GASTRORETENTIVE DRUG DELIVERY SYSTEM

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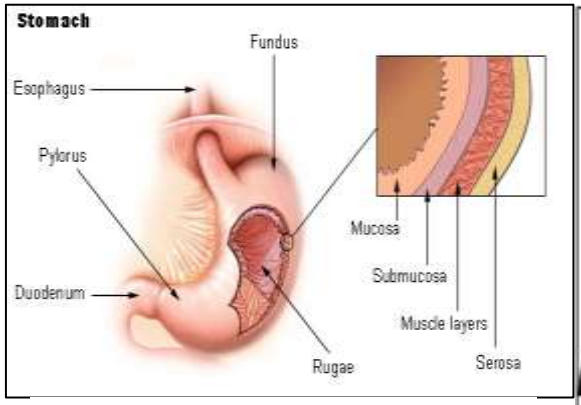


Fig no.1- Anatomy of stomach

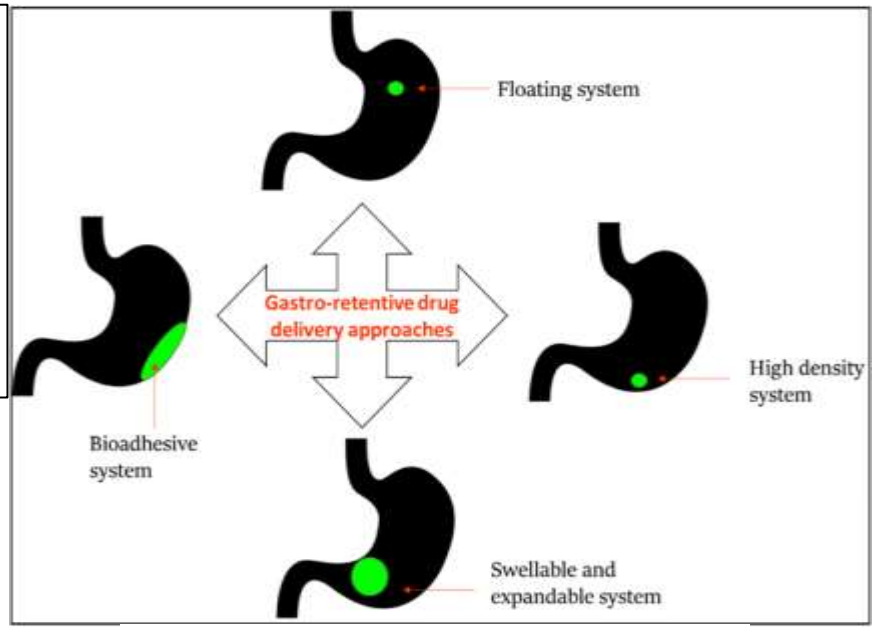
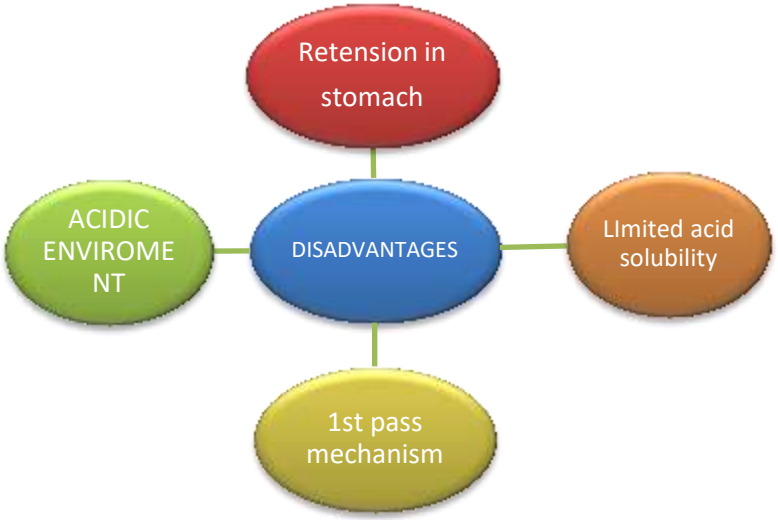


Fig no.2-Gastro retentive approches

INTRODUCTION

The most popular route administration for Systemic action is oral route probabley 90% drug given by Oral route. Oral route mostly prescribed route since it has Patient compliance, ease of ingestion, pain avoidance andVersatibilty to accommodate various type of drug. The short Gastric emptying time and unpredictable short gastric empt-Ing are two problem



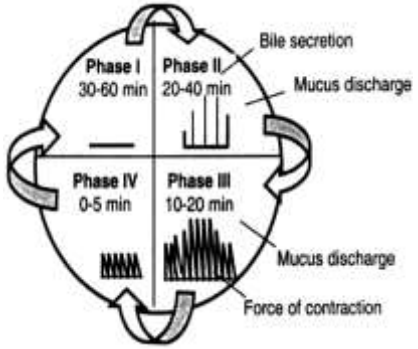
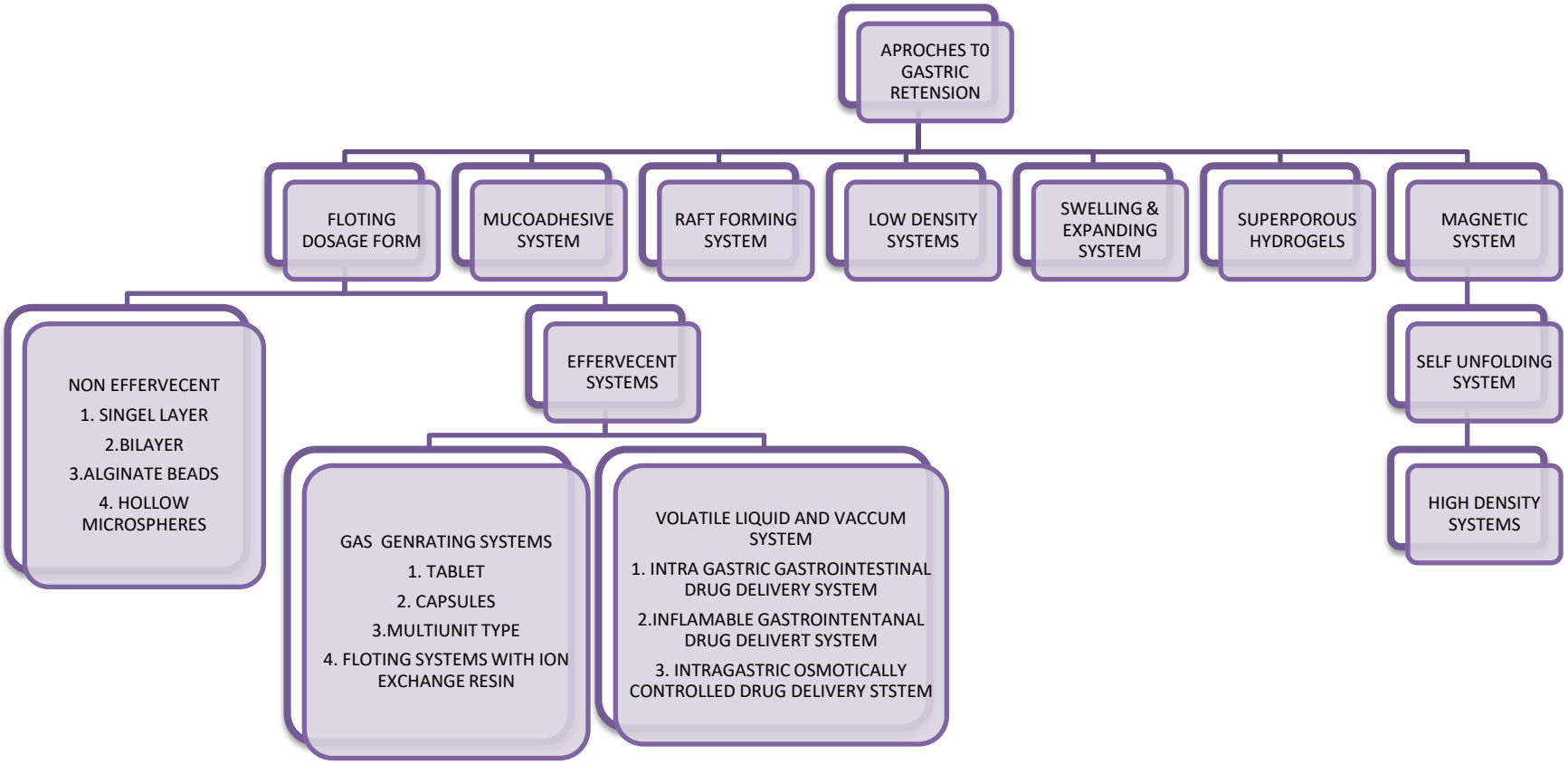


Fig no.3 Phases of GRDDS

APPROCHES FOR GRDDS



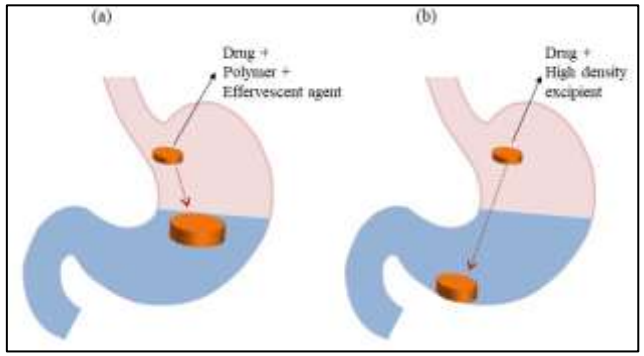


Fig no.4 High density system

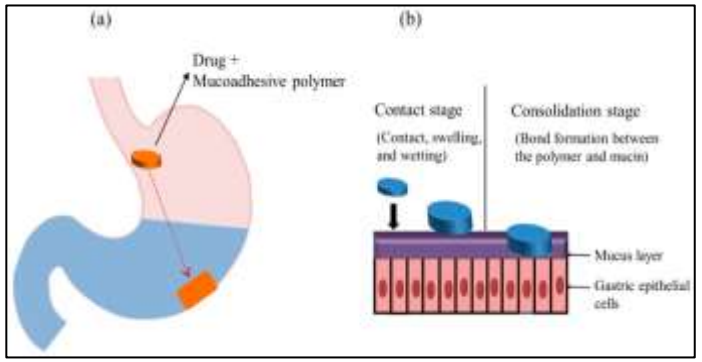


Fig no.5 Gastroadhesive system

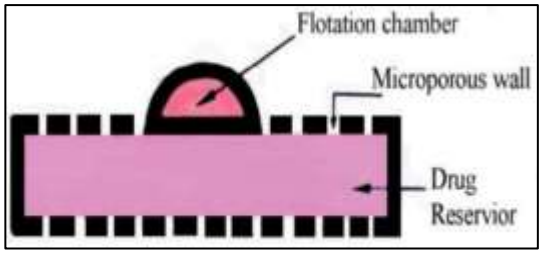


Fig no.6 Floation chamber

1.Floating system

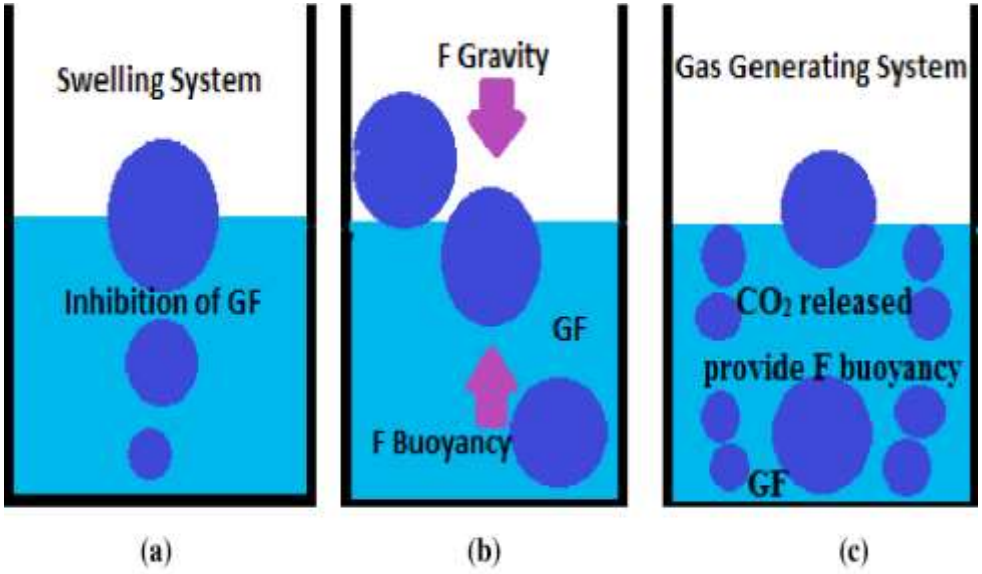


Fig. no.7- Floating system

- Invovled formulation dosage form with density lower than that of stomach content (1.004 gm/cm). These drug remain buoyant 3-4 hr on the gastric content

- Floating systems or dynamically controlled systems are low-density systems that sufficiently buoyancy to float over the gastric contents and remain in the stomach without affecting the gastric emptying rate for a prolonged period of time. This results in an increased gastric retention time and a control of the fluctuations in plasma drug concentration.

ADVANTAGES OF FDDS

- Floating dosage forms such as tablets or capsules will remains in the solution for prolonged time even at the alkaline pH of the intestine.
- FDDS are advantageous for drugs meant for local action in the stomach eg: Antacids
- FDDS dosage forms are advantageous in case of vigorous intestinal movement and in diarrhea to keep the drug in floating condition in stomach to get a relatively better response.
- Acidic substance like aspirin causes irritation on the stomach wall when come in contact with it hence; HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs. 5. The FDDS are advantageous for drugs absorbed through the stomach eg: Ferrous salts, Antacids.

DISADVANTAGES OF FDDS

- Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.
- Drugs such as Nifedipine, which is well absorbed along the entire GI tract and which undergo significant first-pass metabolism, may not be suitable candidates for FDDS since the slow gastric emptying may lead to reduced systemic bioavailability
- One of the disadvantages of floating systems is that they require a sufficiently high level of fluid

- Hoelzel first discovered the effects of dosage form density on the GRT of several animal species.

2.High density system

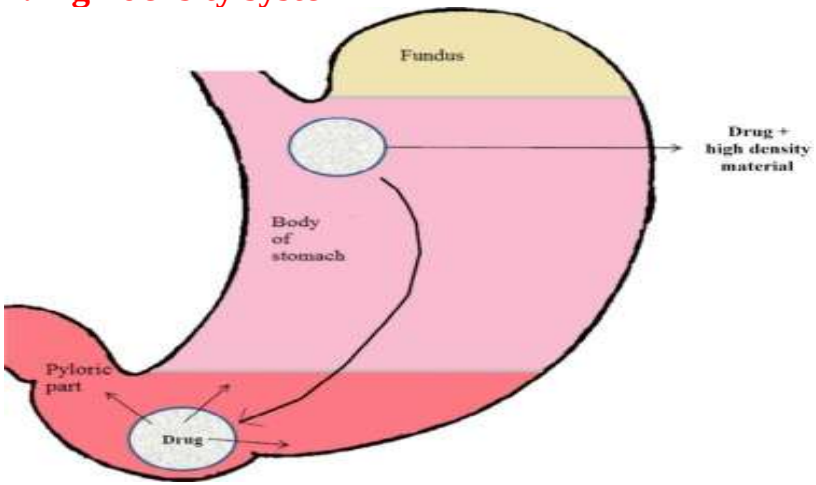


Fig. no.8- high density system

- Involved formulation dosage form with density greater than that of stomach content (1.004gm/cm)
- Major drawback with such system is it technically difficult to manufacture
- These formulations are prepared by coating drug on a heavy core or mixed with inert materials such as iron powder, barium sulphate, zinc oxide and titanium oxide etc
- Sedimentation has been employed as a retention mechanism for pellets.
- Commonly used excipient in high density system inclide barium sulphate ,iron powder and titanium dioxide
- The densities of the tested dosage forms ranged from 0.9 to 10.5 g/cm3.
- The author concluded that high-density materials had slower GRTs than light-density materials.
- Thereafter, the impact of dosage form density on GRT has been studied.
- Garg and Gupta reported that small high-density pellets are able to resist gastric peristaltic movements due to their retention in the antrum rugae or folds, increasing the gastrointestinal tract time from 5.8 to 25 h.
- Even though this system has the potential to improve the GRT, it is difficult to design high-density pellets containing high-dose drugs.
- Moreover, only a few clinical studies on high-density pellet formulations have been reported in the literature; as a result, the clinical significance of these systems is still questionable.
- Therefore, future directions need to be focused on animal studies to investigate the clinical significance of such dosage forms.

3.Inflantable system

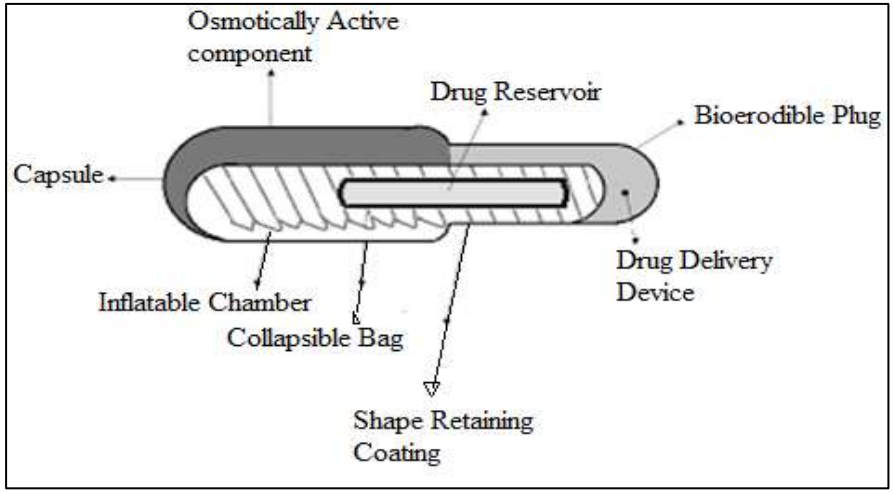


Fig no..9-Inflantable drug delivery

- The inflatable chamber automatically inflat & retain drug reservoir compartment in stomach
- The drug continuously released from reservoir into gastric fluid
- The inflatable floating support is made from a deformable hollow polymeric bag
- nflatable gastrointestinal delivery system The drug continuously released from the reservoir into the gastric fluid
- Intra-gastric osmotically controlled drug delivery system: It is comprised of an osmotic pressure controlled drug delivery device and an inflatable floating support in a biodegradable capsule.

temperature to inflate the bag.

- The osmotic pressure controlled drug delivery device consists of two components; drug reservoir compartment and an osmotically active compartment
- The drug reservoir compartment is enclosed by a pressure responsive collapsible bag, which is impermeable to vapour and liquid and has a drug delivery orifice.
- The osmotically active compartment contains an osmotically active salt and is enclosed within a semi-permeable housing.
- In the stomach, the water in the GI fluid is continuously absorbed through the semi-permeable membrane into osmotically active compartment to dissolve the osmotically active salt.
- An osmotic pressure is thus created which acts on the collapsible bag and in turn forces the drug reservoir compartment to reduce its volume, activate the drug reservoir compartment to reduce its volume and activate the drug release of a drug solution formulation through the delivery orifice.
- The floating support is also made to contain a bioerodible plug that erodes after a predetermined time to deflate the support. The deflated drug delivery system is then emptied from the stomach.

4.GASTROADHESIVE SYSTEM

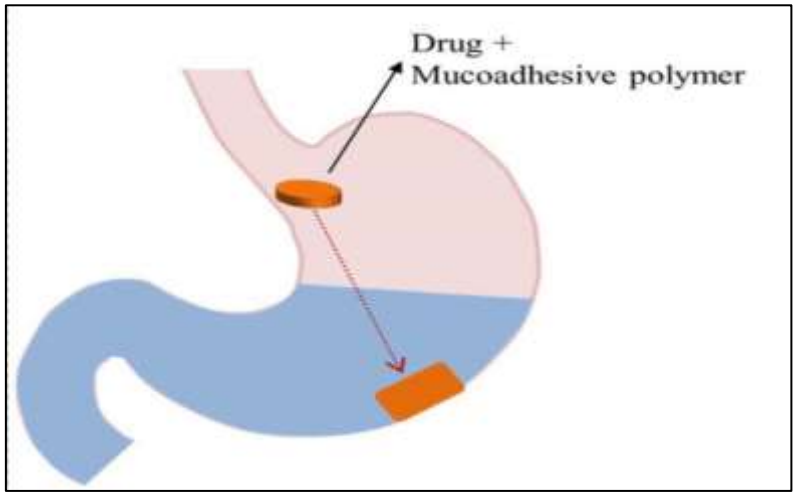


Fig no.10- gastroadhesive system

- The term bioadhesion is defined as adhesion to biological surface 1.e. mucus and/or mucosal surface.
- In instances when the polymeric system interacts with mucus layer only, it is referred as mucoadhesion.
- In order to develop an ideal oral bioadhesive system, it is important to have a through understanding of mucosa, bioadhesive polymers and mucin-polymer interactions in the physiological environment. Intestinal mucosa is composed of high molecular weight glycoproteins hydrated and covering the
- mucosa with a continuous adherent blanket.
- Mucin glycoproteins are rich with fucose and sialic acid groups at the terminal ends which provide a net negative charge in the acidic environment. The thickness of the mucin gel layer varies in different regions of the GIT with thickness ranging
- between 50-500 μm in stomach to 15-150μm in the colon
- The primary function of mucus is to protect the surface mucosal cells from acid and peptidases.
- In addition, it serves as a lubricant for the passage of solids and as a barrier to antigens, bacteria, and viruses.
- The epithelial adhesive properties of mucin are well known and have been applied to the development of GRDDS through the use of bio/mucoadhesive polymers.
- The adherence of the delivery system to the gastric wall increases residence time at a particular site, thereby improving bioavailability.
- A bio/mucoadhesive substance is a natural or synthetic polymer capable of adhering to a biological membrane or the mucus lining of the GIT.
- The adhesion of polymers to a mucus or epithelial cell surface involves various bonding mechanisms, including physical–mechanical bonding and chemical bonding.
- Physical–mechanical bonds can result from the insertion of the adhesive material into the crevices or folds of the mucosa.

MARKETED PRODUCTS

Sr. No.	BRAND NAME	DRUG	REMARK	COMPANY
1	Cifran OD	Ciprofloxacin	Gas generating floating tablets	Ranbaxy
2	Valrelease	Diazepam	Floating capsule	Hoffman- Laroche USA
3	Oflin OD	Ofloxacin	Gas generating floating tablets	Ranbaxy
4	Cytotec	Misoprostol	Bilayer floating Capsule	Pharmacia USA
5	Conviron	Ferrous sulphate	Colloidal gel forming FDDS	Ranbaxy india
6	Topalkan	Al-Mg antacid	Floating liquid	Pierre Fabre Drug

Fig no 11- Marketed product Cifran

Fig no. 12- GRRDS Tablet

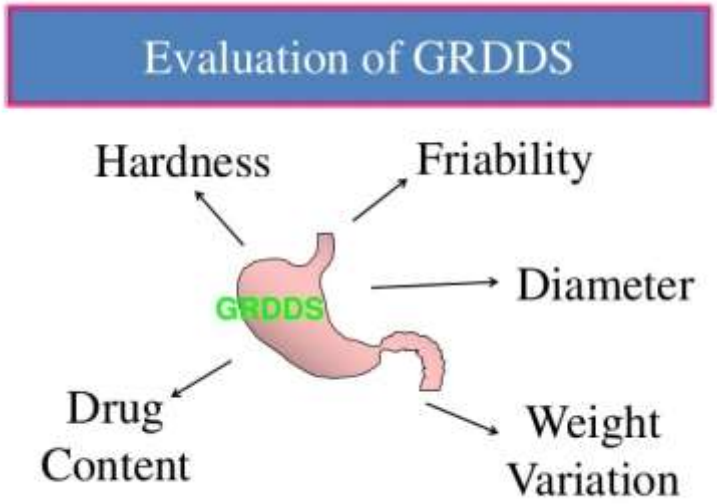


Fig no.13 Evaluation of GRDDS

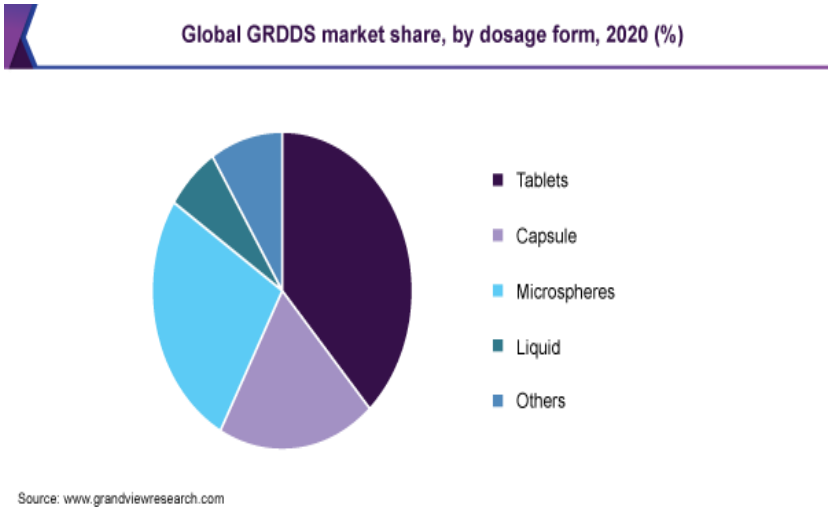


Fig no. 14 Global market share by GRDDS

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SUBJECT: Novel Drug Delivery System

CLASS: Final Year B Pharm

ACADEMIC YEAR: 2021-2022