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Abstract

Pharmaceutical industries have received much interest in pharmaceutical research in the area of oral drug delivery. Oral administration of drug is the most convenient and versatile way due to the simple and comfortable use and flexibility concerning dose strength, and type of formulation. GRDDS is an approach to prolong gastric residence time, thereby targeting site-specific drug release in upper GI tract improving the oral sustained delivery of drug that have an absorption window in a particular region of the GI tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability. This manner may increase patient compliance and provides continuously controlled release administration of sparingly soluble drugs at the particular sites of absorption. More than 55% of drug available in the commercial market used for orally. During the last five decades, little oral delivery has been produced to act as a drug reservoir from which the active ingredients are specified period of time released and at controlled the release rate. Method for preparing GRDDS is simple and straight forward, and as a result economically attractive. An assortment of approaches for gastric retention are floating, non-floating, swelling, bioadhesive, magnetic controlled, and dual working systems etc.

Keywords: Gastro Retentive Drug Delivery Systems (GRDDS); Gastro retention; GI tract; Patents.


Introduction

Oral route is most preferred, favored, promising and versatile route for administration of drugs in systemic action. Because of reasons for their tremendous popularity are their conveniences of application or increase patient’s compliance, ease of administration, low cost, improve bioavailability and ease of
production in an industrial scale [1]. GRDDS is novel site-specific drug deliveries to promoting retention with in the stomach, duodenum or small intestine can prolong drug released to controlled manner. The oral administration approaches to achieve prolong release of drug is the use of gastro-retentive systems. The idea here is to prolong the residence time of the drug delivery in the stomach known as GRT (Gastric Residence Time) [2]. Several types of gastro retentive techniques such as floating systems, super porous hydrogel systems, expandable systems and high density systems etc. can be used [3]. All useful approaches, especially if drug absorption takes place in stomach or upper part of intestine (e.g., duodenum) could be benefits for local drug action in the stomach or for drug with an narrow absorption window. The Gastric Emptying Time (GET) of a dosage form will depends on the density and size of the systems and the fed or fasted state of the patient [4]. GRDDS is enormously beneficial, having rapid drug absorption through GI tract and no risk of drug toxicity [5]. The control of GI transit of oral delivery using gastric dosage forms can increase the drugs bioavailability that exhibit specific site of drugs absorption. Various types of factors controlling the dosage form having GRT (Gastric Retention Time) (GRT) such as density (e.g., range 1.0 - 2.5 g/cm3), particle size (e.g., 1-2 mm), size (e.g., >7.5 mm in diameter), shape (e.g. ring and tetrahedron devices), food intake, frequency of intake (e.g., low frequency of IMMC), posture, age, gender, nature of drugs, nature of the food, sleep, body mass index, GI disease state of the individual chronic disease and drugs administered of cisapride and metoclopramide [6]. Many types of the drugs improve absorption by the duodenum. The bioavailability of many drugs could be optimal and more predictable if drug delivery could be retained in upper region of GI tract for specific period of times or position of drug delivery systems in the duodenum could be controlled [7, 8].

1. Several techniques used to design GRDDS

Many of the oral drug delivery techniques used to improve the gastric-retention in the stomach include; (Figure 1)

(Figure 1). A schematic representation of human stomach with gastro retention techniques.

1.1. Floating systems (FDDS)

Floating Drug Delivery System (FDDS) or Hydro-dynamically Balanced Systems (HBS) are systems that have a density lower that of the gastric fluids so that they remain floating in the stomach [9, 10]. Low-density systems have a density lower than
that of the gastric fluid so they are buoyant. Hydro-dynamically Balanced Systems (HBS) are incorporated buoyant materials enable the device to float. Many buoyant systems have been developed based on powders, granules, micro-particles, film, capsules, tablets, pills, films and hollow microspheres [11]. Floating Drug Delivery Systems (FDDS) classify based on the mechanism of buoyancy and, divided into two types include effervescent and non-effervescent systems showing in Figure (2).

(Figure 2). Flowchart show differents floating drug delivery

1.2. High density system
It is also known as sinking or sedimentation or non-floating systems that retained drug delivery at the bottom or lower region of the stomach [12]. Drug be able to coated or mixed with heavy non toxic materials such as barium sulphate (density = 4.9), titanium dioxide and zinc oxide may be used to formulate high density delivery. These systems with a pellet density of about 3.0 g/cm³ are retained in the pylorus region of the stomach and are capable of withstanding its peristaltic movements. Above a threshold density of 2.4–2.8 g/cm³, such systems can be retained in the lowest position of the stomach. The major limitation of these systems cannot manufacture with large amount of drug due to technical problems, now till date no such system is available in the market and to achieve a density of about approx. 2.8 g/cm³. Density of pellet or tablet should be at least 150 g/ml [13, 14].

1.3. Magnetic systems
Magnetic systems to enhanced the Gastric Residence Time (GRT) is based on incorporation of magnetically active
compounds the simple idea that the site specific drug delivery contains a internal magnet set on the abdomen over the position of the stomach that retained drug delivery in gastric region [15]. Although magnetic delivery seems to work that controls the GI transit of the dosage form, major drawbacks such systems are patient non compliance, external magnet needs to be right position is selected with high degree of precision and accuracy, and very limited used in current markets [16, 17].

1.4. Superporous hydrogel
These conventional types swellable superporous hydrogel system having to improve the gastric residence time and average pore size >100 μm so that they can swell to equilibrium within a minute due to rapid water uptake by capillary wetting through numerous interconnected open pores. Absorption of water by conventional hydrogel is very slow process and several hours may be needed to reach an equilibrium state during which premature evacuation of dosage form may occur. Moreover, they swell to a large size (100 or more swelling ratio) and are intended to have sufficient mechanical strength to withstand pressure by the gastric contraction. This is advised by co-formulation of hydrophilic particulate material like Cross Carmel lose Sodium (CCS) [18, 19].

1.5. Mucoadhesive and bioadhesive systems
Adhesive system is developed by using polymers which enable the delivery device to adhere to mucosal epithelial surface or mucous membrane resulting increase gastric emptying, enhance site specific drug absorption and improved bioavailability. Most promising adhesion mechanisms like hydration, bonding and receptor mediated adhesion used to binds the polymers to the gastric epithelial cell surface and controlled by the dissolution rate of the polymers and enhancing the gastric retention of drug delivery [20, 21]. The major drawbacks such systems are difficulty produce to maintain due to rapid turnover of mucin in GI tract. Some of the most widely used polymeric materials contain PAA (Poly Acrylic Acid), chitosan, sodium alginate, HPMC, polyoxyethylene, gantrez, gumtragacanth, polycarbophil, carbolip, lectins, dextrins and PEG etc [22, 23].

1.6. Expandable systems
Expandable systems are also known as ‘plug type systems’. They achieved larger size in stomach and increased size of whole system goes beyond the diameter of pyloric sphincter (approx. 12-18mm) in their expanded state to preventing pyloric sphincter passage and thus the system retains longer period of time in the stomach [24, 25]. The expansion can be achieved by two systems such as swelling and unfolding system. Swelling system are generally matrix system containing hydrocolloids which by action of hydration, osmotic absorption of water to get swelled and also retain in the stomach because of their mechanical properties. The drug delivery is small enough to be swallowed and swells by the gastric contents. Unfolding systems having biodegradable polymers to produce a carrier such as capsule and then administered upon contact with gastric contents, incorporating a compressed systems get unfolded into the forms which retained longer period of time in the stomach [26].

1.7. Dual working systems
Now, recently combinational mechanism used for Gastro- Retentive Delivery (GRDDS) like swellable and floating, mucoadhesion and floating, mucoadhesion and swelling, mucoadhesion and high density, and floating-pulsatile system [27]. In mucoadhesion and floating systems works on the floatation and bioadhesion principles, a dosage form floats on the gastric content and can bind to gastric mucosal layer and ensure gastro-retention in dual ways. They are bilayer tablet systems containing adhesive polymers and floating layer prevents the undesirable mucoadhesion to buccal and esophageal mucosa. In swellable and floating systems works on the floatation and swelling principles, a core of drug and rate controlling excipients followed by a coating of effervescent excipients, and a coating of swelling excipients is made over the effervescent layer and finally an immediate release coating is layered. In mucoadhesion and high density systems, prolong GRT of drug delivery at the absorption site and facilitate an intimate contact of the dosage form with underline absorption surface and thus contribute to improved drug pharmacotherapy.
In oral controlled release floating-pulsatile systems advantageous that can be released of drug in upper part of GIT after specified time period, no released of drug, increase GRT of drug delivery having lag phase and followed by a mechanism of burst release, less inter or intra-subject variability and reduce the risk of toxicity [28].

2. Literature review of recent novel researches

A number of these advance novel research are very informative and discloses background on the different drug formulations, and review of sustained release drug delivery as review in Table 1. Outline of assorted drugs employed in gastro-retentive drug delivery system is given in the Table 1 mentioned below [29-48].

Table 1. An assortment of drugs employed in GRDDDS

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Dose (mg)</th>
<th>Formulation types</th>
<th>Release time (hrs)</th>
<th>Polymers used</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin HCl</td>
<td>500</td>
<td>Floating tablets</td>
<td>12</td>
<td>Gums Kondagogu and Karaya</td>
<td>[29]</td>
</tr>
<tr>
<td>Captopril</td>
<td>75</td>
<td>Mucoadhesive films</td>
<td>24</td>
<td>HPMC, Carbopol 934, EC</td>
<td>[30]</td>
</tr>
<tr>
<td>diltiazem HCl</td>
<td>500</td>
<td>Floating Microspheres</td>
<td>06</td>
<td>EC, PVP- K90, PVA</td>
<td>[31]</td>
</tr>
<tr>
<td>Ranitidine HCl</td>
<td>150</td>
<td>Floating beads</td>
<td>24</td>
<td>HPMC, Calcium carbonate, alginate</td>
<td>[32]</td>
</tr>
<tr>
<td>Telmisartan</td>
<td>20</td>
<td>SR Microballoon</td>
<td>12</td>
<td>Eudragit RS100, HPMC</td>
<td>[33]</td>
</tr>
<tr>
<td>Mefenamic acid</td>
<td>250</td>
<td>Floating tablets</td>
<td>24</td>
<td>HPMC100SR, alginate sodium, HPMC4000SR, HPMC100000CP, CMC, MC, and eudragit RS</td>
<td>[34]</td>
</tr>
<tr>
<td>Acyclovir</td>
<td>200</td>
<td>Floating matrix tablets</td>
<td>12</td>
<td>Metolose, Sodium CMC</td>
<td>[35]</td>
</tr>
<tr>
<td>Losartan potassium</td>
<td>50</td>
<td>Floating tablets</td>
<td>14</td>
<td>Methocel K15 and Methocel K100</td>
<td>[36]</td>
</tr>
<tr>
<td>Metoprolol tartrate</td>
<td>50</td>
<td>Floating tablets</td>
<td>08</td>
<td>HPMC K4M and HPMC K100M</td>
<td>[37]</td>
</tr>
<tr>
<td>Metoprolol succinate</td>
<td>25</td>
<td>Bioadhesive floating Tablet</td>
<td>24</td>
<td>PEO, Carbopol 71G, HPMC E15, Methacrylic acid, Pectin, Carragenan and Guargum</td>
<td>[38]</td>
</tr>
<tr>
<td>Rosiglitazone maleate</td>
<td>20</td>
<td>Superporous hydrogels</td>
<td>06</td>
<td>Chitosan, Poly vinyl alcohol (PVA)</td>
<td>[39]</td>
</tr>
<tr>
<td>Cefixime</td>
<td>200</td>
<td>Floating tablets</td>
<td>12</td>
<td>HPMC K4M, Carbopol, sodium CMC</td>
<td>[40]</td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>20</td>
<td>Mucoadhesive films</td>
<td>24</td>
<td>Ethyl cellulose, HPMC, Carbopol-934</td>
<td>[41]</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>250</td>
<td>SR tablets</td>
<td>24</td>
<td>HPMC K4M, HPMC K100M, Psyllium husk</td>
<td>[42]</td>
</tr>
<tr>
<td>Atenolol</td>
<td>50</td>
<td>Floating tablets</td>
<td>08</td>
<td>HPMC 100 cps, sodium alginate, carbopol 940 and guar gum</td>
<td>[43]</td>
</tr>
<tr>
<td>Itopride hydrochloride</td>
<td>150</td>
<td>Floating tablets</td>
<td>24</td>
<td>HPMC K100M, HPMC K15M and Carbopol 934 P</td>
<td>[44]</td>
</tr>
<tr>
<td>Domperidone maleate</td>
<td>30</td>
<td>Floating tablets</td>
<td>12</td>
<td>HPMC K4M, HPMC K15M and HPMC K100M</td>
<td>[45]</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>100</td>
<td>Floating microspheres</td>
<td>08</td>
<td>Ethyl cellulose, HPMC</td>
<td>[46]</td>
</tr>
</tbody>
</table>
3. Evaluation parameters

3.1. In-vitro evaluation: For particular systems [28, 49]

- Standardized in-vitro evaluation technique is available for evaluation of GRDDS includes the floating, bioadhesive and swelling system etc. In evaluation of floating systems includes the buoyancy lag time or floating ability test (seconds), floating time, specific gravity or density and resultant weight etc.
- In evaluation of bioadhesive system includes to check bioadhesive strength of a polymer.
- In evaluation of swelling systems includes the swelling index, weight gain, water uptake and continuous monitoring of water uptake

3.2. In-vivo evaluation [28, 49]

- The in-vivo evaluation of the GRDDS is done in dogs, guinea pigs, rats AND pigs as they suitable the anatomic and physiological conditions of human GI tract. In-vivo evaluation of GRDDS includes the radiology, gamma scintigraphy or X-ray, gastroscopy, magnetic marker monitoring or Magnetic Resonance Imaging (MRI), ultrasonography or 13C octanoic acid breath test.

3.3. General in-vitro evaluation [50]

- Many of the general in-vitro evaluation technique is available for GRDDS particularly tablets includes the general description, shape, diameter (mm), thickness (mm), hardness (Kg/cm²), friability (% W/W), average weight, weight variation test (mg ± SD), dissolution or drug release tests, assay, drug loading and drug entrapment efficiency, percentage yield, stability studies for 24 hours, Fourier Transform IR spectroscopy (FTIR) studies and release kinetics. In release kinetics includes the zero and first order release kinetics, higuchi matrix equation, Hixson-crowell cubic root equation, power law or use peppa’s and korsemeyer formula and similarity factor (f² analysis)

4. Patents on gastro-retentive drug delivery system

<table>
<thead>
<tr>
<th>Ziprasidone HCl</th>
<th>20</th>
<th>Gastroretentive tablet</th>
<th>08 &amp; 24</th>
<th>HPMC K4M, Okra gum, Locust bean gum</th>
<th>[47]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ofloxacin</td>
<td>200</td>
<td>Floating matrix tablets</td>
<td>08</td>
<td>HPMC K4M, HPMC 5 cps, Sodium CMC</td>
<td>[48]</td>
</tr>
</tbody>
</table>

Watts PJ and his co-worker (2001) [51] have patented on floating drug delivery composition. There is provided a multi-particulate drug delivery composition adapted for the delivery of a pharmacological agent to the small intestine of a mammal, including drug-containing coated particles, which particles comprise a drug-containing core coated with an enteric polymer that prevents significant release of drug in an acid environment but permits drug release in a more alkaline environment, wherein the particles float when suspended in water.

Mehta B and his co-worker (2003) [52] have patented on floating osmotic device for controlled release drug delivery. This invention relates more particularly to floating osmotic device for immediate delivery of a first active agent followed by continuous controlled delivery of a second agent, which may be same or different from the first active agent, while the device or dosage form drug in the fluid of the environment (e.g., the stomach), thereby being retained in the environment for an extended period of time. The dosage form as described in the present invention is effective for immediate release of one drug followed by continuous, controlled delivery of drug present in osmotic core which is capable of acting locally in gastrointestinal tract or acting systemically by absorption via stomach and upper part of the intestine. The release from the osmotic core depends upon the existence of an osmotic gradient between contents of core and the fluid in the gastrointestinal tract. The drug delivery is essentially constant as long as the osmotic gradient remains constant.

Mohammad H and his co-worker (2009) [53] have patented on gastro retentive drug delivery system comprising an extruded hydratatable polymer. More particularly, the present invention relates pharmaceutical products which are retained in the stomach. In an associated aspect, the invention is concerned with a controlled release drug delivery system for prolonged gastric residence. According to the present invention there is provided a pharmaceutical product for retention in the stomach.
The product is produced by extrusion. The use of extrusion enables the product to take many useful forms. The technology is a versatile system which can be used to deliver drugs in a sustained release manner for local and systemic absorption. A specially designed pharmaceutical dosage form can be provided, usually a solid of different distinctive shape and size that can remain in the stomach for a predetermined time. During residency in the stomach, drug is released from the system in a sustained manner to provide medication for local and/or use. Nandan MC and his co-worker (2009) [54] have patented on a novel gastro retentive delivery of macrolide. The present invention relates to a novel gastro retentive delivery system system of macrolide, comprising a hydrophilic swellable floating matrix system either alone or in combination with a bioadhesive system. The present invention discloses a novel gastro retentive delivery system of macrolide comprising a hydrophilic swellable floating matrix system either alone or in combination with a bioadhesive system, which involves the use of superdisintegrants with hydrophilic polymers and in-situ gelling agents, which can improve the gastro retentive of dosage forms. Further, the controlled release gastro retentive dosage form of the present invention offers enhanced stability of the macrolide in gastric fluid by incorporating an alkali in the matrix system, which not only stabilizes the drug in acidic pH but also controls the drug release by reducing its solubility in stomach by offering alkaline micro-environmental pH. The invention further provides controlled mode of drug release and minimal fluctuation in plasma drug concentration. Gorukanti S and his co-worker (2011) [55] have patented on modified gastro retentive drug delivery system for amine drugs. Oral dosage forms for basic amine drugs, the dosage forms having a gastro-retentive component and a non gastro-retentive component. These dosage forms are capable of providing both IR and SR release rates for these drugs. In addition, they provide for drug release drug in the stomach or intestine of a mammal to which such dosage forms are administered. Such dosage forms include tablets and capsules. Such dosage forms provide improved bioavailability of otherwise poorly bioavailable basic amine drugs. Jiang Q and his co-worker (2011) [56] have patented on gastro retentive drug delivery system, preparation method and use thereof. Surprisingly, the present inventor found that the gastroretentive of pharmaceutical preparations can be achieved effectively by coating the hollow vesicle with a drug-containing layer. Thus, in one aspect, the present invention provides a gas-vesicle-type gastroretentive drug carrier comprising a hollow vesicle and optionally a waterproofing layer and/or isolating layer coated on the surface of the hollow vesicle. In the present invention, the term “gastroretentive drug carrier” refers to any structure or means that can load a drug and deliver it to the stomach to realize gastric retention. In one embodiment of the present invention, the gastroretentive drug carrier comprises a hollow vesicle and optionally a waterproofing layer and/or isolating layer coated on the surface of the hollow vesicle. In another aspect, the present invention provides a new gas-vesicle-type gastroretentive drug delivery system comprising a hollow vesicle or the gastroretentive drug carrier mentioned above and a drug-containing layer coated on the surface of the hollow vesicle. The gastroretentive drug carrier or release system of the present invention may be presented as single chamber type, that is to say, one unit of the carrier or formulation only contains one hollow vesicle. Similarly, the gastroretentive drug delivery system of the present invention may also be presented as multi-chamber type, that is to say, one unit of formulation contains two or more hollow vesicles. The overall density of the formulation can be greatly reduced to less than 1.0 g/cm³ and thereby can float on the gastric juice through the hollow vesicle. Navon N and his co-worker (2011) [57] have patented on baclofen and r-baclofen gastro retentive drug delivery systems. The presents invention to provide solutions to the aforementioned deficiencies in the art, enabling the administration of baclofen or r-baclofen with a reduced daily regimen. Another object of this invention is to provide a drug which may be administered fewer times a day, preferably once a day, to a patient in need thereof. Because of the undesirable side effects and the inconvenient mode of administration of the baclofen commercial product (3-4 times a day), there is a great...
need for an effective controlled release formulation of baclofen or R-baclofen that can provide steady therapeutic levels. The baclofen or r-baclofen gastro retentive dosage forms of this invention are designed to release baclofen or r-baclofen by a combination of immediate and controlled release mechanisms to provide quick onset and steady therapeutic level of baclofen or r-baclofen over time. Due to the design flexibility afforded by the complex structure of the Gastro Retentive Dosage Forms (GRDFs) of this invention, the GRDFs can conveniently release baclofen or r-baclofen in a sustained profile or in a combined immediate and sustained profile over a prolonged period, while maintaining relevant drug plasma levels for extended time intervals.

Masri S and his co-worker (2012) [58] have patented on zaleplon gastro retentive drug delivery system. The present invention relates to gastroretentive drug formulations for the treatment of insomnia. The invention provides a degradable multi-layered gastroretentive dosage form of zaleplon with improved sleep maintenance and minimal residual effects. In one aspect of the invention, the gastroretentive dosage form provides for the controlled release of zaleplon in the stomach and gastrointestinal tract of a patient. In a preferred aspect of the invention, the gastroretentive dosage form of zaleplon comprises a first dosage of zaleplon for immediate release and a second dosage of zaleplon for controlled release, and the gastroretentive dosage form of zaleplon is compacted or folded into a capsule which is easily swallowed and disintegrates rapidly upon contact with gastric juice. Once the capsule disintegrates, the gastroretentive dosage form of zaleplon unfolds rapidly upon contact with the gastric juice. In an even more preferred aspect of the invention, the gastroretentive dosage form of zaleplon comprises an internal layer comprising a first dosage of zaleplon for controlled release; a rigid frame layer; two outer layers and one or two supra-outter layers comprising a second dosage of zaleplon for immediate release. The capsule disintegrates rapidly upon contact with gastric juice, and the gastroretentive dosage form unfolds rapidly upon contact with the gastric juice.

Gerard DE and his co-worker (2012) [59] have patented on gastro retentive drug formulation and delivery systems and their method of preparation using functionalized calcium carbonate. An instantly floating gastro retentive drug formulation comprising at least one functionalized natural and synthetic calcium carbonate comprising mineral and at least one pharmaceutically active pharmaceutical ingredient and at least one formulating aid wherein said functionalized one or more acids and natural or synthetic calcium carbonate is a reaction product with carbon dioxide resulting in carbon dioxide is formed in in-situ by the acid treatment and it is supplied by external source.

Chandanmal PB and his co-worker (2013) [60] have patented on gastro retentive drug delivery system of calcium supplements. Provided are gastro retentive dosage form of calcium and salts thereof and preparing method thereof. Said dosage form comprises (i) absorption enhancing agents (ii) diluents (iii) binders (iv) disintegrants (v) floating agents (vi) polymers (vii) lubricants (viii) anti adherents (ix) preservatives and (x) combinations thereof. Park YJ and his co-worker (2013) [61] have patented on sustained-release preparation using gastro-retentive drug delivery system. The present invention relates to a sustained-release preparation which limits release and absorption of drug using a gastro-retentive system and which can minimize the effect of in vivo environment, and to a method for preparing the sustained-release preparation. More particularly, the controlled release delivery according to this work comprises a swellable polymer, and a first controlled-release base and a second controlled-release base. Therefore, the sustained-release preparation of the present invention may adjust the degree of swelling and floating of a polymer in order to effectively achieve gastric retention. Thus, drugs may ultimately be retained in the GIT over a long period of time, and
the bioavailability of drugs may be improved in order to enable once-a-day administration. Summary of various patents pertaining to gastro-retentive drug delivery system is given in the Table 2 mentioned below [51-61].

**Table 2. Patents Pertaining To Gastro-Retentive Drug Delivery System**

<table>
<thead>
<tr>
<th>Title</th>
<th>Patent No.</th>
<th>Inventors</th>
<th>Published/ GrantYear</th>
<th>Ref.</th>
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<tbody>
<tr>
<td>Floating osmotic device for controlled release drug delivery</td>
<td>US20030064101</td>
<td>Mehta B et al.</td>
<td>2003</td>
<td>[52]</td>
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<tr>
<td>Gastroretentive drug delivery system comprising an extruded hydratable polymer</td>
<td>US20090324694</td>
<td>Mohammad H</td>
<td>2009</td>
<td>[53]</td>
</tr>
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<td>A novel gastroretentive delivery of macrolide</td>
<td>WO201125075A2</td>
<td>Nandan MC et al.</td>
<td>2011</td>
<td>[54]</td>
</tr>
<tr>
<td>Modified gastroretentive drug delivery system for amine drugs</td>
<td>US20110287096</td>
<td>Gorukanti S et al.</td>
<td>2011</td>
<td>[55]</td>
</tr>
<tr>
<td>Gastroretentive drug delivery system, preparation method and use thereof</td>
<td>US20110171275</td>
<td>Jiang Q et al.</td>
<td>2011</td>
<td>[56]</td>
</tr>
<tr>
<td>Baclofen and r-baclofen gastroretentive drug delivery systems</td>
<td>US20110091542</td>
<td>Navon N et al.</td>
<td>2011</td>
<td>[57]</td>
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<tr>
<td>Zaleplon gastroretentive drug delivery system</td>
<td>US20120021051</td>
<td>Masri S et al.</td>
<td>2012</td>
<td>[58]</td>
</tr>
<tr>
<td>Gastro retentive drug delivery system of calcium supplements</td>
<td>WO2013114390A1</td>
<td>Chandanmal PB et al.</td>
<td>2013</td>
<td>[60]</td>
</tr>
<tr>
<td>Sustained-release preparation using gastroretentive drug delivery system</td>
<td>WO/2013/162114</td>
<td>Park YJ et al.</td>
<td>2013</td>
<td>[61]</td>
</tr>
</tbody>
</table>

**Conclusion**

This patents overview comprise vital aspects of GRDDS subjected to the investigate concerns about physiological features in the human stomach, recent advance novel researches study, patent scenarios studies, current and future prospects, and many of the single, multiples and combinative or dual working
techniques used to improve the oral administration of gastric-retention drug delivery in the stomach. The patents analysis and application deals with the GRDDS therefore show assure for therapeutic use in the future. A major consideration of the interplay of this parameter can help in future designing a new victorious application of GRDDS. In general, we have described different patents and its application of the recent marketed trends and future focus of GRDDS. To get advantages of GRDDS drug delivery, Improved bioavailability, therapeutic efficiency of drugs and reduced frequency of dosing. Opportunities in GRDDS particularly in floating or buoyant delivery offers various beneficial future strategies as evident from many recent narrative works used in treating gastric and duodenal ulcers or cancers. The reduced fluctuations in the plasma level of drug (e.g., Levodopa) results from delayed gastric emptying. It can also be exploited for development of various anti-reflux formulations; a HBS™ dosage form offer better control of motor fluctuations. Developing a controlled release delivery for the drugs, have the potential to treat Parkinson’s disease. To explore the eradication of H. pylori by using the narrow spectrum antibiotics (e.g., Ampicillin) released continuously. Oral controlled or sustained drug delivery to the GIT has achieved terrific progress and claimed a good set of therapeutic applications. In the future, it is used in the oral control or sustained release drug delivery and improved number of international patents.

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