceutics13101591.

50. Jagdale SC, Agavekar AJ, Pandya SV, Kuchekar BS, Chabukswar AR. Formulation and evaluation of gastroretentive drug delivery system of propranolol hydrochloride. AAPS PharmSciTech. 2009;10(3):1071-1079. doi:10.1208/s12249-009-9300-8.