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A REVIEW ON GASTRO RETENTIVE DRUG DELIVERY SYSTEM

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Abstract

Gastro-retentive drug delivery systems (GRDDS) have emerged as a promising solution to overcome challenges related to the poor bioavailability of oral drug formulations. GRDDS aim to extend the residence time of drug formulations in the stomach, facilitating controlled and sustained release of active ingredients. This is particularly beneficial for drugs with a narrow absorption window, those unstable in alkaline pH, or those exhibiting increased solubility in acidic environments. Various approaches to achieve gastric retention have been developed, including floating systems, mucoadhesive polymers, magnetic materials, and expandable devices. Each of these strategies aims to prevent premature gastric emptying, thereby enhancing drug absorption and improving therapeutic efficacy. The development of GRDDS requires careful consideration of both in vitro and in vivo evaluations to optimize performance. Techniques like gamma scintigraphy and MRI are commonly employed to assess gastric retention in vivo, although studies involving small animals remain limited. In addition to technical challenges, the physiological variability of the gastrointestinal tract, food effects, and inconsistent gastric emptying rates present barriers to widespread GRDDS adoption. Despite these obstacles, GRDDS have shown promise in the treatment of gastrointestinal disorders, offering the potential for more targeted and personalized therapies. This review provides an overview of recent innovations in GRDDS, examining formulation strategies, evaluation techniques, and clinical applications, while also addressing the challenges that need to be overcome for successful market implementation.

Keywords: Bioavailability, therapeutic window, Floating drug delivery system, Magnetic systems, expendable systems, super porous system.

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Introduction

Oral administration is popular despite of administration. Controlled release drug delivery systems are designed for oral administration. These drug delivery systems release the medication in a predetermined, predictable, and controlled way. They are not suitable for drugs with low bioavailability due to stability or absorption issues. GRDDS can either function as intrinsic controlled-release systems or in conjunction with such technologies to ensure a controlled release of drugs.

GRDFs are created using one of several methods, such as formulating low-density dosage forms that float above gastric fluid (FDDS) or high-density dosage forms. GRDDS is characterised as a system that remains in the stomach for a sufficient duration of time before releasing active moiety in a regulated manner and being metabolised throughout the body. Gastro-retentive drug delivery system (GRDDS) is one such example where the attribute like gastric retention time coupled with the drug release for extended time has significantly improved patient compliance [1].

Anatomically, the stomach is divided into three sections: the fundus, which is closest to the oesophagus; the body, which stores ingested food; and the antrum, the final section that joins the body to the small intestine. The bioavailability of medications taken orally will change depending on the feeding stage. The inter-digestive series of electrical events and cycles, which pass through the stomach and small intestine every 2-3 hours, is what distinguishes the fasted state from other states [2].

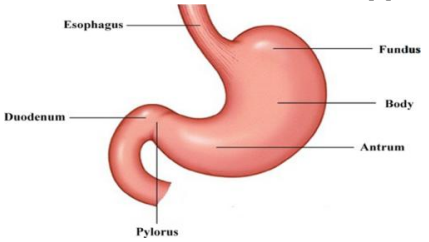

Fig.1- Diagram of human stomach

Stomach physiology

Success of GRDDS relies on the understanding of stomach physiology and related gastric emptying process. Structurally the human stomach is composed of three anatomical regions: fundus, body and antrum (pylorus), as depicted in After a meal, the average volume of a stomach is about 1which varies from 250 to 500 ml during the inter-digestive phases

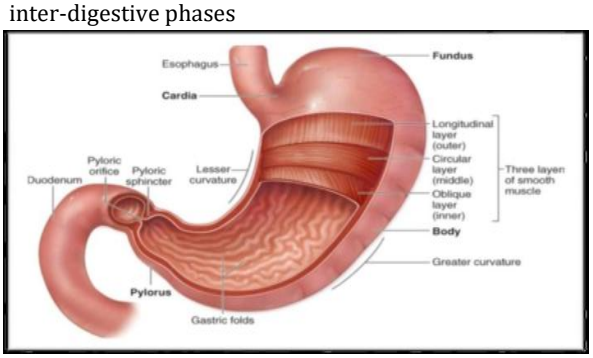

Fig.2 Physiology of stomach

The part made of the fundus and the body acts as a reservoir of any undigested material, while the antrum performs as the principal site for the mixing action. Being the lower part, the antrum works as a pump for gastric emptying by a propelling action. Pylorus acts to separate the stomach from the duodenum and plays a major role in gastric residence time of the ingested materials [3].

The stomach is divided into three parts anatomically

- Body,
- Antrum pylorus,
- Fundus.

Importance of GRDDS in the field of Pharmaceutics

Immediate release oral delivery methods are the most commonly employed to treat disease because they are absorbed only at a specific place. The disadvantages of the instant release dosage form necessitate the development of Gastro-retentive drug delivery methods.

GRDDS success is dependent on an understanding of stomach physiology and the accompanying gastric emptying process. the human stomach is divided into three anatomical regions: the fundus, the body, and the antrum (pylorus) [4].

Approaches for achieving gastric retention

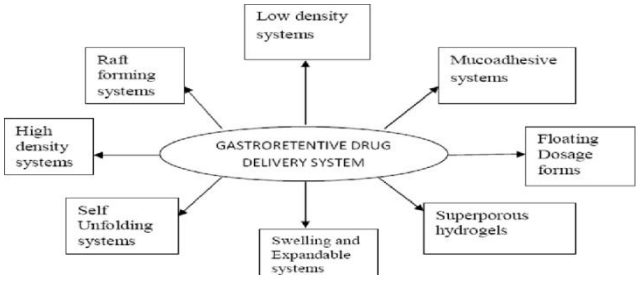

Fig.3.Approaches of GRRDS

Non-floating drug delivery systems

- **High density (sinking) drug delivery system:** The formulation's density exceeds the density of normal stomach content. The materials boost density to 1.5-2.4 gm/cm^3.
- **Bio adhesive or mucoadhesive drug delivery system:** The gastric retention time has extended by adhering the bio adhesive system for gastric mucous membrane The delivery system's adhesion to the stomach wall prolongs residence time, enhancing bioavailability [5].
- Magnetic system: The dose form incorporates a small magnet in this method, and another magnet is placed on the abdomen above the position of the stomach. The external magnet should be set with precision, which may reduce patient compliance.
- Expandable System: These systems have the ability to enlarge and stay in the stomach for prolonged periods of time. These are frequently presented in the form of capsules that include a folded and compressed dosing form. The dosage form expands and the capsule shell breaks down in the stomach environment, making it unable to pass through.
- Raft forming system: To achieve sustained drug delivery, these systems are built with gel-forming polymers and effervescent excipients. Because they provide a barrier between the oesophagus and the stomach, these systems are good at achieving a localised impact. As a result, the device can be used to treat peptic ulcers and gastroesophageal reflux disease. When these systems come into touch with stomach fluid, they swell and create a viscous cohesive gel, resulting in the formation of a continuous layer known as a raft [6].

Physicochemical properties of GRDDS

Physicochemical properties of GRDDS include density, size, and shape of the dosage form, which play major roles in the formulation of GRDDS. The dosage forms having a density lower than the gastric contents can float to the surface, while high-density systems sink to the bottom of the stomach. For an ideal formulation, the density should be in the range of 1.0-2.5 g/cm3. Dosage forms having a diameter of more than 7.5 mm show better gastric residence time (GRT). Circular, spherical or tetrahedron-shaped devices show excellent gastro retentive properties.

Classification of GRDDS

GRDDS are classified into mainly two types:

floating and no floating systems. Floating systems are further classified into effervescent system and non-effervescent systems based on the mechanism of floating, while non-floating systems classified into four different classes based on the mechanism used for gastro retention.

- **Floating or low-density system:** Another approach to increase gastric residence is to lower the density of dosage form than the

normal gastric content. systems remain buoyant due to lower density and provide continuous drug release.

- **Effervescent system:**
  This system uses carbonates (e.g. sodium bicarbonate) to generate in situ carbon dioxide (CO2). Organic acids (e.g. citric and tartaric acids) are added to speed up the reaction, thus reducing the density of dosage form and remaining buoyant in the stomach.
- **Volatile liquid/vacuum type :**

These are further classified into three types.

i) Inflatable system
ii) Intragastric floating system
iii) Intragastric-osmotically controlled system

i. **Inflatable system:**
It consists of a pullout system having a space filled with volatile liquids that evaporate at body temperature. Thus, when these systems are introduced into the stomach, the chamber inflates, and the system floats.

ii. **Intragastric floating system:** It contains a chamber filled with a vacuum and includes a microporous compartment serving as a drug reservoir gum as gel-forming agents. Buoyancy was achieved by adding an effervescent mixture of sodium bicarbonate and anhydrous citric acid [7].

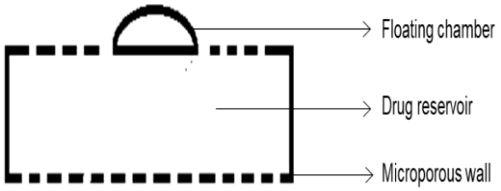

Fig.4. Intragastric floating gastrointestinal drug delivery system

iii. Intragastric-osmotically controlled system: Osmotic control can be achieved using a biodegradable capsule comprising inflatable floating support congestion with an osmotic pressure-controlled drug delivery device.

- Non-effervescent systems : In non-effervescent floating systems, the drug comes in contact with gastric fluid and it swells. It maintains its shape, and its density remains less than one, hence it floats in gastric juice
- Hydrodynamically balanced systems (HBS): These systems mainly consist of a mixture of drugs and hydrocolloids that forms a gelatinous barrier, when it comes in contact with gastric fluid due to swelling of the combination.

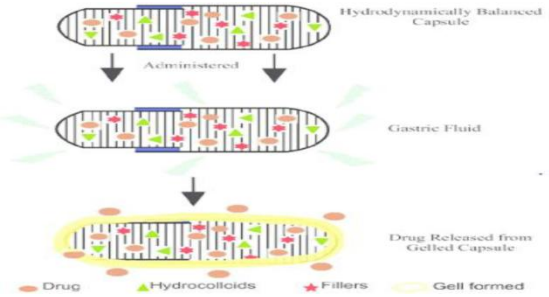

Fig.5.Hydrodynamically balanced system

- **Micro balloons:**
  Micro balloons are described by the gradual addition of drug-containing emulsion into a volatile solvent. On evaporation of the solvent, gas is generated in a dispersed polymer droplet, which results in the formation of an interior orifice in the microsphere of the drug with polymer.
- **Alginate beads:**
  Spherical beads of about 2.5 mm diameter can be made by dropping sodium alginate solution into an aqueous solution containing calcium chloride [8]. Methods of Preparation of Gastro-Retentive Multi particulate System
- **Solvent Evaporation Method:**
  To construct the hollow inner core of a floating multi particulate dosage form, solvent diffusion and evaporation processes can be used. The drug is either dissolved or disseminated in the polymer solution, which has been dissolved in an organic solvent.
- **Ionotropic Gelation Method:**
  Ionotropic gelation is supported by poly electrolytes' capacity to cross link in the presence of opposing ions to form beads.
- **Emulsion Solvent Diffusion Method:**
  The affinity between the drug and the organic solvent is stronger in the emulsion solvent diffusion method than between the organic solvent and the aqueous solvent.
- **Novel Method for Foam Powder:**
  A novel multi-particulate gastro retentive drug delivery method based on low-density foam powder has also been presented and tested in vitro floating microparticles were created using an oil-in-water solvent extraction / evaporation process using polypropylene foam powder, verapamil hydrochloride.
- **Crosslinked polyacrylates:**
  Carbomers, Carbopol® and Poly carbochol (PCP): Carbomers are high-molecular-weight synthetic polyacrylic acids that are cross-linked with polyalcohol allyl ethers such as pentaerythritol polyallelic ether and polyallelic sucrose [9].

Evaluation of gastro-retentive dosage form

- **Buoyancy Lag Time:**
  It is determined in order to assess the time taken by the dosage form to float on the top of the dissolution medium after it is placed in the medium.
- **Specific Gravity / Density:**
  The displacement method, using Benzene as the displacement medium, can be used to calculate density.
- **Resultant Weight:**
  The two fundamental factors that define buoyancy are bulk density and floating time. However, a single measurement of density is insufficient to fully represent buoyancy.
- **Swelling systems:**
  Swelling Index-The dosage form is taken from the SGF at regular intervals after being immersed in a swelling solution at 37°C, and dimensional changes are measured as an increase in tablet thickness or diameter with time.
- **Particle Size and Shape:**
  In comparison to light microscopy (LM), scanning electron microscopy (SEM) delivers better resolution. The most common methods for visualising microparticles are light microscopy (LM) and scanning electron microscopy (SEM) [10].

Current trends in GRDDS

- **Dual working system:**
  These systems are based on floating, bio adhesive, swelling, and bio-adhesion working principles. The therapeutic efficacy of the medicine would be significantly improved by a dual-functioning system, which would overcome the limitations of bio adhesive, swelling, and floating systems [11].
- **Floating osmotic system:** A floating osmotic drug delivery system floats on gastrointestinal fluid using the osmotic pressure principle. These systems are composed of three parts: an osmotic core, a shape-retaining semipermeable membrane, and an outside compression coating composed of gas-generating and gel-forming substances.
- **Floating pulsatile system:**
  Drugs are rapidly and wholly released from pulsatile drug delivery devices after a certain period. However, due to lag time, such systems may remove from the body without releasing drug content.

Challenges ahead with GRDDS

The retention time of the dosage forms in the GIT is one of the determinants of the bioavailability of oral drug delivery systems. In case of GRDDS, it is rather specific to the stomach only. Therefore, for developing a GRDDS, the main challenge is retaining the delivery system in the stomach or the upper part of the small intestine for a long time until all the drugs have been released at a predetermined rate. The process of gastric emptying time is highly variable [12]. Among many other factors, it mainly depends on the dosage form as well as fed or fasted state of the stomach. The gastric retention time is extended in the fed state, whereas shortened by the fasting state. Other physiological barriers and factors like the type of food, caloric content**,** gender and age play significant roles in the variation of gastric emptying time.

Conclusion

In conclusion, Gastro-Retentive Drug Delivery Systems (GRDDS) offer significant advantages in improving patient compliance and reducing side effects by providing controlled and site-specific drug release. These systems, which can be designed using various methods like swelling, bio-adhesion, and effervescence, have shown potential in enhancing bioavailability and controlling drug delivery, particularly for drugs with low bioavailability. However, no single GRDDS is universally ideal for all drug candidates, and careful assessment of each drug's dose, manufacturing process, and appropriate polymer selection is crucial for success. Despite challenges in ensuring in vivo efficacy and the complexity of human GIT physiology, GRDDS is emerging as a promising technology for optimizing drug delivery. More research and tailored formulation designs are needed to overcome obstacles and improve the effectiveness of these systems, particularly for drugs with long first-pass metabolism and limited bioavailability.

Author Contributions

All authors are contributed equally

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Declaration of Competing Interest

The Authors have no Conflicts of Interest to Declare.

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