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Floating Drug Delivery System: A Review

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ABSTRACT

In recent novel drug delivery system floating drug delivery system plays prominent role in the gastro retentive type drug delivery system, it mainly acts by increasing the buoyancy time to float in gastric fluid present in the time, this will not affect the gastric content which is present in the stomach and shows the prolonged period of floating in the GI fluid. The current objective is to review the floating drug delivery system by focusing on present scenario of the advancement and future pharmaceutical importance by the floating tablet in GRDDS. Different class of drugs like antacids, antidiabetics, anticancer and antifungal drugs are formulated into floating tablet. This review article is in focusing on detailed information on floating tablet design, classification, advantages and disadvantages and factors which affects the gastric residence time and its formulation and application of the floating drug.

INTRODUCTION

Gastro retentive drug delivery systems are designed to be retained in the stomach for a prolonged time and release their active ingredients and thereby enable sustained and prolonged input of the drug into the upper part of the GI tract.

After the release of drug, the residual system is going to emptied from the stomach. This results in increased gastric retention time and control of the fluctuation in plasma drug concentration. Gastro retentive drug delivery systems are designed to be retained in the stomach for a prolonged time and release their active ingredients and thereby enable sustained and prolonged input of the drug into the upper part of gastrointestinal tract.

A modified release of drug delivery system with longer residence time in the stomach is particular interest for drugs- acting locally mainly in stomach, having an absorption window mainly in stomach or in the upper part of small intestine; those unstable in the intestinal or colonic environments; or those having low solubility at high pH values.

Drugs which are benefited by this type of floating system are-

1. Drugs that exhibit low solubility at high pH values

   (e.g. diazepam, chlordiazepoxide, verapamil).

2. Drugs which unstable in the intestinal or colonic environment

   (e.g. ranitidine HCl, captopril, metronidazole).

3. Drugs showing narrow absorption window in GIT

   (e.g. furosemide , L-DOPA, paminobenzoic acid, riboflavin).

4. Drugs that disturb normal colonic microbes

   (e.g. antibiotics used for the eradication of *Helicobacter pylori*, such as tetracycline, clarithromycin, amoxicillin).

5. Drugs which are locally active in the stomach

   (e.g. antacids, Misoprostol).

Basic anatomy and physiology of stomach

The stomach is the muscular, J-shaped organ situated in the upper part of the abdomen. Stomach is a part of the digestive system, it is extended from the mouth to the anus. From person to person size the stomach varies, and also from meal to meal.

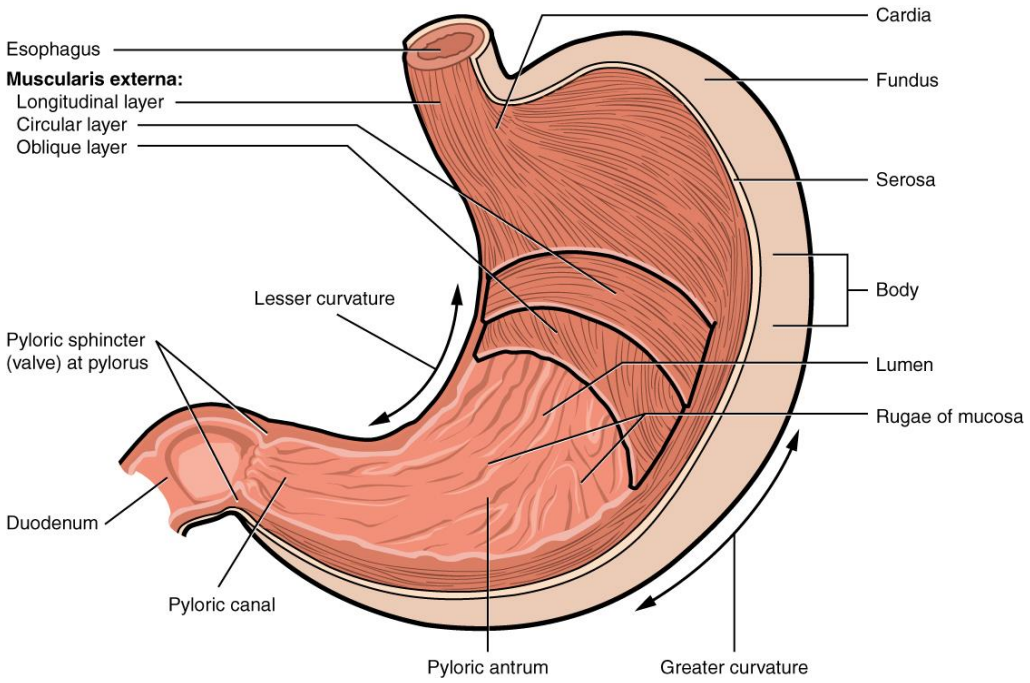

Figure No. 1: Basic anatomy of stomach

The stomach has 3 main functions

- Stomach is the temporary storage for food, which mainly passes from the oesophagus to the stomach where food remains for 2 hours or longer.

- Breakdown and mixing of food by relaxation and contraction of the muscle layers in the stomach.

- Digestion of food.

The mucosa contains specialized cells and glands that produce hydrochloric acid and digestive enzymes to help digest food. The lining of the stomach is protected from the gastric acid mainly by the mucus secreted from the mucosa situated in the cardiac and pyloric region of the stomach, other specialized cells in the mucosa of the pylorus release

the hormone gastrin into the blood. From the mucosa the release of the acid and enzymes is stimulated by the Gastrin, and also helps contracting of the stomach muscles.

Food is broken to form chime which is a thick, acidic, soupy mixture called chyme. Once chyme formation is complete pyloric sphincter relaxes, Chyme then passes into the duodenum. The duodenum plays a big role in absorption of the food we eat. The stomach does not play a big role in absorption of food. It only absorbs water, alcohol and some drugs. During the fasting state, an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the Interdigestive Myloelectric Cycle (IMC).

There are four consecutive phases of activity in the migrating myoelectric complex (MMC).

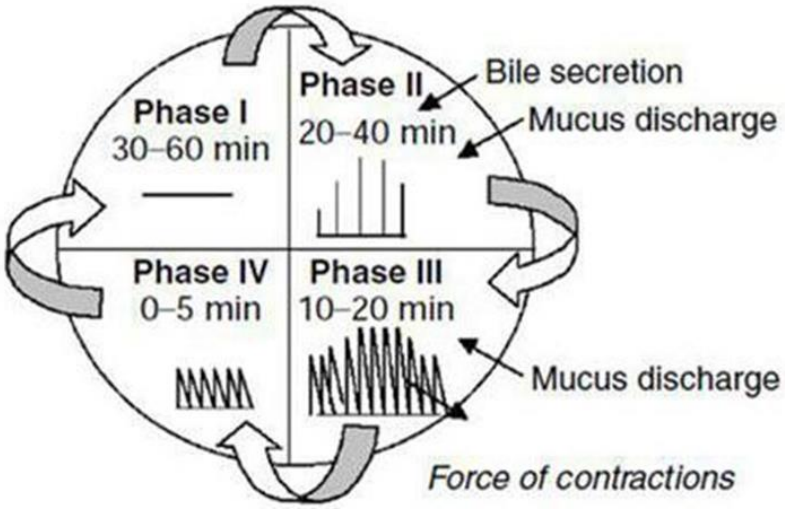

Figure No. 2

1. **Phase I** (basal phase) which lasts from 40 to 60 minutes with limited contractions.

2. **Phase II** (pre-burst phase) which lasts for 40 to 60 minutes with occasional action potential and contractions. As the phase continuous the intensity and frequency also increases constantly.

3. **Phase III** (burst phase) lasts f or 4 to 6 minutes. It includes powerful and regular contractions for short period of time. Due to this wave that all the undigested material is moved out of the stomach down to the small intestine region. It is also known as the housekeeper wave.

4. **Phase IV which** lasts for 0 to 5 minutes and occurs between phases III and I of 2 successive cycles.

ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM

1. Drugs which are absorbed through the stomach or proximal part of the intestine are suitable for floating drug delivery system.

2. Sustained release of the drug from the dosage can be achieved and minimised frequency of the dose administration.

3. Targeted therapy for the local site in the stomach part can be achieved.

4. Drug concentration fluctuation problem is reduced in case of FDDS.

5. Floating system shows improved selectivity in receptor activation.

6. Reduced counter activity of the body is achieved.

7. Extended effective concentration is showed by floating drug delivery system.

8. At the colon, junction minimised adverse activity is achieved.

9. Drugs which are acidic in nature irritates the stomach are formulated into HBS system which reduces the irritation.

10. Drug complete absorption is achieved and drug is available at the intestine by dissolving the drug content in the stomach after gastric emptying it is absorbed through the intestinal region.

DISADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM

1. The drug which is unstable in the acidic environment is not suitable candidates to incorporate in this system, and this system requires high level of fluid in the stomach to float and to work efficiently.

2. Drugs which have solubility and stability problem in the stomach are not suitable for this system.

3. Drugs which undergoes first pass metabolism are not suitable for floating delivery system.

4. Drugs which make irritation to gastric mucosa are not suitable for this system.

5. Dosage form required minimum 200 to 250ml of water for administration.

6. Floating tablet has not having significant advantage over the conventional dosage form.

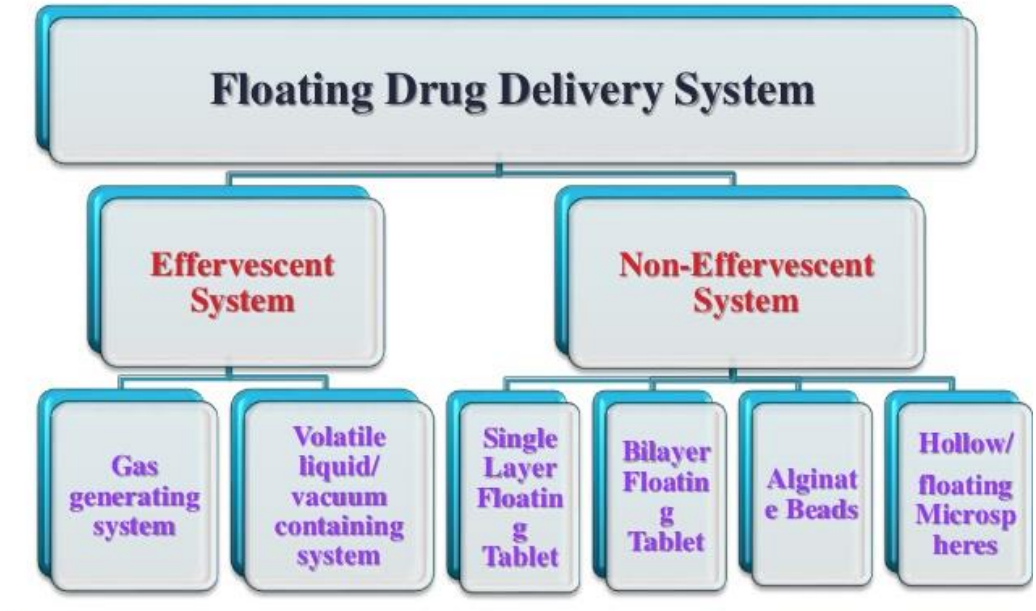

Figure No. 3: CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM

NON EFFERVESCENT SYSTEM

Noneffervescent system floating drug delivery system is based on swelling mechanism of polymer or bioadhesion to mucosal layer in the GI tract. Highly swellable cellulose type hydrocolloids, polysaccharides and matrix-forming material such as polycarbonate, polyacrylate, polymethacrylate, polysterene are the most commonly used excipients in floating drug delivery system. The various types of non-effervescent systems are as follows:

Colloidal Gel Barrier System

They are called as a hydrodynamically balanced system they remain in the stomach due to the presence of the gel forming hydrocolloids due to this gastro retentive time is increased and at the site of the absorption amount of the drug is increased. In this system gel forming agents

are used such are highly soluble cellulose type hydrocolloids which are hydroxypropyl cellulose, hydroxyethylcellulose, hydroxymethyl cellulose, polysaccharides and matrix-forming polymers such as polycarbophil, polysterene[9].

Bilayer floating tablet

A bilayer tablet contains two layers, in which initial dose from the system is released by the immediate release layer, another sustained release layer absorbs gastric fluid, forming an impermeable colloidal gel barrier on its surface, and maintains density less than the gastric fluid that makes to remains in the stomach[10].

Microporous Compartment System

In this system, microporous compartment is present inside at the top and bottom walls contains encapsulated drug reservoir. Peripheral walls of the drug reservoir is completely sealed due to this sealing direct contact of the undissolved drug with gastric surface is prevented. The air which is entrapped in the floating chamber stimulates the system to float over gastric content. The small aperture which is available for gastric fluid entry through which fluid enters and drug is dissolves and available for absorption across intestine[21].

Alginate Beads

from the freeze dried calcium alginate, an multi unit floating dosage forms are developed. An spherical shaped beads of size approximately 2.5mm diameter can be achieved by dropping a sodium alginate solution into an aqueous solution of calcium chloride, which causes the precipitation of the calcium alginate beads which can float over a 12 hours. But compared to solid beads it has a short residence time of 1 hour, and these floating beads gave a prolonged residence time of more than 5.5 hours[7].

Hollow microspheres

It is also called as a Microballons, it is loaded with an drug having an outer polymer shell prepared by an novel emulsion solvent diffusion method. A solution of drug in dichloromethane:ethanol was poured into an agitated aqueous solution of PVA that was controlled thermally at a temperature 400^0C. The gas which is generated in the dispersed polymer droplet by evaporation of dichloromethane formed an internal cavity in the

microspheres of polymer which contains drug in it. This micro balloons will float in the acidic dissolution media containing surfactant for up to 12 hours *in-vitro*[24].

Factors Affecting Gastric Residence Time of FDDS

Gastric residence time of oral dosage form is affected by the several factors which include density, size shape of dosage form, feeding state and also biological factors affect gastric residence time such are age, gender, body mass index, posture, disease state of the body *etc*[15].

Dosage form size and shape

Small size tablets will emptied from the stomach at the digestive phase where large size units are not easily emptied. The floating unit having diameter equal or less than the 7.5mm had a greater gastric residence time (GRT) compare to non-floating units, but for both floating and non-floating units have the similar GRT for units having larger diameter of 9.9mm[30].

Gender Posture and Age

Gastro retentive time for the male is less compared to the female regardless of their weight, height and body surface. In female gastric emptying is lower rate than men even when hormonal changes due to menstrual cycle were minimized[29].

Effect of Food & Specific Gravity

Density of the floating tablet should be less to float in the stomach gastric content i.e.1.0g/cm^3. Presence of the food affects the GRT than buoyancy. GRT is increased under fed condition. GRT for the floating and non-floating single units are shorter in the fasted subjects (less than 2 hour), but after a meal, it is significantly prolonged[23].

Nature of the food & frequency of food

Substances like indigestible polymers or fatty acid salts alters the motility pattern of the stomach in the fed state, it increases the gastric emptying time and prolonging the drug release. Protein rich diet and fat can increases the GRT by 4-10 hours [31].

Table No. 1: Different polymers used in FDDS

Sustained release polymers	HPMC K100M, HPMC K15M, HPMC ELV, Polycarbonate, Sodium alginate, Polyethylene glycol, Carbopol, Eudragit.
Effervescent generating system	Citric acid, Tartaric acid, Citroglycine, Sodium bicarbonate.
Polymers which decrease release	Talc, Dicalcium phosphate, Magnesium stearate.
Polymers which increase release	Mannitol, Lactose
Polymers which increases buoyancy	Ethylcellulose
Inert Polymers	Beeswax, Fatty Acid, Long chain Fatty Alcohol.
Polymers having low density	Foam powder of polypropylene

List of some common natural polymers which are used in floating drug delivery system and their sources.

Pectin	Citrus peel, sugar beet pulp *etc*, tartaric acid.
Guar gum	Endosperm of the seed of *Cyamopsis tetragonoloba*
Chitosan	Shell of marine invertebrate's
Psyllium husk starch	Seed coat of plant which having polysaccharides

Application of floating drug delivery system

Enhanced bioavailability

The bioavailability of the drug is increased significantly enhanced when comparison to the administration of the drug in Gastro retentive floating tablet than the nonfloating type of system polymeric formulations. There are many processes, related to absorption of the drug and transition of the drug in GI tract, that makes the concomitantly to influence the magnitude of the drug absorption[5].

Sustained Drug Delivery

Generally, oral controlled release formulations are having problems such as gastric residence time in the GIT. Hydro Dynamically Balanced System which overcomes the gastric residence problem by retaining in the stomach for longer period due to having bulk density <1 as a

result it floats in gastric contents. These systems are size relatively larger than the pyloric opening so that passing out from the stomach region is prohibited [2].

Site-Specific Drug Delivery

These systems are more advantageous particularly for drugs that are specifically absorbed from stomach or proximal part of the small intestine, e.g., furosemide. Furosemide absorbed primarily from stomach then by the duodenum. It is concluded that a monolithic floating dosage form with having a longer gastric residence time was developed and the bioavailability is increased and observed that 1.8 times more AUC is obtained compare to conventional form of furosemide tablets[9].

Bioavailability or Absorption Enhancement

Drugs which are absorbed from the upper part of the gastrointestinal tract are have poor bioavailability because of site specific absorption hence potential candidates are formulated as a floating drug delivery systems and maximizing their absorption. A floating tablet containing a Metoprolol Succinate in combination of hydrophilic and hydrophobic polymers increases the bioavailability and prolonged period of gastric residence[18].

CONCLUSION

Gastro retentive drug delivery systems are designed to be retained in the stomach for a prolonged time and release their active ingredients and thereby enable sustained and prolonged input of the drug to the upper part of the gastrointestinal tract.

A modified release drug delivery system with prolonged residence time in the stomach is of particular interest for drugs- acting locally in the stomach; having an absorption window in the stomach or in the upper part of small intestine; those unstable in the intestinal or colonic environments; or those having low solubility at high pH values.

Floating drug delivery systems have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.

While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach.

This results in an increased gastric retention time and control of the fluctuation in plasma drug concentration.

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