# A SYSTEM FOR GASTRO RETENTIVE DRUGM DISTRIBUTION: A REVIEW

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## Abstract

*Controlled-release dose formulations have improved essential pharmaceuticals. Yet, physiological issues like limiting and placing the device in the right GI tract and the highly variable stomach emptying process slow development. Bioavailability and peak plasma levels vary. Current gastroretentive drug delivery systems research was covered in this review. Gastric retention summarized physiological issues. Next, we examined high density (sinking), floating, bio- or mucoadhesive, expandable, unfoldable, super porous hydrogel, and magnetic gastroretentive technologies. Gastroretentive medication administration was examined last.*

***Keywords:*** *Oral route, gastroretentive, and GRDDS. Different Methods*

## Objective

This study addresses gastroretentive medicine delivery systems and gastric floating pills. Formulators like them because of their advantages over standard medication delivery systems. The article highlights these advantages and gastroretentive drug delivery improvements.

## Introduction

Oral-systemic circulation. Due to easy dosing, patient compliance, and formulation diversity, pharmaceuticals employ oral controlled release medicine administration. GIT-absorbed drugs are short-lived. Therapy requires many dosages.

Oral sustained controlled release formulations slowly release medication into the gastrointestinal tract and maintain systemic drug concentration to overcome these limits. Oral medication remains in the stomach and softly spreads throughout the gastro intestinal tract1. Gastro retentive drugs release locally and systemically in the upper gastrointestinal tract. Gastro-retentive doses prolong drug stomach retention (GRT).

Over the last few decades, several gastro retentive drug delivery methods have been developed, including high density (sinking) systems retained in the 2,3,4, mucoadhesive systems that bioadhere to stomach mucosa, unfoldable, extendable, or swellable systems that limit stomach emptying through the pyloric sphincter, super porous hydrogel systems, magnetic systems, etc. Site-specific oral controlled release systems are gastro-retentive. Longer-lasting dose formulations must delay and modify gastric emptying. Regulating delivery for optimal absorption and bioavailability is difficult. Target gastrointestinal system cannot restrict dosage form. Drug digestion. Intestinal mucosa contact time impacts medicine absorption.

Incompletely absorbed drugs need minimal intestinal transit. Stomach emptying, motility, physiological, and formulation variables. Gastro-retentive mechanisms keep drugs in the stomach for hours. Stomach retention improves

high pH-insoluble drug absorption, waste, and solubility. Local stomach and proximal small intestine drug delivery is conceivable. 5. Gastro retention facilitates new medical therapies. Mucoadhesion6, floating, sedimentation, expansion, changing forms, or pharmacological agents7, 8, 9 that delay stomach emptying may retain solid doses. These approaches categorized floating medication delivery devices (FDDS). Scientists tested FDDS in-vivo/in-vitro. These methods work for bioavailability-challenged medicines. Industry and academia develop gastroretentive dosage formulations (GRDFs). Floating medications delay gastric emptying. Floating stomachs gently discharge drugs. Improves plasma medicine and GRT. FDDS uses gas-producing, hollow microsphere, and raft-forming technologies. GRDDS uses industry-standard natural polymers. Natural polymers may deliver oral drugs. Biocompatibility, biodegradability, nontoxicity. Natural polymer-floating medicine enhances drug absorption10.

**Basic physiology of Gastrointestinal Tract:** Stomach has fundus, body, and antrum (pylorus). The stomach drains into the antrum. Fasting empties stomachs. States have motility patents. Fasting activates the stomach and intestines every 2–3 hours11. Wilson and Washington12 explain the four-stage interdigestive myoelectric cycle (MMC).

Contraction-based Phase I lasts 40–60 minutes.

1. Phase II (pre-burst) lasts 40–60 minutes with intermittent action potential and contractions. Phase intensity and frequency rise.

Phase III—burst—lasts 4–6 minutes. Rapid contractions. This valve sends undigested food to the small intestine. housekeeper wave.

Phase IV takes 0–5 minutes. Mixed meals stop starvation. Fasting phase II digestive motility contracts constantly. These contractions carry sub-1mm food particles to the pylorus. MMC slows digestion. Oral controlled release dosage forms have short stomach residence duration and irregular gastric emptying, according to scintigraphic investigations.

**Factors affecting gastric retention:**

Many variables impact oral dosage stomach residence time. Pyloric valves allow tiny intestinal particles of 1–2 mm. 13. Fasting stomach pH 1.5–2.0, feeding 2.0–6.0. Stomach water pH 6.0–9.0. Simple medications dissolve better because liquids empty the stomach before acid production. Food viscosity, volume, and calories affect stomach emptying. Nutrient density affects stomach emptying. If calories equal, protein, fat, and carbs don't matter. Acid and calories slow stomach emptying. Diabetes, Chron's, weight, gender, posture, and age impact stomach emptying. Aging slows stomach emptying. Female stomachs empty slowly. Sadness slows, stress speeds. 11. The stomach holds 25–50 ml. Liquid volume affects stomach emptying. Rapid depletion.

Fluids fast. Size affects fed-state stomach emptying. Housekeeping empties large tablets, digesting little ones. Radiolabelled liquid, digestible, and indigestible solid stomach emptying periods vary. Interdigestive migratory complex eject 91mm indigestible particles from stomach. 3–4-minute stomach spasms move fluids and indigestibles via the slightly open pylorus. The cleansing wave increases pyloric opening for bigger indigestibles. Myoelectric phases. Food slows MMC,

prolonging stomach residence (GRT) 12. Many formulation parameters impact gastric residence time. Unlike single-unit formulations, multiparticulate formulations empty stomachs routinely. Single-unit formulations slow food transit more than multiparticulate formulations. 13. Longer-stomaching tetrahedron trans-ring devices. Diameter formula. The stomach held doses above 7.5 mm longer than 9.9 mm.

Concentration impacts gastric emptying. Denser gastric fluids. The dosage unit is further from the pyloric sphincter. Gamma scintigraphy examined stomach emptying invivo. 4.8, 7.5, and 9.9-mm floating and non-floating capsules were used (large). Stomach-floating dosage units.

Peristaltic waves shielded non-floating units near the pylorus from propulsive and retropelling waves. Big floating units had shorter stomach residence durations. Reclining buoyancy alleviated stomach retention. Unfed gastric emptying. One research fed upright participants a little breakfast and another often. The upper stomach's peristaltic wave carried the floating shape to the next digesting phase after meals.

**Suitable drug candidates for gastro retention:**

Slowly and regularly delivered medications work best in the stomach. Reduces pharmaceutical use and negative effects. For therapeutic substances that the stomach cannot absorb, sustained release prolongs the agent's contact duration in the stomach or upper small intestine, where absorption occurs and contact time is normally restricted. 1–3 hours14.

CRGRDF candidates exhibited low colonic absorption but high upper GIT absorption:

- Riboflavin, Levodopa, and Calcium supplements are mostly absorbed through the stomach and upper GIT.
- Antacids and misoprostol are stomach-localized drugs.
- Colon-degradable drugs. Ranitidine HCl with Metronidazole. Amoxicillin.

**Table 1: Good candidates for gastroretentive drug delivery system[15]**

| S.No | Drug & Category | Bioavalibility |
|---|---|---|
| 1 | Verapamil Calcium channel blocker | 20-35% |
| 2 | Nifedipine Calcium channel blocker | 45-65% |
| 3 | Omeprazole Proton pump inhibitor | 35-60% |
| 4 | Atenolol Antihypertesive | 40-50% |
| 5 | Propranolol Antihypertensive | 4-26% |
| 6 | Verapamil Antihypertensive | 18-35% |
| 7 | Diltiazem Calcium channel blocker | 40% |
| 8 | .Lidocaine Local anaesthetic | 35% |
| 9 | Clarithromycin Antibiotic | 50% |
| 10 | Ramipril ACE inhibitor | 28% |

GRDFs have been developed by

academics and businesses. These approaches largely designated GRDFs.

**Approaches to gastric retention:**

Glycoprotein-containing polymers on the stomach epithelial membrane increase oral dose form retention. density methods. Fig.1

**High density approach:**

Such formulations need pellets denser than stomach fluid. 1.5 g/ml. Barium sulfate, titanium dioxide, and other innocuous substances cover the drug.

**Low density approach:**

Low-density systems float. Pellets or pills should float in stomach fluid and softly release medicament. hydrodynamically stable

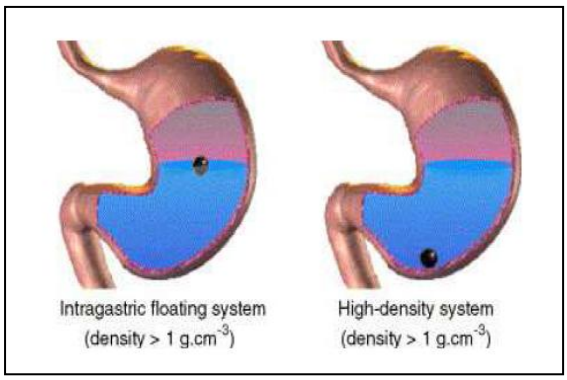


**Fig. 1: Diagram of Gastro retentive drug delivery system (low density and high density systems)**

**1) Floating Drug Delivery systems and itsmechanism:**

FDDS float in the stomach because their bulk density is lower than gastric fluids. Image 2 shows drug gently releasing on stomach contents (a). The dosage form must float on the meal due to low F and stomach content. Weighting floating force dynamics. F is tracked. Figure 2 floats with positive F. FDDS is stabilized and extended by this device16.

F = F buoyancy – F gravity

= (Df – Ds) gv

Where, F= total vertical force, Df = fluid density, Ds= object density, v = volume and g =acceleration due to gravity

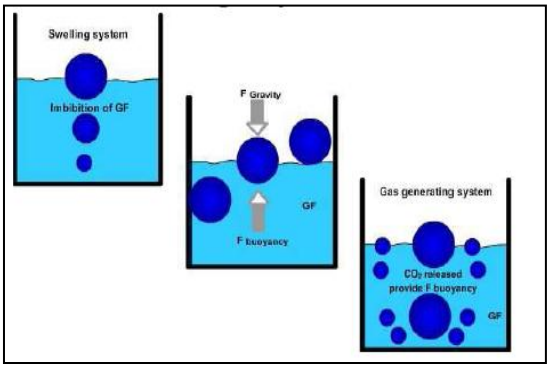


**Fig. 2: Mechanism of floating systems, GF=Gastric fluid**

**Classification of floating system:**

1). Single Unit Floating Dosage Systems

a) Effervescent system

b) Non-effervescent Systems

2). Multiple Unit Floating Dosage Systems

a) Effervescent Systems

b) Non-effervescent Systems

c) Hollow microspheres 3). Raft forming system

**1). Single Unit Floating Dosage Systems:**

**Effervescent systems**

Gas-generating effervescent medication delivery devices gently release medicine and remain buoyant in the stomach (CO2). The effervescent system includes chitosan, methyl cellulose, citric acid, sodium bicarbonate, and tartaric acid17. Penners et al. developed a polyvinyl lactam-polyacrylate tablet that expands quickly in water and stays in the stomach. As gas generated, gas-forming substances floated the device in the stomach18. offamotidine pill. In vitro buoyancy requires gel-forming polymermethocel (K100 and K15M), gas-generating sodium bicarbonate, and citric acid. Tablets released drug steadily and non-Fickian19.

***a)* Non effervescent system**

Non-effervescent systems use gel-forming

or highly swellable cellulose-type hydrocolloids, polysaccharides, and matrix-forming polymers such polycarbonate, polyacrylate, polymethacrylate, and polystyrene. Formulation involves mixing medicine with gel-forming hydrocolloid. This oral dose form swells in stomach secretions to less than 1 g/ml. Air in the expanded matrix buoys the dosage form. Iannuccelli et al. developed an air compartment multi-unit stomach stay system. Calcium alginate core and membrane with air compartment. Leaching water-soluble coating component polyvinyl alcohol (PVA) developed a porous structure that improved membrane permeability and inhibited air compartment shrinkage.

MW20 PVA improves flotation. Wu et al. produced HPMC-PEG 6000 floating sustained-release nimodipine tablets. Floating tablets were compressed after adding nimodipine to poloxamer-188 solid dispersion. Increased HPMC and reduced PEG 6000 lowered in vitro nimodipine release. 21 Single-unit formulations may cling or obstruct the gastrointestinal system, producing pain. "All or none" is the system's main drawback. House-keeper waves may transport the dosage form to the gut. Several unit-dose formulations fix this.

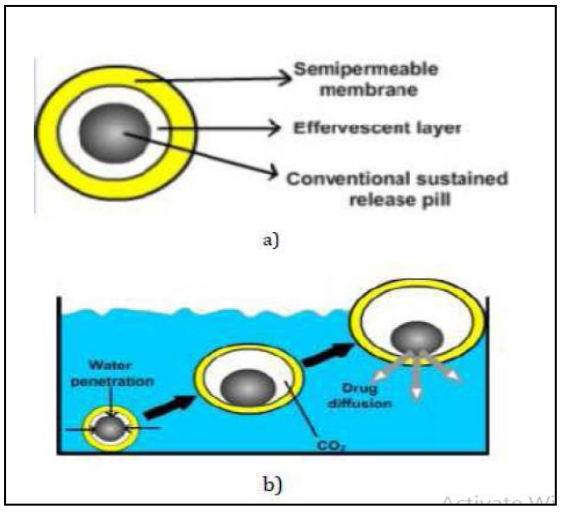


**Fig. 3: a) Different layers b) Mechanism of floatation via CO2 liberation**

Chen et colleagues examined how formulation factors affected floating sustained release verapamil in vitro. Formulations included polymers, excipients, polymer concentration, capsule density, and effervescent agents[22].

**b) Non effervescent systems:**

Effervescent multiple unit systems were further researched. Few studies have considered using chitosan as the polymeric excipient for an indomethacin-containing system. An indomethacin-model HBS was extruded. Slice and dry needle-extruded medicine, chitosan, and acetic acid. In acidic situations, chitosan hydrates and floats, releasing drug[23].

**Multiple Unit Floating Systems:**

Unit dosage formulations decrease dose dumping and inter- and intra-subject medication absorption variability. Air compartments, hollow microspheres from emulsion solvent diffusion, and beads from gelation are multi-unit floating systems. Effervescent and swellable polymers may form multiple-unit FDDS.

**a) Effervescent system:**

Ichikawa et al. created a multiple-type floating dose system with effervescent and swellable membrane layers on sustained release tablets. Separating the inner layer of effervescent components into two sublayers prevented sodium bicarbonate and tartaric acid from combining. Polyvinyl acetate and pure shellac create a swellable membrane surrounding these sublayers. The outer swellable membrane let fluid into the effervescent layer at 37oC. Two effervescent chemicals neutralized to produce CO2 and balloon-like tablets below 1.0 g/ml. (b) Thanoo et al. solvent-evaporated polycarbonate

microspheres. Hollow polycarbonate microspheres floating on dichloromethane and biofluids in SEM (SEM). Stomach and intestinal secretions included drug-loaded microspheres. Drugn-to-polymer ratios enhanced drug24 release and mean particle size. Sheth et al. created hydrodynamically balanced capsules with a uniform drug-hydrocolloid mix that floated on stomach contents until all the medication was released.

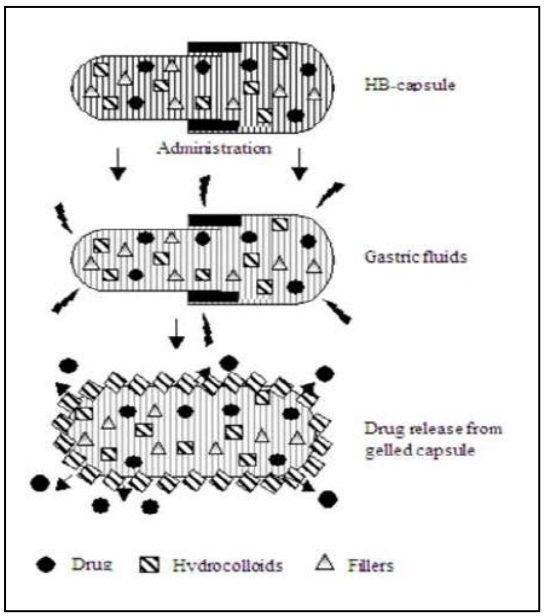


**Fig. 4: Working principle of hydro dynamically balanced system**

**c) Hollow microspheres:**

Polymers float. Joseph et al. created a polycarbonate microsphere-based floating piroxicam dosage form. Solvent evaporation created microspheres. 95% encapsulation. Healthy male albino rabbits were examined in vivo. Pharmacokinetic plasma concentration versus time graphs showed that piroxicam microspheres alone had 1.4 times the bioavailability of the free medication and 4.8 times that of a dosage form including microspheres and the loading dose, enabling sustained drug delivery[26].

**3) Raft forming system:**

Rafts deliver gastrointestinal medicines. Viscous cohesive gel expands stomach contents to form a raft. CO2 lowers bulk density, thus stomach juices float this raft. A gel-forming component and CO2-producing alkaline bicarbonates or carbonates float the system on stomach secretions. Jorgen et al. described a floating antacid raft. Sodium alginate, sodium bicarbonate, and acid neutralizer form a foamy gel (raft) that floats on stomach contents and prevents gastric acid reflux[27].

**Evaluation of Floating Drug delivery system**

1) **Evaluation of powder blend**
a) Angle of Repose
b) Bulk Density
c) Percentage porosity
2) **Evaluation of tablets**
a) Buoyancy capabilities
b) In vitro floating and dissolution behaviour
c) Weight variation
d) Hardness & friability
e) Particle size analysis, surface characterization (for floating microspheres and beads):
f) X-Ray/Gamma Scintigraphy
g) Pharmacokinetic studies

1) **Evaluation of powder blend**

*a)* **Angle of repose**

Angle of repose is "the maximum angle between the powder pile surface and the horizontal plane." Low repose improves flow. Measuring the pile's height (h) and base radius (r) using a ruler gives the angle of repose.

Tan θ = h/r 1

**Bulk density**

Bulk material density. It includes interparticle and intraparticle pore volumes. Particle packing gives bulk. Bulk density Powder density=weight/volume. Packed particles may have large gaps. Powder trapping moves particles and

decreases voids. Powder's bulk volume. Substituting this volume for powder weight in equation (2) yields bulk density.

**Percentage porosity**

Whether the powder is porous or nonporous, the total porosity expression for the calculation

zremains the same. Porosity provides information about hardness, disintegration, total porosity etc.

% porosity, € = void volume x100Bulk volume

% porosity, € = (bulk volumetrue volume) x100True density

**2) Evaluation of floating tablets**

***a)*** **Measurement of buoyancy capabilities of theFDDS:**

***b)*** Weight measures assess floating. The experiment uses deionized water and simulated food. Higher molecular weight polymers with slower hydration rates floated better in simulated meal media than deionized water29.

**In Vitro floating and dissolution behaviour:** USP dissolution tests medications. USP 28 specifies "the dosage unit is allowed to settle to the bottom of the vessel before rotation of the blade". Wire helix twists may anchor floating dose units to tiny, nonreactive substances. USP/BP cannot predict floating dosage form in vitro performance29. Pillay et al. added a helical wire sinker to theophylline's limited water-soluble swellable floating system. The wire helix reduced edema and drug release. To circumvent this constraint, the floating drug delivery device was totally immersed in a ring or mesh structure to increase drug release. Process reliability improved.

A swellable floating system with water-soluble diltiazem released medicine without the suggested technique. Swellable floating devices released medicines by unrestricted swelling, surface exposure, and water solubility.

Compression weighs 10 composite tablets. Typical composite weight divided by 10 has an averaged value issue. Hence, the USP restricts tablet weight deviations to a percentage of the sample average. The USP weight variation test weighs 20 tablets, calculates the average weight, then compares tablet weights to the average. The USP test passes if no more than 2 pills exceed the % limit or change by more than 2 times the limit.

**Hardness & friability:**

"Force required to break a tablet in diametric compression test" is hardness. Hardness crushes tablets. Monsanto, strong Cobb, and Pfizer test hardness. Roche Friabilator measures lab friability. A plastic chamber drops tablets six inches at 25 rpm to stress and abrasion them. Pre-weighed tablets spin 100 times in the friabilator. Compressed tablets that lose 0.5–1% of their weight are typically OK. Effervescent tablets have high friability weight losses, requiring stack packing.

**Particle size analysis, surface characterization (for floating microspheres and beads**):

Dry beads or microspheres are measured via optical microscopy. SEMs characterize surface and cross-sectional morphology.

**XRay/ gamma scintigraphy:**

X-Ray/Gamma Scintigraphy now assesses floating dosage forms. It predicts stomach emptying, GIT transit, and dose form location. X-rays may show radio opaque solid dose form. A camera or scintiscanner may indirectly see a radioactive formulation. Scintigraphy tracks GIT[29] dosage form using a camera utilizing radionuclide rays.

**Pharmacokinetic studies:**

In vivo studies have yielded pharmacokinetic data. Sawicki compared floating pellets in capsules to equal-dose verapamil tablets (40 mg). Floating pellets had greater tmax (3.75 h) and AUC (0-infinity) (364.65ng/ml/1h) than verapamil tablets.

**Recent advances in stomach specific floating dosage forms:**

Sungthongjeen et al. created gas-formed floating multilayer coated tablets. A gas-entrapped membrane, sodium bicarbonate, and hydroxylpropyl methyl cellulose surround a drug-containing core tablet. Gas-entrapped membrane Eudragit RL 30D was selected.

CO2 and polymeric membrane trapping float tablets. Formulation impacts drug release and floating. Direct-compressed tablets floated faster and released medicine faster than wet granulated ones. Raising gas generating agent did not alter time to float but increased medicine release from floating tablets, while increasing coating level of gas-entrapped membrane increased time to float (more than 8 hours) and slightly slowed but maintained drug release.

**Gastroretentive products available in market**

Clarithromycin suspension. In situ sucralfate gels cleaned H.pylori better. FIGC eradicated H.pylori with less clarithromycin than the suspension. The floating clarithromycin gel's extended gastrointestinal residency and stability may kill H. pylori better than the solution.

**Conclusion:**

Several stomach-only medications employ floating drug delivery methods. Buoyant preparation prolongs stomach residence and medication release. Polymer-mediated FDDS alters oral drug distribution. Drug delivery devices must float in stomach fluid. Gastrointestinal illnesses and pharmaceutical half-lives are best treated with these dosage types.

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