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Review Article

Gastroretentive Swellable and Floating Systems: An Innovative and Promising Strategy for Drug Delivery-A Comprehensive Review

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Abstract

Gastroretentive drug delivery systems (GRDDs) have emerged as an innovative and promising approach for enhancing the bioavailability and therapeutic efficacy of drugs with narrow absorption windows in the upper gastrointestinal tract (GIT). Among various GRDDs, swellable and floating systems have garnered significant attention due to their ability to prolong gastric residence time, improve drug dissolution, and facilitate sustained drug release (SDR). This comprehensive review provides a detailed exploration of the principles, mechanisms, and advancements in swellable and floating Gastroretentive systems. The key strategies, such as the use of hydrophilic polymers, gas-generating agents, and superporous hydrogels, are discussed. These systems offer benefits in treating conditions like peptic ulcers, gastroesophageal reflux disease, and infections, where prolonged localized drug action is desirable. A critical assessment of recent preclinical and clinical studies highlights the therapeutic potential of GRDDs in optimizing drug delivery for poorly soluble drugs and drugs with short half-lives. Challenges such as variability in gastric retention, potential toxicity of excipients, and patient-specific factors are also examined. It includes the outlining future trends in GRDDs, focusing on the incorporation of nanotechnology, 3D printing, and biocompatible materials to overcome existing limitations and further enhance therapeutic outcomes. This highlight of review article is initially introduction of GRDDs and their significance, mechanism and their classification of GRDDs, intermediately describe brief on swelling and floating GRDDs system with their application, lastly it describes the recent advances in patent, clinical trials and marketed products for GRDDs swellable and floating system.

Keywords: Drug delivery; GRDDs; floating; swellable; gastroretentive; system; advance approach

1. INTRODUCTION

Drug delivery refers to the methods or processes used to transport a pharmaceutical compound to its target site in the body to achieve a therapeutic effect. The goal of DDs is to optimize the drug's BA, stability, and efficacy while minimizing side effects [1]. These systems can be designed for various routes of administration, such as oral, injectable, transdermal, or inhalation, and may include advanced technologies like nanocarriers, controlled-release formulations, or targeted delivery strategies. By ensuring the right amount of the drug reaches the desired site at the appropriate time, drug delivery systems improve treatment outcomes and patient compliance [2-3].

Gastroretentive Drug Delivery Systems (GRDDs) are specialized DDs designed to prolong the retention of a dosage form in the stomach. These systems are beneficial for drugs that are absorbed primarily in the stomach or upper part of the GIT, have a narrow absorption window, or are unstable in the alkaline pH of the intestines [4]. By staying in the stomach for an extended time, GRDDs can enhance drug BA, provide controlled or sustained drug release, and improve therapeutic efficacy. Types of GRDDS include floating systems, bioadhesive systems, swellable systems, high-density systems, and magnetic systems, each employing different mechanisms to increase gastric retention and optimize drug delivery [3-5].

1.1. *Importance of GRDDs:*

The importance of GRDDs can be highlighted as follows:

- **Prolonged Gastric Retention:** Ensures the drug stays in the stomach longer, allowing extended release and improved therapeutic outcomes.
- **Enhanced Bioavailability:** Increases drug absorption for drugs with a narrow absorption window in the stomach or upper GI tract.
- **Improved Drug Stability:** Protects drugs that are unstable in the alkaline environment of the intestines.

- **Targeted Drug Release:** Ideal for local treatment of gastric conditions (e.g., ulcers or infections like *Helicobacter pylori*).
- **Reduced Dosing Frequency:** By maintaining sustained release, GRDDs can reduce the need for frequent dosing, improving patient compliance.
- **Minimized Drug Wastage:** Prevents premature drug passage into the intestines, maximizing therapeutic efficacy.
- **Controlled Drug Release:** Provides a steady, controlled release of medication over time, reducing fluctuations in plasma drug concentration [6-8].

GRDDs offer several merits and demerits in drug delivery. Merits include prolonged gastric retention, which ensures a sustained release of the drug in the stomach, improving BA, especially for drugs that are absorbed in the upper GIT [9]. GRDDs are beneficial for drugs with narrow absorption windows and those that degrade in the alkaline pH of the intestine. They also reduce dosing frequency, which can improve patient compliance, especially in long-term therapies. Moreover, they can help in local drug action in the stomach, such as in the treatment of gastric ulcers. However, GRDDs also have demerits. Their success is highly dependent on individual gastric motility and emptying, which can vary due to factors like age, diet, and disease conditions [10-11]. Additionally, these systems may not be suitable for drugs that are unstable in acidic conditions or drugs that cause gastric irritation. The size of the dosage form must be large enough to avoid premature gastric emptying but not so large that it causes discomfort [12]. Formulation complexity and higher production costs also pose challenges for widespread use of GRDDS.

1.2. *Significance of Extended Gastric Retention:*

Extended gastric retention is a crucial feature of GRDDs, significantly impacting therapeutic effectiveness and patient compliance [13]. By prolonging the presence of a drug in the stomach, these systems enhance the BA of medications that are primarily absorbed in this region, ensuring that a larger fraction of the drug reaches the systemic circulation. This is particularly beneficial for drugs with a narrow absorption window, as it allows for improved therapeutic outcomes and reduced variability in drug response [14]. Additionally, extended gastric retention can facilitate controlled or sustained release of the drug, minimizing the frequency of dosing and thus improving patient adherence to prescribed regimens. Furthermore, it can enhance the stability of certain medications that may degrade in the more alkaline environment of the intestines, ensuring that patients receive the intended therapeutic benefits [13-16]. The significance of extended gastric retention lies in its ability to optimize drug delivery, improve treatment efficacy, and enhance the overall patient experience.

GRDDs represent a novel approach in drug delivery designed to improve the BA and therapeutic efficacy of drugs that have narrow absorption windows in the upper GIT. By prolonging the gastric retention time, GRDDs enables the drug to remain in the stomach for extended periods, ensuring sustained release and better absorption [17]. This system is especially beneficial for drugs that are poorly soluble in alkaline environments, have a short half-life, or are primarily absorbed in the stomach or proximal small intestine. The various strategies, such as floating systems, bioadhesive systems, and expandable devices, are employed to achieve gastroretention. GRDDs enhances patient compliance by reducing dosing frequency and offers a controlled, localized drug release, making it ideal for treating gastric disorders or improving the therapeutic outcomes of certain systemic diseases [18-19].

2. MECHANISM AND CLASSIFICATION OF GASTRORETENTIVE DRUG DELIVERY (GRDDs)

GRDDs function primarily through mechanisms that enhance the residence time of drugs in the gastric region, improving their absorption and therapeutic efficacy [20]. These systems can be classified into several categories: floating systems, which remain buoyant in gastric fluid, allowing for prolonged retention; swelling systems, which expand upon contact with gastric fluids, increasing retention time; mucoadhesive systems, which adhere to the gastric mucosa; and high-density systems, which settle in the bottom of the stomach and release drugs over an extended period [21-22]. The each classification utilizes distinct mechanisms to optimize drug delivery, targeting specific therapeutic needs while addressing challenges related to drug solubility and absorption in the GIT.

2.1. *Mechanism of Gastroretentive Drug Delivery:*

The several mechanism of GRDDs individually discussed in the below sections.

A. Floating Mechanism: The floating mechanism in GRDDs is designed to keep the dosage form buoyant in the gastric environment, preventing it from sinking. This is typically achieved by incorporating low-density materials or gas-generating agents, which create a structure that is less dense than gastric fluids [23]. When the system is ingested, it floats on the surface of the gastric contents, allowing for prolonged retention in the stomach. This extended residence time enhances the absorption of drugs that have a narrow absorption window, ultimately improving their BA and therapeutic effectiveness. By remaining in the stomach longer, floating systems can also help maintain consistent drug levels in the bloodstream, which is beneficial for chronic disease management [24-25].

B. Swelling Mechanism: The swelling mechanism in GRDDs involves the use of hydrophilic polymers that absorb gastric fluids and expand upon contact. When the system is ingested, the polymers swell and form a gel-like structure, increasing in size significantly [26]. This expansion slows gastric emptying, allowing the dosage form to remain in the stomach for an extended period. By prolonging retention time, swelling systems facilitate controlled and gradual drug release, enhancing the bioavailability of poorly soluble or poorly absorbed medications [27-28]. This

mechanism is particularly effective for achieving sustained therapeutic effects and improving patient compliance in the treatment of chronic conditions.

C. **Mucoadhesion Mechanism:** The mucoadhesion mechanism in GRDDs involves the adhesion of the dosage form to the gastric mucosa. This is achieved through the use of mucoadhesive polymers that interact with the mucus layer lining the stomach [29]. When the system is ingested, these polymers form bonds with the mucus, allowing the dosage form to adhere to the gastric wall. This adhesion prolongs the retention time of the drug in the stomach, facilitating sustained release and improving absorption [30]. The mucoadhesive properties help ensure that the drug remains available at the site of absorption for a longer duration, enhancing BA and therapeutic efficacy, particularly for drugs with limited solubility or absorption windows [29-31]. The various types of GRDDs mentioned in the Fig. 1 as below.

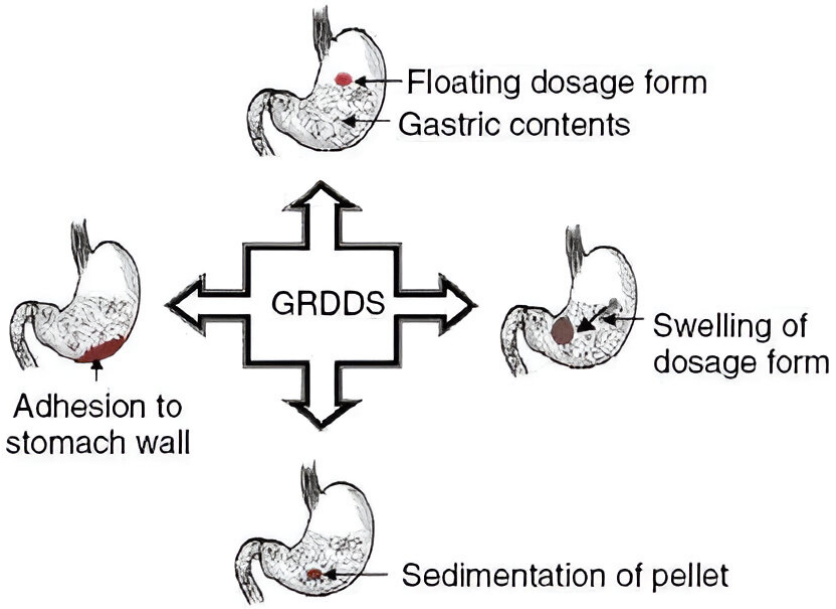

Figure 1: Representation of types of GRDDs and their description [31]

D. **Magnetic Retention Mechanism:** The magnetic retention mechanism in GRDDs employs external magnetic fields to retain the dosage form in the gastric region [32]. This approach involves the incorporation of magnetic materials within the DDs. Once ingested, a magnet placed externally on the abdomen can attract the magnetic dosage form, holding it in place against the gastric wall. This method allows for prolonged gastric residence time and controlled drug release, as the magnetic force keeps the system positioned in an area conducive to optimal absorption [33]. The magnetic retention mechanism is particularly beneficial for targeting specific sites in the GIT enhancing the therapeutic efficacy of various medications while minimizing the need for frequent dosing [32-34].

2.2. *Classification of Gastroretentive Drug Delivery:*

The GRDDs is designed to prolong the retention of dosage forms in the stomach, enhancing drug absorption and therapeutic efficacy, particularly for drugs that have a narrow absorption window or are unstable in the intestinal environment. GRDDs can be classified into several types:

- **Floating Systems:** These remain buoyant on gastric fluids, allowing them to float in the stomach for an extended time.
- **Swelling/Expanding Systems:** These enlarge after ingestion to a size that prevents them from passing through the pylorus, thereby staying in the stomach longer.
- **Bioadhesive Systems:** These adhere to the stomach lining, increasing their retention by resisting gastric motility.
- **High-Density Systems:** These have a higher density than gastric fluids, causing them to sink and stay in the stomach for a prolonged period.
- **Superporous Hydrogel Systems:** These rapidly absorb water, expanding to maintain their position in the stomach.
- **Magnetic Systems:** These use external magnets to retain the dosage form in the stomach by attraction [35-36].

These each system offers unique advantages depending on the drug's properties and the desired release profile. All of them few classes defined more as per the activity and action.

A. **High-Density Systems:** High-Density Systems are a type of GRDDs designed to remain in the stomach for an extended period by sinking to the bottom of the gastric content [37]. These systems are formulated with materials that increase their density to a value greater than gastric fluids, typically above 1.5 g/cm^3. This

increased density allows the dosage form to settle in the antrum (the bottom part of the stomach) and resist being emptied into the intestines by gastric peristalsis [38].

The summarizing the key features of High-Density GRDDs explained in the given Table 1 as below following:

Table 1: List of key features for high density GRDDs [39-40]

Key Feature	Description
Density-Based Retention	The high density ensures that the system does not float or rise in gastric fluids. It remains at the bottom of the stomach, extending the drug's residence time.
Materials Used	Formulated using heavy inert materials such as barium sulfate, zinc oxide, iron powder, or titanium dioxide to increase mass and density.
Suitability for Certain Drugs	Ideal for drugs absorbed in the stomach or with a narrow absorption window in the upper GI tract. Also useful for drugs unstable in alkaline intestinal pH.
Release Profile	Provides sustained drug release over a long period, offering extended therapeutic action, particularly for drugs needing prolonged gastric retention.

This table summarizes the essential aspects of high-density GRDDs systems.

B. Low-Density Floating Systems: Low-Density Floating Systems are a type of GRDDs designed to remain buoyant on the surface of gastric fluids, enabling extended retention in the stomach [41]. They are effective for drugs that are absorbed primarily in the stomach or the upper part of the small intestine. The system has a lower density (less than 1 g/cm^3) than gastric fluids, which allows it to float on top of the stomach content for prolonged periods. This buoyancy helps maintain the drug in the stomach even as gastric emptying occurs [42].

Types: They are classified as following brief description:

- **Effervescent Systems:** These use gas-generating agents like sodium bicarbonate or citric acid. When they come into contact with gastric fluids, they produce CO_2, which allows the system to float.
- **Non-effervescent Systems:** These rely on low-density polymers such as ethyl cellulose or HPMC that enable the dosage form to remain buoyant without producing gas [41-44].

C. Bioadhesive/Mucoadhesive Systems: Bioadhesive/Mucoadhesive Systems are a type of GRDDs that utilize the ability of certain materials to adhere to the mucus lining of the stomach or GIT. This adhesion helps to prolong the retention of the dosage form in the stomach, improving drug absorption and therapeutic effectiveness [45]. These systems work by forming strong bonds between bioadhesive polymers and the mucus layer that coats the stomach or other parts of the GIT. This adherence resists the natural movements of the stomach and intestines, keeping the drug localized for extended periods [46].

Theories of Mucoadhesion: The mucoadhesion theories explained in the Table 2 as below description:

Table 2: List of theories with their details [44-47]

Theory	Description	Key Points
Electronic Theory	Involves the transfer of electrons between mucoadhesive material and mucin.	Formation of electrical double layer, resulting in attractive forces (electrostatic interaction).
Adsorption Theory	Adhesion occurs due to secondary chemical bonds (Van der Waals, hydrogen bonds).	Involves physical forces like Van der Waals, hydrogen bonding, and hydrophobic interactions.
Wetting Theory	Based on the ability of a liquid to spread over a biological surface.	Depends on surface tension and contact angle; applicable mainly to liquid or semisolid systems.
Diffusion Theory	Interpenetration of polymer chains with mucin.	Adhesion occurs as polymer chains and mucin diffuse into each other, forming a stronger network.
Fracture Theory	Focuses on the force required to separate two surfaces after adhesion.	Strength of adhesion is related to the energy required to break the adhesive bond.
Mechanical Theory	Adhesion occurs due to interlocking of the material with the mucosal surface.	Based on physical entanglement between polymer and rough mucosal surfaces.

These theories explain how mucoadhesive materials interact with the mucosal layer to achieve effective drug delivery.

D. Swellable Systems: Swellable Systems are a type of GRDDs designed to significantly increase in size after ingestion by absorbing gastric fluids. These systems contain swellable polymers that expand, making the dosage form too large to pass through the pylorus, which controls the exit of stomach contents into the intestines [48]. This allows the drug to remain in the stomach for extended periods, leading to prolonged drug release and enhanced BA for drugs absorbed primarily in the stomach or upper GIT.

Upon contact with gastric fluids, the system swells to several times its original size, forming a large mass that resists gastric emptying. The common swelling materials include hydrogels like polyacrylate, cellulose derivatives (e.g., HPMC), and cross-linked polymers [49]. They having meritcs on extended gastric retention, improved drug absorption, and controlled, sustained drug release over time. Limitations of swellable systems require adequate fluid intake to expand effectively, and their retention time may vary depending on individual gastric motility [47-49]. These systems are particularly useful for drugs with a narrow absorption window or those that need a controlled release in the stomach.

E. Magnetic Systems: Magnetic Systems are an advanced type of GRDDs that use an external magnetic field to control the retention of the dosage form in the stomach [50]. The DDs contains a small magnetic component, which interacts with an externally applied magnet placed on the patient's abdomen. This method ensures the dosage form stays localized in the stomach or a specific area of the GIT for a prolonged period, allowing targeted and sustained drug delivery [51].

A small magnetic material is incorporated into the drug delivery system. When an external magnet is applied to the abdomen, the magnetic force keeps the system anchored in the stomach.

3. SWELLABLE AND FLOATING GASTRORETENTIVERY DELIVERY SYSTEM

A Swellable and Floating GRDDs is a drug delivery approach designed to prolong the gastric retention time of medications, allowing for extended release and improved BA, particularly for drugs that are absorbed in the stomach or the upper part of the small intestine [52]. These systems work by swelling upon contact with gastric fluids, increasing in size to prevent their passage through the pylorus. Simultaneously, they are formulated to float on the gastric contents due to their low density, maintaining their position in the stomach [53]. This dual mechanism enhances drug absorption by providing a longer window for drug release in the gastric environment, making it ideal for drugs with a narrow absorption window or those that are unstable or poorly soluble in the intestines [54].

3.1. *Swellable Gastro Delivery System:*

A Swellable SGDDs is designed to retain a drug in the stomach for an extended period by expanding in size upon contact with gastric fluids. The system contains polymers that absorb water and swell, increasing in volume to prevent the dosage form from passing through the pylorus into the intestines [55]. This swelling ensures prolonged gastric retention, allowing for sustained or controlled release of the drug. SGDDs is particularly beneficial for drugs with narrow absorption windows or those primarily absorbed in the stomach or upper small intestine, enhancing their bioavailability and therapeutic efficacy [53-55].

An ideal SGDDs should possess several key characteristics to ensure effective and prolonged gastric retention. Firstly, it must have excellent swelling capacity to significantly increase its size upon contact with gastric fluids, preventing premature passage through the pyloric sphincter. The system should demonstrate mechanical strength and integrity after swelling, maintaining its structure to allow for controlled drug release. Additionally, the polymers used should be biocompatible, non-toxic, and capable of rapid swelling while being resistant to degradation in the acidic gastric environment [56]. The system should also release the drug at a controlled rate, providing sustained therapeutic levels without causing irritation to the stomach lining. Lastly, it should be easy to administer, patient-friendly, and stable under various storage conditions to ensure consistent performance [56-57].

Mechanism of Action of Swellable Systems: The mechanism of action of SGDDs is based on their ability to expand and retain in the stomach for an extended period. These systems typically contain hydrophilic polymers that absorb gastric fluids upon ingestion [58]. Once in contact with these fluids, the polymers swell by taking in water, increasing the size of the dosage form. This expansion is critical as it prevents the system from passing through the pylorus into the small intestine. The swollen dosage form remains buoyant or large enough to stay in the stomach, allowing for prolonged residence time. During this period, the drug is gradually released through diffusion or erosion, providing a controlled or sustained drug release profile [57]. As the system stays in the stomach, drugs with narrow absorption windows or those that benefit from extended gastric exposure can be more effectively absorbed, enhancing BA and therapeutic effects. Eventually, the system either degrades naturally or deflates and passes into the intestines once its function is complete [59].

3.2. *Floating Gastro Delivery System:*

A Floating Gastroretentive Drug Delivery System (FGDDS) is designed to prolong the retention of drugs in the stomach by remaining buoyant on gastric fluids. This system incorporates low-density materials that enable the dosage form to float on the stomach's surface, preventing it from passing into the intestines prematurely [58-60]. By maintaining a position in the upper part of the stomach, FGDDS allows for a sustained or controlled release of drugs, particularly those that are better absorbed in the stomach or upper small intestine. This approach improves drug BA, reduces dosing frequency, and enhances therapeutic outcomes, especially for drugs with short half-lives or narrow absorption windows [61]. The FGDDS representation in the Fig. 2 as below following.

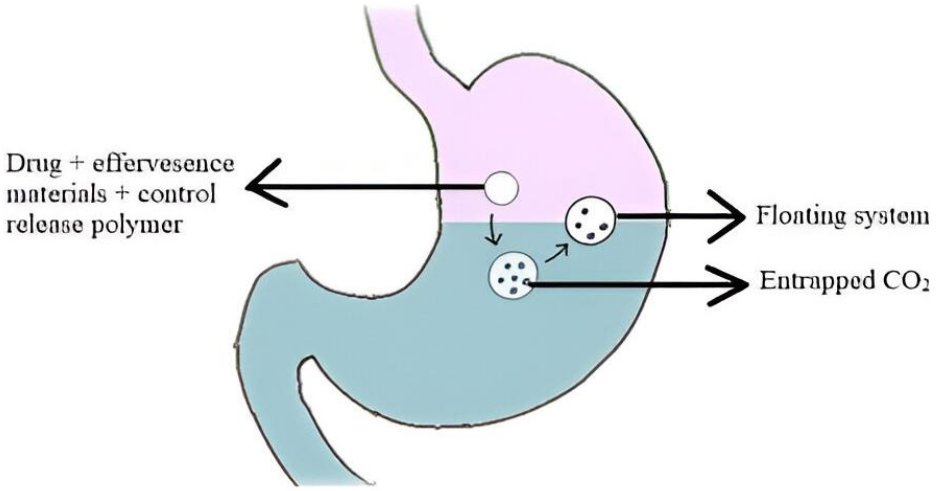

Figure 2: Representation of FGDDs and their details [62]

Types: Floating Gastroretentive Drug Delivery Systems (FGDDs) can be classified into two main types:

- **Effervescent Systems:** These systems rely on gas generation to achieve buoyancy. They contain effervescent components like sodium bicarbonate, citric acid, or tartaric acid, which react with gastric fluids to produce carbon dioxide. The generated gas causes the system to float on the stomach's surface. Examples include floating tablets and capsules that release gas upon contact with stomach acid.
- **Non-Effervescent Systems:** These systems use swellable polymers or gel-forming agents, such as hydroxypropyl methylcellulose (HPMC), that expand and become less dense when they come into contact with gastric fluids. The swollen matrix remains buoyant due to its reduced density, allowing it to float and provide prolonged drug release [61-62].

Both types ensure extended gastric retention, enhancing the bioavailability of drugs with narrow absorption windows in the upper GI tract.

Buoyancy Mechanism in Floating Systems: The buoyancy mechanism in floating drug delivery systems is based on the principle of reducing the system's overall density to remain afloat on gastric fluids. In effervescent floating systems, the dosage form contains gas-generating agents, such as sodium bicarbonate and acids like citric or tartaric acid [63]. Upon contact with gastric fluids, these agents react to release carbon dioxide (CO_2) gas. The gas gets trapped in the polymer matrix or capsule, lowering the overall density of the dosage form, allowing it to float on the surface of gastric contents. The drug is gradually released while the system remains buoyant [64]. In non-effervescent systems, hydrophilic polymers like hydroxypropyl methylcellulose (HPMC) or alginate are used. When these polymers contact gastric fluids, they swell and form a gel-like structure, increasing the volume and decreasing the density of the system [65]. This swollen, low-density matrix stays afloat in the stomach, providing a controlled or sustained release of the drug over time.

These systems ensure prolonged retention in the stomach, allowing for sustained drug release, which is particularly beneficial for drugs that degrade in the intestine or have limited solubility in higher pH environments [66]. Swellable systems utilize polymers that expand upon contact with gastric fluids, while floating systems maintain buoyancy to prevent premature gastric emptying [67]. Together, these technologies improve drug absorption, reduce dosing frequency, and enhance patient compliance. However, challenges such as patient variability in gastric motility and the need for precise formulation design still exist, requiring ongoing research to optimize their clinical application [68].

4. APPLICATIONS OF SWELLABLE AND FLOATING GASTRORETENTIVE SYSTEMS

Swelling and floating gastroretentive systems offer versatile applications in enhancing drug absorption, particularly for medications with a narrow absorption window in the upper GIT. These systems are used to prolong gastric retention, allowing drugs like metformin (for diabetes) and gabapentin (for neuropathic pain) to remain in the stomach for an extended period, improving their bioavailability [69]. They are also applied in the delivery of antibiotics like ciprofloxacin and anti-ulcer drugs such as famotidine, optimizing therapeutic efficacy by controlling drug release [70]. These systems are particularly beneficial for treating chronic diseases, where sustained and localized drug release is crucial for maintaining consistent therapeutic levels. The brief application of swellable and floating GRDDs system as below description [71]. The applications of swelling and floating GRDDs with their features, examples, and related diseases in Table 3 as below.

Table 3: List of several application with the targeting disease and suitable examples [70-72]

Feature	Examples	Disease/Condition
Controlled Release for Chronic Conditions	Metformin, Carvedilol	Diabetes, Hypertension
Delivery of Drugs with Narrow Absorption Windows	Levodopa, Riboflavin, Ciprofloxacin	Parkinson's Disease, Vitamin B2 Deficiency, Bacterial Infections
Gastroretentive Systems for H. pylori Treatment	Clarithromycin, Amoxicillin, Metronidazole	H. pylori Infection, Peptic Ulcer
Enhancing Bioavailability of Poorly Absorbed Drugs	Furosemide, Atorvastatin, Riboflavin	Hypertension, Hyperlipidemia, Vitamin B2 Deficiency

4.1. *Controlled Release of Drugs for Chronic Conditions:*

Swelling and floating gastroretentive systems play a critical role in the controlled release of drugs for chronic conditions, ensuring prolonged gastric retention and optimized drug absorption [73]. By slowly swelling or floating in the stomach, these systems provide sustained and localized drug delivery, which is essential for managing chronic diseases like diabetes, hypertension, and gastroesophageal reflux. Medications such as metformin, for diabetes management, and carvedilol, for heart conditions, benefit from these systems as they maintain steady plasma drug levels, reduce dosing frequency, and enhance patient compliance [74]. This approach is particularly valuable for drugs with a narrow absorption window, improving therapeutic efficacy over extended periods.

4.2. *Delivery of Drugs with Narrow Absorption Windows:*

Swelling and floating gastroretentive systems are highly effective in the delivery of drugs with narrow absorption windows, where drug absorption is limited to specific regions of the GIT, primarily the upper stomach and small intestine [75]. These systems ensure prolonged gastric retention, allowing the drug to be released gradually in the optimal absorption zone. Drugs such as levodopa (for Parkinson's disease), riboflavin (vitamin B2), and certain antibiotics like ciprofloxacin benefit from this approach. By maintaining the drug in the stomach for extended periods, these systems enhance BA, improve therapeutic outcomes, and prevent the premature release of the drug in regions where absorption would be minimal or ineffective [76].

4.3. *Gastroretentive Systems for Helicobacter pylori Treatment:*

Swelling and floating gastroretentive systems are particularly useful in the treatment of Helicobacter pylori infections, as they allow prolonged retention of antibiotics and other therapeutic agents in the stomach, where the bacteria reside [77]. These systems enable controlled and sustained release of drugs like clarithromycin, amoxicillin, and metronidazole, ensuring higher local drug concentrations at the site of infection. By maintaining drug presence in the gastric region for an extended period, gastroretentive systems improve the eradication rates of H. pylori, reduce dosing frequency, and enhance patient compliance, making them highly effective in treating peptic ulcers and other gastric disorders associated with the infection [76-77].

4.4. *Enhancing Bioavailability of Poorly Absorbed Drugs:*

Swelling and floating gastroretentive systems are highly effective in enhancing the bioavailability of poorly absorbed drugs, particularly those with low solubility or short absorption windows in the GIT [78]. By remaining buoyant or swelling in the stomach, these systems allow drugs to be retained longer in the gastric region, promoting gradual and sustained release. This is especially beneficial for drugs like furosemide (a diuretic), atorvastatin (a cholesterol-lowering agent), and riboflavin (vitamin B2), which have limited absorption in the lower GI tract. These systems ensure more efficient drug uptake, resulting in improved therapeutic efficacy and reduced variability in drug levels, leading to better patient outcomes [79].

5. RECENT ADVANCES AND CURRENT APPROACHES IN GRDDs

The recent advances in GRDDs focus on improving the bioavailability and therapeutic efficacy of drugs with narrow absorption windows or low solubility in the GIT. The modern approaches include the development of floating, swelling, and mucoadhesive systems, as well as high-density systems that prolong gastric retention [80]. Innovations like magnetic systems, ion-exchange resins, and novel polymers enhance gastric retention time and control drug release. Patents in this area cover new formulations, polymer compositions, and drug combinations designed to optimize release kinetics [80-82]. The several GRDDs are currently in clinical trials, with some already on the market, including products for drugs like metformin and gabapentin, which benefit from sustained gastric residence to improve absorption mentioned in the below [81]. These systems hold potential for enhanced patient compliance and more effective treatment of chronic conditions.

5.1. *Patent grant status:*

The different patent status in GRDDs with their respective details mentioned in the Table 4 as below following details.

Table 4: List of patents filled and granted for GRDDs medicated formulations

Category	Application No.	Patent No.	Entitle	Inventors	Filling Date	Publication Date
US	16 / 800,742	US 11,147,767 B2	Gastroretentive Formulations	Pilgaonkar	Feb. 25 , 2020	Oct. 19 , 2021
US	111596,123	US8383154B2	Swellable dosage form comprising gellan gum	Bar-Shalom *et al.*	May 11, 2005	Feb. 26, 2013
CA (Canadian)	---	CA2885971C	Gastroretentive drug formulation and delivery systems and their method of preparation using functionalized calcium carbonate	Daniel E *et al.*	2013-10-10	2018-01-02
US	---	US20230115025A1	Gastro-retentive drug delivery system	Hendrik Jan *et al*	2012-07-16	2023-04-13
AU	AU 2015367524 B2	W016/096997	Method for the production of a pharmaceutical delivery system	Susanna Atria *et al.*	2015.12.16	2018-03-15
EP	---	EP4277605A1	A gastroretentive drug delivery system	Vinay Muley *et al.*	2022-01-12	2023-11-22

These above Table 4 the few granted/published patents on GRDDs including Floating and swellable drug delivery system briefly.

5.2. *Clinical Trials condition:*

The several clinical trials data discussed in the below Table 5 as brief description and completion on data from the authorized websites.

Table 5: List of clinical trials status in utilized in the GRDDs

Entitle	NCT No.	Phase	Condition	Sponsor	Interventions	Study types
Magnetic Marker Monitoring of Furosemide-containing Gastroretentive Formulation in Healthy Male Subjects (Fasting and Fed Conditions)	NCT01887379	Phase 1	Gastroretentive Drug Formu-lation of Furosemide	LTS Lohmann Therapie-Systeme AG	Drug: GRDF furosemide	Interventional
Comparison of Prilosec OTC® Versus Zegerid® for Gastric Acid Suppression	NCT00808769	Phase 4		Procter and Gamble	Drug: Zegerid® Drug: Prilosec OTC®	Interventional

5.3. *Marketed Products:*

The several marketed products based on GRDDs have been developed to improve drug BA by prolonging gastric retention time [82-83]. Notable examples include Glumetza®, a controlled-release formulation of metformin used for managing type-II diabetes, which uses a swelling mechanism for extended gastric residence. Gabapentin GR®, for treating neuropathic pain, is another product that enhances drug absorption through sustained release in the stomach [84]. Cifran OD®, a once-daily formulation of ciprofloxacin, uses floating drug delivery technology to improve antibiotic efficacy [85]. These products demonstrate how GRDDs can enhance drug absorption, optimize dosing, and improve patient compliance for conditions requiring long-term therapy. The several marketed products mentioned in the GRDDs in Table 6 as below.

Table 6: List of marketed products in GRDDs with their details

Drug/API	Brand Name	Manufacturer	Application/Use	Approval Date	Ref.
Metformin	Glumetza	Salix Pharmaceuticals	Type 2 Diabetes	July 2005	[86]
Rifampicin	Xifaxan®	Lupin, India	---	---	[87]
Gabapentin	Gralise	Depomed Inc.	Postherpetic Neuralgia	January 2011	[88]
Ofloxacin	Zanocin OD®	Ranbaxy, India	---	---	[89]
Carvedilol	Coreg CR®	GlaxoSmithKline, UK	Gastroretention with osmotic system	---	[90]
Baclofen	Gablofen	Azur Pharma	Spasticity	March 2010	[91]
Ciprofloxacin	Cipro XR	Bayer	Urinary Tract Infection	August 2002	[92]
Gabapentin	Gabapentin GR	Depomed, USA	Polymer based swelling technology: AcuForm™	---	[93]
Levodopa/Carbidopa	Duopa	AbbVie	Parkinson's Disease	January 2015	[94]

These are the recent advances and current approaches in GRDDs, including innovative patents, ongoing clinical trials, and successful marketed products (Table 4, Table 5 and Table 6), highlight the potential of these systems to enhance drug BA, improve therapeutic outcomes, and increase patient compliance, offering promising solutions for the effective treatment of various chronic conditions [93-95].

CONCLUSION

Gastroretentive swellable and floating systems represent a transformative and highly promising approach to enhancing the bioavailability and therapeutic efficacy of drugs that are primarily absorbed in the upper gastrointestinal tract. By extending gastric residence time and providing sustained drug release, these systems offer numerous advantages for treating conditions that require localized action or prolonged drug availability. The integration of hydrophilic polymers, gas-generating agents, and novel materials has advanced the development of these systems, making them versatile and effective for a variety of drug types, including those with poor solubility or short half-lives. However, challenges such as variability in gastric retention, formulation complexities, and patient-specific physiological factors still need to be addressed. Future innovations, including the use of nanotechnology, biocompatible materials, and advanced fabrication techniques like 3D printing, hold the potential to overcome these limitations. Gastroretentive swellable and floating systems represent a forward-looking strategy in drug delivery, promising to improve therapeutic outcomes and patient compliance in the years to come.

List of Abbreviations

GRDDs: Gastroretentive drug delivery systems; **GI:** Gastrointestinal; **SDR:** sustained drug release; **GIT:** Gastrointestinal Tract; 3D: 3 Dimential.

Ethical Approval

Not applicable.

Consent for Publication

Not applicable.

Human and Animal Ethical Right

Not applicable.

Conflict of Interest

The authors declare no conflict of interest, and no funding was required to conduct these review data.

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Availability of Data and Materials

The data supporting this study's findings will be available in the cited references.

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