



Review Article

Gastroretentive Drug Delivery System: A Review

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ARTICLE INFO

Received: 20 Jan. 2023

Revised: 23 Jan. 2023

Accepted: 27 Jan. 2023

Published: 05 Feb. 2023

Keywords:

Gastric retention, Oral controlled release, Floating dosage form, Drug delivery system

DOI:

10.5281/zenodo.5881901

ABSTRACT

The purpose of composing this review of internal drug delivery systems is to combine the recent literature with a particular focus on various bowel approaches that have recently become the leading methodology in the field of orally controlled oral drug delivery. To understand the various physiological problems involved in achieving gastric retention, we have summarized the important factors that control gastric retention. We then checked several previously developed and developed intestinal methods, for example floating, biological or mucosal, expandable, brittle, superporous, high-density (sink) and magnetic and magnetic systems. Finally, the benefits of drug delivery systems in the gut are discussed in detail.

INTRODUCTION

Oral and dental management is the most suitable and suitable tool for any drug delivery system. Oral controlled drugs have recently been obtained from growing drugs for achieving improved therapeutic benefits, such as dose management, adaptation to the patient and flexibility in draft. Drugs that are easily absorbed from the stomach (GIT) and have a short life that is quickly removed by conventional circulation. To achieve proper therapeutic activities, duplicate doses are needed

for these drugs. To prevent this constraint, the development of sustainable edible compounds is an attempt to release the drug slowly to GIT and maintain the concentration of effective drugs in regular circulation for a long time. After oral injection, such drugs are controlled in the stomach and medicine, so that the drug can be constantly presented for gastrointestinal absorption locations.[1]

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



These systems suffer from major challenges: short gastrointestinal protection (GRT) and unexpected killer (received), which can lead to an incomplete drug version of the dose model in the absorption region (stomach or high intestine model) Which leads to a decrease in the effectiveness of the dose. [2] To prepare version of the version dose through orally, desirable, optimal to reach time collected by drug delivery. Long-term maintenance improved in available improvement, increases the duration of the drug version and reduces the drug waste and reducing drugs is a non-soluble wall in the high pH environment [3]. Maintenance time for E and long time (GRT) in the stomach can be beneficial for local work at the top of the micro-intestine, for example, ultra-eye treatment and so on. The delivery of the drug in the prepared stomach is an approach to expanding the stomach residence, and thus focuses on drugs for upper or regular digestive devices for local or regular effects. Invading dosage forms can remain in preparation for long periods, so that the time of maintenance of GRT drugs is maintained. Over the past decades, many methods of delivery of drugs are designed in an aggressive stomach, including high density systems (drowning) on the abdomen, low density (float) that float in the stomach [6, 7] the sludge was systems that cause gastric gastric mucosal systems [8] irreplaceable or comprehensive systems or bugs that limit empty forms through urine in the stomach [9, 10] system The hydrogel is activated [11] magnetic systems [12] and so on. The current audit of various stomach stimuli has recently been reduced by evaluating Article in the field of drug delivery systems.

FACTORS CONTROLLING GASTRIC RETENTION OF DOSAGE FORMS

The destination of gastric and physiotherapy contains the development parameters of infectious dose formats. For the transfer of polycarbonate to

the small intestine, particle size should be within 1 to 2 mm [13]. The most important parameters of storage time (GRT) of oral doses include: density, size and form of doses, consumption and nature, caloric and frequency intake, condition, sex, age, sex, sleep, mass index, patient physical mass index (Patient) Chronic disease, diabetes, etc.) and drug management with penetration at the time of transportation of gastrointestinal tract, for example, drugs as an anti-university (such as tropical regions, percinetic agents (such as codes), [14]. Molecular weight of medicines is also important depending on the essential government [15].

Density of dosage forms

The dose form density also affects the gastric emptying rate and determines the position of the device in the stomach. Dosage forms with lower stomach contents can float to the surface, while regimes with higher density can sink to the bottom of the stomach [16]. Both situations can separate the dosing system from the pylorus. Densities of less than 1.0 g / cm³ are required to indicate buoyancy [17].

Shape and size of the dosage form

The shape and size of dosage forms are important in the design of integrated solid indigestible forms. The average residence time in the stomach is very variable in the case of non-floating dosage forms and depends heavily on their size, which can be large, medium and small units. In most cases the retention time (GRT) is longer, the larger the dosage form, because the larger the dosage form, the faster it reaches the intestine through the pyloric antrum [18]. Drug forms with a diameter of more than 7.5 mm show better gastric survival compared to doses with a diameter of 9.9 mm [17]. Circular and quadrilateral devices have better gastric residence time than other forms [19].

Food intake and its nature



Food intake, viscosity, volume, caloric value and feeding frequency have a profound influence on gastric retention in drug forms. The presence or absence of food in the gastrointestinal tract (GIT) affects the shelf life (GRT) of the dosage form. The presence of food in the gastrointestinal tract (GIT) usually improves the retention time (GRT) of the dosage form and increases the absorption of the drug by allowing the drug to stay in the absorption site longer. Here, too, an increased acid and caloric value indicate a gastric emptying time (GET), which can improve gastric retention with dosage forms [20].

Effect of gender, posture and age

In general, women have a slower gastric emptying rate than men. The influence of posture on the mean gastric residence time (GRT) was not significantly different for individuals who stood, moved, and lay on their back. In the elderly, gastric emptying slows down [21]

POTENTIAL DRUG CANDIDATES FOR GASTRORETENTIVE DRUG DELIVERY SYSTEMS

- 1) Drugs those are locally active in the stomach e.g. misoprostol, antacids etc.
- 2) Drugs that have narrow absorption window in gastrointestinal tract (GIT) e.g. L-DOPA, para aminobenzoic acid, furosemide, riboflavin etc.
- 3) Drugs those are unstable in the intestinal or colonic environment e.g. captopril, ranitidine HCl, metronidazole.
- 4) Drugs that disturb normal colonic microbes e.g. antibiotics against *Helicobacter pylori*.
- 5) Drugs that exhibit low solubility at high pH values e.g. diazepam, chlordiazepoxide, verapamil HCl.

DRUGS THOSE ARE UNSUITABLE FOR GASTRORETENTIVE DRUG DELIVERY SYSTEMS

- 1) Drugs that have very limited acid solubility e.g. phenytoin etc.
- 2) Drugs that suffer instability in the gastric environment e.g. erythromycin etc.
- 3) Drugs intended for selective release in the colon e.g. 5- amino salicylic acid and corticosteroids etc.

APPROACHES TO ACHIEVE GASTRIC RETENTION

High density (sinking) system or non- floating drug delivery system

This approach involves formulating dosage forms with a density that should be greater than the density of the normal stomach contents (~ 1004 g / cubic centimeter). These formulations are made by applying the drug to a heavy core or mixing it with inert substances such as iron powder, barium sulfate, zinc oxide, titanium oxide, etc. [22]. Materials increase the density to 1.5-2.4 grams per cubic centimeter. Densities close to 2.5 g / cm³ appear to be essential for prolonging gastric life [23]. However, the effectiveness of this diet has not been observed in humans [24] and no diet has been commercialized.

Floating drug delivery systems

Floating drug delivery systems are one of the important approaches to achieve gastric retention in order to achieve adequate drug bioavailability [25]. These delivery systems are ideal for drugs with an absorption window in the stomach or upper small intestine [26]. This substance has a lower volume density than gastric juice and therefore stays fresh in the stomach for a long time without affecting the rate of gastric emptying, and the drug is slowly removed from the system at the desired rate. Once the drug is released, the remaining gastric system is emptied. This results in a longer retention time (GRT) and better control of fluctuations in plasma concentrations of the drug. The main requirements for a floating drug delivery system are [22]



- It should release contents slowly to serve as a reservoir.
- It must maintain specific gravity lower than gastric contents (1.004 – 1.01 gm/cm³).
- It must form a cohesive gel barrier.

An inherently low density can be achieved by entrapping air (eg hollow chambers) [27] or by combining materials of low density (such as fats, oils or foam powder) [5, 28, 29]. The following procedures were used to design floating dosage forms for single and multiple unit systems. Recently, a single floating system consisting of polypropylene foam powder, matrix component polymers, drugs and fillers has been proposed [30]. The good buoyancy of these systems can be combined with precise control of the resulting drug release patterns. Single dose forms have been associated with problems such as gastrointestinal tract adhesions or blockages (GIT), which can cause irritation. On the other hand, multi-unit floating systems can be an attractive alternative, as they have been shown to reduce the intrinsic and endogenous availability of active ingredient uptake and reduce the dose-discharge potential [26]. Multi-unit floating system such as multi-unit air chamber system [2], hollow microspheres (small balloons) produced by the emulsion diffusion process [31], fine particles based on foam powder with low density [5], emulsified gelatine granules [32] etc. can spread throughout the gastrointestinal tract, providing an opportunity to obtain a more reliable and longer lasting drug. Based on the buoyancy mechanism, two completely different technologies were used in the development of the floating drug delivery system, namely non-boiling and boiling systems.

Non-effervescent Systems

Normal floating drug delivery systems are usually prepared from cellulose hydrophile or highly divided sugars or matrix-formed polymers such as polyethylates, polycarbonate, polyethylene and polyethylene and polyethylene and polyethylene.

In a approach, the intimate mix of drugs with hydroxyrutocytic gel, which leads to the composition of the stomach after oral and immune management and high density less than the device in the stomach environment [33]. The air that is trapped alongside the polymer lung gives flotation for these dose forms. The most commonly used in these systems includes hydrochloropol hydrochlorules (HPMC), polyvinyl acetate, carbon, agar, sodium gene, calcium chloride, polyethylene oxide, polycarbonate [3]. This system can be divided into sub-species.

Hydrodynamically balanced systems:

The shell of the first set of these systems and prayers. These symmeters are made to achieve hydroids. They are formatting to achieve a dungeon. They are the formula where an empty hole producing one or more prisons. (hydroCOP block), polymodic blocks are mixed and the system is controlled in a balanced balance system. Shell is heavy in relation to water, and the swelling mix makes a helplesed barrier that gives long feather for a long time. Of the continuous channels on the surface that are not in water "in the water and 36]. The base of the cool waste. Waste waste. Based Aisperop LP® [37]. Of the effective distribution depends on the balance of suitable and depending on the effect of the polymer. The many strategies were tested and investigated the company's float center from the company Float Central.

Microballoons / Hollow microspheres:

Drug-containing microspheres / microspheres have been manufactured on another polymer shelf by simple solvent evaporation or solvent diffusion / evaporation [38] (Figure 1) to increase the shelf life (GRT) of the dosage form. Polymers commonly used to develop these systems include polycarbonate, cellulose acetate, calcium alginate, Eudragit S, low methoxy agar and pectin, and more. Small balloons were floated continuously on the surface of an acidic surfactant hydrolysis

medium for more than 12 hours [3]. Microscopic hollow spheres are one of the most promising swimming systems today, as they combine the advantages of a multi-module system with good buoyancy.

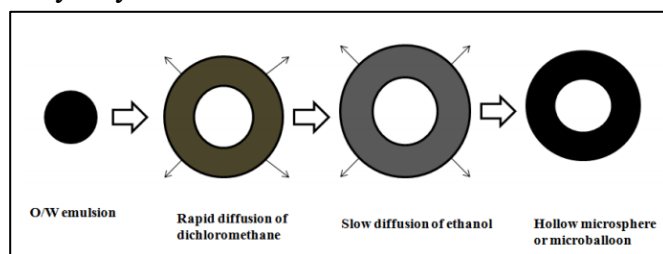


Figure 1. Formulation of floating hollow microsphere or microballoon

Alginate beads: Talukdar and Fassihi [32] recently developed a multi-module swimming system based on cross beads. They are made with low Ca^{2+} + methoxy pectin (anionic polysaccharide) or low methoxylated Ca^{2+} + pectin and sodium alginate. In this process, sodium alginate solution is generally poured into aqueous calcium chloride solution to precipitate calcium alginate. The granules then separate, convex, and dry, creating a porous system that can maintain buoyancy for more than 12 hours. These granules improve gastric retention time (GRT) by more than 5.5 hours [3, 39].

Microporous compartment system: This approach is based on the principle of encapsulating the drug tank in a fine-pored chamber with pores along the upper and lower walls [40]. The end walls of the device were completely closed to allow direct contact of the stomach surface with the undissolved drug. The floating air chamber in the stomach causes the administration system to float in the gastric juice [22]. Gastric juice enters through the mouth and dissolves the drug, with the dissolved drug being continuously transported through the intestines to absorb the drug.

Effervescent (gas generating) systems

Float can be produced by gas bubbles. These dual systems are used with emerging polymers

prepared matrices such as sugars (such as chitosan), brilliant components (such as sodium bicarbonate, citric acid or tartaric acid) [40]. The share of the optimal curtains of citric acid and sodium pepton for gas production 0.76: 1 [19]. In this system, carbon dioxide is exported and causes floating in the stomach (Fig. 2 and Fig. 3). Methods and other reported materials A combination of sodium glycinate and sodium glycinate are multi-unit floating forms that produce gas (carbon dioxide) during consumption, small capsules with sodium bicarbonate, lactose and perilylorridone (PVP) They produce hydroxypropyl methylcellulose (HPMC), floating order depends on the ion exchange technology and other [3]. Binary printing system is also designed or a multi-layer system [41, 42]. Medications and independence can be formulated independently, and gas production can be connected to all layers. More settings include polymer matrix covering with water, but not on carbon dioxide. The main problem of these formulas is to find a good compromise between flexibility, plastics and polymers.

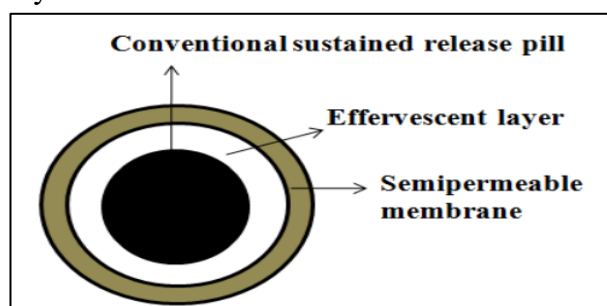


Figure 2. Effervescent (gas generating) systems

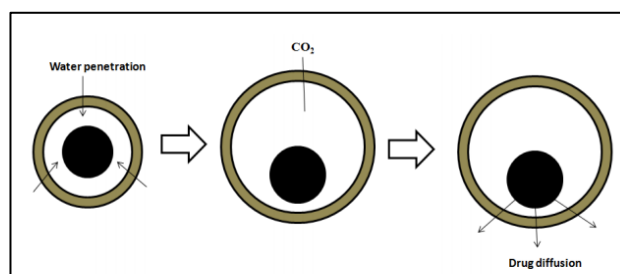


Figure 3. Drug release from effervescent (gas generating) systems

Bioadhesive or Mucoadhesive drug delivery systems

Adhesive drug delivery systems are used as delivery devices in humans to increase the uptake of drugs in a specific way. This approach uses bioadhesive polymers that can adhere to the gastric epithelial surface [43]. Hence, they improve gastric retention lengthening. The adhesive base in this form of the dose can adhere to the surface of the mucous membrane by another mechanism. These mechanisms [44, 45] include:

- 1) The wetting theory, which is based on the ability of bioadhesive polymers to spread and develop intimate contact with the mucous layers.
- 2) The diffusion theory, which proposes physical entanglement of mucin strands the flexible polymer chains, or an interpenetration of mucin strands into the porous structure of the polymer substrate.
- 3) The absorption theory, suggests that bioadhesion is due to secondary forces such as Vander Waal forces and hydrogen bonding.
- 4) The electron theory, which proposes attractive electrostatic forces between the glycoprotein mucin network and the bio adhesive material.

Common materials used for bioadhesion include polyacrylic acid, chitosan, cholestyramine, sodium alginate, hydroxypropylmethyl cellulose (HPMC), sucralfate, tragacanth, dextrin, polyethylene glycol (PEG) and polylactic acid, and others. Effective maintenance is very difficult due to the rapid circulation of mucus in the gastrointestinal tract (GIT).

Expandable, unfoldable and swellable systems

The gastric dosage form tolerates gastric passage if it is larger than the pyloric sphincter. However, the dosage form should be small enough to be swallowed and should not lead to gastric obstruction either alone or in combination. Hence, their configuration [46, 47] is necessary to create

an expandable system for increasing gastric retention time (GRT):

- 1) a small configuration for oral intake,
- 2) an expanded gastroretentive form, and
- 3) a final small form enabling evacuation following drug release from the device.

Therefore, the portability of the stomach increases with a combination of large size and high rigidity of the dosage form for resistance to peristalsis and mechanical contraction of the stomach. Non-folding and inflation systems have been explored, and recent efforts have been made to develop an effective method of drug delivery in the intestine. Non-collapsible systems consist of biodegradable polymers. They are available in various geometries, for example as a four-sided, ring-shaped or corrugated membrane (4 labeled discs or 4-point crossover) made of a biodegradable polymer, compressed into a capsule that extends into the stomach [48, 49]. The systems of the gastrointestinal tract (GIT) are also retained due to their mechanical properties. The swelling is usually due to the osmotic uptake of water, and the dosage form is small enough to be swallowed by gastric juice (Figure 4). Scalable systems have disadvantages such as the problematic storage of easily hydrolyzable polymers, biodegradable polymers and the relatively short mechanical shape memory of the Bloom system, which is not difficult to build and is inexpensive. Dosage forms can cause short-term obstruction, intestinal adhesions and gastropathy [19]

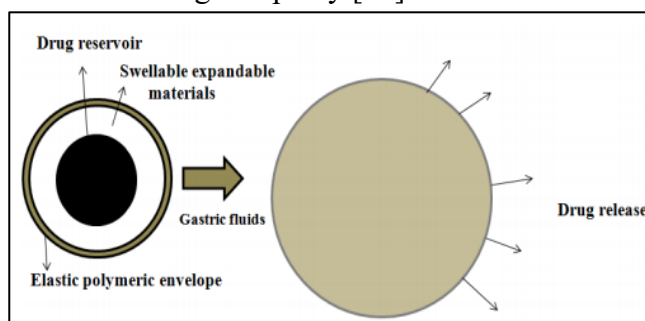


Figure 4. Drug release from swellable systems

Super porous hydrogel systems

These scalable systems differ enough from traditional types to allow separate classification. This approach to improving gastric retention time (GRT) scales very weak hydrogels with an average pore size greater than 100 microns due to the rapid uptake of water by capillary hydration through many interconnected open pores within a minute. 51]. They swell strongly (swelling ratio: 100 or more) and are constructed in such a way that they have sufficient mechanical strength to withstand the pressure of gastric contraction. This is recommended through the formulation of a hydrophilic particulate material [52].

Magnetic Systems

This approach to improving gastric retention time (GRT) is based on the simple principle that the dosage form contains a small internal magnet that is attached to the stomach above the stomach position. Although the magnet system appears to be working, the external magnet must be positioned with an accuracy that can compromise patient compliance [45]. The drugs commonly used to formulate gastric drugs and some commercially resistant gastric products are listed in Table 1 and Table 2, respectively.

ADVANTAGES OF GASTRORETENTIVE DRUG DELIVERY SYSTEMS

Table 1. Commonly used drug in formulation of gastro retentive dosages forms [17, 22]

Dosage form	Drugs
Floating Tablets	Acetaminophen, Acetylsalicylic acid, Ampicillin, Amoxicillin trihydrate, Atenolol, Captopril, Cinnerzine, Chlorpheniramine maleate, Ciprofloxacin, Diltiazem, Fluorouracil, Isosorbide dinitrate, Isosorbide mononitrate, pAminobenzoic acid(PABA), Prednisolone, Nimodipine, Sotalol, Theophylline, Verapamil
Floating Capsules	Chlordiazepoxide HCl, Diazepam, Furosemide, L-DOPA and Benserazide, Nicardipine, Misoprostol, Propranolol, Pepstatin
Floating Microspheres	Aspirin, Griseofulvin, p-nitro aniline, Ibuprofen, Terfenadine, Tranilast
Floating Granules	Diclofenac sodium, Indomethacin, Prednisolone
Powders	Several basic drugs
Films	Cinnerzine

Table 2. Gastroretentive products available in the market [22, 53]

Brand name	Active Ingredient
Cifran OD	Ciprofloxacin
Madopar	L-DOPA and Benserazide
Valrelease	Diazepam
Topalkan	Aluminum -magnesium antacid
Almagate FlatCoat	Aluminum -magnesium antacid
Liquid Gavison	Aluminium hydroxide,
Convicon	Ferrous sulphate
Cytotec®	Misoprostal

- 1) The availability of dynamics of treatment factors can be highly improved for those who are interested in high radius by delivery of metal drugs than non-invasive drug management. There are many factors of absorption and transportation in GIT drugs that affect the absorption of drugs [54].
- 2) For semi-relative drugs, continuous emission can lead to pharmaceutical flaps, and the dose frequency can also be reduced by improving adaptation to the patient.
- 3) They also have advantage in their traditional system because they can be used to overcome the stomach reality pads (GRT), as well as the time of stomach discharge (received). Since these systems are expected, they penetrate gastric fluids without increasing the level of employment, because bulk density is less than the stomach.
- 4) Delivery of drugs in an attacker stomach can produce medications from the dose and release that benefit from internal treatment in the accurate stomach and intestine. Therefore, it is useful in treating micro-intestinal disorders.
- 5) Slow delivery is controlled, the dose dose model provides sufficient local methods in the patient's location, leading to a reduction or cancellation of systematic drug exposure. The delivery of drugs on the site leads to a reduction in unwanted effects.
- 6) Dose formats in the stomach reduce the concentration fluctuations and the effects of the drug. Therefore, accepted side effects can be provided to focus on the concentration of courier. This function is especially important for drug treatment index [55].
- 7) Internal drug delivery can reduce antibody activity and thus increase the effectiveness of the drug.
- 8) The reduction in the fluctuations in drug concentrations makes it possible to achieve improved selectivity in receptor activation.
- 9) The continuous release of the drug from the protective doses of the stomach makes it possible to extend the time in the critical concentration range and thus to increase the drug effect and improve the chemical results.

CONCLUSION

According to Peiill literature, gastric stomach drugs can be concluded that many potential drug benefits with limited vital capabilities are limited to the upper gastrointestinal tract (GIT) and can be effectively delivered, so that Absolute vital access and pharmaceutical and non-pharmatic parameters, research, increase, increase, increase the need for an optional dose model for specific property. Another promising research field is the removal of *Helicobacter pylori*, which now has to remain bacteria for chronic gastritis and gastrointestinal ulcer. Although this real religion organism is very sensitive to many antibiotics, complete removal requires maintaining high concentrations of antibiotics in mucous membranes for a long time. An important advantage is to consider the domain of the stomach. When the drug (during meals or separation of food) is an important parameter. To develop a more effective metal model, a real challenge for medical technology. In fact, the drug delivery system should be sufficient in the stomach that is not compatible with normal member functions. All drug release systems (high density, floating, floating, flexible, flexible, non-flexible, sticky, magnetic, etc.) are interesting and presenting their advantages and disadvantages. There are currently a lot of work on the development of different types of stomach delivery systems for different drugs. In the future, they are expected to be increasingly important,



ultimately improve the efficiency of different types of drugs.

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HOW TO CITE: Suraj Kothule, Smita Aher, Rishikesh Bachhav, Gastroretentive Drug Delivery System : A Review, *Int. J. in Pharm. Sci.*, 2023, Vol 1, Issue 2, 75-85. <https://doi.org/10.5281/zenodo.5881901>

