IOCN 2023 The 4th International Online Conference on Nanomaterials
05–19 May 2023 | online
nanomaterials MDPI

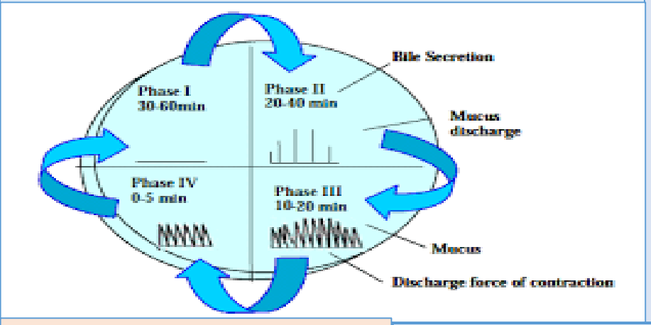
NANOMATERIALS FOR GASTRO RETENTIVE DRUG DELIVERY

Presented By:-
Mr. Ravindra Popat Mali Research Scholar, PSG VPM, College of Pharmacy, Shahada, Nandurbar, India. Email ID: ravi.mali.55@gmail.com

Gastro Retentive Drug Delivery System's (GRDD's) aims to hold the dosage form in this stomach to attain desired activity by the formulator against the challenges involved with the body.

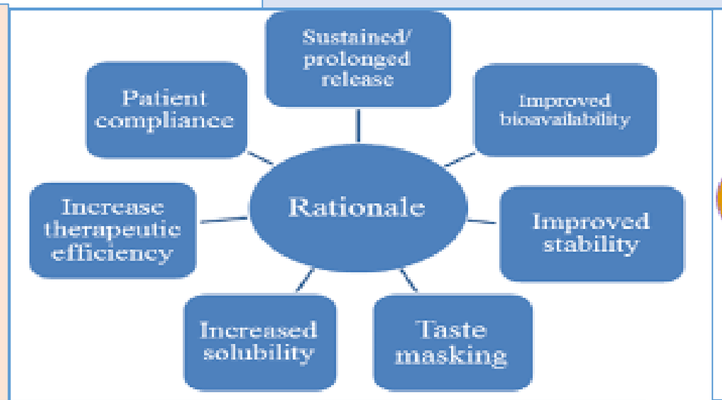
Introduction:

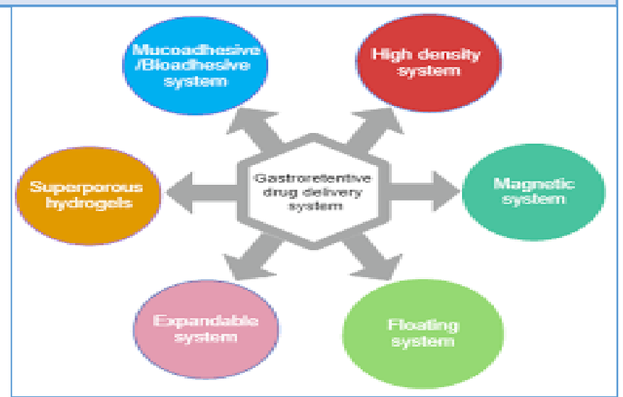
Drug delivery via the oral route is one of most preferred route in state of patient compliance among the other routes. The absorption window is the influential parameters due to which most commercially available modified release dosage forms are acting in this physiological region for their desired effect.



Factors Affecting Gastro Retention

- Size
- Shape of dosage form
- Particle size
- Density
- Fed or unfed state
- Frequency of feed
- Nature of meal
- Caloric content
- Gender
- Age
- Posture
- Nature of drugs
- Formulation related factors
- Polymer type, nature & concentration of excipients
- Single unit/multiple unit
- Patient related factors (BMI, Chronic disease, Physical activity)





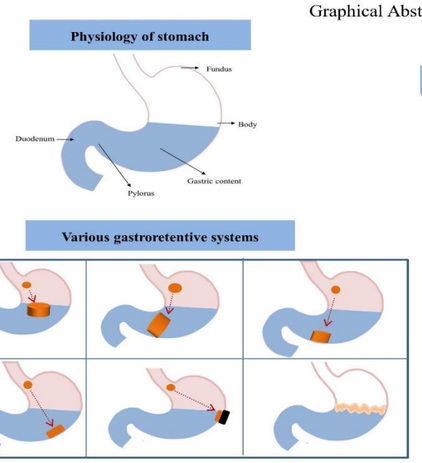
Advantages:

- Drug delivery with narrow absorption windows in the area of the small intestine.
- A longer residence time in the stomach may be beneficial for local effect in the upper part of the small intestine. E.g. to treat peptic ulcer disease.
- Drugs that are easily absorbed after release in the gastrointestinal tract, such as cyclosporine, captopril, ranitidine, amoxicillin, ciprofloxacin, etc., are expected to improve their bioavailability.
- Compliance is achieved through treatment once a day.
- Reduces the frequency of administration.
- Targeted treatment for local disease of the upper digestive tract.
- The bioavailability of therapeutic drugs can be significantly improved especially drugs metabolized in the upper GIT by this gastro retentive drug delivery method compared to administration of non-gastro retentive drugs.
- Gastric retention drug delivery can produce prolonged and sustained release of drugs from dosage forms for local treatment in the stomach and small intestine.
- Therefore, they can be used to treat diseases related to stomach and small intestine.
- The drug delivery of gastric retention can minimize the side effect of human body, thereby improving the efficiency of the drugs.
- Extend the retention time of the dosage form at the absorption site.
- Excellent accessibility.
- Due to first pass metabolism, drug bioavailability increases.
- By slowly releasing the drug at a controlled rate, drug minimized mucosal irritation.

Disadvantages:

- Need to increase the level of gastric juice.
- Not suitable for the following drugs: Problems with solubility in gastric juice, Causing G.I stimulation, Inefficient in acidic environment.
- Drugs intended for selective release in the colon.
- Due to the constantly updated state of gastric mucus wall lead to unpredictable compliance.
- Hydrogel based swelling system require longer time to swell.
- After multiple administrations, the increased size of the drug delivery systems poses a threat to life due to the potential danger of permanent retention in stomach.
- Super porous systems have disadvantages such as problematic storage of easily hydrolyzed, biodegradable polymers.
- Drugs that absorb equally well through GIT. E.g. Isosorbide dinitrate, Nifedipine.
- Floating drug delivery systems require high fluid level in stomach to float and work effectively.

Graphical Abstracts



Evaluation of Gastro Retentive Drug Delivery System

***In Vitro* Evaluation Parameters**

- Particle size and morphology
- Drug entrapment study
- Measurement of tablet tensile strength
- Floating lag time (FLT), Total floating time (TFT), Floating strength
- Swelling studies
- Viscosity and Rheology
- In vitro unfolding study
- Ion exchange capacity, moisture content
- In vitro drug release
- Gel strength
- Drug-excipient interaction study

***In Vivo* Evaluation Parameters**

- GRT and bioavailability of the drug
- Various diagnostic imaging techniques including gamma scintigraphy, radiology, gastroscopy, ultrasonography, and magnetic resonance imaging (MRI) can be applied for in vivo evaluations of GRDD's.

Approaches for Gastroretentive Drug Delivery System

Pharmacological Approach: Co-administration of drugs with GI altering agents such as Anti-muscarinic agents e.g. atropine, benztropine which delay gastric emptying.

Physiological Approach: Use of fat derivatives e.g. Triethanolamine myristate which stimulate duodenal or Jejunal receptors which slow gastric emptying.

Pharmaceutical Approach: Pharmaceutical approach is one of the most relevant approach used to attain gastric retention as first two approach pose alteration to physiology of the body and may lead to undesired consequences to circadian rhythm of the body.

High Density System:
Approach involves use of heavy materials with formulation strategy of coating it with heavy material or mixing it with iron powder, Zinc oxide, Barium Sulphate which tends the formulation to settle in the stomach giving retard action due to high density of formulation. The formulation of this system is challenging and no such marketed formulation exists in market.

Low Density System/Floating System:
It is also known as low density system. They are also considered as one of the most developed formulations as they do not change the motility activity of the GIT. Many commercial formulations are available worldwide with this approach.

Super porous Hydrogels:
This dosage forms have polymers pore size less than 100 which rapidly causes swelling of polymer which is primary properties of this formulation as delayed swelling may lead to premature evacuation of the dosage form.

Mucoadhesive System:
This system in charge retain the dosage form by adhering in the gastric region different natural, synthetic & semi-synthetic polymers are used for the development of muco-adhesive system. This adhesion leads to retention in GRDD's with the desired release profile with appropriative tailoring of the formulation.

Magnetic System:
This system simply implies placement of magnetic system inside the formulation variable and the other magnetic system which will be placed above the abdomen to retain in the formulation in the gastric region to achieve gastric residence time.

Stomach has four main regions, Cardia 2) Fundus 3) Body & 4) Pyloric, Cardia is located on superior region of the stomach projects as opening region. Further extending downward the upper curve to the left of the cardia is called fundus which is store of undigested material just below the fundus the central part of the stomach is called body. The pyloric region an essential region of mixing of food in the stomach consist of the parts pyloric antrum, pyloric canal and pylorus which connects to the duodenum. The communication between the pylorus and small intestine happens with pyloric sphincter. The concave region is called lesser curvature and the convex as greater curvature. Stomach consist of 4 basic layers i.e. Mucosa, submucosa, muscular & serosa.

Ideal drug candidate for GRDD's

- ✓ Locally acting drugs in stomach
- ✓ Drugs having narrow absorption window in GI tract
- ✓ Drugs having narrow absorption window in intestine or colonic conditions
- ✓ Drugs having a low solubility in GI

Drugs those are unsuitable for GRDD's

- ✓ Drugs that have very limited acid solubility e.g. Phenytoin etc.
- ✓ Drugs that suffers instability in the gastric environment e.g. Erythromycin, Rabeprazole, Clarithromycin, Esomeprazole etc.
- ✓ Drugs intended for selective release in the colon e.g. 5-amino salicylic acid and corticosteroids etc.

Nano Formulations Targetting Gastroretentive System

❖ **Zero-valent Iron Nanoparticles**

Zero-valent iron nanoparticle (ZVINP) are gastro retentive high-density component was made of barium sulfate, and the release retarding agent was carbopol. The optimized pellets immediately sank in the sinking time test, but the inclusion of carbopol enabled them to delay iron release for 19 hours in vitro.

❖ **Gliadin Nanoparticles**

Amoxicillin-containing mucoadhesive gliadin nanoparticles (GNP) and their efficacy in eliminating Helicobacter pylori. The mucoadhesive property of GNP increased as the concentration of gliadin increased. Typically, the maximum amount of nanoparticles that were still present was 82.4 percent, indicating that GNP had a stronger mucoadhesive propensity and was more specific for the stomach.

❖ **Floating Nanospheres**

The creation of amphiphilic materials based on (meth)acrylate and (meth)acrylamide derivatives that are capable of self-assembling in core-shell structures could be of great interest given that poly(meth)acrylates are biocompatible materials that are widely used in humans.

❖ **Dendrimer Nanocarriers**

Dendrimers are one of a kind polymers whose size and structure are clearly defined. One of the most common structures found in all biological systems is dendritic architecture. In contrast to linear polymers, the following elements can be distinguished in the structure of dendrimer: a center, dendrons, and surface dynamic gatherings. The monomer molecules known as dendrons, or dendrimer arms, are linked to the core, resulting in the formation of layers and successive generations (their growth is constrained by space).

Conclusions:

Over the years, a number of mechanisms, including magnetic, effervescence, swelling, floating and sinking, have been proposed. Only a few of the proposed systems have demonstrated efficacy in vivo, despite the majority displaying promising dissolution profiles and in-vitro retention. The most common marketed forms at this time are polymeric swelling monolithic systems.

Nanoparticles are very effective for targeted drug delivery in stomach, dendrimers, iron oxide nanomaterials, antibiotics like amoxicillin to treat esophageal reflex. Novel drug delivery systems such as nanoparticulate based drug delivery systems, colloidal carriers and miscellaneous delivery systems are introduced to overcome some limitations of large dosages. These systems mainly help in reducing the toxicity and increase the efficacy of drugs and thus increase the therapeutic effect in treatment at site of action.

In future perspectives, Nanomaterials based GRDD's initiatives may need to concentrate on a combination strategy in order to improve product quality, considering the pharmaceutical industry. In addition, a QbD strategy can be utilized to better comprehend how formulation and process variables affect the performance of the final product.