# GASTRORETENTIVE MEANS OF DELIVERY: A SYSTEMS ANALYSIS

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## ABSTRACT
*This study combines and describes gastro retentive techniques, which are now the main approach for site-specific oral controlled release medication delivery. Gastro-retentive medication delivery is used for oral medicine administration (GRDDS). To overcome oral delivery issues such poor bioavailability, dosage forms are often kept in the stomach and slowly released. Gastric retention reasons and cures helped us grasp numerous physiological issues. In vitro gastro retentive device testing.*

***KEYWORDS:*** *GRDDS, oral drug administration, bioavailability, and gastric retention.*

## INTRODUCTION
Oral systemic administration dominates. 90% of oral medicines. Prefer solid oral medicines. Oral method is more popular because to patient compliance, discomfort avoidance, and medication diversity. Drug administration temporarily retains and empties the stomach. Poor absorption zone medication release reduces dosage response.

Medication absorption is weak and vary due to physiological factors and GI transit, notably stomach residence duration. Gastric retention promotes intestinal absorption. [1] A regulated and repeatable medication delivery system is being developed to prolong therapeutic plasma drug concentration and minimize dose frequency and variation at steady state. Innovative GRDDS (gastro retentive drug delivery system). Stomach-held GRDDs. Slow-release drugs with an absorption window are GRDDSs. Extended gastric retention may benefit medications absorbed from the proximal GIT, less soluble at alkaline pH, or encountered in the lower GIT. GRDDS boost drugs:

• Bioavailability

Therapeutic efficacy and dosage decrease.

• Long-term therapeutic level stability reduces therapeutic level fluctuations.

Minimize drug waste

• Increases medication solubility at high pH. (e.g. weakly basic drugs like domperidone, papaverine)

Gastroretentive medicine administration prolongs stomach residency time for upper gastrointestinal tract (GIT) site-specific drug release for local or systemic effects. Gastroretentive dose forms may prolong pharmaceutical GRT. [3]

**Gastric Emptying Time (Get) and Motility**

We fast. GET transports medicines from stomach to intestine. Most drugs are gut-absorbed. Gastric emptying speeds medication absorption. Gastric degraders start quicker. Delaying gastric emptying dissolves poorly soluble alkaline pH medicines that are mostly absorbed from the stomach or proximal intestine. [4]

**Demerits**

- Floating systems require plenty of stomach fluids. Higher dosages need additional water.
- Contractile waves may eliminate

floating dose forms from sleeping postures. Avoid floating dosages before bed.

- GRDDS eliminates low-solubility, unstable in high acidic conditions, and stomach mucosa-irritating drugs.
- Bio/mucoadhesives have thick, fast-turnover mucus.
- Swellable dose form must swell quickly before stomach escape and surpass pylorus aperture.
  - Diet, pH, and stomach motility impact gastric retention. Several factors complicate buoyancy prediction.
  - Bioadhesive medical devices may bond esophageally.
  - After meals, 6GRDDS helps digestion remain.
  - Hydrogel swells slowly.
- Large medicine delivery systems might cause stomach retention and death.

**Need For Gastric Drug Delivery System**

- Medication absorption is site-specific. Targeted or maximum medicine distribution is needed.
- 7GI-absorbed medicines (GIT).
- Alkaline-degradable medicines.
- Time-dependent gastric emptying medications.

- Specific illness medication in the stomach and proximal small intestine.

**Floating Systems**

Gastric retention enhances drug absorption. Floating drug delivery is novel. It's needed for stomach or upper small intestine-absorbed drugs. This method does not alter long-term stomach emptying. Low-density method (lower than gastric fluid). Keep your stomach buoyant to slowly release the drug.

Medication releases after stomach emptying. GRT rises and plasma medication concentration variation is regulated. Floating drug delivery needs. [10]

3. Storage.
4. Maintain stomach specific gravity below 1.004–1.01gm/cm3.
5. Create a gel seal.

**Mechanism of Floating Drug Delivery Systems:** Delayed medication release and stomach contents. Stomach residual system elimination post-discharge. Buoyancy retention requires little stomach contents and the right floating force (F) to retain dose form above meal surface. Floating force kinetics instruments. F (time-dependent) force submerges it.

Higher positive force F enhances object flow in Fig. FDDS and intragastric buoyant capacity fluctuations are improved.

$F = F_{buoyancy} - F_{gravity}$

$= (D_f - D_s)\, gv$

Where,

F= total vertical force, $D_f$ = fluid density,

$D_s$ = object density, v = volume and

g = acceleration due to gravity.

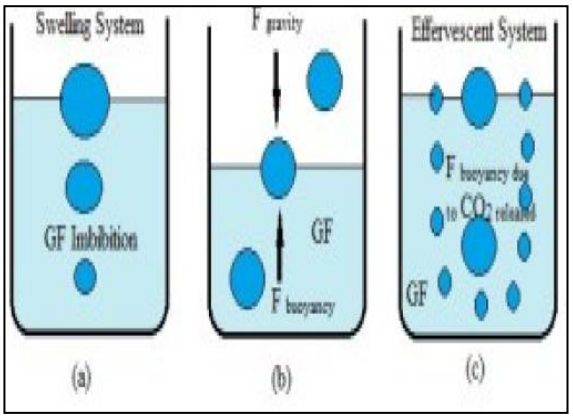


**Fig 1: Mechanism of floating drug delivery systems, gf: gastric fluid, $co_2$: carbon dioxide**

**Low Density Systems**[11]

Low-density FDDSs. Stomach fluids float these systems. The stomach-floating drug-releasing device. Post-medication stomach emptying.

Bubbly GRDS: non-effervescent systems bubbly systems

**Non Effervescent Systems**

Gel-forming or highly swellable cellulose-type hydrocolloids, polysaccharides, or matrix-forming polymers such polyacrylate, polycarbonate, polystyrene, and polymethacrylate generate non-effervescent systems. These methods float dosage forms by tightly combining medication with a gelforming hydrocolloid, which swells in stomach fluid after oral administration and retains shape and bulk density below unity inside the outer gelatinous barrier. Air-trapped polymer floats these dosage forms. Medication release is stored in gel. Subtypes:[12]

**Hydrodynamically balanced systems**

In these single-unit dosage forms, hydrocolloids from HPMC, hydroxyethyl, hydroxypropyl, sodium carboxymethyl, polycarbophil, polyacrylate, polystyrene, agar, carrageenans, or alginic acid float over stomach contents. Drug-polymer capsules are hydrodynamically balanced. The capsule shell dissolves in water and forms a gelatinous barrier, buoying the dose form in stomach fluid (Dhiman et al., 2011) 13. Surface erosion keeps the interior layers hydrated and dosage form buoyant. Low-density fat compositions reduce erosion.

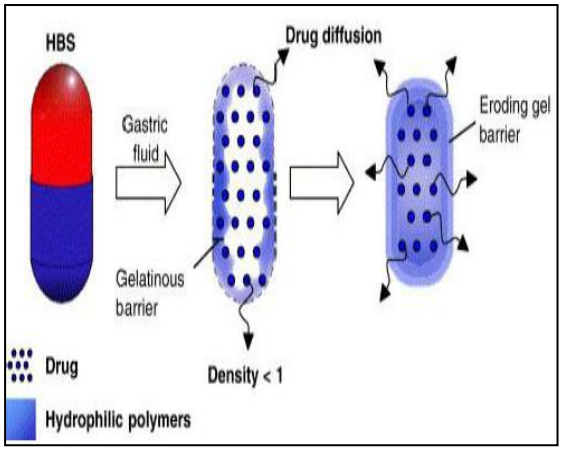


**Fig. 1: Mechanism of hydrodynamically balanced systems.**

**Micro porous compartment system[14]**

Top- and bottom-porous microporous compartments contain drug reservoirs. Sealing the device's edges prevented undissolved medicine from entering the stomach. Air-filled stomach chambers house the delivery mechanism. The intestines absorb drugs from gastric fluid.

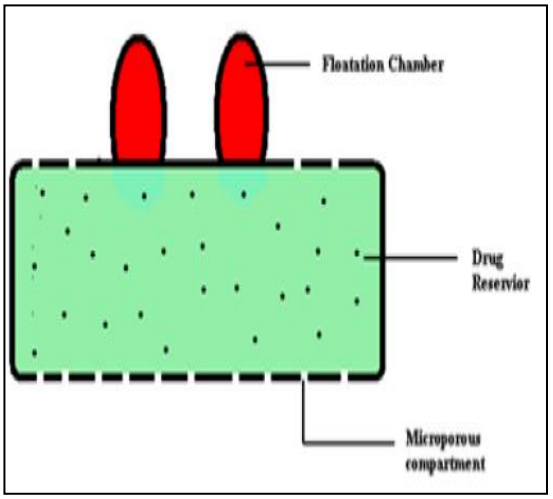


**Fig. 2: Microporous compartment system.**

**Alginate beads:[15]**

Emulsion gelation produces multi-unit gastroretentive sustained-release dosages of water-soluble medicines like ranitidine hydrochloride. By gently mixing oil and water phase with sodium alginate, beads encapsulated polymer and oil were extruded into calcium chloride solution. Long-lasting beads give stomach medicine.

**Hollow microspheres:[16]**

Hollow microspheres' multiple-unit construction and good floating make them buoyant structures. Solvent diffusion creates drug-loaded hollow microspheres. The drug's ethanol: dichloromethane solution and enteric acrylic polymer were added to agitated PVA at 400 C. Dichloromethane evaporation created gas phases in scattered polymer droplets and cavities in drug-loaded microspheres.

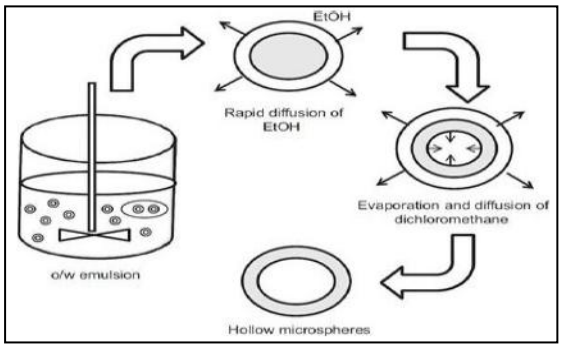


**Fig. 3: Solvent diffusion technique.**

**Effervescent Systems:**[17]

Effervescent systems make carbon dioxide (CO2) gas from carbonates like sodium bicarbonate and organic acids like citric acid and tartaric acid, lowering their density and floating over stomach contents. At body temperature, liquid matrices evaporate gas. Gas-vacuum effervescent systems.

**1) Gas generating systems:**[18]

Reacting sodium bicarbonate, citric acid, and tartaric acid produces CO2. The system's jellified hydrocolloid layer traps gas, decreasing its specific gravity and letting it float over stomach contents. Multiple-layered seed tablets are used. Inner layer: effervescent sodium bicarbonate and tartaric acid. PVA shellac swells the outer membrane.

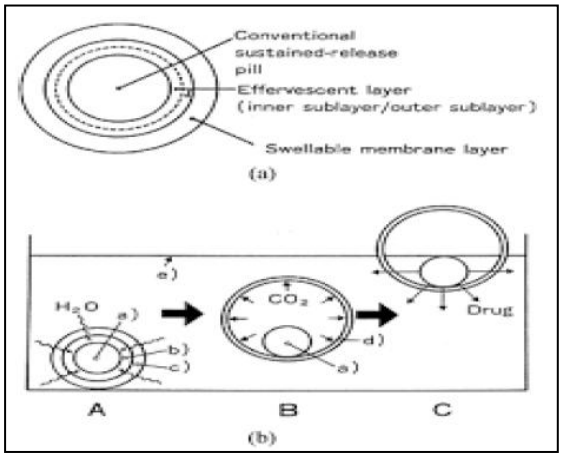


**Fig. 4: Gas generating sytems.**

These can be further divided into

**Floating capsule**

They are made from a sodium bicarbonate-sodium alginate solution. Acidic environments create CO2 gas. The system floats because the moisturizing gel captures this gas.

**Floating pills**

Unit-dose sustained release formulations. Two-layer sustained-release tablets. Swellable membrane surrounds effervescent substances. System membranes swell before sinking. Effervescent agents release CO2, floating the system.

**Floating system with ion exchange resin**

These systems are usually made using resin beads filled with bicarbonates. Coating it with insoluble yet water-permeable ethyl cellulose follows. The system floats and emits CO2.

**Volatile liquid containing systems**[19]

A pressure-responsive bladder divides these chambers. Drug and volatile liquid in first and second chambers. Inflating a stomach compartment with ether or cyclopentane that gasifies at body temperature may sustain a medication delivery system's GRT. A bioerodible plug consisting of Poly vinyl alcohol, Polyethylene, or other materials degrades over time, releasing gas and deflating the chamber after a specified period to allow spontaneous stomach evacuation. Inflated reservoirs discharge medicine into stomach fluid. Classifications follow.

**Intragastric floating gastrointestinal drugsystem**[20]

These devices may float in the stomach because the floating chamber is a vacuum, air, or a harmless gas, and the drug reservoir is in a microporous compartment (fig 1).

**Inflatable gastrointestinal delivery system**

Inflatable liquid ether expands in the stomach when heated to body temperature. These devices use a polymeric matrix

impregnated with medication in an inflated chamber and a gelatin capsule. Oral administration fractures the capsule, releasing the drug reservoir and enlarged chamber. Inflatable chambers automatically maintain medicine reservoirs in stomach fluid.

**Intragastric-osmotically controlled drug deliverysystem**

Osmotic pressure distributes medication from its bioerodible capsule. Dissolving capsules deliver intragastric-osmotically regulated medication. A hollow polymeric bag containing a liquid that gasifies at body temperature inflates the inflatable floating support.

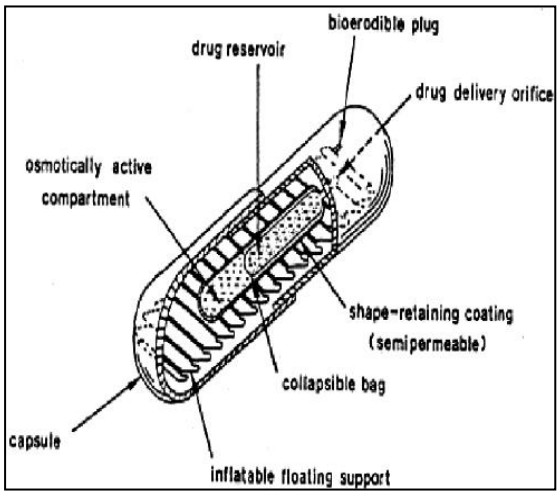


**Fig. 5: Intragastric-osmotically controlled drug delivery system.**

**High Density Systems**

High-density systems need stomach content denser than 1.004 gm/cm3. Medications are coated on heavy cores or blended with iron powder, barium sulphate, zinc oxide, titanium oxide, etc. 1.5–2.4 g/cm3.

Sedimentation may trap tiny pellets in stomach rugae at the pyloric area. Rugae-trapped thick pellets (3g/cm3) resist stomach wall peristaltics. Density, not diameter, impacts GI transit. Near-threshold density extends gastric residence.

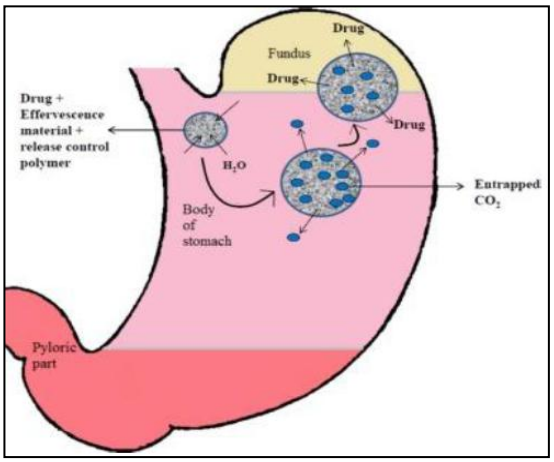


**Fig. 6: High density systems.**

**Swelling and Expanding Systems**

These dosage types enlarge and contract the pylorus. Water and osmosis generate edema, which traps plug-type devices near the pyloric sphincter. Gastric retention and controlled delivery formulations stay in the stomach for hours. Swelling and molecular weight polymers delay release for controlled and sustained release. Stomach fluid swells polymers. Hydrophilic polymer networks inflate due to physical chemical cross connections. Crosslinks inhibit polymer breakdown.

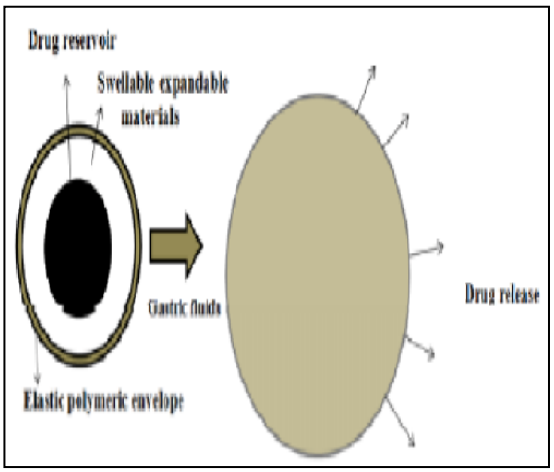


**Fig. 6: Swelling and expanding systems.**

**Muco/Bio-Adhesive Systems**

Site-specific medication absorption. Bioadhesive polymers attach to stomach mucosal epithelial surface, prolonging gastric retention. Cationic, anionic, or neutral polymers exist. HPMC, carbopol, sodium carboxy methyl cellulose, sodium

alginate, gelatin, and guar gum are used. Wetting theory permits bioadhesive polymers to spread and intimately contact mucin layers.

• Diffusion theory involves mucin strands tangling with soluble or penetrating polymers.

• Absorption theory explains bioadhesion as Vanderwaal forces and hydrogen binding.

• Electrostatic hypothesis proposes glycoprotein mucin network and bioadhesive material attract.

• Polymers adhere to mucous membranes in different ways:

❖ **Hydration mediated adhesion:** Hydration makes hydrophilic polymers sticky and mucoadhesive.

❖ **Bonding mediated adhesion:** Bonding may be mechanical or chemical. Ionic, covalent, or vanderwaal forces may be present in chemical bonds between the polymer molecule and the mucous membrane.

❖ **Receptor mediated adhesion:** It occurs when certain polymers interact with particular receptors that are expressed on stomach cells. The polymers might be neutral, anionic, or cationic.

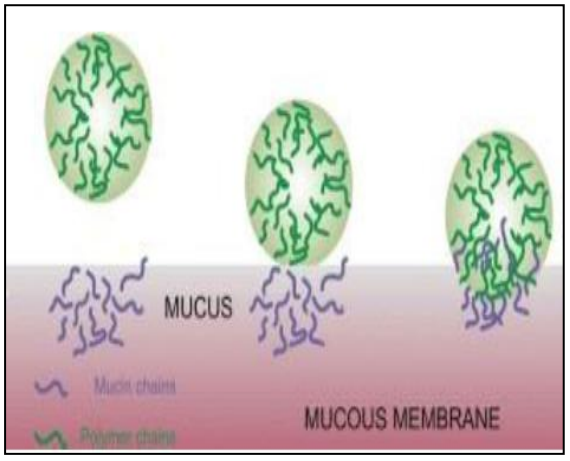


**Fig 7: Muco/bio adhesive systems.**

**Magnetic Systems:**

The stomach's powerful magnet prevents gastroretentive capsules' magnetic material from escaping. The predicted effects can only be obtained by carefully modifying magnet location, making such systems doubtful despite multiple successful testing. Modern, portable magnetic field generators may facilitate this.

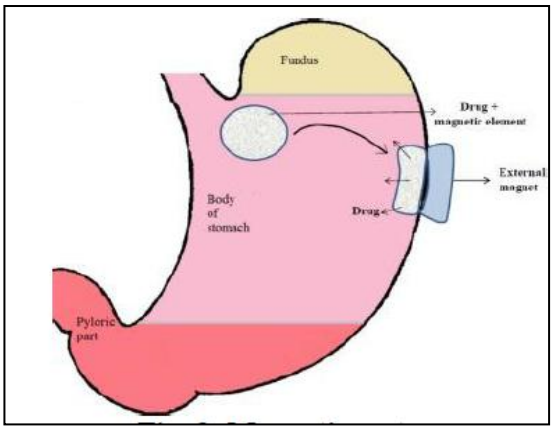


**Fig. 8: Magnetic systems.**

**Raft Forming Systems:**

Rafts deliver gastrointestinal medicines. Floating rafts reduce reflux (GERD). Stomach fluids produce a raft of viscous cohesive gel. CO2 lowers bulk density, thus stomach juices float this raft. Gel-forming agents and alkaline bicarbonates or carbonates float CO2 on stomach juices.

**Superporous Hydrogel Systems:**

Swellable superporous hydrogels vary. Traditional hydrogel takes hours to absorb water, which may induce premature dosage form evacuation. Superporous hydrogel swells to equilibrium size in minutes by capillary soaking via linked open pores. They grow and withstand stomach contractions. Co-formulated Ac-Di-Sol is hydrophilic.

**Evaluation of grdds**

**Pre compression parameters**

1) **Bulk density:** First, a measured amount of medication powder was added to a 10 ml measuring cylinder. Using the formula, the apparent bulk density in g/ml was obtained from the bulk volume. Bulk density=weight of powder/bulk volume

2) **Tapped density:** Following shaking to break up agglomerates, a 10 ml

measuring cylinder was filled with medication powder from each batch. After recording the initial volume, the cylinder was permitted to tap under its own weight at 0.5 cm intervals on a hard surface. Tapping continued until volume stabilized. Tapped density=weight of powder/tapped volume

3) **Hausner's ratio (HR):** This was calculated as the ratio of tapped density to bulk density of sample **HR=Tapped density/bulk density**

4) **Carr's compressibility index:** The Compressibility Index of the powder blend was determined by the below formula

**Carr"s compressibility index = Tapped density-bulk density/tapped density*100**

5) **Angle of repose:** The funnel method calculated powder mix angle of repose. The funnel held the properly weighed powder combination. The funnel was raised to barely touch the powder mixture. Powder mixture flowed through the funnel. The angle of repose was calculated using the powder cone's diameter and the following equation:

6) $\tan \theta = h/r$

Where,

h= height of the powder cone and r= radius of the powder cone.

**Standard values of angle of repose.**

| Angle of repose | Flow property |
|---|---|
| >250 Excellent | Excellent |
| 250-300 | Good |
| 370-400 | Fair beyond |
| 400 | Poor |

**Post Compression Parameters**

1) **Weightvariation test:** weight variation The prescribed process was followed to weigh 20 formulation pills on a citizen electronic balance. 20 tablets were randomly selected from each batch and weighed individually to evaluate weight variation.

2) Percentage Deviation (PD) $=w_{avg} - w_{initial}/w_{avg}$ Where,

$W_{avg}$ = average weight and $W_{initial}$= initial weight

**Standards for uniformity of weight as per I.P.**

| Avg. wt. of tablet | % Deviation |
|---|---|
| 80 mg or < 80mg | 10 |
| 80mg to < 250 mg | 7.5 |
| 250mg or more | 5 |

3) **Hardness test:** Hard tablets withstand mechanical shock. Monsanto Hardness Meters assessed tablet hardness by dimetric compression. Three random tablets were hardness-tested. Mechanical stability demands 2-4 Kg/cm2 tablet hardness.

4) **Friability test:** Roche Friabilator measured tablet friability. It's a %. Before entering the Friabilator, the pills were weighed. The Friabilator was ran 100 times or 25 rpm for 4 minutes. Pills were weighed again. Friability % was calculated using this formula.

[34]% Friability = initial weight-final weight/initial weight

*100

- Percentages Friability of tablets less than 1% are considered acceptable.

5) **Floatation studies:** Invitro buoyancy is measured by FLT and total floating time (TFT). FLT and TFT are measured by placing tablets in a 250 ml beaker with 200 cc 0.1N HCL. The floating lag time and total floating time are the time it took the tablet to rise to the surface and float.

**Drug content uniformity:** Invitro buoyancy is measured by FLT and total floating time (TFT). FLT and TFT are measured by placing tablets in a 250 ml beaker with 200 cc 0.1N HCL. The floating lag time and total floating time are the time it took the tablet to rise to the surface and float.

**Drug release study:** USP XXIII type-II paddle-type dissolving test device discharged floating tablets with 900 cc 0.1 N HCl at 50 rpm and 37±0.5°C. A pre-filtered syringe replaced 5 ml of samples with new dissolving media at predefined intervals. UV Visible spectrophotometers estimated drug release by measuring API's max (nm) absorbance following dilutions.

## CONCLUSION

Gastro-retentive medication delivery systems enhance bioavailability and gastrointestinal residence duration. They will enhance dosing intervals and patient compliance beyond GRDDS by substantially increasing medicine release time. GRDDs improve gastric mucosa medication concentrations, improving stomach pharmacotherapy. Systemic, localized, and reduced dose frequency GRDDS decreases contraindications, systemic toxicity, and drug dependence. The research implies that gastro retentive drug distribution may improve low-bioavailability medicines since their absorption is limited to the upper gastrointestinal tract.

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