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Gastro-Retentive as Most Promising Drug Delivery System

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

The aim of any research work is to find the complications associated with the drug or formulation and find the conclusion of what can be the best possible way to solve them. It has been observed that drugs with short half-life, pH-dependent solubility and having absorption window in upper part of GIT forms good drug candidate for gastro retentive system. Since the formulation reside at a particular site and releases the drug in a controlled manner. In this review article, we have focussed on a thorough understanding on the gastric region, which helped in selecting drugs, various types of gastro retentive systems, new outcomes from recent literature, and important evaluation parameters to attain formulation objective and various marketed products available.

Keywords: Stomach; gastric residence time; bioavailability; absorption window.

1. INTRODUCTION

Although many routes found to be successful in achieving the therapeutic objective, oral route has its own importance and place due to its many advantages. The first most important is its easy administration, which lead to better patient compliance, other advantages are like dose

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strength flexibility, low cost of manufacturing, delivery of drugs for longer period of time using the concept of control release and more over bioavailability issue can be solved by reformulating, hence one can reach higher level of patient compliance[1]. According to one of the study it has been found that 50% of the drugs are available in the market as oral drug delivery system. So one can go for gastro-retentive drug delivery system (GRDDS) as such approach where the feature of gastric retention time combined with the controlled drug release for required extended time. Being so popular the oral conventional drug delivery system facing some unforeseen constraints which lead the evolution of the researchers to such new delivery system. One the limitation which always created restriction in formulating oral preparation is drugs less solubility at higher pH of intestine. It can be solved by just retaining the preparation in stomach for prolonged period of time, and this can become easily possible with gastro retentive system [2].

To keep the dosage form in the stomach, a variety of methods are now in use. Floating, effervescent, bio-adhesive, swelling, and expanding systems are a few examples, as are delayed stomach emptying devices such raft forming systems. Apart from the formulation part one should also consider the gastro-intestinal (GI) tract. The GIT is composed of several regions with varying the gastro-intestinal anatomy, motility, biochemical environment such as secretions, microbial flora, and expression of transporters which ultimately decide absorption characteristic of drug [3]. As soon as the drug administered orally, all other process such as drug absorption, active or passive transport, efflux by P- glycoprotein, metabolism by cytochrome-p450 also come in synchronisation simultaneously, thus one can say the delivery site can say has its higher influence in designing the drug's pharmacokinetic profile [4]. In comparison to these traditional dosage forms, gastro retentive approach can be perfectly designed so that the drug remain in the stomach for a prolonged, as well as predictable time. Ultimately the drug's gastric residence time gets extended and bioavailability aspect can be improved [5].

2. ANATOMY AND PHYSIOLOGY OF STOMACH

One should have thorough understanding of GIT before proceeding to make gastro retentive system. This is because some time the physiological aspects itself becomes barrier for attaining therapeutic objective.

One of the pouch like looking part of our digestive system is stomach. The stomach lies between the oesophagus and small intestine. During resting or empty condition the stomach gets contracted in to numerous folds which we call as rugae, which gets expanded when food or water enters to attain its bulk. The four main basic types of secretary cells, epithelial cell that covers the stomach and extends into gastric pits and glands.

1. Mucous cells which helps secretion alkaline mucus
2. Parietal cells which helps in secretion hydrochloric acid
3. Chief cell which secrete pepsin enzyme
4. G –cells which helps in secretion hormone gastrin.

The stomach is divided into three divisions, each of which performs a different function, according to popular perception.

- Fundus
- Body
- Antrum (pylorus)

Whenever we eat food or take any medicine, the ingested material get stored in the fundus and body which acts as primary site for storage of such undigested food. Whereas pyloric region part helps in mixing and further movement. Such alternating moving activity and relaxation of gastro intestinal activity can be expressed in cyclic pattern. There are main four distinct periods of such activity as shown below [6].

2.1 Different Physiological Features of Stomach

Gastric pH: it is always advisable to determine pH of gastric content in both fasted and fed state and its found that fasted healthy subject have approximately 1.1 whereas fed healthy subject have 3.6.

Volume: individuals with resting volume is approximately in the range of 25-50 ml.

Gastric Content Secretions Includes: The acid, pepsin and gastrin enzyme, and mucus approximately 50-60 ml with about nearly 4 mm of hydrogen ions.

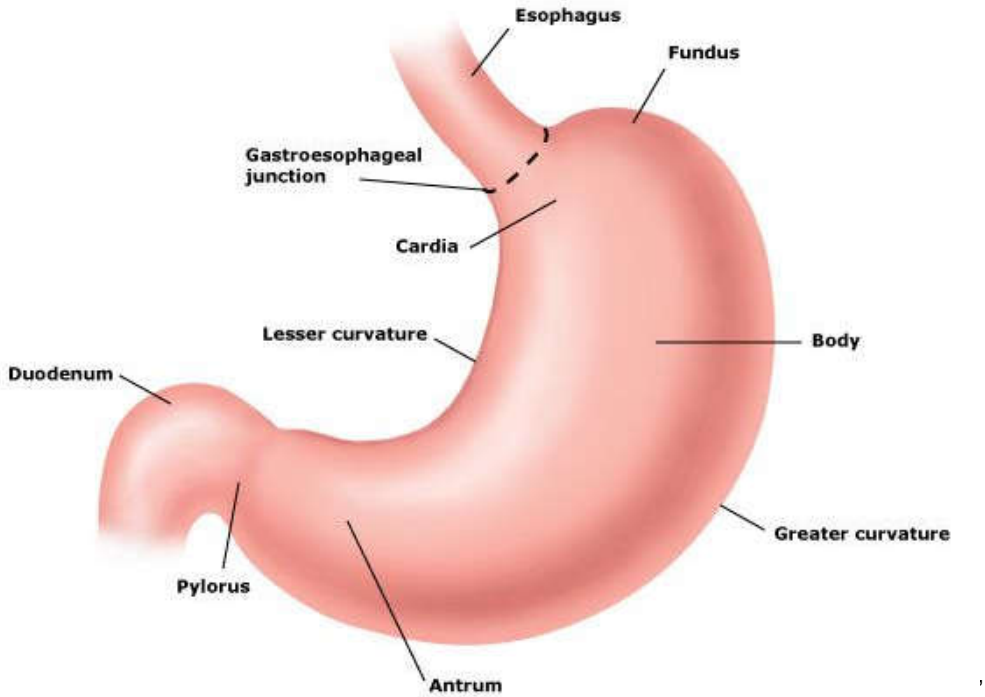

Fig. 1. Anatomy of stomach
Ref:www.harvard-wm.org/anatomy

Table 1. Gastro-intestinal motility phases

Name of phase	Duration in minutes	Activity
Phase-I (Basal)	30-60	Relaxation without contraction
Phase-II(pre-burst)	20-40	Gradual increasing sequential contractions
Phase-III(brust)	10-20	4-5 Contractions per min
Phase-IV	0-5	Dissipating contractions between Phase I and

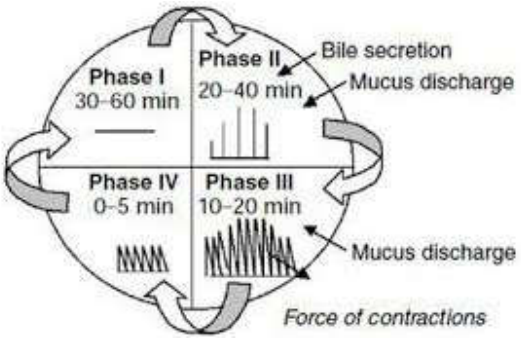

Fig. 2. Gastro-intestinal motility phages
Ref: Swapnil More et al Journal of Drug Delivery & Therapeutics. 2018; 8(4):24-35

Food on Gastric secretion: Approximately 3 liters of gastric secretions will be added to the food each day.

3. FACTORS TO BE CONSIDERED IN GASTRIC RETENTION OF DOSAGE FORMS

Because the human body physiology differs from person to person, several parameters must be addressed in order to keep a dosage form at a specific location, some of which are listed below.

3.1 Density of Dosage Forms

One of the factors that has a stronger impact on dosage form retention is density, which influences not only gastric emptying time but also helps determine the placement of the system in the gastric area. If you prepare a dosage form with the density lass than gastric content it will start floating on the surface where as a dosage form with greater density try to sink to bottom

and get moved further. In both the circumstances the dosage form gets departed from pyloric region. One can achieve gastric retention using either of the situations. To possess floating property, the dosage from should have density less than one gm/cm3 is required [7].

3.2 Shape and Size of the Dosage Form

One of the aspect of dosage form which has greater influence on gastric retention time is size and shape of the formulation. Especially when floating mechanism is involved in gastric residence. It has also been observed that larger sized dosage form have greater buoyancy time. One must give due consider to shape and size of the dosage forms while designing. When compared to one with a diameter of 9.9 mm, an ideal size of 7.5 mm has shown to have a better stomach residence time. In compared to other shapes, ring and tetrahedral shaped devices have shown to have a longer stomach residency period [8].

3.3 Food Intake and its Nature

The food we take has greater influence on gastro intestinal motility hence gastric residence time of dosage form. It has been observed that during fasting gastric residence decreasing while during fed condition gastric residence is increasing this is also leading the dosage form to get enough time for absorption.one can conclude presence of food has positive effect**.** Along with the type of food, the amount of food consumed, the nature of the food, the volume viscosity of the food, the frequency of feeding, and the caloric content of the food, all of these factors have a substantial impact on the stomach retention of dosage forms. Furthermore, as acid levels and caloric value increase, such as when eating a fat-rich food, the stomach emptying time of dose forms improves [9].

3.4 Effect of Gender, Posture and Age

Males have a higher metabolic rate than females, which would be factual. As a result, females have a slower stomach emptying rate, resulting in a longer gastric retention period. Apart from gender, the influence of posture on stomach retention time has been investigated in persons who are either upright, supine, or ambulatory, and it has been discovered that none of these postures have a significant effect. However, in the case of the old people, gastric emptying is slowed due to age related factor [10].

4. APPROACHES TO DESIGN GASTRO RETENTIVE DRUG DELIVERY SYSTEM

4.1 Effervescent System

The effervescing property of mixed ingredient is used in such matrix systems. These system contain one or more hydrophilic polymer such as chitosan blended with effervescent compound such as citric acid and sodium bicarbonate. These system when taken orally come in contact with water content of gastric juice the polymer swell and liberated carbon dioxide get trapped into swollen polymer due to which system gets floating property. Based on source floating agent these are further classified as.

1. Volatile liquid containing system
2. Gas generating system.

These systems typically include two compartments: a flotation compartment and a drug reservoir compartment, where the drug is present in solid form. There are three different types of flotation mechanisms [11].

4.1.1 Intragastric floating system

These system uses vacuum mechanism for achieving floating They have two chambers: one is the floatation chamber, which can be vacuum-sealed or filled with an inert gas, and the other is the drug reservoir, which is encased in a microporous membrane and releases the medication in a regulated manner.

4.1.2 Inflatable delivery systems

These systems also have two chambers: the floatation chamber, which is made up of a liquid, such as ether, that expands with body temperature to fill the drug storage chamber at the plantation site. The medicine is delivered slowly from the reservoir chamber into the gastric fluid, depending on the rate of ether evaporation.

4.1.3 Intragastric osmotically controlled system

These system also comprise of two chambers the floatation chamber, contains osmotic active compound which exert osmotic pressure and drug reservoir compartment separated from floating compartment by bioerodible polymer plug which slowly erodes after a predetermined time, from which the drug release is intragastirc osmotically controlled. The deflated drug delivery system is then emptied from the stomach.

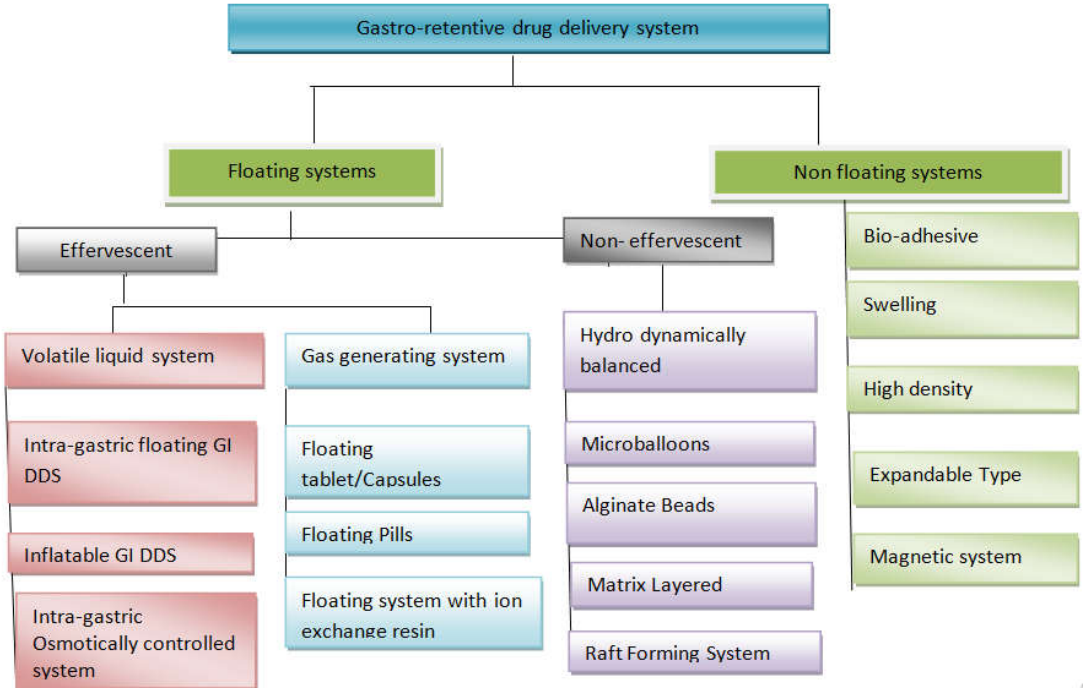

Fig. 3. Flowchart showing different approaches for gastro-retentive drug delivery systems
Ref: B. Venkateswara Reddy et al/JGTPS/Volume 4, Issue 1, January-March 2013

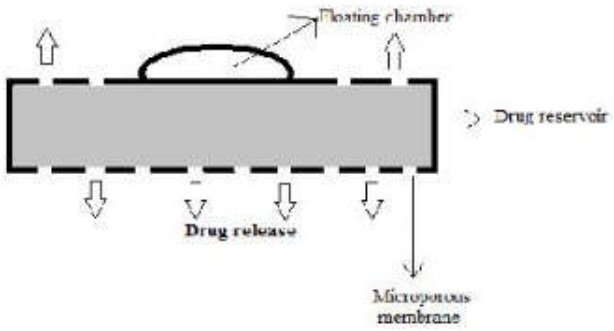

Fig. 4. Intragastric floating

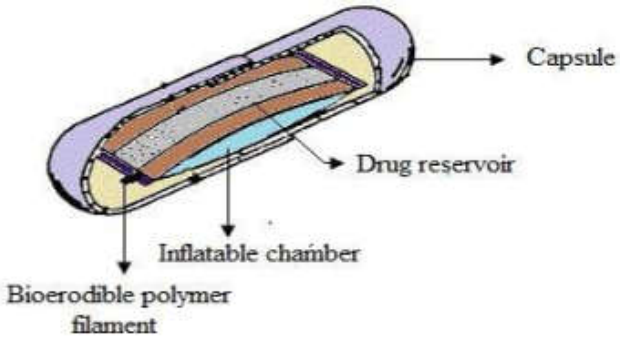

Fig. 5. Inflatable

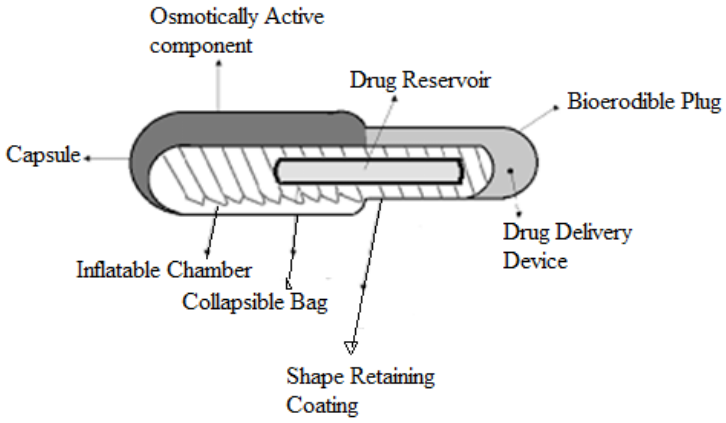

Fig. 6. Intragastric osmotically controlled
Ref: B. Venkateswara Reddy et al/JGTPS/Volume 4, Issue 1, January-March 2013

4.2 Gas Generating System

4.2.1 Floating capsule/tablet

The formulation is enclosed in a capsule shell formed of polymers (e.g. Alginate) that floats on the surface of the stomach content and so provides gastric retention in this type of gastro retentive drug delivery method [12].

These are made with the goal of providing sustained release by using a variety of polymers that can float in the stomach due to a swelling process, extending the formulation's gastric retention duration [13].

4.2.2 Floating microspheres

These formulations are part of the gastro retentive system, which has a lower density than gastric fluid, allowing the microparticles to stay suspended in the stomach for a longer period of time**.** These microspheres are made from a biodegradable polymer called Eudragit and are made using the solvent evaporation process. When these microparticles float in the stomach, the medicine is delivered slowly and at the rate desired [14].

4.2.3 Ion-exchange resin systems

The cationic or anionic polymeric resin (cationic or anionic) in the ion exchange resin has the ability to release the medicine at a controlled rate. The medicine will be chosen based on the ionic nature of the resin. A cationic resin, for example, is used to transport cationic drugs, and the drug resin complex is known as resinate. When these resinates come into touch with the hydronium ion in gastric content, the adsorbed medication is released [15].

4.3 Non Effervescent System

These non-effervescent system uses swelling mechanism to achieve floating property. The polymer used here are polysaccharides hydrocolloids and some matrix forming polymers such as polycarbonate, polystyrene and polymethacrylates etc. depending upon the method of preparation and drug incorporation, these further discussed as follows.

4.3.1 Hydro dynamically balanced

These HB system uses gel forming property of hydrocolloids. In this system drug is incorporated with one or more polymers which are present in single unit. As they come in contact with water the polymer swell provides the buoyancy. Depending upon the water penetration the drug release can can be controlled. A.K. Nayak et al. Prepared Ofloxacin HBS capsule by simple blending of ofloxacin with different polymers. HBS ofloxacin capsules showed sustained drug release over a period of time 6 h. [16].

4.3.2 Micro-balloon

These are hallow preparations that look like balloons and contain a medication. Balloon structures can be made from both natural and synthetic polymers. They're made using the emulsion solvent diffusion method. The main releasing mechanism was discovered to be diffusion. These tiny balloons have good in vitro

floatability, and another advantage is that as the polymer concentration rises, drug release decreases dramatically [17].

4.3.3 Alginate beads

These multiunit spherical shaped beads are made using a simple precipitation procedure in which the alginate solution is dropped directly into an aqueous solution containing calcium chloride, where it precipitates as calcium alginate beads. These porous devices can sustain their floating state for up to 12 hours [18].

4.3.4 Matrix layered:

Single Layer Floating Tablets: these are prepared by simple dispersion technique. By direct blending drug with hydrophilic polymer. The resulting blend is then compressed in to a tablet. These tablets upon contact with gastric juice swell and provide buoyancy to the preparation [19].

Bilayer Floating Tablets: A bilayer tablet seems to have two layers: one immediate release layer that releases the initial loading dose from the system which provide the required therapeutic concentration and another maintenance dose layer that absorbs gastric fluid and forms an impermeable colloidal gel barrier on its surface, allowing the dosage form to float in the stomach by having a bulk density less than the gastric fluids.

4.3.5 Raft forming systems

A raft is a simple flat log or plank that floats on water and can be used for transporting. It is often float on the surface. The raft formation mechanism involves when a viscous cohesive gel of a system on contact with gastric fluids, absorb the surrounding water, in which each portion of the cohesive gel expands and forms a continuous layer over the other called a raft. Because of its decreased density, this raft floats on stomach contents. usually these systems contain hydrocolloid polymer with carbonate or bicarbonate which are accountable for generation carbon dioxide which make the system less dense which float on gastric content Alginates are one of the most widely used biopolymers. Alginate is commonly used as an excipient in pharmaceuticals because of its thickening, gel-forming, and stabilising qualities. For almost 30 years, alginate-based raft-forming formulas have been sold under a variety of brand names, including Gaviscon [20].

4.4 Bioadhesive Systems

These systems make use of the polymer's capacity to adhere to mucus, and the close contact between the drug delivery system and the epithelial surface on a specific spot promotes gastric retention and hence bioavailability. There are numerous polymers with bio adhesion properties, such as alginate and pectin.

4.5 Swelling Type

These system provides floating behaviour due to their swelling property, they swell to an extent that the formulation becomes a physical barrier which floats on gastric content and prevent its backflow called reflux which is one of desirable gastro retentive property. Such significant size changing behaviour is related to crosslinking property of hydrophilic polymer. Non-floating systems, often known as plug type systems, are a sort of non-floating system. The cross-linking also provides for gradual dissolution, increasing stomach retention and allowing for more controlled drug release [21].

4.6 High Density System

Withstanding the peristaltic movement is the main mechanism for achieving gastric retention. In this non floating system formulation sink settle at the bottom to an extent which becomes immovable. Such density forming preparation are made by using high density substances such as titanium dioxide. These formulations have density greater than 3g/cm3, which is sufficient with stand peristaltic movement [22].

4.7 Expandable Type

Folded systems are another name for GRDDS. These are made in such a way that when they come into contact with stomach content, they expand. These typically comprise of a drug-loaded bilayer polymeric film created by solvent casting, which releases the drug by an unfolding mechanism when exposed to light. The unfolding of the dose form in the stomach within 15-20 minutes after delivery results in gastric retention [23].

4.8 Magnetic System

GRDDS medication and polymer will be loaded into a small magnet in this type. To manage drug release, an external magnet will be used to locate the internal microscopic magnet present in

the stomach. However, such a formulation is not very successful because it is difficult to monitor drug release using an external magnet due to low patient compliance [24].

5. RECENT LITERATURE REVIEW ON GRDDS

Appala et.al [25] prepared floating matrix tablet using Gemofloxacillin a broad spectrum antibiotic. The drug was good solubility in acidic pH of gastric region which helped the formulator floating system as formulation. The tablet were prepared using excipients such as HPMC K4M, HPMC K15M, and POLYOX WSR 1105 Avicel PH102. The formulation was successful in achieving buoyancy up to 6 hours.

Fatema and shahi et al. [26**]** prepared Metoprolol beta one selective adreno receptor blocking agent as gastro retentive system. While formulating the researcher found drug was undergoing rapid first pass metabolism which resulted in poor bioavailability. When formulated using HPMC K100 M, mannitol, PVP, sodium bicarbonate, with MCC it was possible to solve the problem associated with it. The study that the formulation is able to release the drug in controlled manner to attain the objective.

Khalid El say [27] found that Carvedilol an antihypertensive drug was facing narrow absorption window and short half-life as complication to treat the condition, when the drug formulated in to gastro retentive system the formulation was to solve the both issue and fron invitro study it has confirmed that the drug was released in controlled manner for more than 12 hours.

Naufal et.al [28] prepared floating tablet using HPMC, citric acid and sodium carbonate by wet granulation. During the formulation development they found the drug Glipizide and Metformin have poor bioavailability due their absorption window. The researcher were able to solve third drawback by making as gastro retentive system. From the in vitro study it has revealed now the drug release in controlled manner over a period of 14 hours.

Jedi et.al [29] prepared effervescent floating tablet of Proponolol a beta adrenergic blocker in hypertension using excipient such as compritol-888 ATO, Precirol ATO5, HPMC K4M, HPMC K15M, Avicel PH200. The drug was absorption window due to which drug was showing 16% bioavailability. The formulation was able to solve smoothly the bioavailability issue and able to control the release by increasing residence time for hours.

Ramu and Pandiyan [30] prepared tablet using HPMC K100M, carbopol 974 and xanthan bum Avicle PH 102 and sodium bicarbonate. During the formulation researcher found selected drug Hydrochlorothiazide diuretic having poor solubility and absorption window in upper part of GIT which helped the formulator in deciding preparation of bio adhesive system increase gastric residence. Now the preparation is able to release drug in controlled manner over a period of time more than 12 hours.

Baratam and vijavratna [31] selected Levofloxacillin a third generation floroquinone a broad spectrum antibiotic. The floating tablets were prepared using HPMC, MCC as release retardant polmers and sodium bicarbonate as gas forming agent and found that the polymers were successful in controlling release of drug up to 12 hours.

Hendrika et al. [32] found that drug Amoxicillin new generation antibiotic was unable to treat infection cause by H..Pylori due to its less contact time at mucus surface which main region for disease causing organism. When formulated in to gastro retentive system it was able to release 90% drug at target site. The formulation was prepared by extracting pectin from banana peel. They used inotropic method to make the formulation.

Koppula subbarao et al. [33] formulated Rospinirol HCL a non ergoline dopamine antagonist tablet which was showing low bioavailability due to its short half-life. The tablet was prepared using HPMC K15M, Sodium alginate, guar gum, sodium bicarbonate. The prepared floating tablets were successful in sustaining drug release due to increased residence by 12 hours.

Limpongsa et al. [34] selected Diclofenac a non-steroidal anti-inflammatory drug, while selecting the drug candidate the researcher observed that drug was having pH dependent solubility that is low solubility in gastric content along with short half-life which helped the researcher in formulating GRDDS using HPMC, MCC and SLS. The formulation was able to solve solubility problem by providing hydrophilic environment.

Mohapatra et al. [35] studied the effect of various natural polymer such as gum karaya, guar gum combined with HPMC to make gastro retentive system for Losartan an antihypertensine drug. From the study it is found these natural polymers able to enhance gastric retention. From the in-vitro dissolution study it has been confirmed the polymers have positive effect in retarding drug release and found the formulation is able to release 98.7% of drug over a span of 12 hours.

Siahaan et al. [36] discovered that the drug Cemitidine a H2 receptor antagonist having short half and upper part of GI as absorption window retarding maintain required concentration. When the drug formulated into GRDDS using sodium alginate as release retardant formulator was able to get required result of sustaining release characteristic and from invivo study has confirmed that Cmax, Tmax, AUC and hence bioavailability has increased.

Sindoor et al. [37] selected Lafutidine a H2 antagonist the drug is having short half-life less than 2 hours and thus having low bioavailability problem. The formulator addressed this issue by formulating it into in-situ gel formulation using various natural excipients such as gellan gum xantan gum, sodium alginate and sodium citrate and calcium chloride as gas forming agent. The researcher successful in formulating oral in-situ gel meeting the requirement and found the formulation is able to release more than 12 hours.

Bangun et al. [38] studied effect of muco-adhesive alginate beads of Turmeric a potent anti-inflammatory, antiulcer agent to treat the ulcer. The alginate beads were prepared by gelation method. The polymers exhibited required adhesion property and from in-vireo study it has been confirmed the formulation was successful in treating hydrochloric acid induced ulcer in rats.

Gourishyam pasa et al. [39] prepared Ciprofloxacillin a broad spectrum antibiotic floating tablet. It is found that drug was unable to maintain required concentration which resulted in poor bioavailability. But when formulated in floating system it was able to release 99% drug over a period of time 12 h hence addressing the complication occurred during formulation.

Pashikanti et al. [40] observed that Ciprofloxacillin a broad spectrum antibiotic was showing pH dependent solubility in gastric content. This drug residence issue was solved by developing into gastro rententive system using sodium alginat5, HPMC K100M as polymer. The formulation was able to float and release drug in controlled manner to target site to address pH dependent solubility.

6. EVALUATION CHARACTERIZATION

Each and every aspect must be considered while evaluating the final formulation. Because these are control keys to attain formulation objectives. Some of them are described in brief.

6.1 Floating Lag Time and the Buoyancy Duration

All of the sudden the formulation or the preparation will not float on the surface. When the preparation is poured in beaker for testing first it settle at bottom after some time it revert back on the surface to provide the floating behaviour to the preparation. And this is known floating lag time, this should be be minimum around 30 seconds to 2 minutes. The total time for which the floats on the surface is called floating time. These two evaluation factors are assessed using a beaker containing 0.1N HCL as medium [41].

6.2 Drug Release Study

As these are controlled release formulations, the best choice to study their drug release is paddle type i.e type-II USP apparatus. The drug release study will help us in assessing in vitro bioavailability of drug from the formulation. So attempt should be done to create environment which is similar to gastric content. Such as temperature, dissolution medium speed of paddle and other factors such as sampling method replenishment of fluid, spectroscopic method etc. to such an extent the study should provide results with greater accuracy [42].

6.3 Determination of Drug Entrapment

The drug entrapment efficiency will help us in understanding how efficiently the polymer is able to hold the drug during its formulation and also reveals whether the bound is able to release at desired extent. This is usually determined by measuring free drug infiltrate solution by suitable spectroscopic method. The amount of drug entrapped in system was calculated by the following equation:

%Drug entrapment= Theoretical drug loaded (g) - free drug (g) Theoretical drug loaded (g) ×100

6.4 Swelling Studies or Water Uptake Studies

The swelling studies is done to determine whether the polymer under consideration is cable of interacting with water content of gastric fluid to provide required buoyancy and how well the polymer retard drug release of the preparation. This study is done to determine the swelling property polymer because only upon swelling there will be formation of diffusion layer and drug will come out through that diffusion layer in controlled manner. Swelling property is measured by taking weight difference of the polymer before and after placing formulation in 0.1N HCL [43] percent swelling index was calculated using the following formula:

%Swelling index=Wt-W0/Wt×100

6.5 Physical Parameters

All the official quality control test must be conducted whenever a new formulation is prepared. For tablet formulation hardness, friability, weight variation, thickness etc. and if the preparations are solutions then viscosity etc. are carried out.

6.6 Drug Content

The drug content measurement for the formulation aids in determining whether the medication is uploaded in the required concentration in the polymer to produce correct drug levels. The drug content of the formulation was determined by putting the needed amount of sample into 20 ml of methanol and sonicating it for 15 minutes to eliminate any solubility-related mistakes. After that, the solution was filtered with a 0.45 filter. The drug content was determined using spectrophotometry. Typically, the average of three judgments was used [44].

6.7 *In vivo* Radiographic Studies

The in-vitro study does not give any guaranty the formulation provide same drug levels when administered. One has to go for in-vivo study in order to predict and provide therapeutic drug levels. To conduct in vivo studies the formulation is modified by including radio opaque substance. This is done by replacing some portion of drug with radio opaque substance keeping other things constant. Before in vivo study all the formulation factors such as hardness, floating lag time, and floating duration etc tested in order to avoid any error. Three male volunteers were chosen for the radiography research according to the study protocol. The samples were prepared as described above and swallowed by volunteers along with a glass of water. Following consumption, the individual will be photographed using an X-ray technique in the abdomen region. The x-ray pictures will be obtained at pre-determined intervals according to the study to establish the length of time the sample drug remained in the gastric region (mean gastric time) [45].

6.8 Drug Release Kinetics

The release kinetic study for various gastro retentive system has been conducted for various model such as Fickian, Non Fickian and anomalous models and found that these polymeric system follows Fickian as main model, though other mechanism is involved but these of are minor importance for example relaxation of polymer chain. This process is due to non-Fickisn or anamolous diffusion. In Fickian diffusion, the drug first penetrates the glassy polymer, which then swells and becomes rubbery, followed by drug diffusion, which is influenced by a variety of parameters, including the length of the polymer chain [46].

The data analysed from in vitro studies were fitted to different equations i. e Zero order, First order, Higuchi model and Kosermeyer-Peppas model.

6.9 Physical Stability Studies

The physical stability studies is done to ensure the drug in the formulation is intact to produce therapeutic effect. It also confirms that there are no interaction between the ingredients and also processing method used can the used in future for further formula development. One must conduct stability study according to the guidelines by laid down by International Conference on Harmonization (ICH). According to the guideline final formulation is packed in a container and placed in stability study chamber by selecting required temperature and humidity. During the study the sample was taken out tested for few important evaluation characteristics such as harness or viscosity, floating time drug content etc. based on the

result stability profile generated and decision will be taken to state whether the formulation is stable or not [47].

7. GASTRO-RETENTIVE FORMULA-TIONS AVAILABLE IN MARKET [48]

Many mind blowing and satisfying products are available in the market, few of these are mentioned below,

1. Ciprofloxacillin available as CIFRON OD a gastro retentive system formulation available in dose strength 1 gram used to various systemic infections manufactured by Ranbaxy India.
2. CYTOTECH Misoprostol 200 mg gastro retentive system used to treat gastric ulcer condition produced by Pfizer India and USA.
3. GAVISCON Aluminium hydroxide gel available in market as oral in situ gel as antacid manufactured by Glaxo Smith Kline India.
4. A Metformin preparation available as GLUMETZ used to treat diabetic condition produced by Demomed Canada.
5. OFLIN OD an Ofloxacillin- 400 mg available as gastro retentive system used to treat genital, urinary, respiratory and other soft tissue manufactured by Ranbaxy India.
6. MEDOPAR, Levodopa and Benserzide mixture formulation available as gastro retentive with dose 100 and 25mg respectively used to treat Parkinson manufactured by Nicholas Piramal India.
7. VALRELEASE a Diazepam 15mg gastro retentive system used to treat anxiety, muscle spasms and alcohol withdrawal symptoms. Produced by Roche laboratories USA.

7. CONCLUSION

In this review article we tried to gather all possible recent information in the field of grdds. From the above review study we can imagine how far the gastro retentive system helps in solving the problem associated with it and also getting the required objective. One can take help from such formulation in their drug candidate falls in the portfolio which has been outlined in this study. Moreover the study helps in evoking the researchers to put new steps towards further advancement.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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