

A Review on

GASTRO-RETENTIVE DRUG DELIVERY SYSTEM

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Abstract

The aim of this review is to focus on the various gastro retentive approaches by investigate, compile, and present in most concise way, where the gastroretentive has gained immense popularity in the field of oral drug delivery. In the field of oral drug delivery gastro-retentive drug delivery play an important role. There are various types of GRDDS approaches which can be utilized to retain the dosage form in the stomach and release the drug slowly for an extended period of time. The various GRDDS approaches include high density, low density, mucoadhesive, expandable, magnetic systems and superporous hydrogel system. GRDDS has proved to be effective in both local and systemic actions to treat gastric or duodenal ulcers. Gastro-retentive drug delivery system can be utilized to prolong the residence time of delivery system in the stomach. Where the stomach and duodenum are separated by the pylorous, which has an important role in residence time of the ingested substances in the stomach. GRDDS can be used to overcome challenges related with conventional oral dosage forms.

Keywords

Gastro-retentive, GRDDS, Oral route, GIT, various approaches, floating system, non-floating system, bioadhesive system.

Introduction

In 1968, Davis firstly discovered the concept of floating drug delivery system (FDSS) after experience gagging or choking by some persons while swelling medicinal pills. The GI-Tract is the most important route for the delivery of drugs to the systemic circulation. (Vishwanath Reddy M, 2011). Oral administration is the most convenient and popular despite continuous improvement

in drug delivery approaches owing to patient comfort and ease of administration. Oral controlled release drug delivery system has recently been of increasing interest in pharmaceutical field to achieved therapeutic advantages. These drug delivery systems release medication in a predetermined, predictable and controlled way.

Gastro-retentive drug delivery is an approach to prolong gastric residence time by targeting site-specific drug release in the upper gastrointestinal tract for local or systemic effect. It improved therapeutic patient compliance by reducing the frequency of dosing. (kuldeep VINCHURKAR, 2022).

GRDDS are feasible for drugs that have low absorption in the lower part of GIT, are unstable and poorly soluble at alkaline pH, it show local activity at the upper part of the intestine for eradication of Helicobacter pylori. (Fujimori J.). It including super-porous hydrogel, bio/ mucoadhesive, raft forming, ion exchange, low and high density systems, expandable. (Thapa P.)

Physiology of GIT

The GIT can be divided in to three main regions: stomach, small intestine (duodenum, jejunum, and ileum), large intestine. The GIT is a continuous muscular tube, extending from the mouth to anus, which functions to take in nutrients and eliminate waste by such physiological processes as secretion, motility, digestion, absorption, and excretion.

The organization of the GIT from stomach to large intestine. The stomach is J- shaped enlargement of GIT, which can be divided in to four anatomical regions: Cardia, Fundus, Body and Antrum.

The main functions of stomach are to store and mix food with gastric secretions before emptying its load through pyloric spinchter and into small intestine at a controlled rate suitable for digestion and absorption. Gastro-retentive dosage forms release the drug in a controlled manner to their and

absorption. Gastro-retentive dosage forms release the drug in a controlled manner to their specific site of action. It is one of the site specific delivery of the drugs at stomach. (Hemendrasinh J Rathod).

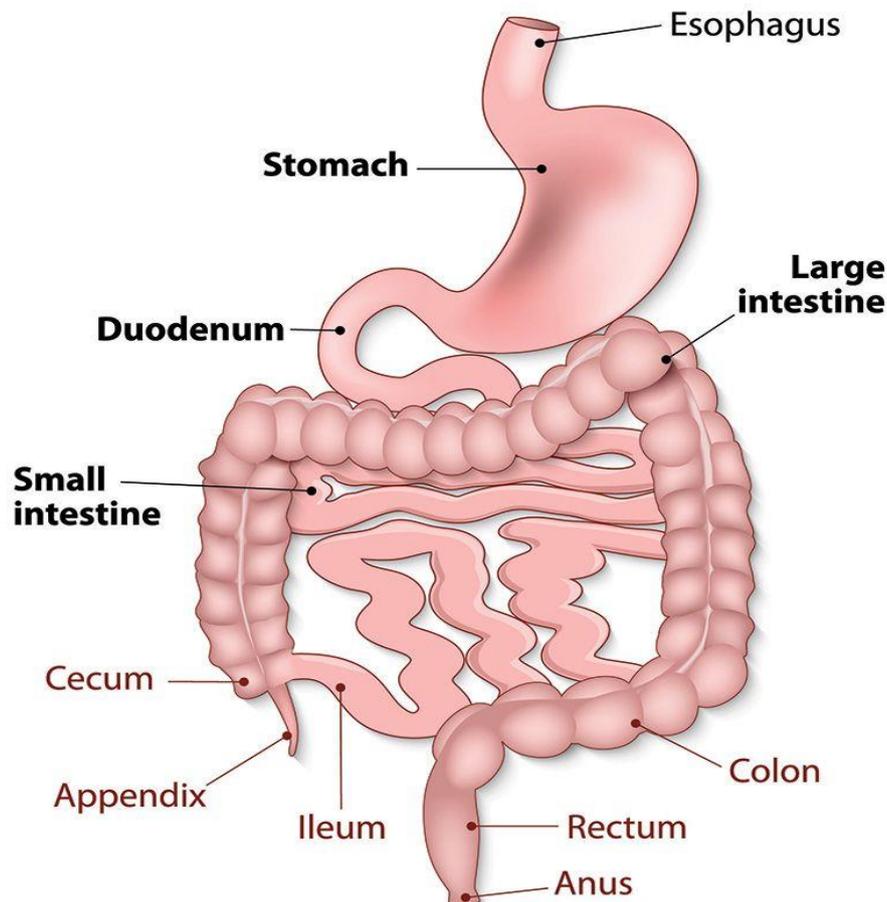


Figure 1: Anatomy of GI Tract

Advantages of GRDDS:

1. One of safest route of administration.
2. Reduces dose and dose frequency.
3. It helps in targeting of drugs.
4. It reduces the side effect.
5. Improved bio-availability.
6. Sustained release can be achieved.
7. It can be used for wide range of drugs.
8. Minimizes fluctuation of drug concentration in blood. (Satinderkakar, 2015).

Disadvantages of GRDDS:

1. Drugs having stability and solubility problems in highly acidic gastric environment.
2. Swellable dosage form must be capable to swell fast before it exits from stomach and achieve size larger than pylorus.
3. Presence of food is preferable, food delays emptying time of food and dosage form.
4. Floating system require high level of fluids in stomach for floating. Therefore, more water intake is prescribed with such dosage forms. (Meenakshi jassal, 2015).

Need for GRDDS

1. Drugs that are less soluble or are degraded by the alkaline pH, they encounter at the lower part of GIT.
2. Drugs that are absorbed from the proximal part of the GIT.
3. Drugs that are absorbed due to variable gastric emptying time.
4. There are local or sustained drug delivery to the stomach. (S. Satish babu, 2017)

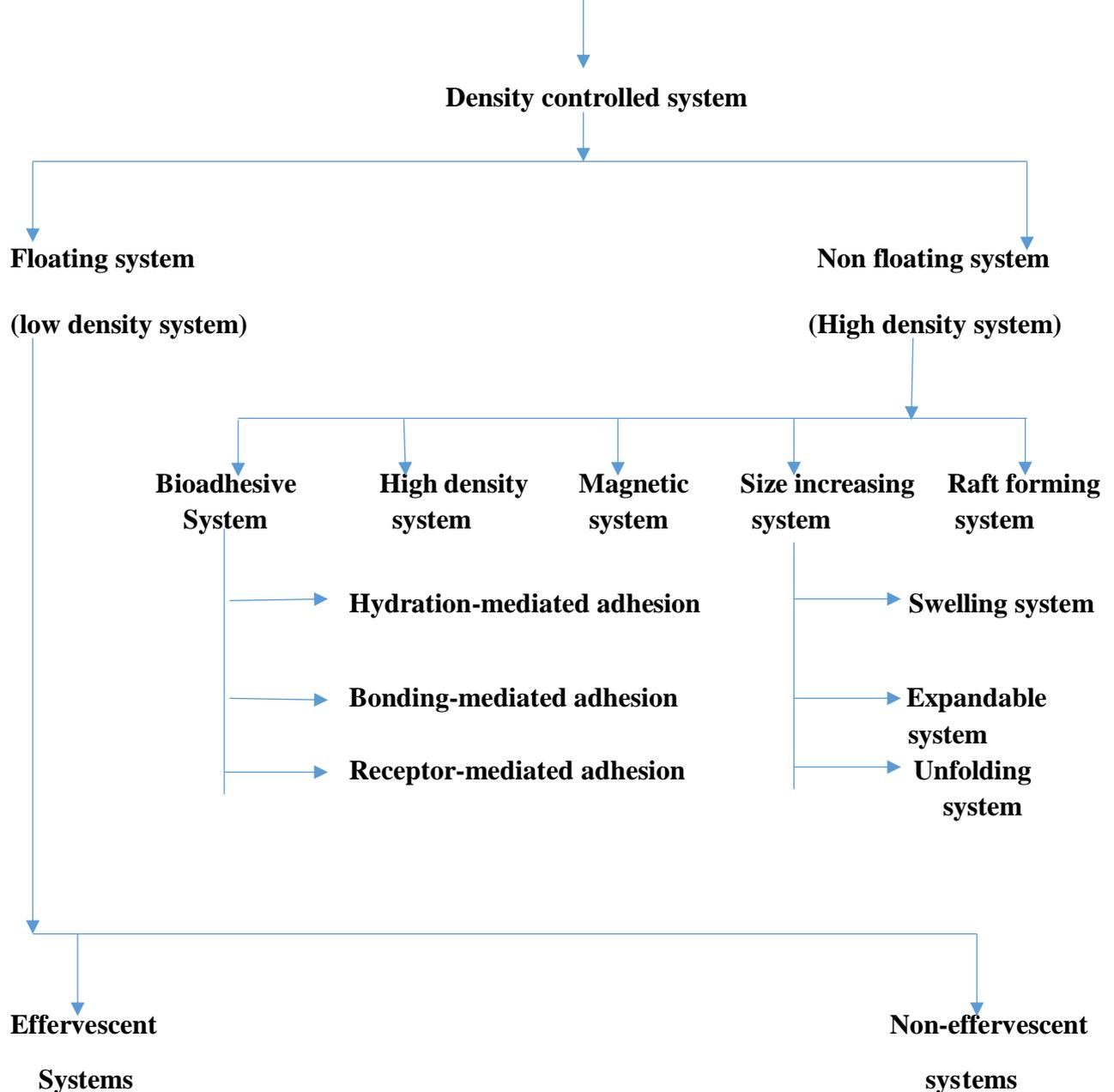
Application for GRDDS

1. Enhanced bioavailability
2. Sustained drug delivery
3. Site specific drug delivery system
4. Absorption enhancement
5. Reduced fluctuation of drug concentration

Approaches of GRDDS

- High density system
- Low density system
- Mucoadhesive system
- Raft forming system
- Swellable system

Table 1: Gastro-retentive drug delivery system



High density system

In this type of system, drug can be coated or mixed with heavy non-toxic materials such as Barium sulphide and Titanium dioxide etc. the high density system uses its weight as

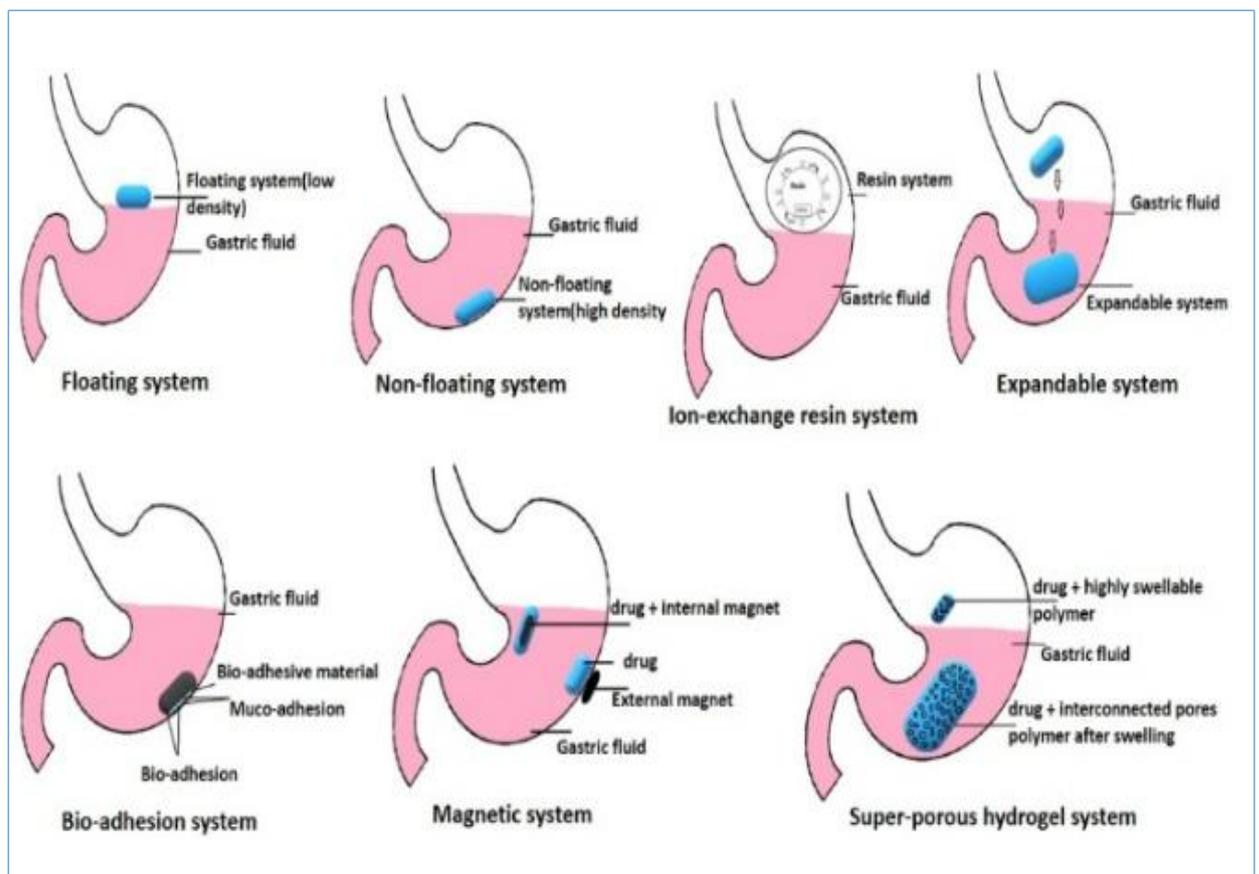
mechanism. To enhance the gastric residence of drug in stomach its density must exceed the normal stomach content (1.004g/ml).

Low density system

Lower density system lowers the density of dosage form than the normal gastric content. It comes under the low density approach. Which is also called as Hydrodynamically balanced system. In this the density of pellets should be less than 1g/ml.

Floating system

This system remains buoyant due to lower density and provide continuous drug release. It increases GIT of drug and improve its bioavailability. This system was first introduced by Davis in 1968. It is helpful in the drug which have locally action in the proximal portion of GIT. (Mandar J Bhandwalkar, 2020).



Mucoadhesive / bioadhesive system

In this system mucoadhesive polymers are used which hold the epithelial surface in the stomach. These some theories have been used to explain the fundamental mechanism of bio-adhesion / muco-adhesion.

1. Wetting theory: to spread and develop immediate attachment with the mucous membranes.
2. Electronic theory: there are attractive electrostatic forces in between glycoprotein mucin network and bio/mucoadhesive polymers.
3. Adsorption theory: surface forces resulting in chemical bonding. etc. (Vikram kumar sahu, 2011).

Swelling and Expandable system:

This system is capable of expanding and retain in the stomach for longer periods. It is usually formulated as a capsule containing dosage form folded and compact form. (Shailaja Pant, 2016). Swelling drug delivery system meant to prolong the stay of a drug inside the stomach. So as to achieve controlled blood plasma level. It becomes larger in size.

Non-effervescent system:

It is based on the mechanism of swelling of polymer or bioadhesion to mucosal layer in GI tract. In this highly swellable cellulose derivatives or gel forming polymers are used. It mixing the drug with forming polymer. After oral administration these dosage form swells in contact with gastric fluids and attains a bulk density of less than 1g/ml. (Shivram Shinde, 2013).

Effervescent system:

It includes a gas generating agent volatile liquids. Effervescent system has been applied for single or multiple unit systems. When this system comes into contact with gastric field, CO₂ is liberated due to the reaction of effervescent agent with gastric fluid.

It is divided into two types:

- i. Volatile liquid or vacuum containing system.
- ii. Gas generating system.

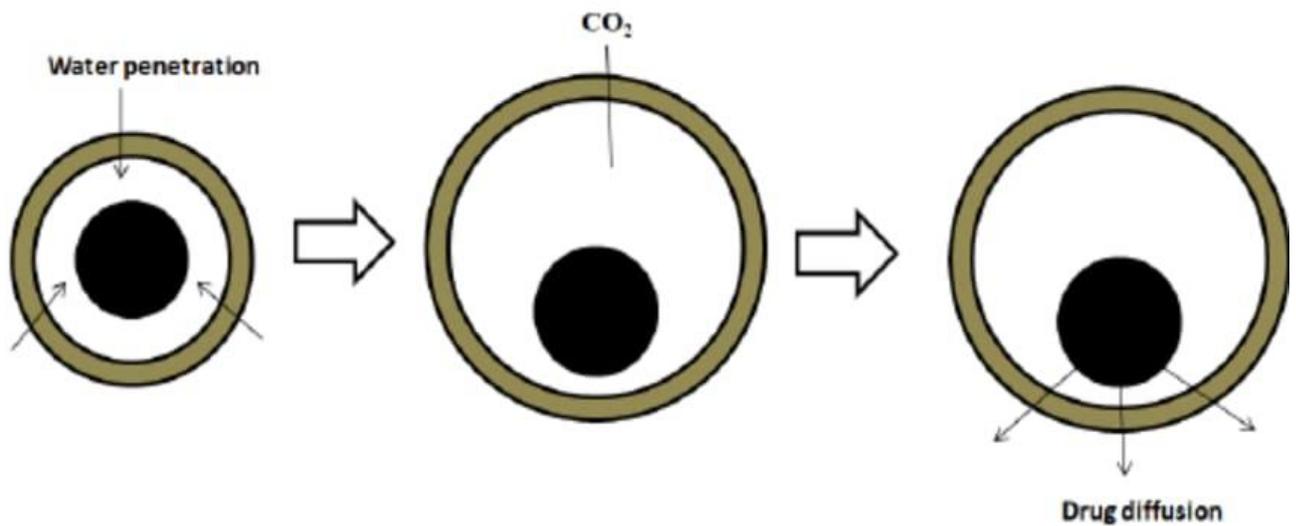


Figure 2: Drug release from effervescent system

Microballons / hollow microsphere: It loaded with drugs in their other polymers. In this system shelf were prepared by simple solvent evaporation or solvent diffusion.

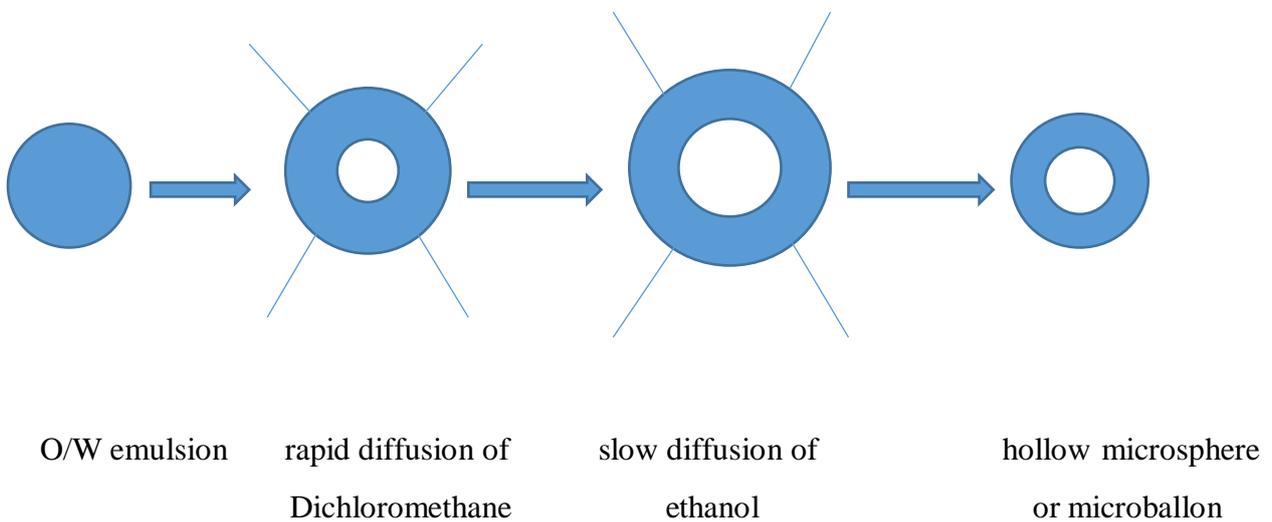


Figure 3: microballons

Table 2: COMMONLY USED DRUG IN FORMULATION OF GRDDS

Tablets	Ziduvudine, Pentoxifyllin, Chlorpheniramine Maleate, Nemodipine, Amoxicillin Trihydrate, Ciprofloxacin, Atenolol, Diltiazem, Verapamil HCL, Nimodipine, Ampicillin, Theophylline, Sotalol, Furosemide.
Capsules	Furosemide, Propranolol, Pepstatin, Celiprolol HCL, Diazepam, Misoprostal, Urodeoxycholic Acid,.
Microspheres	Verapamil, Aspirin, Iboprufen, Nicardipine, Theophylline, Nifedipine, Griseofulvin, Terfenadine.
Powders	Several Basic Drugs-Riboflavin, Sotalol, Theophylline.
Granules	Diltiazam, Isosorbide Mononitrate, Indomethasin, Diclofenac Sodium, Ranitidine Hcl, Fluorouracil.
Beads	Loratadine, Ranitidine, Diltiazem Hcl.
Bilayer Tablets	Diltiazem HCL, Lovastatin, Metoprolol Succinate, Atenolol.
Films	Albendazole, Prednisolone, Quinidine Gluconate, Cinnarizine.

Table 3: Good drugs for GRDDS

S.No	Drug and category	Bioavailability
1	Propranolol Antihypertensive	4-26%
2	Atenolol Antihypertensive	40-50%
3	Verapamil Calcium Channel Blocker	20-30%
4	Nifedipine Calcium Channel Blocker	45-65%
5	Omeprazole Proton Pump Inhibitor	35-60%
6	Verapamil Antihypertensive	18-35%
7	Ramipril ACE Inhibitor	28%

Table 4: GRDDS products available in markets

Drugs	Brand Name
Ciprofloxacin	Cifran OD
Diazepam	Valrelease
Ferrous Sulfate	Conviron
L-DOPA And Benserazide	Madopar
Aluminum-Magnesium Antacid	Almagate Flatcoat
Aluminum Hydroxide	Liquid Gavison

Conclusion:

We have seen many drugs have been formulated as floating drug delivery system with an objective of sustained release and restricting the region of drug release to stomach.

In this GRDDS the most important criteria which has to be looked into for the production of a floating drug delivery system is that the density of the dosage form should be less than that of gastric fluid.

The GRDDS dosage forms serve the best in the treatment of disease related to the GIT and for extracting a prolonged action from a drug with a short half-life.

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