REVIEW ARTICLE

Gastro-retentive Drug Delivery Systems and their *In Vivo* Success: A Recent Update

S N Vaidya*, S Agrawal, P Jirvankar

Datta Meghe College of Pharmacy Salad (H), Datta Meghe Institute of Higher Education and Research (DU) Wardha-442002, Maharashtra, India

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ABSTRACT

In recent times, GRDDS has become a common tool for the administration of oral drugs. Holding the medication longer in the stomach and releasing it gradually is a common technique. In particular, its limited bioavailability helps get around some of the problems with traditional oral administration. GRDDS are being built utilizing floating systems with or without effervescence, plug-type swelling systems, and muco-adhesion methods. To guarantee improved stomach retention and longer drug release, a carefully planned *in vivo* study is also required, in addition to *in vitro* testing. Gamma scintigraphy and magnetic resonance imaging (MRI) are two widely used methods for measuring how long an organism spends in its stomach. For this type of drug delivery system, assessing their overall effectiveness in living organisms, particularly in smaller animals like mice or rats. There have been relatively few published studies using beagle dogs, rabbits, and human subjects *in vivo*, despite a plethora of promising *in vitro* results. GRDDS is not as widely available in the market as it might be due to a variety of factors, including dietary influence, variable stomach emptying rates, and variability in gastrointestinal problems. This review paper highlights the limitations and challenges of the most recent *in vivo* research of GRDDS, which will need to be resolved in the near future.

Keywords: Floating tablet, Effervescence, Polymer swelling, *In vitro* Bioavailability

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INTRODCTION

Among the various types of medicine developed for human use, oral formulations have taken center stage. The majority of traditional oral administration methods frequently have limited bioavailability because of things like quick stomach emptying. However, in order to solve this issue, a number of novel pharmaceutical devices, notably controlled release drug delivery systems, have been developed as a result of recent technological breakthroughs. In the case of the gastro-retentive drug delivery system (GRDDS), characteristics like extended medication release and stomach retention duration have significantly improved patient adherence. Interest in this novel delivery mechanism has been spurred by the intrinsic drawbacks of conventional oral medication administration methods. The absorption of certain drug molecules that are primarily lost in thought in the commencement of the stomach, is hampered by the rapid gastric emptying caused by traditional oral medications. Medications with low solubility in the stomach can increase their solubility by extending their time in the stomach. Many medications, including ranitidine HCl, metronidazole, and captopril, are prone to disintegrate in the colon. Drugs having short half-lives must be dosed regularly to have the required therapeutic effects since they are quickly eliminated from the body's circulation. However, an oral sustained-controlled release formulation with extra gastric retention abilities can address these drawbacks by slowly delivering the medication in the stomach and sustaining a sufficient drug level in the bloodstream for an extended period of time. In addition to its systemic effects, GRDDS has shown effectiveness in healing esophagitis, duodenal ulcers, and stomach ulcers by eliminating Helicobacter pylori from the submucosal tissue of the stomach. GRDDS formulations have been in existence for more than thirty years. The basic production techniques and associated *in vitro* analyses are also well-established. There have been a lot of reviews on GRDDS released recently. These reviews mostly concentrate on the *in vitro* characterisation studies and formulation elements of GRDDS that have been carried out by various researchers. Nevertheless, the quantity of gastro-retentive formulations available for sale is rather small. Given their critical roles in the effective marketing of all medications, it is imperative that the *in vivo* study on GRDDS be carefully examined in order to ascertain the pharmacokinetic characteristics of the developed systems. Our analysis of the literature indicates that, as of right now, no reviews explicitly look at the *in vivo* efficacy of GRDDS, especially in light of more recent research. This review aims to summarize *in vivo* investigations on GRDDS with particular attention to gastro-retention periods, pharmacokinetic characteristics, and difficulties encountered by investigators during assessments.

**Author for Correspondence: sunita.pharmacy@dmiher.edu.in*

Physiology of Stomach

Understanding stomach physiology and the linked gastric emptying process is crucial for the success of GRDDS. The human stomach consists of three anatomical regions: fundus, body, and antrum (pylorus), as depicted in Fig. 1. After eating, a stomach's usual size is about 1.5 liters, varying from 250 to 500 milliliters when empty. The fundus and body act as a storage for undigested material, while the antrum is where most of the mixing action takes place. The antrum operates as a pump to aid in gastric emptying in the lower digestive system. The pylorus separates the stomach from the duodenum and plays a crucial role in controlling the amount of time that ingested substances stay in the stomach. However, the gastric movement pattern varies when in fasting compared to when fed. The arrangement of stomach movement is characterized by alternating periods of relaxation. Each cycle consists of four stages and has a duration of 90 to 120 minutes as detailed in Table 1. The migrating motor complex (MMC) is the usual term for the stomach's movement pattern.

Table 1: Four phases of migrating motor complex (MMC)

Phase	Description	Duration (min)
Phase I (basal phase)	Idle condition without any contraction	30 to 60
Phase II (pre-burst phase)	Intermittent contractions	20 to 40
Phase III (burst phase)	The regular contraction at maximum frequency leads the excellent material to move distally.	10 to 20
Phase IV	Transition period between phases III and I	0 to 5

From Talukder and Fassihi [21].

Approaches for Developing Gastroretentive (GR) Systems

Scientists have utilized various methods to extend the amount of time drugs remain in the stomach and improve their release. Increasing the density of the new formulation (Fig. 2) to 2.5 to 3.0 g/ml was done to enable it to withstand peristaltic movement *in vivo* and remain intact even if the gastrointestinal tract is disrupted. It was estimated that the usual time it takes for food to move through the digestive system would rise to anywhere between 5.8 to 25 hours [7, 22].

One of the primary drawbacks of this kind of technology, according to Chawla et al. [23], was the requirement for a larger dosage size in order to get the intended high density. Another novel idea was to use a magnetic field to hold the dose form in the stomach. The magnetically active components of the dose form will be present. To keep the medication in place, an external magnet had to be applied to the abdomen, covering the stomach region (Fig. 3). The primary barrier to this delivery system's *in vivo* deployment, despite its creative design, was patient noncompliance [24]. Through the use of a novel expanding and swelling mechanism (Fig. 4), GRDDS has demonstrated significant efficacy in assisting the dose form to stay in the stomach in both *in vitro* and *in vivo* investigations [25, 26]. A device designed to grow greater than the pyloric sphincter's diameter and continue to in situ was reported by Bolton and Desai [27] (Fig. 4).

Conversely, the system's capacity to inhibit the pyloric sphincter led to being dubbed "plug type systems." The polymer expanded and absorbed water when it came into contact with stomach fluid [18, 28–30]. The right polymer (or combination of polymers) with the ideal molecular weight/viscosity grade and swelling properties allowed the dosage form to achieve a sustained-release feature.The development of this type of dosage form has evolved further with the introduction of new polymers with super-porous characteristics, which allow them to grow to a stable size in less than a minute. When the dosage form interacts with GI fluid, capillary wetting through several connected open pores, each on average larger than 100 μm, causes the polymer to swell rapidly (swelling ratio exceeding 1:100) [31]. A novel version of GRDDS has been created by utilizing the floating characteristic that all dosage forms in GI fluid show [32]. The dosage form's density eventually drops below that of the stomach fluid, which has a density of between 1.004 and 1.010 g/ml. Many factors determine how quickly the polymer in the formulation swells, such as sort, viscosity grade, the presence of swelling boosters or wicking agents, etc. [33–35]. This determines the delay in time. The formulation's parameters also dictate how long the medicine floats and how quickly it releases the drug *in vitro*. The degree to which floating behavior is successful also depends on the patients' physiological circumstances, including whether or not they are fasting, how much gastric fluid is in their stomachs, and other variables. The used dose form is discharged from the stomach after the required medication release [36]. As shown in Fig. 5 [37–41], an additional characteristic called fizziness was introduced to improve the floating performance (time and duration) of this swelling-based floating delivery method.

The dosage form contained a combination of many fizzy chemicals, including citric acid, tartaric acid, and sodium bicarbonate. Carbon dioxide (CO2) is released When these parts arrive into interaction with the contents of the stomach. This CO2 is then absorbed by the hydrocolloid system that has gelled. These bubbling and expanding mixes help the medicine form ascend and remain floating for a longer amount of time by bringing its density down below that of stomach fluid [37]. Apart from monolithic systems, two- and three-layer have been considered for this combination approach's design in order to incorporate two medications with different release patterns [37]. While another medication is integrated into the outer layer for quick release, one drug and its components are specially built into a sustained release layer with a gas producing device. Additionally, attempts were attempted to employ mucoadhesive or bioadhesive drug delivery methods for the aim of gastro-retentive therapy. The dose form's purpose was to stick to the inside of the stomach lining and endure prolonged movement of the digestive system (Fig. 6).

The location was especially designed to improve local medication absorption in an affected stomach region, which was favorable. Promising constituents for this kind of design include excipients including CMC, pectin, and

gliadin. Another novel strategy to improve gastro-retention characteristics is to combine a floating or swelling mechanism with muco-adhesion. When coupled with carbon dioxide bubble trapping referred to as the raft forming system—is another way to increase patient compliance during gastroretention. This specific delivery strategy, which begins as a solution, contains carbonates or bicarbonates as fizziness-producing agents together with sodium alginate, the polymer that gels in the body. The medication delivery devices are kept afloat by their expansion and production of a thick, cohesive gel containing trapped carbon dioxide bubbles upon contact with stomach juice. Because raft forming devices may produce a protective barrier on top of the stomach fluid, they are frequently used in the treatment of gastroesophageal reflux [48,49].

***In vitro* Evaluation of Gastro Retentive Drug Delivery System (GRDDS)**

Testing GRDDS in a laboratory setting is essential to ensure its effectiveness in the body. In this context, the primary focus is on floating lag time, floating duration, and formulation composition. Typical characteristics of tablet formulation include firmness, tendency to break, aesthetics, amount of medication, consistency of dosage, variability in weight, and drug release in simulated body conditions [37]. Research studies utilizing various gastroretentive drug delivery systems commonly employ simulated stomach fluid and deionized water to evaluate floating characteristics like floating length and floating lag time [50]. In order to study differences in the medication formulations' buoyant capabilities, both mediums are utilized. Moreover, the swelling characteristics and speed of dose shapes made of polymers are evaluated in a dissolving solution (0.1N HCl) for at least 8 hours to confirm The process of medication release and drifting. This includes determining the increase in weight or swelling of the pill after retrieval at the end of the experiment [46]. Drug release is tested using artificial stomach juice *in vitro*. Specimens are extracted from the dissolve containers and thinned at certain time points in order to analyze the drug concentration [51]. By utilizing SEM at different levels of magnification, a microscopic analysis is conducted to assess the surface characteristics of the dosage form. Additional studies are being conducted on stomach-retaining beads and microspheres to enhance the formulation's composition and processing features, such as drug loading, measurement of particle size, and efficiency in drug entrapment. Spectrophotometers, optical microscopes, and particle size analyzers are frequently used for specific tests *in vitro* evaluation.

***In vivo* Gastric Retention as a Surrogate for Pharmacokinetic Investigation**

To prove the effectiveness of any GRDDS in a living organism, it is necessary to conduct a well-designed study using the right animal model or healthy human subjects. Turner et al. [54] mention the challenge of determining stomach retention and bioavailability in smaller animal species when administering high tablet doses. Consequently, studies on GRDDS formulation often demonstrate stomach retention in larger animals such as dogs or humans, along with important *in vitro* tests like dissolution, floating lag time, and floating duration.

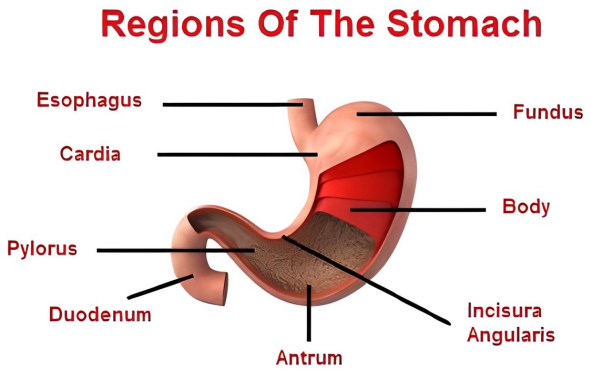

Figure 1: Diagram of Human Stomach

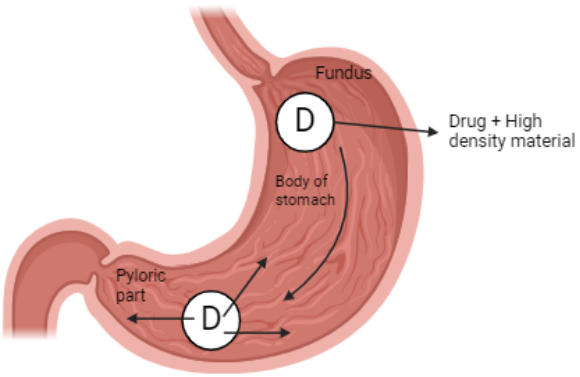

Figure 2: Gastro-retentive drug delivery system based on high density

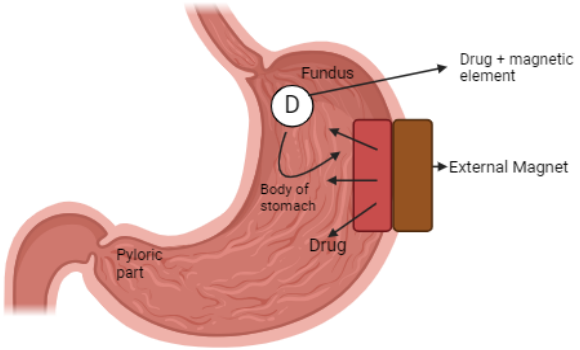

Figure 3: Gastro-retentive drug delivery system based on application of magnetic force

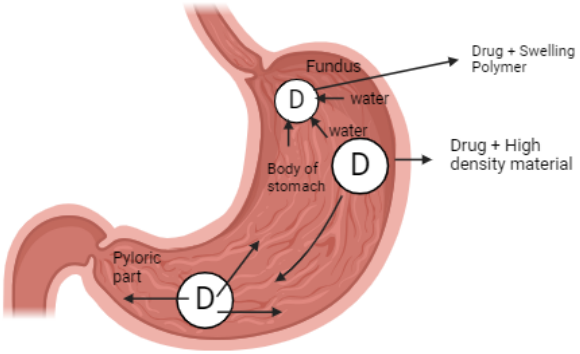

Figure 4: Gastro-retentive drug delivery system based on polymer swelling

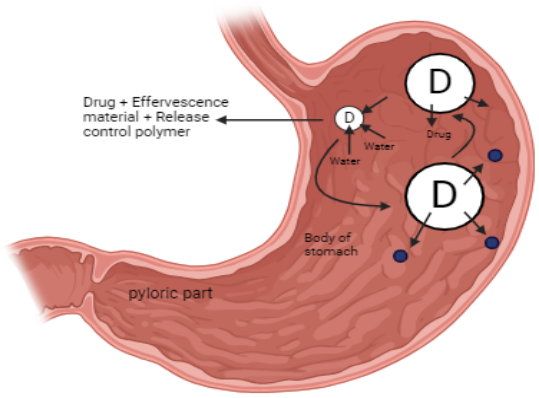

Figure 5: Gastro-retentive drug delivery system based on combination of polymer swelling and effervescence

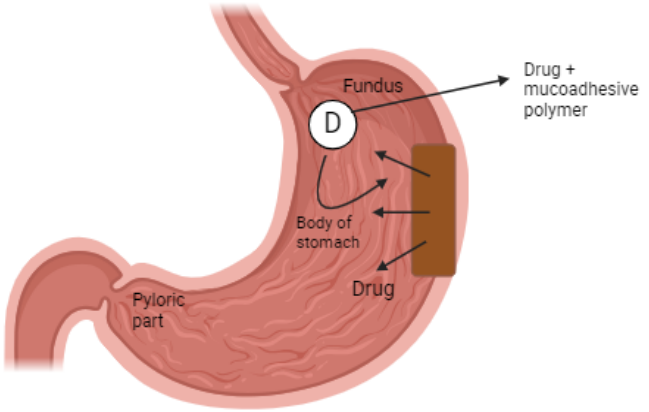

Figure 6: Gastro-retentive drug delivery system based on muco-adhesion

It is believed that the prolonged presence of the stomach in the body can enhance the effectiveness of the treatment when compared to standard dosage forms. There are many advanced visualization methods that are beneficial in this respect. Gamma scintigraphy is a widely used and advanced method for evaluating gastroretentivity in humans. A neutron source is utilized to stimulate the dosage form that contains a small amount of radioisotope with a brief half-life to release gamma rays, which are then captured as an image and examined by a computer. Repeat write-up below. Badve and his team created empty calcium pectinate capsules that have diclofenac sodium to enhance the chronopharmacological impacts. The empty spheres floating were made of beads with a bulk density lower than 1 g/ml and a porosity of 34%. Gamma scintigraphy was used in a study on live rabbits to demonstrate that beads can remain in the stomach for as long as 5 hours. Recent studies have also shown that floating tablets and microspheres can effectively remain in the stomach and carry various therapeutic compounds like ascaridole and repaglinide [57-59]. MRI is a safe technique that uses magnetic fields and radiowaves to confirm the *in vivo* presence of a GRDDS by displaying the entire anatomical structure and the location of the administered dose form. Iron oxide with superparamagnetic properties is used in vision applications. Steingoetter et al. [60] used this approach to study the stomach's holding onto Gd-DOTA in a floating tablet containing Fe3O4, as well as the tablet's position and duration in individuals. Radiography, also known as X-ray, is another way to incorporate a radio opaque substance into GRDDS. This technique has been used to evaluate stomach emptying, rate of dosage breakdown, and movement through the esophagus. However, there are concerns about safety with this technique as prolonged exposure to X-rays could result in health problems [62]. However, this approach has the advantage of demonstrating efficacy in both human participants and animals such as dogs and rabbits [63-67]. Gastroscopy is a common procedure utilized for the diagnosis and monitoring of the gastrointestinal tract (GIT). This method utilizes fiber optics or a video system to determine the location of the dosage form. Individuals undergoing an uncomfortable procedure can be given a mild sedative to assess how long the stomach holds onto a specific dosage form [68]. Nonetheless, Dhiman et al. [51] noted that dogs need full anesthesia for the procedure.

***In vivo* Success of GRDDS in the Context of Pharmacokinetic Properties**

Numerous studies have shown that the oral GRDDS has been extensively investigated in drug delivery research for the past thirty years. Nevertheless, only a few of them have been supported by evidence from living organisms. The next parts provide a timeline overview for both animal and human participants, with each group organized separately.

Animal Study

Klausner and his colleagues created a unique controlled release mechanism for Levodopa by utilizing elastic polymer membranes that elongate, unfold, and become stiffer. Research was conducted on live beagle dogs that had been pre-treated with carbidopa. The given equation was used to establish the place of the medication form within the GI system through X-ray scanning. Moreover, sequential blood samples were gathered and analyzed for the medication being administered. The improved controlled release Levodopa GRDDS was able to sustain levels of Levodopa (>500 ng/ml) for a period of 9 hours. When compared to non-GR controlled release particles and oral solution, the average absorption time was noticeably greater. Jain together with others. Developed repaglinide floating microspheres using calcium silicate and Eudragit. Male Using Sprague Dawley rats, the organ distribution was investigated. While albino rabbits were given water containing floating microspheres labeled with 99mTc orally. Following gamma scintigraphy to assess a gastric residence time of 6 hours, The stomach and intestinal organs of the rats were removed when they were slaughtered. The examination substance was evenly spread in organs and demonstrated a relative bioavailability 3.17 times greater than the tablets currently available on the market. Shishu and Aggarwal [69] conducted an *in vivo* study to assess the effectiveness of calcium alginate beads containing 5-fluorouracil for treating tumors. The use of a floating system across various units decreased the rate of stomach cancers in mice by 74%, compared to a mere 25% reduction with a conventional tablet form. Pande and his colleagues created microspheres with cefpodoximeproxetil for use as gastroretentive drug delivery systems (GRDDS). The process used to produce microspheres containing drugs

consisted of solvent evaporation, with HPMC and ethyl cellulose used to manage the release speed. Microspheres with suspension of cefpodoximeproxetil, each as much as 10 mg/kg, were given orally toA pair of male albino rat groups. Samples of blood taken from the retroorbital region were centrifuged at specific time intervals to isolate plasma samples for analysis via HPTLC.

This study discovered that the drug had a bioavailability 1.5 times greater when in microsphere form compared to when in suspension form. Guan and team demonstrated that a famotidine-filled floating osmotic capsule was superior to the current arrangement. The capsules, containing glycerin and diethyl phthalate, were created using novel technology with asymmetric membranes. Polyethylene oxide WSR N-80, with a molecular weight of 200,000, was utilized in creating the extended release floating granules contained in the capsule casings. The perfect mix led to the continuous release of drugs for 12 hours in a laboratory environment while also sustaining buoyancy. During a meticulously designed *in vivo* study, six male beagle dogs were administered 40 mg floating capsules (Test) and 20 mg commercial tablets of famotidine (two tablets per dose as Reference), with blood samples collected for 36 hours. The maximum concentration of blood for the Reference formulation was 0.334 µg/ml, while it was 0.187 µg/ml for the Test formulation capsule. Also, the Reference tablet peaked in plasma concentration after 2.083 hours, compared to the Test capsule which took 4 hours to reach the same level. The floating capsule remained effective for approximately twice as long as the standard tablet, having a half-life of 23.634 hours compared to 13.178 hours. The AUC0-∞ for the Reference tablet was 31.411 µg/ml as expected, whereas the Test capsules showed a result of 50.4 µg/ml. Therefore, the newly developed capsule exhibited a relative bioavailability around 1.605 times higher than the existing market formulation. Research conducted on animals showed that a medication designed to remain in the stomach was more effective than a traditional one. Khan and Dehghan discovered that albino rabbits had higher bioavailability of atorvastatin calcium when given floating tablets instead of standard ones. The tablets experienced a buoyancy delay of around 56 ± 4.16 seconds, with a duration of effects lasting 6 hours and an increase in bioavailability by 1.6 times. Yin et al. [73] discovered that most of the absorption of cephalexin takes place in the stomach, indicating that enhancing a gastro-retentive formulation might boost its bioavailability. Tablets with Cephalexin for gastric retention were formulated by utilizing HPMC K100M as a binder and sodium bicarbonate as a gas-generating agent. The tablets that were made showed a buoyancy duration lasting more than 12 hours and a delay of under 15 seconds, indicating an appropriate extended-release pattern for 12 hours during testing. An experiment was conducted in beagle dogs, both fed and fasting, to compare how standard capsules and extended-release tablets are metabolized in their bodies. The reference formulations had a substantially lower relative bioavailability of 39.3%, whereas Cephalexin floating tablets demonstrated a much greater relative bioavailability of 99.4% with a prolonged drug release pattern. Nonetheless, the investigation revealed a notable impact on the extended-release pills' pharmacokinetics. Thakar and his colleagues performed a live research experiment on rabbits to evaluate the efficacy of floating tablets containing baclofen [4]. With a floating delay of 4 to 5 seconds and a floating time of more than 12 hours, the tablets demonstrated good gastro-retentive qualities when sodium bicarbonate was used to produce gas and Polyox WSR 303 and HPMC K4M to reduce edema. In line with the traits seen in a lab setting, the enhanced floating drug release system remained in the stomach for longer and shown a bioavailability increase of 2.34 times that of the existing product. Zhu and team found that the efficacy of famotidine mini-tablets *in vivo* was enhanced by the blend of bioadhesion and floating techniques. Together with sodium bicarbonate and carbopol 971P for gas production and bioadhesion, respectively, HPMC K4M was used as a polymer to extend release time and cause swelling. During tests on rats, the bioavailability of the mini-tablets increased by 1.62-fold. Qi and his colleagues were able to achieve positive results in a living organism using a floating tablet coated with compression that contained ofloxacin. The pills contained sodium bicarbonate as an effervescent agent, sodium alginate as a medication release modifier, and hydroxypropyl cellulose as a compression coating agent. The tablets' *in vitro* properties, like a 30-second floating delay and a 12-hour floating period, correlated closely with its 172% comparative bioavailability between the evaluated market formulation on Bunnies from New Zealand. Kadivar and his team showed in their research that a sustained release tablet of imatinibmesylate can effectively stay in the stomach and work well in the body by using a mix of floating mechanism and effervescence withBenecel™ Hydroxypropylmethylcellulose (HPMC) K4M, Alginate of sodium with carbomer 934P. During testing, gastro-retentive tablets in New Zealand rabbits showed 1.5 times greater bioavailability than standard Gleevec tablets.

Human Study

Employing a blend of hydroxyethyl cellulose, sodium bicarbonate with sodium carboxymethylcellulosea swelling/effervescence mechanism, Chen and colleagues [76] created tablets that stay in the stomach to release the blood pressure drug losartan. Tablets were discovered to float for almost 16 hours in a controlled laboratory setting, and in just 3 hours, they expanded to a width of 2 cm. The tablets also demonstrated pH-dependent medication release over a 24-hour period. During testing, the improved tablets' bioavailability over Cozaar was around 164% higher in healthy human subjects. The gastro-retentive floating tablets demonstrated beneficial pharmacokinetic properties as predicted: in comparison to the commercial formulation, the maximum residence time (MRT) and Tmax values rose while the Cmax values dropped. The efficiency of gastro-retentive cefuroxime axetil tablets in comparison to traditional Zocef® tablets for antibiotic therapy was proven by Bomma and Veerabrahma [66]. To enhance the tablets, effervescence (citric acid, calcium carbonate) and swelling (HPMC and Polyox 303) methods were used in their production. The enhanced pills lasted 225 ± 30 minutes in the human body, according to x-ray scans, and had In

laboratory testing, a floating delay of less than 30 seconds and a floating period of more than 12 hours are required. For testing, eight healthy human volunteers were given the identical pills. When compared to the Zocef tablet, the floating tablets demonstrated better bioavailability. Regarding the test and reference groups' *in vivo* outcomes, a significant difference was seen in Cmax, Tmax, t1/2, AUC0–∞, and mean residence duration ($P < 0.05$). When compared to regular tablets, the extended-release cefuroxime axetil tablets showed a 1.61-fold increase in proportional bioavailability. The *in vivo* effectiveness of nicotinamide at a high dosage of 600 mg, the active component of GRDDS, was patented by Meijerink et al. In the formulation, Hypromellose was employed as an edema inducer. Eight adult volunteers in good health had their pharmacokinetic profiles evaluated. Blood and urine samples were taken at predetermined intervals. The newly created medication kept subjects' Nicotinamide levels in the blood rise for at least eight hours following consumption. The use of powdered aloe vera gel with ellagic acid in a dual-layer floating tablet containing Bismuth sodiumand Benecel™ Hydroxypropylmethylcellulosewas investigated as a possible treatment for stomach ulcers in a research done by Ranade et al. [78]. The researchers found that ellagic acid reduced ulcers by 75% when combined with other treatments, whereas ellagic acid reduced ulcers by 57% when administered alone. The pills had a total drug release of 92% and a floating duration of 4 hours *in vitro*, indicating their effectiveness. Abouelatta and colleagues [79] used the ionotropic gelation technique in a separate investigation to confirm the effectiveness of calcium pectinate beads loaded with cinnamon in gastro-retentive emulsion gel. Researchers found that healthy human volunteers performed better *in vivo* than conventional tablets, with average elevations in AUC0-∞ of 1.79 and 3.80 times, respectively, and AUC0-24. It is important to note that the beads containingLabrafaclipophile WL 1349 (oil phase) with glycerylmonooleate, and pectin (base) demonstrated instantaneous *in vitro* floating capabilities. While a number of GRDDS that employ diverse creative manufacturing methodologies have demonstrated efficacy in educational settings, their economic viability has been limited.

Challenges with Gastro Retentive Drug Delivery System (GRDDS)

The time duration that dosage forms remain in the gastrointestinal system determines the bioavailability of oral drug administration modalities. GRDDS focuses mostly on the stomach. The primary problem in establishing a GRDDS is maintaining the delivery system in the stomach or upper small intestine until all drugs are administered at a constant rate. Time spent emptying the stomach (Gastric emptying time) varies substantially. Gastric retention duration is primarily determined by the dose type and the stomach's fed or fasted condition, with fed states lasting longer and fasting states lasting shorter. Additional physiological barriers and factors, such as meal type, calories, gender, and age, have a significant influence on the variability of stomach emptying time [82]. Because of its large caloric content, a high fat meal greatly slows down stomach emptying. Furthermore, Mojaverian et al. [83] found that patients' GRT can differ based on their gender and age [1]. The pylorus is essential for stomach retention of any GRDDS, measuring 2 to 3 mm during digestion and growing to 12.8 ± 7.0 mm in the inter-digestive phase. Particles must be less than 5 mm in diameter to pass through the pylorus and enter the duodenum [84]. Another element to consider is the size of the pylorus and peristaltic movement in animals (such as dogs and rabbits) vs humans [85]. As a result, *in vivo* efficacy studies should be interpreted with caution. The stomach residence duration, which is connected to the efficacy of the dosage form, is determined by factors such as the dosage form's size and shape, the individual's illness status, and BMI. Nonetheless, data suggest that in some circumstances, multiple-unit GRDDS provide more dependable and constant drug release than single-unit GRDDS. Time and gastric emptying can cause a single unit gastro-retentive dose form (GRDF) to escape the stomach before becoming effective [5]. So, in order to construct the greatest GRDDS feasible, the main challenges to overcome are controlling concerns with stomach emptying rate and ensuring the medication is delivered at the appropriate rate over a lengthy period of time before being metabolized [86].

CONCLUSIONS

Based on a review of various published studies and thorough examinations of commercial products, it has been determined that there is no one gastro-retentive system that is the most suitable for every drug candidate. Nevertheless, most patients have shown numerous benefits from using GRDDS. Each medication candidate or combination must be examined individually for dose requirements and manufacturing feasibility. Choosing the proper polymer is critical for formulations with a high dosage. This option is critical for attaining the compressibility necessary to take use of the high API content. Nonetheless, the optimum polymer should be selected depending on its dose form; a little amount that assures considerable stomach retention is preferable. While numerous ways have been presented, such as floating, bio-adhesion, effervescence, sinking, magnetic, swelling, and so on, their *in vivo* use has not been properly examined. In terms of formulation, the major tendency has turned toward the use of swelling polymer matrix and effervescence to create floating delivery systems. Despite the multiple potential benefits of this delivery system, it is just now emerging as a significant innovative drug delivery method because to the severe commercial obstacles it faces. GRDDS are predicted to become increasingly popular in the near future due to their capacity to transport medications more efficiently into systemic circulation. However, due to the complexities of pharmacokinetic and pharmacodynamic factors, it is critical to demonstrate their efficacy through well-designed *in vivo* studies for a specific medicine.

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