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DESIGN, DEVELOPMENT, AND APPLICATIONS OF GASTRO-RETENTIVE FLOATING DRUG DELIVERY SYSTEM: AN UPDATED REVIEW

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Abstract:

Gastro-retentive floating drug delivery systems (GRFDDS) have emerged as a pivotal strategy in the design of oral sustained release formulations. These systems aim to improve the bioavailability and therapeutic efficacy of drugs by increasing their gastric residence time. GRFDDS are particularly beneficial for drugs that are poorly soluble in the alkaline pH of the intestine, drugs with a narrow absorption window in the upper gastrointestinal tract (GIT), and those intended for local action in the stomach. Various techniques, including effervescent and non-effervescent mechanisms, have been employed to ensure the buoyancy of the dosage form. The present review provides an updated and critical insight into the design principles, formulation strategies, polymers and excipients used, evaluation techniques, and current clinical applications of GRFDDS. Moreover, recent advancements, challenges, and future prospects are discussed to understand the evolving role of these systems in drug delivery science.

Keywords: *Gastro-retentive drug delivery system, Floating dosage forms, Buoyancy, Controlled release, Gastric residence time.*

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1. INTRODUCTION:

The oral route is widely recognized as the most favorable and convenient method for drug administration, accounting for nearly 90% of all marketed pharmaceutical products [1]. However, the efficacy of conventional oral drug delivery systems is often compromised due to factors such as unpredictable gastric emptying time, short gastric residence, and poor drug solubility in the intestinal environment [2]. To overcome these physiological constraints, Gastro-Retentive Drug Delivery Systems (GRDDS) particularly floating drug delivery systems (FDDS) have been developed to enhance drug bioavailability and sustain drug release within the upper gastrointestinal tract [3].

GRFDDS are dosage forms engineered to remain buoyant in gastric fluid for prolonged periods, thereby maximizing drug release at the desired absorption site [4]. These systems exploit the concept of low-density formulations that float on gastric fluid and resist gastric emptying. Floating systems can be broadly categorized into effervescent systems (based on gas generation) and non-effervescent systems (based on polymer swelling or matrix integrity) [5]. The extended gastric retention is highly beneficial for drugs that are absorbed in the stomach or proximal small intestine, are unstable at intestinal pH, or have limited solubility in alkaline conditions [6].

The development of GRFDDS involves a multidimensional approach, integrating physicochemical properties of the drug, formulation excipients, physiological factors, and mechanical design considerations. Moreover, polymers play a critical role in maintaining matrix integrity, modulating release, and ensuring floating behavior [7]. The utility of natural, semi-synthetic, and synthetic polymers in developing these systems has been widely reported in the literature [8].

Several marketed products such as Madopar® (levodopa), Valrelease® (diazepam), and Cifran OD® (ciprofloxacin) utilize gastro-retentive strategies to improve therapeutic outcomes [9]. The research interest in GRFDDS has significantly grown over the last decade due to advances in polymer science, formulation technology, and in vitro–in vivo correlation techniques [10].

2. Mechanism of Gastro-Retentive Floating Drug Delivery Systems (GRFDDS)

The central goal of gastro-retentive drug delivery systems (GRDDS) is to increase the gastric residence time (GRT) of a dosage form to improve drug absorption in the upper gastrointestinal tract (GIT). Among the various GRDDS, floating drug delivery systems (FDDS) are the most widely explored. FDDS work based on the principle of buoyancy, i.e., they float on gastric fluids and avoid premature passage into the intestine [11].

2.1 Floating Mechanism

The floating behavior of a dosage form is governed by the density difference between the dosage form and the gastric content. To remain buoyant, the formulation must have a bulk density less than that of gastric fluid, which is approximately 1.004–1.010 g/cm³ [12].

Once administered, the floating system swells and/or forms a gel barrier to trap gas (either internally generated or externally present), reducing its density. The formulation floats on the stomach contents, releasing the drug slowly at a desired rate [13].

2.2 Types of Floating Systems

Floating systems can be categorized into:

(a) Effervescent Systems: These systems generate carbon dioxide gas (CO_2) upon contact with gastric fluids, usually through the reaction of acidic components (e.g., citric acid) with carbonates or bicarbonates (e.g., sodium bicarbonate) [14]. The CO_2 gets trapped within the matrix, making the dosage form buoyant. Effervescent systems can be:

- Single-layer tablets: Contain gas-generating and gel-forming agents.
- Bilayer tablets: One layer for immediate release and the other for sustained floating.
- Multiple-unit systems: Capsules containing multiple floating beads or tablets.

(b) Non-effervescent Systems: These rely on gel-forming polymers such as hydroxypropyl methylcellulose (HPMC), xanthan gum, or alginate that swell upon hydration, forming a low-density, floating structure without generating gas [15]. Such systems often use Hydrodynamically balanced systems (HBS), Alginate beads, Microballoons (hollow microspheres)

2.3 Role of Hydrodynamics and Gastric Motility

Gastric emptying is influenced by several physiological factors like Fasting or fed state, Posture, Size and shape of the dosage form, Caloric content of gastric content, Patient variability (age, disease, gender) [16]

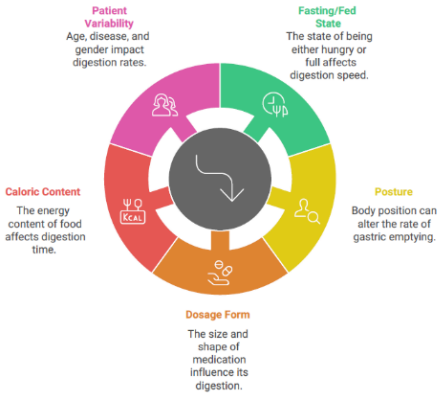

Fig 1: Factors influencing gastric emptying.

In the fasted state, the Migrating Myoelectric Complex (MMC) clears the stomach every 90–120 minutes, reducing GRT. In the fed state, gastric emptying is delayed, enhancing the retention time of floating systems [17].

2.4 Advantages of Floating Mechanism

a) Prolonged gastric retention, allowing drug release in a controlled manner.
b) Improved bioavailability of drugs absorbed in the stomach or upper intestine.
c) Reduced dosing frequency, enhancing patient compliance.
d) Local delivery to treat gastric infections (e.g., *Helicobacter pylori*).
e) Minimized drug waste, especially for unstable drugs in the intestinal environment [18][19].

3. Design Strategies for Gastro-Retentive Floating Drug Delivery Systems (GRFDDS)

The successful formulation of GRFDDS relies on a strategic combination of physiological, physicochemical, and mechanical design considerations to ensure prolonged gastric retention, controlled drug release, and effective therapeutic outcomes. Several dosage form designs and strategies have been developed over the years to achieve and maintain gastric buoyancy. These include effervescent, non-effervescent, hollow microspheres, multi-unit systems, and floating raft systems.

3.1 Factors Affecting GRFDDS Design:

A robust formulation must take into account:

- Drug properties: solubility, pKa, absorption window, stability at low pH.
- Dosage form density: must be <1.0 g/cm³ for effective floatation.
- Gastric motility and emptying rate: varies with fed/fasted state.
- Food interaction: high-fat meals can increase retention time [20-22].

3.2 Effervescent Floating Systems

Effervescent systems are designed to release CO_2 through the interaction of acid and carbonate sources (e.g., citric acid and sodium bicarbonate). The gas generated gets entrapped in the gel matrix formed by swellable polymers, providing buoyancy.

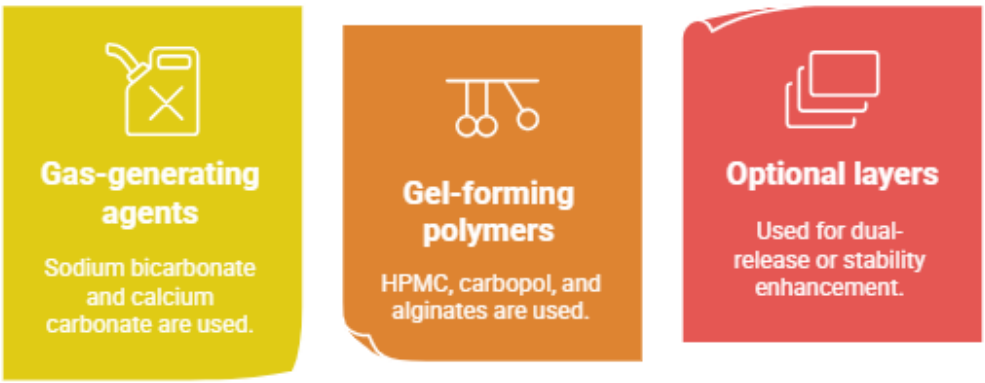

Fig 2: Formulation components

Non-Effervescent Floating Systems: These systems do not generate gas but rely on the swelling or gelling properties of hydrophilic polymers to decrease system density and maintain buoyancy. Types are

- Hydrodynamically balanced systems (HBS): Matrix-forming polymers like HPMC and ethyl cellulose maintain buoyancy.
- In situ gel systems: Liquid formulations that gel upon contact with gastric acid.

- Floating beads and tablets: Prepared using ionotropic gelation or freeze-drying techniques [23][24].

Floating Hollow Microspheres (Microballoons)

These are low-density, hollow spherical particles that remain buoyant on gastric fluid. They offer increased surface area, uniform drug distribution, higher entrapment efficiency. Preparation methods include solvent evaporation, emulsion diffusion, and spray drying, it is used for drugs like propranolol, metronidazole, and riboflavin [25].

3.3 Multi-Unit Floating Dosage Systems

These systems consist of multiple small units (pellets, beads, granules) encapsulated within a single dosage form. Benefits include reduced risk of dose-dumping, consistent gastric retention, even in variable pH or motility states; minimized inter-patient variability [26].

3.4 Floating Raft System

Primarily used for liquid dosage forms, these systems form a viscous cohesive gel or raft on contact with gastric acid. Common in anti-reflux formulations (e.g., alginate-based Gaviscon®).

Mechanism: Sodium alginate reacts with gastric acid to form a viscous gel.

Gel entraps CO_2 and floats on gastric contents, forming a protective raft [27].

3.5 Innovations in GRFDDS Design

Recent trends include:

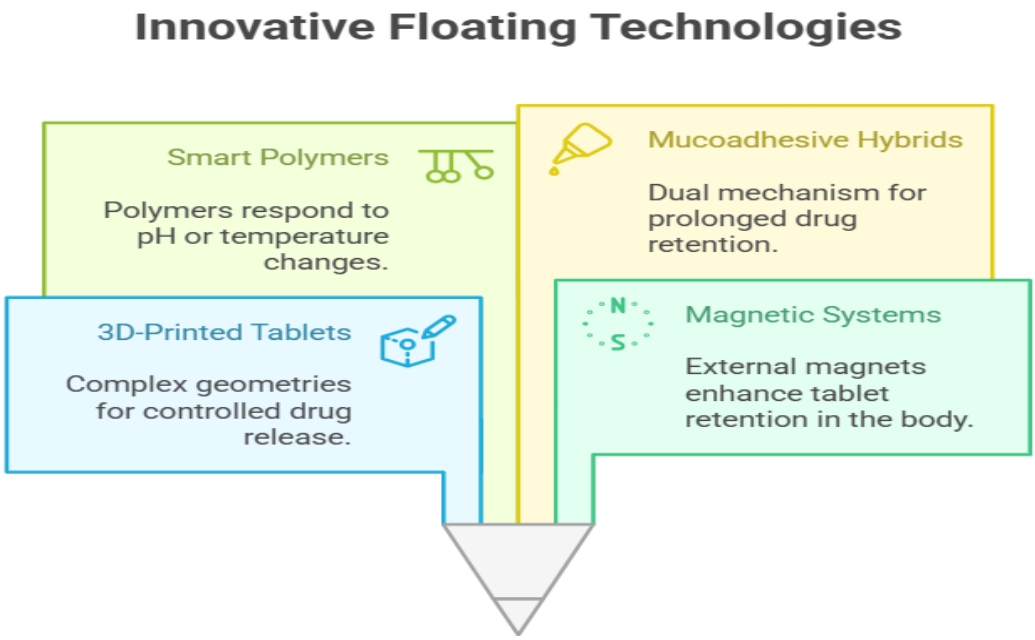

Fig 3: Recent trends in GRFDDS

These innovations aim to personalize therapy, improve precision, and enhance therapeutic outcomes [28][29].

4. Polymers and Excipients Used in GRFDDS

Polymers and excipients are the backbone of gastro-retentive floating drug delivery systems (GRFDDS). They contribute to matrix formation, swelling, buoyancy, drug release modulation, and overall structural integrity. The selection of an appropriate polymer directly influences the floating behavior, drug release kinetics, and gastric residence time of the dosage form.

4.1 Ideal Characteristics of Polymers for GRFDDS

An ideal polymer used in GRFDDS should:

- Be non-toxic and biocompatible.
- Have good swelling and gelling abilities.
- Exhibit controlled hydration rate.
- Maintain mechanical strength in acidic conditions.
- Be compatible with the drug and other excipients [30].

4.2 Types of Polymers Used in GRFDD

Polymers used in GRFDDS are broadly classified into:

(a) Natural Polymers: These are biodegradable and generally safe, widely used in matrix formulations and gel systems.

Polymer	**Function**	**Example Use**
Guar gum	Swelling & matrix former	Sustained floating tablets
Xanthan gum	Gel-forming	pH-independent release
Sodium alginate	Raft formation & ionotropic gelation	In-situ gels
Chitosan	Mucoadhesive & pH-sensitive	Coated beads/microspheres [31][32]

(b) Semi-Synthetic Polymer: These are chemically modified natural polymers, offering improved functional properties.

Polymer	Role in GRFDDS
Hydroxypropyl methylcellulose (HPMC)	Primary matrix former, swelling agent
Carboxymethyl cellulose (CMC)	Floating support and drug release control
Ethyl cellulose (EC)	Insoluble film former, used in multilayer tablets

Different grades of HPMC (e.g., K4M, K15M, K100M) are chosen based on viscosity and gel strength [33].

(c) Synthetic Polymers: These are man-made materials offering precise control over formulation behavior.

Polymer	Role
Polyvinyl alcohol (PVA)	Film-forming and matrix support
Eudragit® RL/RS	pH-independent release & buoyancy
Polylactic-co-glycolic acid (PLGA)	Biodegradable sustained release microspheres [34]

4.3 Excipients in GRFDDS:

Besides polymers, excipients play key roles in ensuring system performance.

Excipient	Purpose
Sodium bicarbonate	Gas-generating agent for effervescent systems
Citric acid/tartaric acid	Acid sources for CO_2 generation
Lactose, mannitol	Fillers to adjust tablet density
Magnesium stearate	Lubricant for tablet compression
Gelatin/PEG	Capsule formation and surface modifiers [35]

4.4 Polymer Combinations and Their Synergistic Effects:

Many GRFDDS formulations employ binary or ternary polymer combinations to achieve desirable release and buoyancy profiles. For example:

- HPMC + EC: Enhances matrix integrity while modulating release.
- Xanthan gum + chitosan: Improves mucoadhesion and gel formation.
- Sodium alginate + PVA: Offers better structural retention in raft systems [36].

4.5 Polymer Role in Micro/Nano Formulations:

In modern GRFDDS, polymers are used to prepare:

- Floating microspheres using HPMC, Eudragit RS/RL.
- Nanoparticles for high surface area drug release.
- Mucoadhesive nano-floating carriers combining chitosan and PLGA.
- These systems offer enhanced control, site-specific targeting, and reduced variability in gastric retention [37,38].

Table: Comparative Overview of Polymers in GRFDDS

Polymer	Type	Function in GRFDDS	Advantages	Limitations
HPMC (Hydroxypropyl Methylcellulose)	Semi-synthetic	Matrix formation, gelation, release modulation	Widely available, multiple viscosity grades	May swell excessively, slower drug release
Xanthan Gum	Natural	Swelling, gelation	Biodegradable, non-toxic	Sensitive to ionic strength
Sodium Alginate	Natural	Ionotropic gel formation, raft systems	Forms gels at low pH, fast response	Brittle, low mechanical strength
Chitosan	Natural	Mucoadhesion, gel formation	Biocompatible, pH responsive	Poor solubility at neutral pH
Ethyl Cellulose (EC)	Semi-synthetic	Sustained release coating, low permeability	Water-insoluble, excellent film former	Non-biodegradable, slow hydration
Carbopol	Synthetic	Thickener, bioadhesion	Strong mucoadhesion, low concentration required	pH-sensitive swelling
Polyvinyl Alcohol (PVA)	Synthetic	Binder, film former in microspheres	High mechanical strength, biocompatible	Not biodegradable
Eudragit® RL/RS	Synthetic	pH-independent sustained release	Customizable permeability	High cost, polymer interaction concerns
Guar Gum	Natural	Swelling and controlled drug release	Readily available, low cost	Microbial instability, batch variability
PLGA (Polylactic-co-glycolic acid)	Synthetic	Biodegradable microspheres/nanoparticles	FDA approved, customizable degradation profile	Expensive, complex formulation process

5. In Vitro and In Vivo Evaluation of GRFDDS

The performance of gastro-retentive floating drug delivery systems (GRFDDS) is validated through a series of in vitro and in vivo tests. These evaluations ensure that the dosage form meets the intended design specifications in terms of buoyancy, drug release, and gastric retention.

5.1 In Vitro Evaluation Techniques

a. *Buoyancy Test:* This test evaluates two key parameters: floating lag time (time taken to float) and total floating duration. An ideal GRFDDS should exhibit a short lag time (<2 minutes) and prolonged floatation (>12 hours). This simulates the gastric retention behavior under physiological conditions and is considered essential for preliminary screening of formulations [39].

b. *Swelling Index:* Swelling index indicates the water uptake capacity of the polymer matrix, which directly affects the formulation's buoyancy and drug release. A higher swelling index typically correlates with extended floating time and controlled drug diffusion through the hydrated gel barrier. It is particularly relevant in non-effervescent GRFDDS [40].

Swelling Index (SI) = [(Wt - W0) / W0] × 100

(Where Wt = weight after swelling, W0 = initial weight)

Drug Release Studies: Controlled and sustained drug release is the core objective of GRFDDS. Drug release is evaluated in acidic media (pH 1.2), simulating gastric conditions. The resulting data is interpreted using mathematical models such as Higuchi, Korsmeyer–Peppas, and zero/first-order kinetics to identify the release mechanism [41].

Matrix Integrity and Erosion: Maintaining matrix integrity is vital for prolonged gastric retention. Excessive erosion or disintegration can lead to premature gastric emptying. The physical stability of the formulation is monitored over time to assess its robustness in acidic environments.

Density and Porosity: Formulations must possess a density lower than gastric fluid to remain buoyant. Measuring porosity helps predict the rate of water penetration, gas entrapment, and swelling—all of which influence floatation and drug release.

5.2 In Vivo Evaluation Techniques

Radiographic Imaging (X-Ray): Used to confirm gastric retention by incorporating radiopaque markers such as barium sulfate into the dosage form. Sequential imaging tracks its location in the gastrointestinal tract. While effective, this method is limited by radiation exposure and lack of functional insight into drug release [41].

Gamma Scintigraphy: A highly sensitive nuclear imaging method that enables real-time tracking of the formulation using gamma-emitting isotopes. It provides data on gastric retention time, disintegration behavior, and transit kinetics, and is often considered the gold standard, albeit with cost and regulatory limitations [42].

Pharmacokinetic Analysis: This method quantifies the absorption characteristics of the drug, particularly Cmax, Tmax, and AUC values. GRFDDS typically demonstrate prolonged Tmax and reduced Cmax fluctuations, which are indicative of controlled absorption and improved bioavailability.

1. *Ultrasonography*: A non-invasive imaging technique that visualizes dosage form movement within the stomach. Although less precise than scintigraphy, it is safer for human studies due to the absence of **radiation.**

5.3 In Vitro–In Vivo Correlation (IVIVC)

IVIVC is critical for predicting in vivo behavior from in vitro data. A Level A correlation (point-to-point) is ideal and supports regulatory approval and batch-to-batch consistency. However, achieving IVIVC in GRFDDS is often complicated by variability in gastric motility, pH, and fed/fasted states.

6. Clinical Applications and Marketed GRFDDS Products

Gastro-retentive floating drug delivery systems (GRFDDS) have demonstrated immense therapeutic value in the clinical management of diseases that benefit from localized action in the stomach or enhanced absorption in the upper gastrointestinal tract (GIT). By prolonging the residence time in the stomach, GRFDDS not only improve drug absorption and bioavailability but also offer reduced dosing frequency, better patient compliance, and targeted delivery.

6.1 Clinical Applications

i. *Drugs with Narrow Absorption Windows:* Drugs like levodopa, riboflavin, and ciprofloxacin are primarily absorbed in the

upper GIT. GRFDDS improve therapeutic efficacy by maintaining the drug in the absorption zone for an extended period.

ii. *Drugs Unstable in Alkaline pH:* Some drugs degrade rapidly in the intestinal (alkaline) environment but remain stable in gastric acid. For example, ranitidine and metformin exhibit better stability and absorption in the stomach.

iii. *Localized Stomach Action:* Diseases such as gastric ulcers, gastritis, or Helicobacter pylori infections require the drug to act directly on the stomach lining. GRFDDS enhance the local therapeutic effect and reduce systemic exposure. Antibiotics like amoxicillin, clarithromycin, and metronidazole are often formulated in this way.

iv. *Sustained Release for Chronotherapy:* GRFDDS allow chronotherapeutic alignment of drug release, such as in nocturnal acid breakthrough in GERD patients, by floating overnight and releasing drugs like famotidine in a controlled manner.

v. *Drugs with Low Solubility at High pH:* Certain drugs (e.g., furosemide) are more soluble in acidic pH and exhibit poor solubility in the intestine. Floating systems enhance dissolution in the stomach before transit to the intestine.

6.2 Marketed GRFDDS Products

Here's a curated table of prominent floating systems already available in the market:

Table: Selected Marketed GRFDDS Products

Product Name	Active Drug	GRFDDS Type	Indication	Manufacturer
Madopar® HBS	Levodopa + Benserazide	Hydrodynamically balanced capsule	Parkinson's Disease	Roche
Valrelease®	Diazepam	Floating capsule	Anxiety	Hoffmann-La Roche
Cifran OD®	Ciprofloxacin	Floating matrix tablet	Bacterial infections	Ranbaxy
Almagate®	Almagate	Floating antacid tablet	Hyperacidity	Astellas
Liquid Gaviscon®	Sodium alginate + sodium bicarbonate	Raft-forming system	GERD	Reckitt Benckiser
Conviron®	Ferrous sulfate	Floating controlled release	Iron deficiency anemia	Solvay Pharma
Mosapride GR®	Mosapride citrate	Gastro-retentive tablet	Gastroparesis	Abbott
Metformin SR	Metformin HCl	Floating sustained-release tablet	Type 2 Diabetes	Multiple brands
Ofloxacin SR	Ofloxacin	Floating matrix tablet	GI infections	Cipla

7. Recent Advancements and Emerging Trends in GRFDDS

Over the past decade, gastro-retentive floating drug delivery systems (GRFDDS) have evolved from simple effervescent tablets to complex, multifunctional platforms incorporating smart polymers, precision release mechanisms, and advanced manufacturing techniques. These innovations aim to overcome limitations of conventional systems such as variability in gastric retention, formulation rigidity, and drug release inconsistency while enabling personalized therapy, better targeting, and regulatory compliance.

7.1 Use of Smart Polymers and Stimuli-Responsive Systems

Recent studies have focused on stimuli-responsive polymers that adapt to physiological changes in pH, temperature, or enzymes. These "smart" polymers allow site-specific drug release and controlled swelling, enhancing therapeutic efficiency.

- pH-sensitive systems: Remain stable in acidic gastric pH but degrade in intestinal pH.
- Thermo-responsive systems: Use temperature-sensitive polymers (e.g., poloxamers) for in situ gelation.
- Mucoadhesive-floating hybrids: Combine floatation and mucosal adhesion for dual gastric retention mechanisms [43][44].

7.2 Nanotechnology-Based Floating Systems

Nano-floating systems offer enhanced solubility, stability, and targeting efficiency. Examples include:

- Floating nanospheres, liposomes, and nanoemulsions for drugs with poor solubility.
- Use of PLGA, Eudragit, or PEGylated polymers to formulate nanoparticle-based carriers.
- These systems are being investigated for chemotherapeutics, peptides, and biologics, which are typically unstable in the gut [45].

7.3 3D Printing in GRFDDS

The advent of 3D printing technology enables tailor-made floating systems with complex geometries that enhance floatation and drug release control.

- Fused Deposition Modeling (FDM) and Inkjet printing are used to fabricate gastro-retentive tablets with specific porosity and density.
- 3D-printed tablets can contain multiple compartments, each with a distinct release profile, facilitating chronotherapy [46].

7.4 Magnetically Controlled GRFDDS

These systems embed a magnet or magnetic particles into the dosage form. An external magnet can be applied to control:

- Position of the dosage form in the stomach.
- Duration of retention.
- Local delivery, especially for stomach-specific infections or tumors.

Though still under investigation, such systems have shown promise in animal and small-scale human studies [47].

7.5 Floating Osmotic Systems

Osmotic pumps have been adapted for gastro-retentive applications, combining floatation with zero-order drug release. They work independently of gastric motility and provide precise, consistent release profiles over 12–24 hours [48].

7.6 **Biodegradable and Eco-friendly Systems**

Environmental safety and regulatory scrutiny have led to the development of biodegradable GRFDDS using natural polymers like gum karaya, gelatin, and tamarind seed polysaccharides. Green manufacturing methods using minimal organic solvents. These align with green pharma initiatives and are better suited for chronic therapies [49].

Personalized GRFDDS and AI-Guided Formulation

With the growth of AI/ML in pharmaceutical formulation, predictive modeling helps:

- Optimize polymer ratios.
- Predict drug release profiles.
- Simulate in vivo performance (e.g., via in silico IVIVC models). This helps design patient-centric GRFDDS based on gender, age, diet, and gastric physiology variations [50].

7.8 Regulatory and Industrial Trends

- FDA and EMA are increasingly requiring biorelevant in vitro models and IVIVC data.
- Quality by Design (QbD) and Process Analytical Technology (PAT) are being incorporated for better control.
- Pharmaceutical giants are investing in multifunctional delivery platforms, combining gastro-retention, sustained release, and mucoadhesion in a single dosage unit [51].

8. Challenges, Limitations, and Future Perspectives in GRFDDS

While gastro-retentive floating drug delivery systems (GRFDDS) have made significant strides in enhancing oral bioavailability and therapeutic effectiveness, their clinical and industrial success still faces multiple challenges. These arise from physiological variability, formulation complexities, and regulatory barriers, all of which limit universal adoption across drug classes.

Physiological Challenges

Variability in Gastric Emptying

Gastric motility is highly variable across individuals and affected by age, gender, posture, disease state, and fed/fasted condition. In the fasted state, the Migrating Myoelectric Complex (MMC) can lead to sudden expulsion of dosage forms. This variability makes predictable retention difficult [52].

Floating Failures in Fasted State

In absence of food, gastric contractions are stronger and more frequent, increasing the risk of dosage form expulsion before complete drug release. GRFDDS are better suited for the fed state, but that introduces compliance issues regarding administration timing [53].

i. Limited Absorption Window

a. Even with extended gastric retention, drugs with absorption windows only in the duodenum or jejunum may not benefit. For instance, certain peptides, proteins, or macromolecules are still poorly absorbed due to enzymatic degradation and tight junction barriers [54].

8.2 Formulation and Technological Limitations

a) *Floating Lag Time:* Systems that do not float immediately after administration can fail to retain in stomach and enter the intestine prematurely.

b) *Drug Dose and Loading Limitations:* Floating systems are less suitable for high-dose drugs or drugs requiring rapid onset, as the floatation mechanism generally supports sustained release. Uniform distribution of drug and gas-forming agents in the matrix is technically challenging [55].

c) *Complex Manufacturing Processes:* Multilayer tablets, hollow microspheres, and 3D-printed formulations demand precise control, often leading to scalability and cost challenges. Reproducibility and long-term stability under humidity-sensitive conditions are concerns [56].

8.3 Regulatory and Commercial Challenges

- IVIVC for GRFDDS is hard to establish due to the dynamic nature of gastric physiology.
- There's a lack of standardized testing protocols for in vitro floating and retention behavior.
- High development and validation costs restrict commercial entry, especially for generic companies.
- Regulatory agencies may demand additional in vivo imaging studies (e.g., scintigraphy), which increases timelines and cost [57].

8.4 Future Perspectives

Despite the limitations, ongoing innovations suggest a strong future for GRFDDS:

i. *Integration with Artificial Intelligence:* AI/ML-based formulation modeling can reduce development time and optimize floating and release profiles based on simulated gastric environments [58].

ii. *Personalized GRFDDS:* Use of patient-specific data (e.g., gut microbiota, gastric pH) to design customized floating systems using 3D printing and biosensors.

iii. *Mucoadhesive*: Floating Hybrid Systems: Combining mucoadhesion and floatation ensures dual retention mechanisms for drugs needing localized action or extended release.

iv. *Smart Polymers and Biopolymers:* Future systems may use biosmart materials that respond to stimuli like pH, enzyme activity, or pressure, optimizing release.

v. *Floating Bio-Nanocomposites:* Nano-sized floating systems with targeting ligands and biodegradable carriers offer hope for drugs with narrow therapeutic windows or poor solubility.

vi. *Industrial Adaptation:* Enhanced QbD, PAT, and continuous manufacturing techniques will facilitate the scale-up of GRFDDS with consistent quality [59].

9. CONCLUSION:

Gastro-retentive floating drug delivery systems (GRFDDS) offer a promising solution to the limitations of conventional oral drug delivery by enabling prolonged gastric retention, controlled drug release, and enhanced bioavailability particularly for drugs with narrow absorption windows, poor solubility at higher pH levels, or those requiring localized gastric action. Over time, GRFDDS have evolved from basic effervescent matrices to advanced technologies such as mucoadhesive systems, nanoparticles, 3D-printed platforms, and AI-assisted smart devices, with polymers playing a critical role in modulating drug release through their swelling, gelling, and buoyancy properties. Despite their advantages, GRFDDS face challenges including gastric motility variability, manufacturing scalability, drug-loading limitations, and regulatory complexities. However, emerging innovations in intelligent polymer design, predictive modeling, and personalized delivery are paving the way for more effective and patient-centered therapies. The future of GRFDDS lies in the integration of materials science, artificial intelligence, and personalized medicine to deliver more precise, efficient, and user-friendly drug delivery systems.

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