Gastro-Retentive Drug Delivery System: An Advanced Comprehensive Review

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ABSTRACT

Gastro-Retentive Drug Administration Mechanism represents a cutting-edge method of orally regulated drug administration designed to prolong GI residence time and enhance therapeutic efficacy. Immediate-release oral medication form frequently have obstacles notably irregular stomach emptying, PH fluctuations, enzymatic degradation, and reduced bioavailability for drugs with narrow absorption window. GRDDS overcome these challenges by conserving the prescribed dose in the gut through mechanisms such as floating, mucoadhesion, swelling, high density, magnetic retention, and raft formation. Proper drug selection is critical, with ideal candidates including drugs exhibition narrow upper gastrointestinal absorption window, better solubility in acidic, pH short half-life, local gastric action, and low dose requirements. Recent technological advancements have significantly improved GRDDS performance. Hybrid multi-mechanistic systems, 3D printing, artificial intelligence-assisted formulation design, nanotechnology integration, biodegradable smart hydrogels, and floating microspheres have enhanced gastric retention time beyond 12 hours, improved bioavailability by 1.5-3 fold, and enabled controlled drug release exceeding MRI have further strengthened formulation optimization and in vitro-in vivo correlation. Despite certain limitation, including dependence on gastric motility and regulatory challenges, GRDDS demonstrate strong clinical potential in managing chronic and gastric-specific disorders such as Parkinson's disease, type 2diabetes, peptic ulcer disease, and Helicobacter pylori infection. Continued innovation is expected to establish GRDDS as a cornerstone of next-generation oral medication distribution.

Keywords: *Gastro Retentive Drug Delivery Systems (GRDDS), Gastro Residence Time, Controlled Release, Floating Drug Delivery Systems, Smart polymers.*

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INTRODUCTION

Oral drug delivery continues to dominate the pharmaceutical market as the most preferred and patient-friendly route of drug administration. Its widespread acceptance is attributed to convenience, non-invasiveness, cost-effectiveness, ease of large-scale manufacturing, and improved patient adherence compared to parenteral or transdermal systems. Tablets, capsules, suspensions, and other oral formulation account for a significant proportion of commercially available medicines worldwide. Despite these advantages, conventional oral dosage forms are often associated with important physiological and biopharmaceutical limitations that compromise therapeutic outcomes[1].

A significant obstacle in the distribution of oral medications involves variability of gastric emptying time. The stomach exhibits complex motility patterns governed by the migrating motor complex (MMC), which alternates between fed and fasted states. In the fasted states, indigestible solid dosage forms are rapidly cleared from the stomach during phase 3 of the MMC, often within 1-2 hours. In contrast, the fed state may prolong gastric residence, but this is highly dependent on meal composition, caloric content, and individual physiology. Such variability results in unpredictable drug absorption and plasma concentration profiles. Additionally, enzymatic degradation in the gastrointestinal tract. pH variability (By the stomach's elevated acidity & the intestine's relating neutrality), and limited permeability across the intestinal epithelium further complicate drug delivery[2].

These limitations are particularly significant for medications that demonstrate a limited window of absorption in the upper GIT , typically in stomach or proximal small intestine. Once such drugs pass beyond their optimal absorption site, their bioavailability drastically decreases. Similarly, drugs with PH-dependent solubility-those that dissolve better in acidic

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*Author for Correspondence: grajitha@spmvv.ac.in environments- may precipitate in the more alkaline intestinal fluids, leading to reduce systemic exposure. Furthermore, certain drugs are designed to work locally within the Gut, like antibiotics for *Helicobacter pylori* eradication or agents for gastric ulcer therapy. Conventional formulations may not provide sufficient gastric retention to achieve optimal therapeutic levels at the target site[3].

To overcome these limitations, Gastro Retentive Drug Administration Mechanism, constitute a cutting-edge method within controlled release technology. GRDDS have been customized to lengthen the interval of residence of typical dosage, ensuring that the medication remains in the gut for longer intervals.via retaining formulation in the gastric environment, GRDDS facilitate prolonged drug dissolution in acidic media and controlled release at or near the primary absorption site. This strategy enhances bioavailability, reduce dosing frequency, minimizes therapeutic efficacy and patient compliance[4].

The design of GRDDS relies on overcoming physiological barriers such as gastric motility and pyloric emptying. Over the past decade, multiple retention mechanisms have been explored, including floating systems with low density, bioadhesive systems that attach to gastric mucosa, expandable systems that increases in size to hinder transit across the pyloric cavity & enhanced density networks that settle in gut folding. However, recent developments between 2023 and 2025 reflects a paradigm shift toward multi-mechanistic retention strategies, where floating, swelling, and mucoadhesion are combined within a single dosage form. Such hybrid systems aim to compensate for the limitations of individual approaches and provide more reliable and reproducible gastric retention[5].

Another significant advancement is the incorporation of stimuli-responsive sophisticated polymers. These elements adapting to environmental triggers comprising PH, temperature, ionic strength, enabling controlled swelling, gel formation, or drug release in response to gastric conditions. Smart hydrogels and responsive polymeric matrices enhance both retention efficiency and release precision[6].

The application of three-dimensional (3D) printing technologies has further revolutionized GRDDS development. Additive manufacturing permits absolute influence on tablet design, density distribution, internal porousness, & medication layering[7].

Personalized gastric-retentive formulations tailored to patient-specific pharmacokinetic needs are now a realistic possibility. Similarly, the incorporation of nanostructured drug carriers, such as nanoparticles, nanocrystals, and lipid-based systems, within gastro-retentive matrices improves drug solubility, stability, and mucosal penetration[8].

Modern GRDDS research also emphasizes the use of biodegradable and biocompatible polymers to enhance safety and reduce the risk of gastro obstruction. Natural polymers such as chitosan, alginate, and cellulose derivatives are increasingly preferred due to their favourable regulatory and toxicological profiles[9].

Advance in real-time in vivo imaging techniques, including gamma scintigraphy and magnetic resonance imaging (MRI), now allow researchers to monitor gastric retention behaviour directly in human subjects. These tools have significantly improved in vitro-in vivo correlation and formulation optimization[10].

Clinically, the demand for GRDDS has expanded due to the rising prevalence of chronic gastric disorders, *Helicobacter pylori* infections, Parkinson's disease requiring levodopa therapy, metabolic disorders such as type 2 diabetes treated with metformin, and other conditions requiring sustained upper GIT drug exposure. By addressing pharmacokinetic unpredictability and site-specific delivery challenges, GRDDS represents a sophisticated evolution in oral controlled release systems11.

In conclusion, gastro-retentive drug delivery systems embody a strategic advancement in pharmaceutical technology aimed at enhancing drug bioavailability, therapeutic performance, and patient outcomes. Through integration of advanced materials, smart design principles, and innovative manufacturing technologies, GRDDS continue to redefine the future of oral drug delivery.

SUITABILITY OF DRUGS FOR GRDDS

Gastro Retentive Drug Administration Mechanism, are optimized to broaden the interval of residence of medication in gut. thereby enhancing drug absorption and improving therapeutic efficacy. However, not every medication is a good fit for GRDDS. The selection of a drug for gastro-retentive systems depends on its physiochemical properties, pharmacokinetic behaviour, pharmacodynamic profile, and therapeutic requirements. Proper drug selection is critical for achieving clinical success and ensuring formulation efficiency.

CRITERIA FOR DRUG SUITABILITY

Drugs considered ideal for GRDDS generally exhibit the fallowing characteristics[12-18]:

1. Narrow Absorption Window in the Upper GIT

Certain medications are tend to be absorbable in the Gut or duodenum. If such drugs pass quickly into the lower intestine, their absorption decreases significantly. GRDDS prolongs GI retention, ensuring that medication remains in the optimal absorption region for a longer time, thereby improving bioavailability.

2. Better solubility in Acidic pH

Certain drugs exhibit higher solubility in acidic conditions compared to alkaline environments. Since the stomach maintains a PH of 1-3, drugs with better solubility in acidic PH benefit from prolonged gastric residence. This enhances dissolution and absorption. Weakly basic drugs are particularly suitable in this category.

3. Local Action in Gut:

Some drugs have been created to act locally in stomach, such as drugs used for peptic ulcers of Helicobacter pylori infections. For such drugs, extended gastric retention ensures prolonged content with the gastric mucosa, enhancing therapeutic effectiveness.

4. Low solubility at Alkaline pH

Drugs that show reduced solubility in the alkaline environment of the intestine may have poor absorption if they leave the stomach. Retaining these drugs in the acidic gastric environment improves their dissolution rate and bioavailability.

5. Short Half-Life Requiring Sustained Release

Medication having limited biologically determined shelf-lives must be taken often to sustain therapeutic plasma levels. Incorporating such drugs into a GRDDS formulation provides sustained release, reduces dosing frequency, improves patient compliance, and maintains consistent drug levels.

6. Instability in Intestinal Environment

Certain drugs degrade in the alkaline PH of the intestine or are susceptible to enzymatic degradation. Retaining these drugs in the stomach can reduce degradation and improve therapeutic outcomes.

7. Low Dose Requirement

Drugs administered in low doses (generally less than 1 gram) are more suitable for GRDDS. High-dose drugs require larger dosage forms, which may be difficult to retain in the stomach effectively.

DRUGS SUITABLE FOR GRDDS

Several drugs have been successfully formulated using gastro-retentive systems dues to their favourable properties[19-23]:

- **Riboflavin (vitamin B2)** –Riboflavin has limited window for upper GI absorption. Prolonging gastric retention improves its absorption and bioavailability.
- **Levodopa-** An anti-Parkinsonian drugs mainly utilized in the upper GIT. GRDDS enhances its therapeutic effectiveness by maintaining drug concentration in the absorption site.
- **Metformin HCl-** An antidiabetic drug that shows enhanced solubility in acidic PH. Gastro-retentive formulations improves its absorption and reduce gastrointestinal side effects.
- **Ranitidine HCl-** An H2receptor blocker used for gastric ulcers. It acts locally in the stomach; therefore, prolonged gastric retention improves its therapeutic action.
- **Ciprofloxacin-** An antibiotic with improved solubility in acidic medium. GRDDS enhances its dissolution and absorption.
- **Furosemide-** A diuretic with limited window for upper GI absorption. Gastro-retentive formulations help maintain stable plasma concentrations.
- **Diltiazem-** A calcium channel blocker with a short half-life. Sustained-release gastro-retentive formulations help maintain stable plasma concentrations.
- **Amoxicillin-** Commonly used for Helicobacter pylori eradication. Prolonged gastric residence increases its effectiveness against gastric infections.
- **Indomethacin**- It is an NSAID where gastric targeting may improve therapeutic medication with limited window of absorption. GRDDS enhances its absorption and reduces dosing frequency.

These examples demonstrate how proper selection of drugs based on pharmacokinetics and physiochemical properties significantly enhances the performance of gastro-rententive systems.

Table 1: Drug suitability for GRDDS

Criteria	Explanation	Drug Examples
Limited window for upper GI absorption	Drug is mainly absorbable in gut or upper GIT; Prolonged retention enhances bioavailability	Ribovastin, Levodopa, Gabapentin, Furosemide
Better solubility in acidic PH	Drug dissolves better in gastric PH (1-3), improving dissolution and absorption	Metformin HCL, Ciprofloxacin
Local action in stomach	Drug acts directly on gastric mucosa; prolonged contact increases effectiveness	Rantidine HCL, Amoxicillin (H. pylori therapy)
Low solubility at alkaline PH	Drug dissolves poorly in intestinal PH; gastric retention improves availability	Ciprofloxacin, Diltiazem
Short half-life requiring sustained release	Frequent dosing needed; GRDDS provides prolonged therapeutic effect	Diltiazem, Levodopa
Instability in intestinal environment	Drug may degrade in alkaline or enzymatic intestinal conditions	Riboflavin
Low dose requirement (< 1 g)	Smaller dosage form improves gastric retention efficiency	Gabapentin, Ranitidine HCL

DRUGS UNSUITABLE FOR GRDDS

Despite the advantage of GRDDS, certain drugs are not appropriate candidates[24-28]:

1. Drug Unstable in Acidic PH
Drugs that degrade in the conditions that are acidic in the gut are unsuitable. Example such as, erythromycin is acid-labile and undergoes degradation in gastric condition.

2. Drugs Absorbed Throughout the Entire GIT
When a medication is uniformly taken up by the digestive system prolonging gastric retention provides no significant advantages. In such cases, conventional sustained-release formulations are more appropriate.

3. Drugs Causing Gastric Irritation
Medications that cause stomach mucosal irritability should not be prescribed for prolonged gastric residence, as they may increase the risk of ulceration or discomfort.

4. High-Dose Drugs (>1 g)
High-dose drugs require larger dosage forms, which may not be efficiently retained in the stomach. This limits their suitability for gastro-retentive systems.

The success of Grdds largely depends on appropriate drug selection. Ideal candidates include drugs with narrow depends on windows, enhanced solubility in acidic PH, local gastric action, short half-life, and low dose requirements. Conversely, drugs unstable in acidic conditions, absorbed throughout the GIT, causing gastric irritation, or requiring high doses are unsuitable for GRDDS. Therefore, careful evaluation of physiochemical, pharmacokinetic, and pharmacodynamic properties is essential for developing effective and clinically successful gastro-retentive formulations.

Table 2: Drug unsuitability for GRDDS

Category	Reason for unsuitability	Drug Example
Drugs unstable in acidic pH	Degrade in gastric acidic environment; lose activity before absorption	Erythromycin, Penicillin G
Drugs absorbed throughout entire GIT	Uniform absorption along intestine; no benefit from prolonged gastric retention	Paracetamol, Propranolol
High-dose drugs (> 1 g)	Require large dosage form; difficult to retain in stomach	Amoxicillin (high-dose therapy), Metformin (high-dose formulations)

CLASSIFICATION OF GRDDS

Gastro Retentive Medication Administration Mechanisms are optimized to lengthen the gastric intervals of residence of drugs in the gut, Classification of GRDDS is mainly based on the mechanism by which the stomach holds onto the dose form. These mechanisms ensure improved bioavailability, controlled drug release, and enhanced therapeutic efficacy from drugs with specific absorption requirements[29-38].

1 Floatind Drugs Delivery Systems (FDDS)

Principle
The density of floating systems for drug administration is intended to be less than that of stomach fluids (about 1,004 g/cm [3). Because of this, the dose form floated on the external; surface of the stomach fluids without altering the rate at which the stomach empties, The medication has been released gradually & remains under control while floating.

Types

a. Effervescent systems
These systems contain substances that produce gas, for instance sodium bicarbonate along with organic acids such as citric acid & tartaric acid. When the dosage from comes into interaction with GI fluids, carbon dioxide (co_2) was generated. This gas becomes trapped within a polymer matrix, decreasing density and enabling buoyancy.

b. Non-effervescent Systems
These systems rely on swellable polymers like Hydroxy Propyl Methylcellulose (HPMC) & chitosan.When it comes into touch with GI fluids, the polymer becomes hydrated & produces a gel around the tablet, reducing its density and allowing it to float.

Advantages
- Simple and cost-effective formulation
- Suitable for controlled and sustained release
- More effective in fed state (presence of gastric contents improves floating)

Limitations
- Dependence on sufficient gastric fluid volume
- Possible floating lag time before buoyancy occurs

2. Bio adhesive / Mucoadhesive systems

Principle
These devices use bioadhesive polymers to stick to the stomach mucosa. The adhesion occurs due to hydrogen bonding, electrostatic, and physical entanglement between polymer chains and mucus glycoproteins.

Common Polymers
- Carbopol
- Chitosan
- Polycarbophil

- Sodium alginate

Mechanism
After administration, the dosage from attaches to the mucus layer of gut. The adhesion lengthens gastric interval of residence & enhances local drug action, especially useful for drugs targeting gastric conditions.

Challenges
- Continuous mucus turnover reduces adhesion duration
- Variability in adhesion strength due to physiological factors

3. Expandable / Swelling Systems

Principle
Expandable systems are designed to swell rapidly after ingestion, increasing in size beyond the pyloric opening (approximately 12-18 mm). This prevents the dosage form from passing into the intestine.

Mechanism
Hydrophilic polymers absorb gastric fluid and expand significantly. The swollen dosage from remains mechanically retained in the stomach.

Material Used
- Superporous hydrogels
- Cross-linked polymers

Advantages
- Strong mechanical retention
- Independent of gastric fluid density

Risks
- Improper design may cause gastric obstruction
- Requires precise formulation control

4. High-Density Systems

Principle
These systems have a density greater than 2.5 g/cm^3. Due to their high density, they immerse & remain in lower GIT, particularly in gastric folds.

Material used
- Barium sulphate
- Zinc oxide
- Iron powder

Limitations
- Limited clinical success
- Manufacturing challenges in achieving high density uniformly
- Risk of irritation due to heavy materials

5. Superporous Hydrogel Systems

Features
Superporous hydrogels contain interconnected pores that allow rapid water absorption. They swell within minutes after contact with gastric fluid.

Benefits
- Rapid swelling ensures immediate gastric retention
- High mechanical strength prevents collapse
- Can retain large volumes of water

These systems combine the advantages of swelling and mechanical strength for effective retention.

6. Magnetic Systems

Mechanism
In magnetic systems, a tiny inner magnet incorporated into dose form. An external magnet was applied over the stomach to control and maintain the dosage form's location in stomach.

Limitation
- Requires an external magnetic device
- Poor patient compliance
- Practical limitations in routine therapy

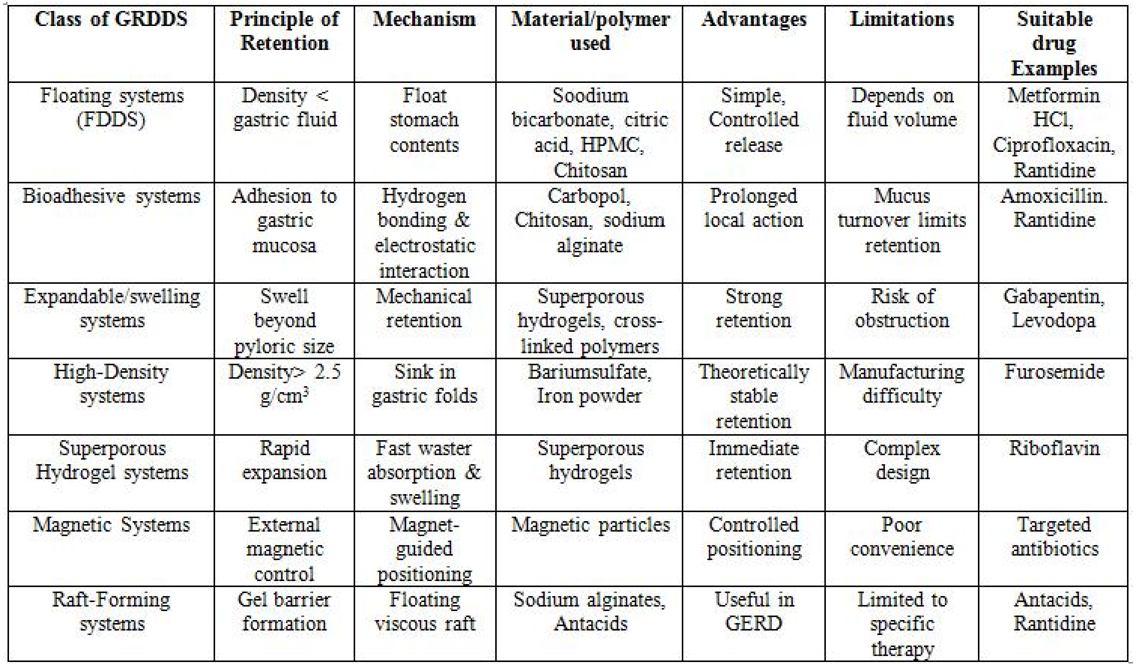
7. Raft-Forming Systems

This devices mainly utilized in the management of Gastroesophageal Reflux Disease (GERD).

Mechanism
Upon contact with gastric fluids, the formulation forms a thick gel or raft which floats atop the stomach fluids, which operates as a protective layer, obstructing acid reflux into oesophagus.

These systems were commonly used in antacid formulations and provide rapid symptomatic relief.

Table 4: Classification of GRDDS



Class of GRDDS	Principle of Retention	Mechanism	Material/polymer used	Advantages	Limitations	Suitable drug Examples
Floating systems (FDDS)	Density < gastric fluid	Float stomach contents	Soodium bicarbonate, citric acid, HPMC, Chitosan	Simple, Controlled release	Depends on fluid volume	Metformin HCl, Ciprofloxacin, Rantidine
Bioadhesive systems	Adhesion to gastric mucosa	Hydrogen bonding & electrostatic interaction	Carbopol, Chitosan, sodium alginate	Prolonged local action	Mucus turnover limits retention	Amoxicillin. Rantidine
Expandable/swelling systems	Swell beyond pyloric size	Mechanical retention	Superporous hydrogels, cross-linked polymers	Strong retention	Risk of obstruction	Gabapentin, Levodopa
High-Density systems	Density> 2.5 g/cm^3	Sink in gastric folds	Bariumsulfate, Iron powder	Theoretically stable retention	Manufacturing difficulty	Furosemide
Superporous Hydrogel systems	Rapid expansion	Fast waster absorption & swelling	Superporous hydrogels	Immediate retention	Complex design	Riboflavin
Magnetic Systems	External magnetic control	Magnet-guided positioning	Magnetic particles	Controlled positioning	Poor convenience	Targeted antibiotics
Raft-Forming systems	Gel barrier formation	Floating viscous raft	Sodium alginates, Antacids	Useful in GERD	Limited to specific therapy	Antacids, Rantidine

LITERATURE REVIEW

Recent advancement in Gastro Retentive Medication Administration Systems, focus in improving gastric retention time, enhancing bioavailability, and achieving predictable controlled release. Traditional single-mechanism system such as floating or Mucoadhesiveformulation often show variability due to physiological factor like gastric motility and pH fluctuations. To overcome these limitations, modern research emphasizes hybrid systems, advance fabrication technologies, nanotechnology integration, smart polymers sophisticated evolution techniques[39-43].

1. Multi-Mechanistic Hybrid System

One of the most significant trend is GRDDS research is the development of multi-mechanistic hybrid systems. These systems combine two or more retention mechanisms-such as floating, swelling, and mucoadhesion-within a single dosage form.

For example, a formulation may initially float due to gas generation while simultaneously swelling to increase its size beyond the pyloric opening. Additionally, mucoadhesive polymers may allow the system to adhere to the gastric mucosa, further prolonging retention. By integrating multiple mechanisms, these systems minimize the weaknesses associated with individual approaches, such as floating lag time or mucus turnover. Hybrid systems have demonstrated improved reliability, prolonged gastric residence, and enhanced drug absorption compared to single mechanism GRDDS.

2. 3D Printed GRDDS

Three-dimensional 3D printing has now considered a game-changing innovation in pharmaceutical formulation. In GRDDS, 3D printing enables customizable geometry, allowing precise control over the size, shapes, and internal architecture of the dosage form.

This technology supports personalized drug release by modifying parameters such as infill density and structural design. As a result, profiles of release of medications can be tailored for meeting patient-specific needs for therapy. Furthermore, 3D printing allows controlled density distribution within the dosage form, ensuring optimal floating behaviour while maintaining mechanical strength. Although promising, constraints with huge-scale manufacturing & regulations approval remain under investigation.

3. Nanotechnology Integration

Nanotechnology serves as an emergent role in boosting GRDDS performance. Researchers have developed formulations in which nanoparticles are embedded within floating or swelling matrices. This combination provides both prolonged gastric retention and nanoscale drug delivery benefits.

Nanoparticles enhance mucosal penetration owing to their decreased size & increased surface area, resulting in improved absorption. They also protect drugs from degradation in harsh gastric conditions, thereby improving stability. Additionally, Nano-encapsulation improves solubility of poorly water-soluble drugs. These advancements significantly enhance therapeutic efficiency and pharmacokinetic performance.

4. Smart Polymers

Smart or stimuli-responsive polymers represent another important innovation in GRDDS research. These polymers respond to environment triggers notably, activity of enxzyme, pH, temperature.

PH-responsive polymers swell or release drugs specifically in acidic gastric conditions. Temperature-responsive hydrogels adjust their structure at body temperature, ensuring controlled expansion and sustained drug release. Enzyme-triggered systems release drugs in response to gastric enzymes, providing site-specific and controlled delivery. Smart polymers improve precision and minimize drug wastage while enhancing therapeutic outcomes.

5. Advanced Evaluation Techniques

Modern evaluation techniques have improved the assessment of GRDDS performance. Gamma scintigraphy and Magnetic Resonance Imaging (MRI) permits real time visual representation of gastric retention & dosage form location within the stomach. Pharmacokinetic modeling helps predict drug absorption and plasma concentration profiles. *In vitro In vivo Correlation (IVIVC)* studies establish relationship between dissolution data and actual biological performance, ensuring formulation reliability.

Recent publications report significant progress in GRDDS technology, including gastric retention times exceeding 12 hours, bioavailability enhancement of 1.5 to 3- fold, and controlled drug release extending beyond 24 hours. These advancements demonstrate the growing potentials of innovative gastro-retentive systems in improving therapeutic efficacy and patient compliance.

NEW TECHNOLOGIES IN GRDDS

Recent technologies advancements have significantly enhanced the design, performance, and clinical applicability of Gastro-retentive Drug Delivery Systems (GRDDS). Emerging technologies focus on precision manufacturing, intelligent formulation design, improved safety, and enhanced therapeutic outcomes[44-48].

1. 3D Printing

Three-dimensional (3D) printing has revolutionized pharmaceutical manufacturing by allowing precise control over dosage form architecture. In GRDDS, 3D printing enables fabrication of hallow floating tablets with internal cavities that reduce density and enhance buoyancy. These hallow structures improve floating time while maintaining mechanical integrity.

Additionally, 3D printing allows development of multi-layered systems, where different drug layers can provide

4. Biodegradable Smart Hydrogels

Biodegradable smart hydrogels represent a safer alternative to traditional expandable systems. These hydrogels swell in the stomach and gradually degrade into harmless byproducts after drug release.

Controlled degradation minimize the risk of gastric obstruction, which is a concern in expandable systems. Smart hydrogels can also be engineered which react to environmental stimulus like pH & temperature, allowing absolute control on release of medication kinetics.

Their biocompatibility & reduced safety risks make biodegradable hydrogels highly attractive for long-term therapy.

5. Floating Microspheres and Microballoons

sustained & immediate release profiles in a single form of dose. This is particularly beneficial for combination therapies.

Another major advantages is the ability to design complex geometries that optimize surface area, density distribution, and swelling behaviour. Customizable designs enables personalized medicine, where drug release profiles can be tailored according to patient needs. Despite its promise, large-scale manufacturing and regulatory validation remain areas of ongoing development.

2. Artificial Intelligence in Formulation

Artificial Intelligence & Machine Learning have been used as emerging tools in pharmaceutical formulations. AI algorithms can predict optimal polymer ratios based on physiochemical properties of drugs. This reduces trial-and-error experimentation and accelerates formulation development.

AI models also helps optimize buoyancy and release kinetics by simulating polymer swelling, drug diffusion, and erosion mechanisms. Predictive modeling ensures consistent gastric retention and controlled drug release. Furthermore, AI enhances quality control by identifying critical formulation parameters that influence performance.

By integrating computational tools with experimental research, AI-driven GRDDS development improves efficiency, reduces cost, and enhances reproducibility.

3. Nanofiber-Based GRDDS

Nanofiber-based system are prepared using electrospinning techniques that produce ultra-thin fibres with high surface area. These nanofibers exhibit rapid swelling upon contact with gastric fluid, promoting effective gastric retention.

The large surface area enhances drug loading and facilitates controlled release. Nanofibers also demonstrate improved adhesion to the gastric mucosa due to increased contact GRDDS promising for targeted gastric therapy.

However, challenges include large-scale production and maintaining uniformity of fiber morphology.

Floating microspheres, also known as microballons, are multiple-unit dosage systems with hollow internal cavities. Their low density allows them to float on gastric content for prolonged periods.

These systems provide a large surface area for drug release and ensure uniform gastric distribution. Unlike single-unit tablets, microspheres reduce the risk of dose dumping and provide more consistent plasma drug concentrations. They are particularly useful for drugs requiring sustained release and enhanced bioavailability.

Advantages of GRDDS

GRDDSoffer several therapeutic and clinical advantages[49-51]:

1. Enhanced bioavailability for drugs with narrow absorption window.
2. Reduced dosing frequency due to sustained release.
3. Improved patient compliance, especially in chronic therapy.
4. Reduced plasma drug fluctuation, minimizing side effects.
5. Targeted gastric therapy for local diseases.
6. Better management of chronic diseases such as diabetes and hypertension.
7. Improved therapeutic index through controlled drug release.
8. Reduced drug waste by optimizing absorption.
9. Potential for local ulcer treatment and gastric infections.
10. Improved stability fro acid-stable drugs retained in gastric environment.

Disadvantages and Limitations

Despite their benefits, GRDDS have certain limitations[52-54]:

1. Dependence on gastric motility and emptying rate.
2. Variability between fed and fasted states affecting retention time.
3. Not suitable for acid-liable drugs.
4. Risk of gastric irritation for certain drugs.
5. Complex formulation techniques requiring careful optimization.
6. Higher production costs compared to conventional dosage forms.
7. Possibility of dose dumping in poorly designed systems.
8. Risk of gastric Obstruction, particularly in expandable systems.
9. Limited suitability for high-dose drugs.
10. Regulatory challenges for novel technologies like 3D printing and nanotechnology.

Application of GRDDS

GRDDS have wide clinical applications, particularly in chronic and gastric-specific diseases[55-57]:

1. Parkinson's disease (Levodopa)
2. Type 2 diabetes (Metformin)
3. Hypertension (Diltiazem)
4. Peptic ulcer disease
5. Therapy of Helicobacter pylori eradication.
6. Management of Gastroesophageal reflux disease (GERD)
7. Vitamin supplementation (e.g., Riboflavin)
8. Antibiotic therapy requiring gastric targeting
9. Local treatment of gastric tumours
10. Controlled NSAID delivery for reduced systemic effects

In conclusion, emerging technologies such as 3D printing, artificial intelligence, nanofibers, smart hydrogels, and floating microspheres are transforming GRDDS into highly precise and efficient drug delivery platforms. While certain limitations remain, their strong clinical potential in managing chronic and gastric-specific diseases makes them a promising area of pharmaceutical research and development.

CONCLUSION

Gastro retentive medication administration mechanisms, represents as extremely hopeful strategy to enhance oral drug therapy. By lengthening gastric interval of residence, these systems, improve bio-availability, ensures regulated release, & optimize therapeutic outcomes for medications with limited absorption window & localised gastric activity.

This integration of advanced materials, smart polymers, nanotechnology, and 3D printing has transformed GRDDS into a next-generation drug delivery platform. Despite certain physiological and manufacturing challenges, continuous research and technological innovation are expanding the scope of GRDDS application.

Future directions include:

- AI-guided formulation design
- Personalized medicine
- Biodegradable expandable systems
- Commercial scale-up technologies

With sustained scientific advancement, GRDDS are expected to become mainstream in advanced oral controlled drug delivery.

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