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Floating Drug Delivery System: An Update of Preparation and Classification of Formulation

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ABSTRACT

This review focus on the types of floating drug delivery systems and mechanism of floatation to achieve gastric retention. Floating drug delivery system can remain in gastric region for several hours and prolong the gastric residence time of drugs. Prolonged gastric retention ease bioavailability, reduces drug waste, enhance the solubility of drugs that are less soluble in a high pH environment. The controlled gastric retention of solid dosage forms may be achieved by the mechanism of mucoadhesion, floatation, sedimentation, expansion, modified shape systems or by the administration of pharmacological agents that delaying gastric emptying. Based on these approaches, floating drug delivery systems appear to be advantageous delivery systems for control release of drug.

1. INTRODUCTION:

Floating drug delivery system (FDDS) is one of the type of drug delivery system used for oral administration of such drugs that required prolong the gastric residence in the stomach. Prolonged gastric retention improves bioavailability, reduces drug waste, improves the solubility of drugs that are less soluble in a high pH environment (1-9). FDDS is a hydro-dynamically controlled denseness system with sufficient buoyancy to float over the gastric contents and stay buoyant within the abdomen. The most purpose for developing these systems is to boost the protection of a product to increase its length of action (10).One in all such difficulties is that the ability to confine the indefinite quantity kind within the desired space of the channel. To beat this physiological drawback, many drug delivery systems with prolonged internal organ retention time are investigated. Tries square measure being created to develop a controlled drug delivery system which will offer therapeutically effective plasma drug concentration levels for extended durations, thereby reducing the dosing frequency and minimizing fluctuations in plasma drug concentration at steady state by delivering drug in a very controlled and consistent manner (11,12). The controlled viscous retention of solid indefinite quantity forms could also be achieved by the mechanism of mucoadhesion, floatation, deposit, expansion, changed form system or by the administration of medicine agents that delaying viscus remotion. supported these approaches, floating drug delivery system consider to be the promising delivery systems for management unleash of drug (13).

2. DRUG CANDIDATES APPROPRIATE FOR FDDS

- Drugs having slender absorption window in disagreeable person (e.g. L-DOPA, furosemide, riboflavin)(17).

- Medicine those square measure regionally active within the abdomen (eg. Misoprostol, antacids) (18).

- Medicine those square measure unstable within the enteral or colonic surroundings (e.g. captopril, histamine blocker HCl, metronidazole) (19).

- Medicine that disturb traditional colonic microbes (e.g. antibiotics used for the demolition of Helicobacter pylori, like bactericide, clarithromycin, amoxicillin)(20).

- Medicine that exhibit low solubility at high pH scale values (e.g. diazepam, benzodiazepine, and verapamil)(21).

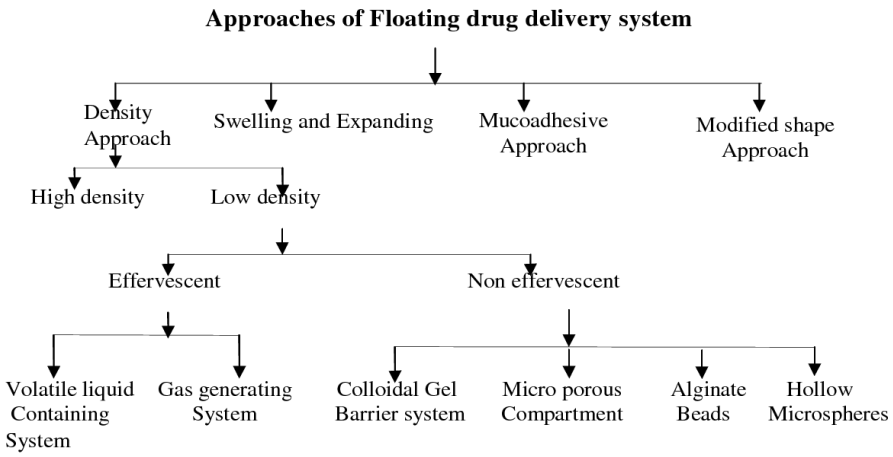

Figure 1: Various approaches to gastric retention

3. ADVANTAGES OF FDDS

- The Floating systems are advantageous for drugs meant for local action in the stomach. eg. antacids.

- Acidic substances like aspirin irritate the abdomen wall once they are available in contact with abdomen. Thus, FDDS could also be helpful for the administration of antacid and different similar medicine.

- The Floating systems are advantageous for medicine absorbed through the abdomen.eg. ferric salts, antacids.

- Thus, expected that a drug will be fully absorbed from floating dose types if it remains within the resolution form (22).

4. DISADVANTAGES OF FDDS

- Need high quantity of fluid in abdomen to float.

- Not possible for those medicine having solubility or stability issues in internal organ fluids (23).

5. ANATOMY AND PHYSIOLOGY OF GIT

Anatomically the stomach is divided into three regions: fundus, body, and pylorus. The stomach is an expanded section of the digestive tube between the oesophagus and small intestine. Gastric emptying occurs during fasting as well as fed state. The pattern of motility

is however distinct in the two states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hrs. This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC), which is further divided into following 4 phases.

Part I (basal phase)

With contractions up to 40 to 60 min with rare contractions.

Part II (pre burst part)

With intermittent impulse and contractions, it lasts for 40 to 60 minutes and therefore the intensity and frequency also will increase step by step throughout the phase progresses.

Part III (burst phase)

It includes intense and regular contractions for short amount and stays up to 4 to 6 minutes. It's conjointly called the housekeeper wave.

Part IV

It occurs between phases III and I of two consecutive cycles and lasts for 0 to 5 minutes.

The pattern of contractions changes from fasted thereto of fed state when taking mixed meal. This is conjointly known as organic process motility pattern and it produces out continuous contractions as in part II of fasted state. Throughout the fed state onset of migrating myoelectric cycle is delayed ensuing in reduced internal organ voidance rate (24).

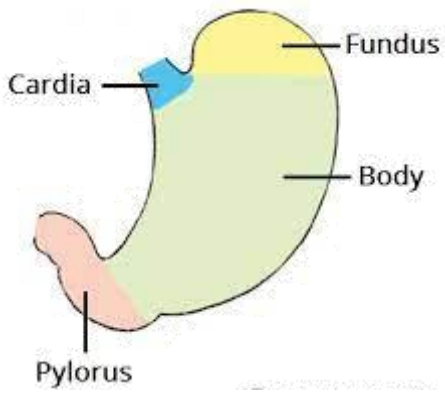

Figure 2: Diagram of stomach

6. GASTRIC MOTILITY

Gastric motility is controlled by a posh set of neural and secretion signals. Nervous management originates from the enteric nervous system, parasympathetic and sympathetic systems. An outsized battery of hormones has been shown to influence organ motility, eg.ch internal secretion and cholecystokinin act to relax the proximal abdomen and enhances contractions within the distal abdomen. The bottom line is that the way of GI motility likely are a result from smooth muscle cells combine a large number of integrating and stimulating cells (25). Liquid without delay go through the porta in spurts, however, solids should be reduced to a diameter of 1-2 millimeter before passing porta gatekeeper. The internal organ volume is very important for dissolution of the dosage form *in vivo*. The resting volume of the abdomen is 25-50 ml. There's an outsized distinction in organ secretion of traditional and achorhydric individuals. Internal organ hydrogen ion concentration conjointly has pronounced impact absorption of the drug from delivery system. The pH of abstinence abdomen is 1.2-.2.0 and in fed conditions a 2.0-6.0(26).

7. FACTORS AFFECTING GASTRIC RETENTION

The gastric retention time (GRT) of dose type is controlled by many factors that have an effect on their efficacy as a gastroretentive system.

7.1. Density

Density of dosage form should be less than gastric content.

7.2. Size

Dosage form unit with a diameter of more than 7.5 mm are reported to have an increased GRT challenge with those with a diameter of 9.9 mm.

7.3. Shape of dose type

Polyhedron and circular devices with a flexural modulus of 48 and 22.5 kilo pounds per sq. in (KSI) area unit rumored to possess higher GRT.

7.4. Single or multiple unit formulation

Multiple unit formulations show a more predictable due to failure of units, allow co-administration of units with contrasting release profiles or containing incompatible

substances and enable a larger margin of safety against dosage form failure compared with single unit dosage forms.

7.5. Fed or unfed state

Underneath fast conditions, the GI motility is characterized by periods of robust motor activity or the migrating myoelectric advanced (MMC) that happens 1.5 to 2 hours. The MMC sweeps undigested material from the abdomen and, if the temporal arrangement of administration of the formulation coincides therewith of the MMC, the GRT of the unit can be expected to be very short. However, within the fed state, MMC is delayed and GRT is significantly longer.

7.6 Nature of meal

Feeding of undigested polymers or carboxylic acid salts will alter the motility pattern of the abdomen to a fed state, so decreasing the viscous voidance rate and prolonging drug unleash.

7.7. Caloric content

GRT might be increased by 4 to 10 hours with a meal that's high in proteins and fats.

7.8. Frequency of feed

The GRT might increase by over 400 minutes once a consecutive meal are compared with one meal due to the low frequency of MMC.

7.9. Gender

Mean ambulant GRT in males (3- 4 hours) is a smaller amount compared with their age and race-matched feminine counterparts (4-6hrs), despite the burden, height, and body surface.

7.10. Age

Elderly people, particularly those over 70, have a considerably longer GRT.

7.11. Posture

GRT will vary between supine and upright ambulant states of the patient.

7.12. Concomitant drug administration

Anticholinergic like antidote and propantheline, opiates like opiate and prokinetic agents like metoclopramide and cis a pride.

7.13. Biological factors

Diabetes and Crohn's disease (27-30).

8. CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM

8.1. Effervescent floating drug delivery system

These are matrix type system prepared with the assist of swellable compound like hydroxypropyl methylcellulose and chitosan beside effervescent compounds viz. baking soda, citric acid. These are developed in such a selected way that when it comes in reality with gastric juice; CO_2gets liberated and is confine in swollen hydrocolloids.

8.1.1 Gas generating systems

Low-density FDDS relies on the discharge of CO_2upon contact with gastric juice once oral administration. These are developed in such a way that once they come in contact with abdomen, CO_2 gets liberated due to reaction with acidic gastric content and that get trapped within the gel-based matter. It produces an upward motion of the dose type and maintains its buoyancy. Ultimately it causes a decrease in relative density of dose type and therefore resulting into a float on the chime (31).

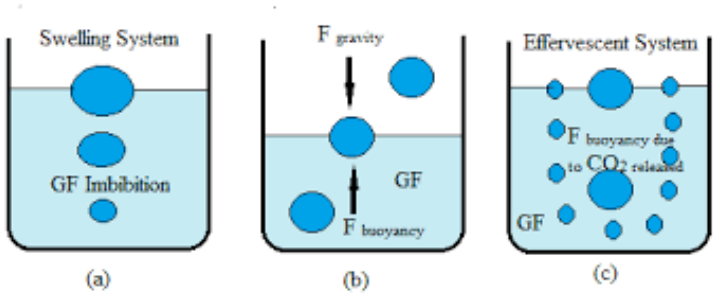

Figure 3: Mechanism of floating beads (GF- gastric fluid).

8.1.2 Osmotically controlled drug delivery system

This isosmotically controlled floating system during which a tool comprised of a hollow deformable unit in convertible folded type. Housing would be connected to its deformable

unit internally divided into a primary and second chamber separated by a tight, pressure sensitive movable unit. the primary chamber typically contains a vigorous drug, whereas the second a volatile liquid, like cyclopentane or ether get vaporized at a physiological temperature to provide a gas, sanctionative the drug reservoir to float. The unit gets expelled from the abdomen, with the help of bioerodible plug that allowed the vapour to flee (32).

8.2 Non-effervescent FDDS

Non-Effervescent Floating Drug Delivery Systems includes a gel-forming (or) swellable polyose variety of hydrocolloids created from polysaccharides together with matrix forming polymers like polycarbonate, polymethacrylate, and vinyl benzene. The routine formulation technique involves the blending of the drug with gel forming hydrocolloids that swell in contact with gastric fluid upon oral administration and maintains the integrity of form and a bulk density barrier, the air trapped by swollen compound confer buoyancy to the dosage forms (32).

8.2.1. Colloid barrier systems (Hydrodynamic balanced systems)

This system prolongs gastric retention time and maximizes the quantity of drug that reaches its absorption site in solution form. It primarily contains drug with gel forming hydrocolloids to stay buoyant on the abdomen content. Such a system incorporates one or a lot of gel-forming cellulose type substance eg. hydroxypropyl methylcellulose (HPMC), polysaccharides and matrix forming polymers like polycarbophil, vinyl benzene, and polyacrylate. Upon contact with gastro-Intestinal (GI) fluid, the hydrocolloids within the system hydrates to get a mixture gel barrier to its encompassing (33).

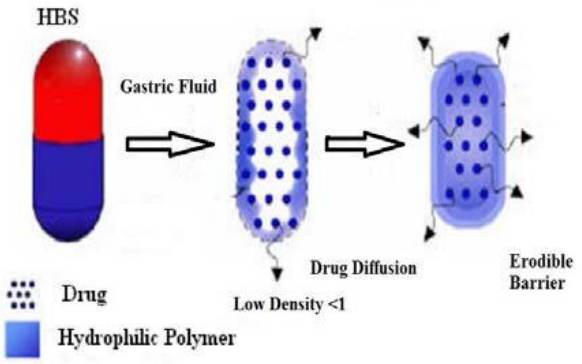

Figure 4: Mechanism of hydrodynamically balanced system

8.2.2. Microporous compartment systems

This technology incorporates the encapsulation technique of a drug reservoir within a microporous compartment together with pores at prime and bottom walls. The peripheral wall of the drug reservoir compartment is completely locked to stop any direct contact of the internal organ surface with the undissolved drug. within the abdomen, the floatation chamber composed of entrapped air causes the delivery system to float over the internal gastric content. Gastric fluid enters through the aperture, to the extent that it prevents theirs exist from the drug and carrier the dissolved drug for continuous transport across the gut for absorption.

8.2.3. Floating Microspheres/Micro balloons

Hollow microspheres also referred as micro balloons are thought as best buoyant system. It is composed of central hallow space within the microsphere. Hallow microsphere is loaded with a drug in their outer polymer shelf square measure fictional by a novel solvent diffusion technique for emulsion (32).

8.2.4. Alginate beads/Floating beads

Multi-unit floating dose forms have been developed from calcium alginate spherical beads of about 2.5 mm linear unit in diameter and maybe fictional by adding sodium alginate solution into a solution of calcium chloride, leading to the precipitation of calcium alginate, additionally beads are separated, snap-frozen in liquid nitrogen and freeze-dried at 400 °C for 24 hr, results in the generation of a porous system. This fictional system would maintain a floating force for over 12 h and these floating beads give an extended duration of over 5.5 hr.

8.3. Raft-forming systems

Raft-forming systems are in a lot of attention for the delivery of antacid and drug delivery for gastro infection and disorders. On contact with gastric fluid, a gel-forming solution swells and forms a viscous cohesive gel entrapped with CO_2 bubbles (33).

Table 1: Lists of drugs explored in floating dosage forms

Dosage forms	Drugs explored in floating dosage forms	Ref.
Microspheres	Aspirin, Griseofulvin, P-nitroaniline, Ibuprofen, Ketoprofen, Terfenadine, Tranilast.	34
Granules	Diclofenac sodium, Indomethacin, Prednisolone.	35
Capsules	Chlordiazepoxide HCl, Diazepam, Furosemide, L-Dopa and Benserazide, Misoprostol, Nicardipine, Propranolol HCl, Ursodeoxycholic acid.	35
Tablet/Pills	Acetaminophen, Aspirin, Amoxicillin trihydrate, Ampicillin, Atenolol, Captopril, Ciprofloxacin, Cinnarizine, Furosemide, 5-Fluorouracil, Isosorbide mononitrate, Diltiazem, Isosorbide dinitrate, Nimodipine, Para amino benzoic acid, Prednisolone, Quinidine, Verapamil HCl, Riboflavin, Sotalol.	35-36
Alginate beds	Diclofenac sodium, Famotidine, Nevirapine, Riboflavin, Pantoprazole	36
in-situ colloidal gels	Clarithromycin, Furosemide, Ofloxacin.	35-36
Films	5-Flurouracil, Propranolol, Metoprolol.	35-36

9. POLYMERS USED IN FORMULATION OF FDDS

9.1. Hydrochlorides

HPMC 1000, HPMC 4000, β-cyclodextrin, sodium alginate, HPC-L, CP 934 P, HPC, Eudragit S, Metolose S.M.100, PVP, HPC-H, HPC-M, HPMC K15, Polyox, HPMC K4, Acrylic polymer, E4M and Carbopol.

9.2. Inert fatty materials

Beeswax, fatty acids, gelucires.

9.3. Effervescent agents

Sodium bicarbonate, citric acid, tartaric acid, Disodium glycine carbonate, Citroglycin.

9.4. Release rate accelerants

Lactose, mannitol.

9.5. Release rate retardants

Di-calcium phosphate, talc, magnesium stearate.

9.6. Buoyancy increasing agents

Ethyl cellulose

9.7. Low-density material

Polypropylene foam powder (Accurel MP 1000)

10. ANALYSIS OF FORMULATIONS

There are various analytical methods such as UV-spectroscopy, IR spectroscopy, HPLC, etc that are routinely used for quality control of floating drug delivery systems (37-58).

11. CONCLUSION

FDDS promises to be a potential approach for gastric retention. Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extends the time of drug absorption. FDDS become an additional advantage for drugs that are absorbed primarily in the upper part of GI tract. A large number of companies are focusing towards commercializing this technique.

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