International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 96-107 www.ijprajournal.com ISSN: 2456-4494

Recent Approaches in Controlled Release Gastroretentive Drug Delivery System: A Review

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Date of Submission: 01-05-2024 Date of Acceptance: 10-05-2024

ABSTRACT: The oral route is the most recommended method for administering drugs due to its ease of use, patient compliance, and formulation versatility. However, this approach has several drawbacks, such as a restricted gastric residence time (GRT) for medications that are absorbed from a particular area of the gastrointestinal tract (GIT) and for sustained drug delivery systems. Many strategies have been put forth to lengthen the gastric retention duration of the delivery system in the upper gastrointestinal tract in order to get around these restrictions. The gastro retentive dosage form (GRDF), which targets site-specific drug release in the upper section of the GIT, extends the GRT. GRDFs improve the bioavailability of medications with a restricted therapeutic window and allow continuous, prolonged drug release; thus, they increase the time between doses. This page aims to summarize the several gastro retentive methods. We have enumerated the key variables influencing gastric retention in order to comprehend the different physiological challenges associated with achieving gastric retention. The evaluation criteria for medication delivery systems that are gastro retentive are finally discussed. This study provides a quick overview of the current state of play for the several major gastro retentive drug delivery technologies that have been developed to date, including magnetic systems, high density (sinking), floating, bio- or mucoadhesive, expandable, unfoldable, ultra porous hydrogel, and others.

KEYWORDS: Floating Delivery, Gastro retentive system, Gastric retention time, Gastric emptying time.

I. INTRODUCTION

Oral drug administration continues to be the primary method despite significant breakthroughs in drug delivery. Patients comply with therapy at high rates since it is inexpensive and simple to administer[1,2]. Drug release is regulated and consistent with controlled-release drug delivery systems (CRDDS)[3,4]. A necessary condition for the effective administration of oral CRDDS is that the medication must be well absorbed throughout the gastrointestinal tract (GIT)[5]. The typical oral dosage form offers a precise medication concentration in the systemic circulation, but it also has significant variability in plasma drug levels and no control over drug administration[6].The goal of the gastro-retentive drug delivery system (GRDDS) is to target site-specific medication release in the upper gastrointestinal tract (GIT) by extending the stomach residence period[7].

There are several ways to retain food in the stomach, including floating systems, which include low density in the gas generating system, and swelling systems, in which the dosage form floats in the gastric fluid because the component density should be lower than the stomach[8].

The dosage form in the bio adhesive system sticks to the mucosal surface; numerous theories underlie these systems. In the high-density system, the dosage form stays in the distal portion of the stomach because its mass is greater than that of the gastric fluid. The dosage form in the super porous hydrogel system swells as a result of water absorption via the porous material via a capillary wetting process. Polymers are present in raft forming systems, which are systems that float above the stomach contents and swell to form an insitu gel layer. Systems swell and unfold in expandable approaches, and this happens via diffusion[9].

Anatomy and Physiology of Stomach:

The stomach, which is situated between the oesophagus and small intestine, is the most dilated part of the digestive system. The duodenum's stomach opening is controlled by the pyloric sphincter. The fundus, body, antrum, and pylorus are the four anatomical parts that make up the stomach[9].

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Volume 9, Issue 3 May-June 2024, pp: 96-107 www.ijprajournal.com ISSN: 2456-4494

Stomachfunction:

The fundus is the stomach's main component; the body and antrum make up the stomach's greater portion. Food is ground and sieved by the antrum, while the fundus and body handle the storing. Gastric pits are absent from the mucosa that makes up the stomach[9].Figure no.1 represents physiology of stomach.

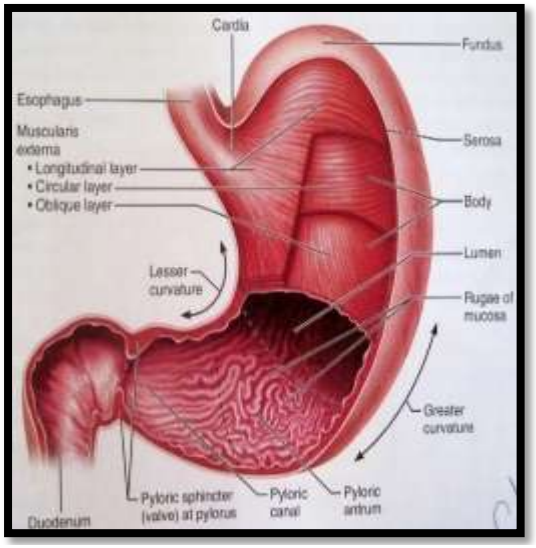

Fig no: 1 Physiology of stomach

Gastric Motility and Gastric Empty Rate: There are two different gastrointestinal motility and secretion patterns for the fed and fasting states. Figure no.2 represents phases of gastric motility and gastric emptying rate.

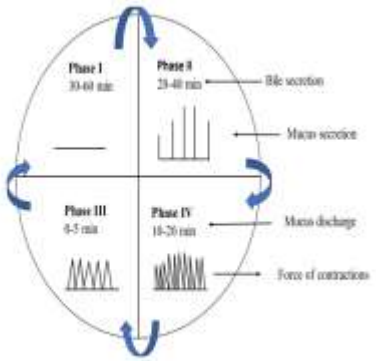

Fig no: 2 Phases of Gastric motility and gastric emptying rate

The condition of feeding affects the oral medication's bioavailability. An inter-digestive electrical event known as the inter-digestive myoelectric cycle or migrating motor complex(MMC) is what defines the fasting state. It's broken up into four stages[10].

a) Phase I (base phase), which lasts for 40–60 minutes and occasionally experiences contractions

b) The pre burst period, or period II, lasts for 40–60 minutes and is characterized by sporadic contractions and potential.

c) Phase III, or the burst phase, lasts for four to six minutes. During this time, there are brief but frequent, strong contractions. The undigested food is moved from the stomach into the intestine as a result of these spasms. We call these "housekeeper waves."

d) Phase IV lasts for 0–5 minutes and happens twice in a row, in between cycles III and I.

The contraction pattern that occurs after ingesting a mixed meal shifts from a fed to a fasted state; this is referred to as the digestive motility pattern. The food particles are reduced to less than 1 mm in size by these contractions, at which point they are sent in suspension form to the pylorus. The delayed start of MMC during the fed state causes the pace of stomach emptying to slow down[10].

Need for Gastro Retention[11]

1. Drugs that are absorbed from the proximal part of the gastrointestinal tract
2. Drugs with lower solubility or those that break down at an alkaline p^H
3. Drug absorbed as a result of a varied timing of stomach emptying.
4. Local or long-term medication administration to the proximal small intestine and stomach in order to address certain ailments.
5. Treatment of H. Pylori-induced peptic ulcers.

Potential Drug Candidates for Stomach Specific Drug Delivery System[12]:

1. Drugs that function locally within the stomach, like antacids and misoprostol
2. Drugs with a limited window of absorption in the gastrointestinal tract (GIT), such as riboflavin, furosemide, para amino benzoic acid, and L-dopa.
3. Drugs that disrupt the normal microbiota in the colon, such as antibiotics targeted against Helicobacter pylori; these include drugs that are unstable in the intestinal or colonic environment, such as metronidazole, captopril, and ranitidine HCl.

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4. Drugs that show poor solubility at high pH levels, such as verapamil hydrochloride, diazepam, and chlordiazepoxide.
5. Substances that shouldn't be used with stomach-specific medication delivery system
6. Drugs with extremely low acid solubility, such as phenytoin, etc.
7. Drugs that are unstable in the stomach environment, such as erythromycin, etc.
8. Drugs designed for the colon's selective release, such as corticosteroids and 5-amino salicylic acid.

Advantages of Gastro Retentive Drug Delivery System

1. It lowers the frequency of doses, which improves patient compliance.
2. The buoyancy increases the gastric residence period.
3. Improved treatment outcome from short half-lives medications
4. It is possible to delivery drugs to the stomach at a specific site.
5. Designing for continuous release can help prevent gastric discomfort.
6. Because a single floating unit, like microspheres, releases medication equally, there is no chance of dose dumping.
7. For local action in the upper portion of the small intestine, such as the treatment of peptic ulcer disease, a longer duration spent in the stomach may be beneficial.
8. Drugs that are quickly absorbed in the GI tract upon release, such as ranitidine, ciprofloxacin, and cyclosporine, should have improved bioavailability.

Disadvantages of Gastro Retentive Drug Delivery System

1. Floating systems need a lot of fluids in the stomach in order to function properly. Thus, with this dosage form, it is recommended to drink more water.
2. A floating dose form in a supine posture, such as when sleeping, may be carried away by contractile waves, if it is not greater in size. Thus, the patient shouldn't take their floating dosage form right before bed.
3. It is not possible to combine medications that irritate the stomach mucosa, have very low solubility in acidic environments, or have stability issues in highly acidic environments into GRDDS.
4. A swelling dosage form should rapidly expand within the stomach to surpass size of pyloric aperture before exiting. It needs to be able to withstand Phase III of MMC's housekeeper waves.
5. There are numerous factors that affect gastric retention, including pH, food presence, and stomach motility. Since these variables fluctuate, it is impossible to predict the buoyancy.

   These kinds of systems are not appropriate for drugs that have stability and solubility issues in the gastrointestinal tract.

II. GASTRO RETENTIVE TECHNIQUE:

There are several techniques available for gastro retention. Figure no.3 represents different gastro retentive techniques.

Fig no:3 schematic representation of different Gastro retentive techniques

1.Floating Drug Delivery Systems (GRFDDS):

These are low-density systems float in the stomach for an extended amount of time without slowing down the process of gastric emptying since their density is less than that of gastric fluid (1.004 gm/cm3). There are two main categories for GRFDDS[13].

1.Non effervescent systems
2.Effervescent systems

Non- Effervescent System[14]:

Gel-forming or highly swellable cellulose type hydrocolloids, polysaccharides, or matrix-forming polymers like polyacrylate, polycarbonate, polystyrene, and polymethacrylate are typically used to produce non-effervescent floating drug delivery systems[15,16].the intimate blending of a drug with a

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hydrocolloid that gels and comes in contact with stomach fluid after oral administration while maintaining a relative integrity of shape and a bulk density below unity in the stomach environment[17].Because of their tendency to remain lodged close to the pyloric sphincter, this sort of system is also known as a "plug type system.

Effervescent System:

Drug delivery system floating in stomach that is either empty, partially full, or filled with an inert gas. An organic solvent (such as ether or cyclopentane) can volatilize and release gas into the floating chamber, or CO_2 can be created when organic acids and carbonate bicarbonate salts react effervescently. These devices contain a hollow, deformable unit that may be extended or collapsed, and it returns to the collapsed position after a predefined period of time, allowing a thin, floatable system to spontaneously exit the stomach[10].

a) Gas Generating System:

When the mixture is placed in the beaker, it sinks and rises and floats due to the effervescent reaction between the carbonate/bicarbonate salts, citric/tartaric acid, and CO_2. This reaction occurs in the presence of water[18].Figure no.4 represent gas generating approach for floating drug delivery.

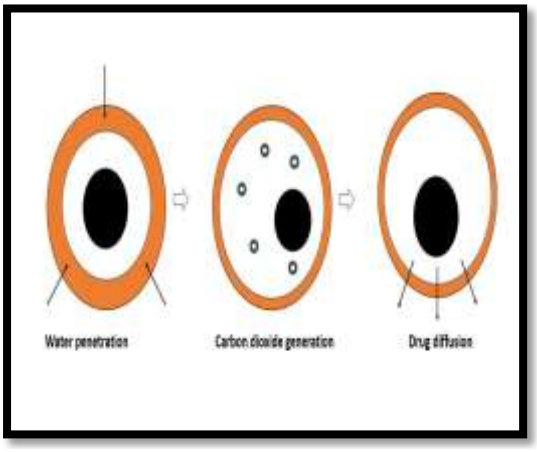

Fig no:4 A approach of Gas Generating System

b) Volatile Liquid Containing System:

It consists of the liquid inside an inflatable chamber similar to ether, which at body temperature produces gas and causes the inflation chamber to expand. Following ingestion, the capsule releases the drug reservoir along with the inflatable because of the formation of carbon dioxide gas bubbles caused by the incorporation of carbonates or bicarbonate by contact with gastric region[19].Figure no.5 represents volatile liquid containing system.

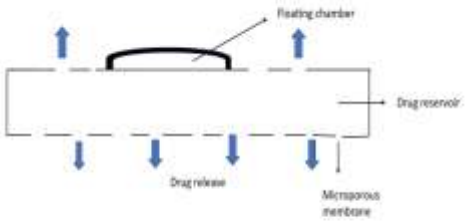

Fig no:5 Volatile liquid containing system

2. Raft Forming System:

In this process, a viscous gel containing trapped carbon dioxide bubbles on contact with gastric fluid is created by carbonates or bicarbonates. Formulation often typically contains antacid such as aluminium hydroxide or calcium carbonate to minimize gastric acidity. They create a layer on upper of gastric fluids which are often used in GI treatment as with water[20]. Figure no.6 represents raft forming system.

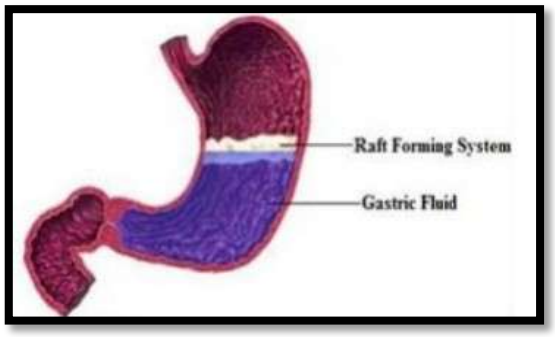

Fig no: 6 Raft forming system

3. High-Density Systems:

These systems, which are confined within the stomach's rugae and can endure its peristaltic movements, have a density of about 3 g/cm3. Above a threshold density of 2.4–2.8 g/cm3, such systems can be retained in the lower part of the stomach[21]. Pellets are small enough to be held in the rugae, or folds, of the stomach body close to the pyloric region-the area of the organ with the lowest position when in an upright position-sedimentation has been used as a retention mechanism. Robust pellets (about 3g/cm3) enclosed in rugae also have a tendency to endure the stomach wall's peristaltic motions. The average GI transit time of pellets can

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 96-107 www.ijprajournal.com ISSN: 2456-4494

be extended from 5.8 to 25 hours; this depends more on the density of the pellets than on their diameter. It appears that a density around the threshold density is required to significantly extend the gastric residence duration. Excipients such iron powder, zinc oxide, barium sulfate, and titanium dioxide are frequently utilized. Figure no.7 represents high density system. Density can be increased by these materials by 1.5–2.4 g/cm3[22,23,24]

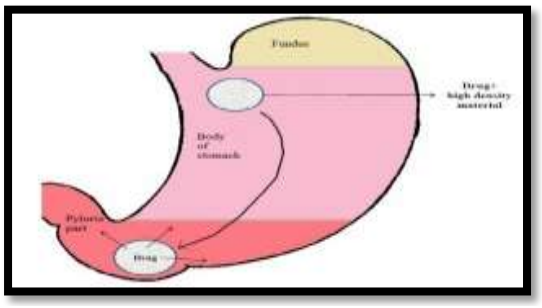

Fig no: 7 High density system

4.Swelling and Expanding Systems:

Swelling and expanding systems(Figure no.8) are dosage forms that, after swallowing, swell to an extent that prevents their exit from the pylorus[25]. The dosage form is therefore kept in the stomach for an extended amount of time. Since these systems have a tendency to become logged at the pyloric sphincter, they are referred to as "plug type systems." The drug delivery device can cause swelling and controlled drug release when it comes into contact with gastric fluid because the polymer absorbs water and swells. The presence of physical-chemical crosslinks in the hydrophilic polymer network causes the polymer to swell extensively. Housekeeper waves are suppressed by the bulk, which permits gastric retention and keeps the stomach in a "fed" state [26,27].

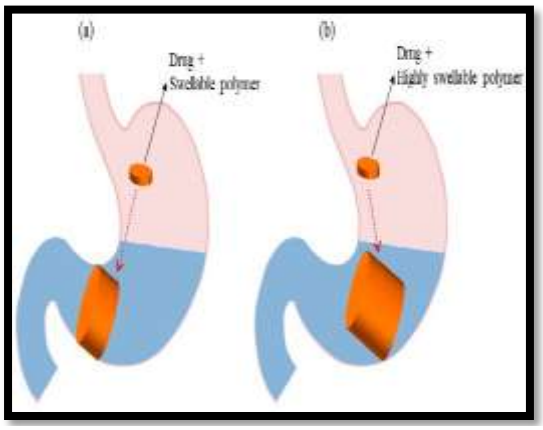

Fig no: 8 Swelling and expanding systems

5.Super Porous Hydrogels:

In this approach to enhance gastric retention time (GRT) super porous hydrogels having average pore size > 100 micrometres expand to equilibrium size in less than a minute because of their quick absorption of water through capillary wetting through multiple interconnected open pores. They have a huge swelling ratio (100 or more) and are designed to be strong enough to withstand pressure from the contraction of the stomach. This is accomplished through co-processing with croscarmellose sodium, a hydrophilic particle substance. This, during synthesis, creates a dispersed phase within the continuous polymer matrix ("super porous hydrogel composites"). For more than 24 hours, the super porous hydrogel composites will remain in the upper GIT [28,29,30]

6. MagneticSystem and Self-Unfolding Systems:

This is made up of an abdomen-placed magnet over the stomach location and a little inside magnet. These systems are a kind of treatment where a magnetic substance is present. The removal of the substance is prevented by applying a powerful enough magnet to the stomach region of the body. The capacity to mechanically grow in proportion to the initial dimensions is referred to as the self-unfolding systems. This increase keeps the medication from passing through the pylorus and preserves its prolonged stomach stay. A drug may be incorporated into the polymer composition of the gastro retentive system or it may be added as a separate part. When stomach juice comes into touch with the hydrogel, it expands[31,32].Figure no.9 represents magnetic and self-unfolding systems.

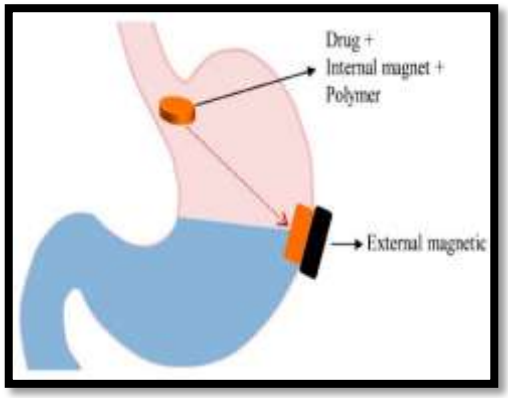

Fig no: 9 Magnetic System and Self-Unfolding Systems

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7.Bioadhesive or Mucoadhesive Systems:

Bioadhesive is the term used to describe mechanism of adhesion to the mucosal or biological surface. Interaction of polymers with mucosa termed as Mucoadhesion. The mucin gel layer's thickness varies depending on the area; in the stomach, ranging between 50-500 micrometers, while in the colon, it is between 15-150 micrometers. The adhesive qualities of the layer are determined by the concentration of glycoproteins in the layer. These systems are used for the buccal, oral, rectal, and vaginal routes of administration. The GI tract's self-protecting mechanisms are maintained by the goblet cells constant production of mucus for protective action[33].Figure no.10 represents bio adhesive or mucoadhesivesystems.

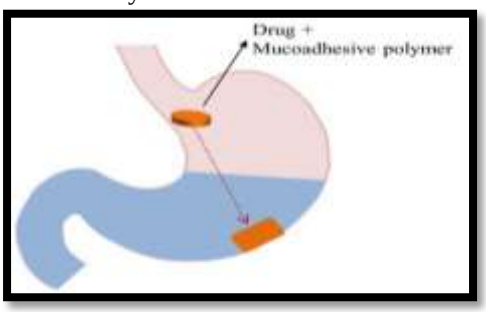

Fig no: 10 Bio adhesive or Mucoadhesive Systems

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Factors Controlling GRDDS[34,35,36,37]

1. **Density:** High density dose forms sink to the bottom of the stomach, low density dosage forms may float to the top. For floating property, an appropriate density of less than 1.0 gm/cm³ is needed.
2. **Size:** Size should have a diameter of greater than 7.5 mm.
3. **Shape:** Dosage forms with spherical or circular shapes have superior properties than those with other shapes.
4. **Single or multiple unit formulation**: Because they have a predictable release profile, multiple units are preferred.
5. **Fed or Unfed State:** During a fast, gastric retention time falls as a result of an increase in stomach motility.
6. **Meal Type:** To extend the gastric retention period, a high concentration of fatty acids and other indigestible polymers are produced by variations in stomach motility.
7. **Feeding Frequency:** Depending on how frequently food is consumed, a low frequency of migrating myoelectric complex (MMC) can contribute to GRT up to 400 times.
8. **Caloric Content:** A high-protein and high-fat diet can increase GRT by four to ten hours.
9. **Gender:** Men have a higher GRT than women do.
10. **Age:** GRT is less common in young children and infants and more common in elderly people. People above 70 (>70) exhibit prolonged GRT.
11. **Posture:** GRT can vary from the patient's supine to upright ambulatory phases.
12. **Disease State:** Individuals with stomach disorders including diabetes, crohn's disease, hypo- or hyperthyroidism, duodenal ulcers, etc., have altered GRTs.
13. **Concomitant Drug Intake:** Taking certain drugs along with depressants or boosters of gastric motility can affect gastric reflux therapy (GRT).

III.POLYMERIC MATERIALS IN GASTRO RETENTIVE FORMULATIONS:

1.Hydroxypropylmethyl Cellulose (HPMC)

The most often used hydrophilic carrier material in the production of oral controlled drug delivery systems is hydroxypropyl methylcellulose (HPMC)[38]. In HPMC, also referred to as hypromellose, a cellulose ether, one or more of the three hydroxyl groups from the cellulose glucopyranose units have been altered, forming ether linkages. As a result, it is a semisynthetic polymer made from highly purified natural pulp that is etherified using a methyl chloride and propylene oxide mixture to produce a non-ionic, water-soluble cellulose ether[39]. The two brands under which the most widely used HPMC is marketed are Methocel® and Pharmacoat®.

2.Chitosan

Chitosan is the term used for the N-deacetylated form of chitin. It is a naturally swellable polymer. chitosan that includes main amino groups, which exhibit mucoadhesive qualities, controlled release action, in-situ gelation, and increased permeability Because chitosan is a non-toxic, biodegradable, and biocompatible polymer, it can be directly compressed or granulated and used in oral extended-release tablets[37].

3.Carboxymethyl cellulose (CMC)

Carboxymethyl cellulose (CMC) is a water-soluble, semisynthetic, nontoxic cellulose derivative that has carboxymethyl groups (-CH_2-COOH) bonded to some of the hydroxyl groups of

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the glucopyranose repeating units of the cellulose backbone via an ether bond. NaCMC's anionic carboxylate groups may enhance the gel-viscosity properties of nonionic hydrocolloids like HPMC and HEC through interactions with them[40].

4. Natural Gums

Natural polymers have many useful uses in biology and medicine because they have advantageous qualities including safety and biocompatibility. Drug release from swellable systems has been effectively controlled by the use of natural polymers as hydrocolloids in addition to synthetic cellulose ethers[41]. Together with other polysaccharides like chitosan and alginates as well as natural polymers like pectin and gelatin, natural gums such as xanthan gum, guar gum, gellan gum, and carrageenans are natural hydrocolloids or gel-forming agents that can swell in contact with gastric fluid, maintain relative shape integrity, and have a bulk density less than the gastric content[42].

5.Guar gum

Guar gum is obtained from the seeds of the legume family plant Cymopsistetragonolobus. Guar gum swells quickly in the presence of water with a translucent suspension because of its dual composition, which consists of an insoluble component and an approximately 85% water-soluble portion known as guaran. Because of the mannose units, cohesive structural gels are formed when borate ions are added to hydrated guar gum[39]. In the pharmaceutical business, guar gum improves viscosity and functions as a disintegrant and binder when used in solid dosage forms[42].

6. Gellan Gum

Gellan gum works as a crosslinking agent when Ca^{2+} ions are present, which allows for in-situ gel formation. When coupled with Ca^{2+} ions, gellan gum can be used as a crosslinking agent in in-situ gels.

7. Xanthan Gum

Xanthan gum is utilized in food, cosmetics, and topical and oral medication formulations due to its non-toxicity and non-irritating properties[43].

8. Poly (ethylene oxide) (PEO)

High molecular weight PEO has shown to be an excellent option for controlled release dosage forms due to its ability to sustain API release through the rate at which the polymer swells and erodes. High molecular weight PEO may form dense polymeric networks in aqueous conditions, which makes it viscoelastic in its inflated state[44]. For highly swellable and mechanically robust matrix tablets, PEO is therefore relevant as an addition to enhance their mechanical qualities[45].

Twenty tablets were selected randomly for the test, and the percentage of drug content was found. If the tablets contained at least 85% or at least 115% (100±15%) of the prescribed amount of drug, the test was considered to be passed.

Assay

Each formulation's drug content was determined by triturating 20 tablets and dissolving the powder to the equivalent of one hundred ml of 0.1N hydrochloric acid using a 30-minute sonication process. After passing through a 0.45µ membrane filter and being appropriately diluted, the absorbance of solution was measured spectrophotometrically at the API's λ_{max} (nm) using 0.1 N hydrochloric acid as a blank. Density Usingvernier callipers, the thickness of each tablet formulation was tested by placing the tablet between two arms of the vernier calipers[47].

In-Vitro Buoyancy Studies

Floating lag time was defined as the amount of time needed for the tablet to rise to the surface and float.

IV.EVALUATION OF FLOATING TABLETS

Pharmacopeial Tests[45]

Hardness

By applying diametric compression, a Monsanto Hardness Tester was used to determine the tablets hardness. Mechanical stability is thought to be achieved with a tablet hardness of 2-4 kg/cm^2.

Friability

Using a Roche Friabilator, the tablets' friability was assessed. After taking 20 tablets, the initial weight (W_0) was recorded, and the tablets were weighed again after being dedusted in a drum for a predetermined amount of time (100 freefalls in a Roche Friabilator). The weight decrease as shown by the equation below was used to compute the percentagefriability.

A weight loss of little more than 1% is acceptable[46].

Percentage Friability = (Initial weight-Final weight)/Initial weight*100

Content Uniformity

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The tablets were added to 0.1N HCl in a 100 mL beaker[48,49].

Weight (%) = W_f / W_f + W_s * 100

W_s = weight of the settled microspheres

W_f = weight of the floating microspheres

In-Vitro Dissolution Study

The USP XXIII type-II dissolution test apparatus (Paddle type) was used for the In vitro dissolution research of the floating tablets. The dissolution media used was 900 ml of 0.1 N HCl, which was mixed at 50 rpm and 37±0.5°C. Using a syringe equipped with a pre-filter, 5 ml of the samples were taken out at pre-arranged intervals. The volume taken out was replaced with the same amount of new dissolving media each time. After the appropriate dilutions, the resultant samples were examined for the presence of the drug release by measuring the absorbance at $\lambda_{max}$of API (nm) using a UV Visible spectrophotometer[50].

Kinetic modelling of drug release

To determine the kinetic modeling of drug release, the dissolution profiles of all the formulations were fitted into first-order, zero-order, Higuchi, and Korsmeyer-Peppas models.

In Vivo Evaluation for Gastro-Retention

X-ray and gamma scintigraphy are widely utilized evaluation methods for floating dosage forms in contemporary pharmaceutical practice. This technique aids in pinpointing the location of dosage forms within the gastrointestinal tract (GIT), facilitating the prediction and correlation of gastric emptying time with the passage of the dosage form through the GIT. Here the inclusion of a radio opaque material into a solid dosage form enables it to be visualized by X rays. Similarly, the inclusion of aγ emitting radionuclide in a formulation allows indirect external observation using a γ camera or scinti scanner. In case of γscintigraphy, the γ rays emitted by the radionuclide are focused on a camera, which helps to monitor the location of the dosage form in the GIT. The Formulated Tablets (Tranilast Eudragit S ($BaSO_4$) Isardipine (HPMC) system) and for In Vivo studies two healthy male volunteers administered hard gelatin capsules packed with micro ballons (1000 mg) with 100 mL water. X-ray photographs at suitable intervals were taken[46].

Two phases:

Phase I (fasting conditions): In an open randomized crossover design with five healthy volunteers (two females and three men), tablets were consumed in sitting position and 100 ml of tap water was provided. Phase II (fed states): Following a typical breakfast, four patients in a crossover design were given capsules with either MR or normal contents. Heparinized tubes were used to collect venous blood samples at pre-arranged intervals following dosage. Gamma scintigraphy was used to track the in-vivo behavior of coated and uncoated beads, as well as prepared floating beads, in a study including 12 healthy human volunteers with a mean age of 34 years.

Tablet density

It is a crucial floating tablet parameter. Only when the tablet's density is lower than that of stomach fluid will it float (1.004). The relationship below is used to calculate the density.

$$V = r^2hd = m/v$$

V = tablet volume (cc);R= Tablet radius (cm)
h = tablet crown thickness (g/cc)
m = tablet mass

Patents of gastro retentive drug delivery system:
Some of patented gastro retentive formulations are listed below in table no.1

Table 1: Patents of some gastro retentive delivery [47,48,49]

PATENT NUMBER	PATENT TITLE	INVENTOR
US5232704	Sustained release bilayer buoyant dosage form	IlkkaLarma MaaritBackman
US5169638	Buoyant controlled release powder formulation	Dennis Andrew Timmins Peter
US5972389	Gastric retentive, oral drug dosage forms for the controlled release of sparingly soluble drugs and insoluble matter	John W. Shell Jenny Louie-Helm
US5443843	Gastro retention system for controlled drug release	William J. Curatolo Jeelin Lo
US4767627	Drug delivery device that can be retained in the stomach for controlled period of time.	Larry J. Caldwell Colin R. Gardner

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US4814179	Floating sustained release therapeutic compositions	Daniel E. Gerard Joachim Schoelkopf
US4167558	Novel sustained release formulations	Jiri Lisal Jaroslava JAMAEINOVA
US4140755	Sustained release tablet formulations	ShethPrabhakar R Tossounian Jacques L
0013876A1	Novel floating dosage form	BrajBhushanLohray Sandip B. Tiwari
6,207,197B1	Gastro retentive controlled release microspheres for improved drug delivery	Lisbeth Illum Nottingham
US8586083B2	GRDDS comprising an extruded hydratable polymer	Hassan Mohammad Littleport
EP2061438A1	Extended release gastro retentive oral drug delivery systems for valsartan	Nikhil Javant ParthibanLakshman
US5169639	Floating tablet	Anand R. Baichwal John N. Staniforth

Marketed products of gastro retentive drug delivery system: Some of the marketed gastro retentive formulations are listed below in table no.2

Table 2: Marketed gastro retentive products [49,50]

Drug	**Brand name**	**Drug**	**Brand name**
Diazepam Floating capsule	Valrelease®	Diazepam Floating capsule	Valrelease®
Aluminium Hydroxide	Liquid Gavison	Aluminium Hydroxide	Liquid Gavison
Benserazide and L-Dopa	Madopar®	Benserazide and L-Dopa	Madopar®
Misoprostol	Cytotech®	Misoprostol	Cytotech®
Aluminium-Magnesium antacid	Topalkan®	Aluminium – Magnesium antacid	Topalkan®
Metformin HCL	Glumetza GRTM	Metformin HCL	Glumetza GRTM

V.CONCLUSION

Improved bioavailability and regulated medication delivery are two potential benefits of the gastro retentive drug delivery system. The use of a gastro-retentive medication delivery device has the potential to improve drug gastric retention. An increasing number of drug delivery systems will be developed in order to optimize the distribution of molecules demonstrating regional variability in drug absorption, as a result of a growing understanding of the impact of GIT physiology on drug delivery. As delivery technologies become more advanced, more gastro-retentive drug administration methods will be developed to maximize the delivery of compounds with long half-lives, low bioavailability, and extensive first pass metabolism. After reviewing the literature, we came to the conclusion that gastro-retentive drug administration has a number of potential benefits for medications whose absorption is poor. A gastro retentive drug delivery device maximizes the patient's benefit. There are now several methods for extending the duration of gastric retention. These include modified shape systems, high density systems, polymer bioadhesive systems, swelling and expanding systems, floating drug delivery

systems also referred to as hydrodynamically balanced systems and other delayed gastric emptying devices.

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