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A Review on Floating Drug Delivery Systems

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ABSTRACT: The purpose of writing review on Floating Drug Delivery System (FDDS) was to compile the recent literature with specific focus on the principal mechanism of floatation to achieve gastric retention. The recent developments of FDDS including the physiological and formulation variables affecting gastric retention, approaches to design single-unit and multiple-unit floating systems, and their classification and formulation aspects are covered in detail. FDDS improves the drug bioavailability and patient compliance by increasing the gastric residence time and controlling the drug release. Gastro-retentive systems can remain in the gastric region for several hours for significantly prolong residence time of drugs by which improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high PH environment. This review summarizes the in vitro techniques, in vivo studies to evaluate the performance and application of floating systems, and applications of these systems. These systems are useful to overcome several problems encountered during the development of a pharmaceutical dosage form.

Keywords: Floating drug delivery systems, multiple unit, bioavailability, gastric residence time.

I. INTRODUCTION

Drug delivery is defined as the method or process of administering a pharmaceutical compound to achieve a therapeutic effect in humans or animals. Drug delivery refers to approaches, formulations, technologies, and systems for transporting a pharmaceutical compound in the body where they are needed to safely achieve its desired therapeutic effect. Quick elimination of the drug from the blood circulation and frequent dosing are the problems associated during the administration of drug[1]. The goal of any drug delivery system is to provide a therapeutic amount of drug to proper site in the body to achieve promptly and then maintain a desired drug concentration. To achieve this, recent development in this technology has provided viable dosage alternatives that can be administered via different routes of administration. Various routes that are used include oral, topical, nasal, rectal, vaginal and ocular, etc. but out of these routes, oral route of drug deliveryis considered as the most favored and practiced way of delivery, due to the following reasons: Ease of administration, Ease of production, Low cost, High levels of patient compliance[2].

The oral route is most preferred, favored, promising and versatile route for administration of drugs insystemic action. Oral route of administration has been received more attention in the pharmaceutical field because of the more flexibility in the designing of dosage form than drug delivery design for other routes[3]. The primary aim of oral controlled drug delivery system should be better absorption and enhanced bioavailability, and to control the released rate of drug. The development of oral sustained- controlled release formulations is an attempt to release the drug slowly into the gastrointestinal tract (GIT) and maintain an effective drug concentration in systemic circulation for a long time and hence, significantly prolong the gastric residence time of drugs. How-ever this case is found very difficult to occur incase of conventional dosage forms[4].

Gastro retentive drug delivery system (GRDDS) is a novel site-specific drug deliveries to promoting retention with in the stomach, duodenum, or small intestine can prolong drug release in a controlled manner. Prolonged gastric retention reduces drug waste and improves solubility of drugs that are less soluble in high pH environment[6]. It is the formulation of a drug with gel forming hydrocolloids meant to remain buoyant in the stomach contents. This can be achieved by the mechanism of muco-adhesion, flotation, sedimentation, expansion, modified shape systems

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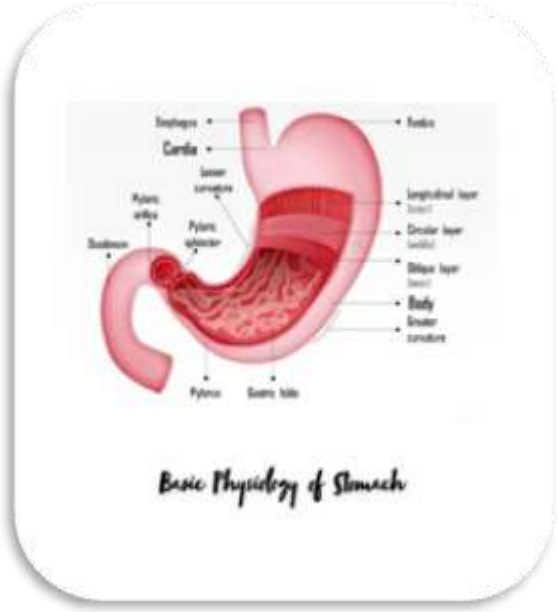
or by the administration of the pharmacological agents, that delay gastric emptying. Based on these approaches, floating drug delivery systems (FDDS) seems to be the promising delivery systems for control release of drugs[7-9].

The successful development of oral controlled drug delivery systems requires an understanding of the three aspects of the system, namely.

- ✓ The physiochemical characteristics of the drug
- ✓ Anatomy and physiology of GIT and
- ✓ Characteristics of dosage forms.

Basic Physiology of Gastrointestinal Tract[10]: Anatomically, the stomach is divided into 3 regions: fundus, body and antrum (pylorus). The proximal part made of fundus and body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions.

Fig:1 Basic Physiology of stomach



Stomach

The stomach is situated in the left upper part of the abdominal cavity immediately under the diaphragm, which is an expanded section of the digestive tube between the oesophagus and small intestine. Its size varies according to the amount of distention: up to 1500 ml following a meal; after food has emptied, a collapsed state is obtained with resting volume of 25-50 ml. The wall of the stomach is structurally similar to the other parts of the digestive tube, with the exception that stomach has an extra, oblique layer of smooth muscle inside the circular layer, which aids in the performance of complex grinding motions[9]. The mean value of PH in fasted healthy person is 1.1± 0.15, after intake of food the PH may rise to levels in the 3.0 to 4.0 level due to the buffering capacity of proteins. However, in fasted state, gastric secretion in women is lower than that of men[10].

Gastrointestinal motility

Gastric motility is controlled by a complex set of neural and hormonal signals. Nervous control originates from the enteric nervous system as well as parasympathetic and sympathetic system[11]. Two distinct patterns of gastrointestinal motility and secretion exist corresponding to the fasted and fed states. As a-result the bioavailability of orally administered drugs will vary depending on the state of feeding. In the fasted state, it is characterized by an inter-digestive series of electrical event and cycle, both through the stomach and small intestine every 2-3 hrs. This activity is called inter-digestive myoelectric cycle or migration motor complex (MMC).

MMC is often divided into four consecutive phases: basal (phase i), pre-burst (phase ii), burst (phase iii), and (phase iv) interval[12].

- ✓ Phase I (basal phase) lasts from 30-60 min with rare contractions.
- ✓ Phase II (pre burst phase) lasts for 20-40 min with intermittent action potential and contractions. As the phase progresses the intensity and frequency alsoIncreases gradually.
- ✓ Phase III (burst phase) lasts for 10-20min. It includes intense and regular contraction for short periods. Due to this contraction all the undigested material is swept out of the stomach down to the small intestine. This is also known as housekeeper wave.
- ✓ Phase IV lasts for 0-5min and occurs between phases III and I for two consecutive cycles.

Gastric empty rate

To achieve gastric retention, the dosage form must resist premature gastric emptying. For this, the dosage form must be able to withstand in the stomach against the force caused by peristaltic waves. Furthermore, once its purpose has been served the dosage form should be removed from the body with ease.

Advantages of FDDS

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- ✓ Floating dosage forms such as tablets or capsules will remain in the solution for prolonged time even at the alkaline PH of the intestine.
- ✓ FDDS dosage forms are advantageous in case of vigorous intestinal movement and in diarrhoea to keep the drug in floating condition in stomach to get a relatively better response.
- ✓ Acidic substances like aspirin causes irritation on the stomach wall when come in contact with it hence; FDDS formulations may be useful for the administration of aspirin and other similar drugs.
- ✓ The FDDS are advantageous for drugs absorbed through the stomach e.g. Ferrous salts, Antacids. Improve drug absorption, because of increased GRT and more time spent by the dosage form at its absorption site.
- ✓ Controlled delivery of drugs. It minimizes the mucosal irritation by releasing drug slowly.
- ✓ Treatment of gastrointestinal disorders such as gastro oesophageal reflux.
- ✓ Ease of administration and improves patient compliance by decreasing dosing frequency.
- ✓ Site-specific drug delivery to stomach can be achieved by minimizing the side effects[13].

Disadvantages of FDDS

- ✓ Floating system is not feasible for those drugs that have stability problem in GI tract.
- ✓ These systems require a high level of fluid in the stomach for drug delivery to float and work efficiently.
- ✓ The residence time in the stomach depends upon the digestive state. Hence, FDDS should be administered after the meal.
- ✓ Not suitable for the drugs that cause gastric lesions e.g. NSAIDS.
- ✓ The floating system in patients with achlorhydria can be questionable in case of swellable systems[14].

Desired properties for FDDS

The device must comply with following criteria:

- ✓ It must have sufficient structure to form a cohesive gel barrier.
- ✓ It must maintain an overall specific gravity lower than that of gastric contents
- ✓ It should dissolve slowly enough to serve as a drug reservoir[15].

MECHANISM OF FLOATING DRUG DELIVERY SYSTEM

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. It includes floating dosage forms (gas-generating systems and swelling or expanding systems), mucoadhesive systems, high density systems, modified shape systems, gastric-emptying delaying devices and coadministration of gastric-emptying delaying drugs. Floating drug delivery systems (FDDS) have always 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[16]. The system is floating on the gastric contents where the drug is released slowly at the desired rate from the system.The apparatus operated by measuring continuously the force equivalent to F (function of time) that is required to maintain the submerged object. This apparatus helps in optimizing floating drug delivery systems with respect to stability and durability of floating forces produced inorder to prevent the drawbacks of unforeseeable intragastric buoyancy capability variations[17].

F = F buoyancy – F gravity = (Df – Ds)v

Where,

F = total vertical force, Df = fluid density, Ds = object density, v = volume and g = acceleration.

FACTORS AFFECTING GASTRIC RESIDENCE TIME OF FDDS

Formulation factors

Size of the tablet: Diameter of the dosage form units 9.9 mm compared with a diameter of more than 7.5 mm are reported to have less gastric residence time.

Density of tablet: A dosage form having a density less than that of the gastric fluid floats, since it is away from the pyloric sphincter, the dosage unit is retained in the stomach for a prolonged period. A density of less than 1.0g/ml i.e. less than that of gastric contents has been reported.

Shape of tablet: Six shapes (ring, tetrahedron, cloverleaf, string, pellet, and disk) were screened in-vivo for their gastric retention potential. The tetrahedron rings exhibited nearly 100% retention at 24hr.

Viscosity grade of polymer: Low viscosity polymers (e.g., HPMC K 100 LV) were found to be more beneficial than high viscosity polymers (e.g., HPMC K4M) in improving floating properties. In

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addition, a decrease in the release rate was observed with an increase in polymer viscosity.

Idiosyncratic factors:

Gender: Mean ambulatory gastric residence time in males is less when compared with females. In male it is 3.4 ± 0.6h while in females it is 4.6 ± 1.2h, irrespective of the weight, height and body surface.

Age: People especially those over 70 years, have a significantly longer gastric residence time.

Posture: upright – protects floating forms against postprandial emptying

Supine – no reliable protection against early and erratic emptying.

Concomitant intake of drugs: Anti-Cholinergic like propantheline and atropine, opiates like codeine and prokinetic agents like Cis-pride and metoclopramide, can affect floating time.

Feeding regimen

Gastric residence time increases in the presence of food, leading to increased drug dissolution of the dosage form at the most favourable site of absorption.

Table:1 Marketed available floating products

Brand Name	Drug	Dosage form	Polymers used	Manufacturers
CIFRAN O. D	Ciprofloxacin	Tablet	Xanthan gum and sodium alginate	Ranbaxy
Liquid GAVISON	Mixture of Alginates	Liquid	Alginates	GlaxoSmithKline
MADOPAR HBS	Levodopa and BENSERAZIDE	Capsule	HPMC	Roche
GLUMETZA	Metformin Hydrochloride	Tablet	HPMC	DEPOMED

APPROACHES TO GASTRIC RETENTION: Different approaches have been pursued to increase the increase the retention of oral dosage forms in the stomach. These systems have been classified on the basis of principle of gastric retention[18].

1. **High density systems:** These systems, which have a density of 3g/cm³, are retained in the stomach and capable of withstanding its peristaltic movements[19]. These formulations are prepared by coating drug on a heavy core or mixed with inert materialssuch as iron powder, barium sulphate,zinc oxide and titanium oxide. The major drawback with these systems is that it is technically difficult to manufacture them with a large amount of drug (>50%) and achieve required density of 2.4-2.8g/cm³.
2. **Swelling and expanding systems:** This system is also called as "plug type systems", since they exhibit tendency to remain logged in the pyloric sphincters. These are the dosage forms, which after swallowing swells to such an extent that their exit from the pylorus is prevented; as a-result dosage form is retained in the stomach for a prolonged period of time[20]. The extensive swelling of these polymers is due to the presence of physical chemical cross links in the hydrophilic polymer network.

Expandable systems are capable of expanding and retain the stomach for long periods. These are usually formulated as capsule containing dosage forms folded and compact form[21].After being exposed to stomach environment, capsule shell disintegrates and dosage form expands preventing its exit through the stomach.

3. **Mucoadhesive and bio-adhesive systems:** Bio-adhesive drug delivery systems are used to localize a delivery device with in the lumen to enhance the drug absorption in a site-specific manner. This approach involves the use of bio-adhesive polymers, which can adhere to the epithelial surface in the stomach. Some of the most promising excipients that are commonly used include polycarbophil, Carbopol, lectins, chitosan, CMC and gliadin, etc[22].
4. **Floating systems:** Floating systems have a bulk density less than gastric fluids though the system is floating on the gastric contents. After release of drug, the residual system is emptied from the stomach. Floatation can be achieved by incorporating floating chamber filled vacuum, air, or inert gas.

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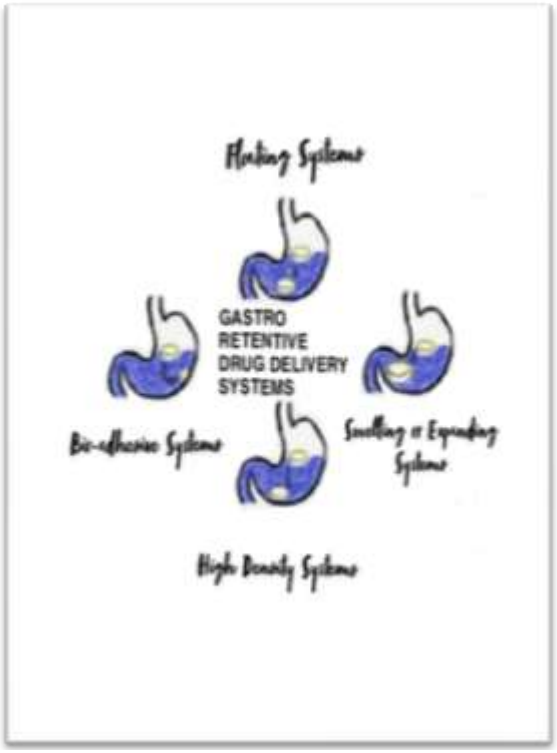
5. **Modified systems:** Systems with non-disintegrating geometric shape moulded from silastic elastomers or extruded from polyethylene blends, which extend the GRT depending on size, shape and flexural modules of drug delivery device[23].



CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEMS: Based on buoyancy these are classified as follows:

A. **Single Unit Floating Dosage Systems:**
a)Effervescent systems (Gas-generating systems)
b) Non-effervescent systems

B. **Multiple Unit Floating Dosage Systems:** a) Non-effervescent systems
b) Effervescent systems (Gas-generating systems)
c) Hollow microspheres

C. Raft Forming Systems

A. **Single Unit Floating Dosage Systems**: Single unit dosage forms are easiest to develop but suffers from the risk of losing their effects too early due to their all-or-none emptying from the stomach and, thus they may cause high variability in bioavailability and local irritation due to large amount of drug delivery at a particular site of GIT[24].

Effervescent systems or Gas-generating systems: The matrices which are prepared using swellable polymers like HPMC, polysaccharides like chitosan, effervescent components like sodium bicarbonate, citric acid and tartaric acid or chambers containing a liquid that Gasifies at body temperature. The optimum stoichiometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be0.76:1. Thus, carbon dioxide is released which cause the beads to float in the stomach[25].

Non-effervescent systems: This dosage forms use a gel forming or swellable cellulose type hydrocolloids, polysaccharides, and matrix forming polymers like polycarbonate, polymethacrylate and polystyrene. The formulation method includes a simple approach of thoroughly mixing the drug and the gel-forming hydrocolloid. After oral administration this dosage form swells in contact with gastric fluids and attains a bulk density of <1. The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so formed swollen gel-like structure acts as a reservoir

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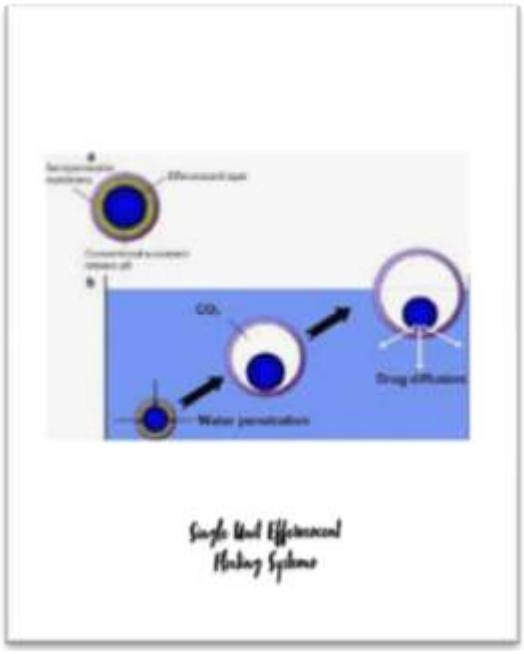
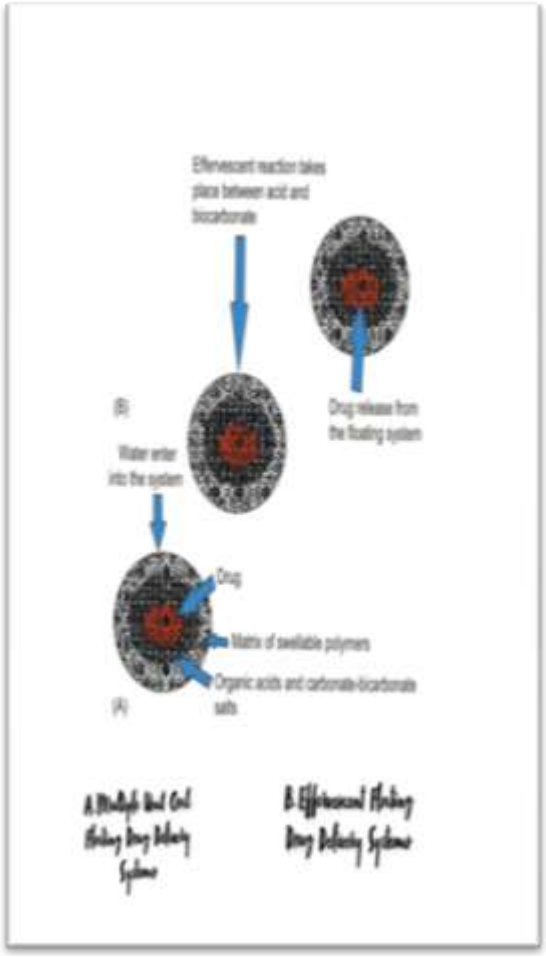
and allows sustained release of drug through the gelatinous mass[26].



B. Multiple Unit Floating Dosage Systems: Multiple unit dosage forms may be an attractive alternate since they have been shown to reduce inter and intra-subject variabilities in drug absorption as well as to lower the possibility of dose dumping[27].

Non-effervescent systems:A few workers have reported the possibility of developing such system containing indomethacin, using chitosan as the polymeric excipient. A multiple unit HBS containing indomethacin as a model drug prepared by extrusion process is reported[28]. A mixture of drug, chitosan and acetic acid is extruded through a needle, and the extrudate is cut and dried. Chitosan hydrates and floats in the acidic media, and the required drug release could be obtained by modifying the drug-polymer ratio[29].

Effervescent systems (Gas-generating systems):A multiple unit system comprises of calcium alginate core and calcium alginate/PVA membrane, both separated by an air compartment was prepared. In presence of water, the PVA leaches out and increases the membrane permeability, maintaining the integrity of the air compartment. Increase in molecular weight and concentration of PVA, resulted in enhancement of the floating properties of the system. Freeze-drying technique is also reported for the preparation of floating calcium alginate beads. Sodium alginate solution is added drop wise into the aqueous solution of calcium chloride, causing the instant gelation of the droplet surface, due to the formation of calcium alginate. The obtained beads are freeze-dried resulting in a porous structure, which aid in floating[30].



Hallow microspheres: A controlled release system designed to increase its residence time in the stomach without contact with the mucosa was achieved through the preparation of floating microspheres. Techniques involved in their preparation include simple solvent evaporation, and solvent diffusion and evaporation. The drug release and better floating properties mainly depend on the type of polymer, plasticizer and the solvents employed for the preparation[31].

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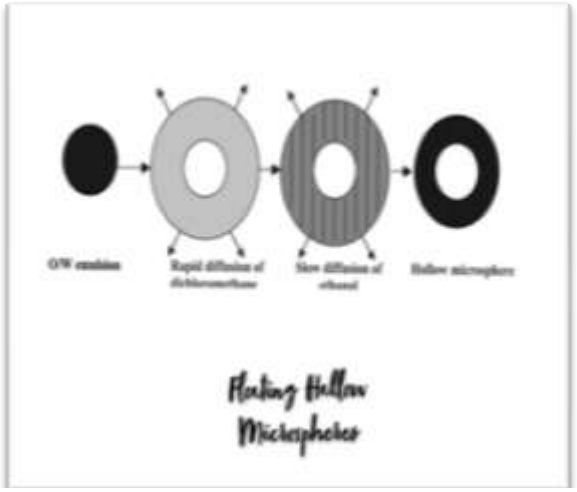
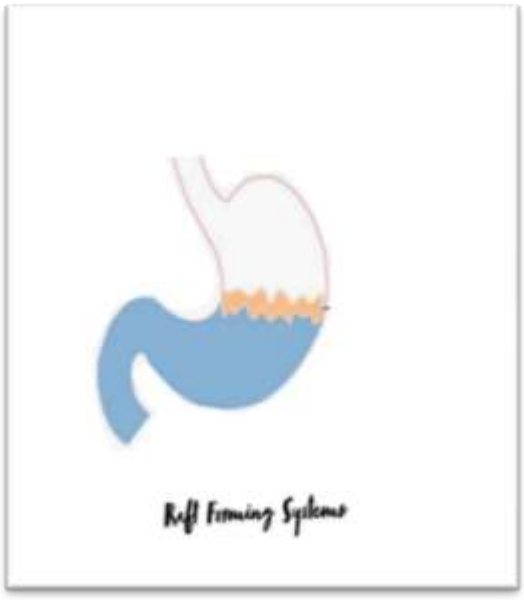


C. Raft Forming Systems: The basic mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, where in each portion of the liquid swells forming a continuous layer called a raft. The raft floats because of the buoyancy created by the formation of CO2 and acts as a barrier to prevent the reflux of gastric contents like HCl and enzymes into the oesophagus[32]. Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of to make the system less dense and float on the gastric fluids.



POLYMERS AND OTHER INGREDIENTS USED IN PREPARATION OF FLOATING DRUGS:

Polymers: Polymers are used, so as to target the drug delivery at specific region in the GI tract i.e. stomach. Polymers are the macromolecule compound containing many monomer units joined to each other by bonds. These are further classified as:

Natural polymers: Natural gums (obtained from plants) are hydrophilic carbohydrate polymer of high molecular weight. They are generally insoluble in organic solvents like hydrocarbon and ether. It includes:

Guar gum – Naturally occurring galactomannan polysaccharide. It hydrates and swells in cold water forming viscous colloidal dispersions or sols.

Chitosan- Is a natural polymer obtained by deacetylation of chitin. It is non-toxic, biodegradable, biocompatible and have anti-bacterial property.

xanthum gum- Is a high molecular weight extracellular polysaccharide produced by pure culture aerobic fermentation of carbohydrate.

Gellan gum –Is an anionic, high molecular weight, deacetylated extracellular, linear polysaccharide. This gum has an outstanding flavour release, high gel strength, an excellent stability, process flexibility.

Sodium alginate - It consists of sodium salts of alginic acid, which is a mixture of polyuronic acids composed of residues of d-mannuronic acid and L-guluronic acid.

Synthetic polymers: These are either purely synthetic or they are modified form of natural polymer known as semi-synthetic. It includes:

Hydroxy propyl methyl cellulose –It is a semi-synthetic, inert, viscoelastic polymer, used as an excipient and controlled- delivery component in oral medications.

Eudragit – Eudragit L, S and FS types are used as ente3ric coating agents because they are resistance to gastric fluid.

Ethyl cellulose –Used in pharmaceutical formulations such as taste-masking of bitter actives, moisture protection, stabilizer, extended release multi-particulate coating[33].

Inert fatty materials (5%-75%): Edible, inert fatty materials having a specific gravity of lessthan one can be used to decrease the hydrophilic property of formulation and hence increase buoyancy. E.g. Beeswax, fatty acids, long chain fatty alcohols, GELUCIRE® 39/01 and 43/01.

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Evaluation Parameters Of Gastroretentive System:

Hardness test: Randomly sampled twenty tablets in each batch of formulations should be used for the determination of hardness with the help of Monsanto type hardness tester[34].

Weight variation test: Twenty tablets selected at the random are weighed accurately and the average weight of the tablet is calculated. Then the deviation of individual weight from the average weight is calculated

Thickness test: The individual crown to crown thickness of ten tablets is determined using slide callipers for each batch[35].

Floating lag time: It is the time by the tablet to emerge on to the surface of dissolution medium and is expressed in seconds or minutes

Angle of repose: The maximum angle possible between the surface of a pile of powder or granules and the horizontal plate. The granules were allowed to flow through the funnel fixe3de to a stand at definite height(h). The angle of repose was then calculated by measuring the height and radius of the heap of granules formed[36].

$\tan\theta = h/r$

$\theta = \tan^{-1}(h/r)$

θ = Angle of repose

h = height of the heap

r = radius of the heap

Determination of In vitro Dissolution Study: The test for buoyancy and in vitro drug release studies are usually carried out in simulated gastric and intestinal fluids maintained at 37˚C. In practice, floating time is determined by using the USP dissolution apparatus containing 900ml of 0.1 HCl as a testing medium maintained at 37˚C. The time required to float the HBS dosage form is noted as floating time.

Size and shape evaluation: It play a major role in determining the solubility rate of the drugs and thus potentially its bioavailability. The particle size of the formulation was determined using sieve analysis, air elutriation analysis, photo analysis, optical microscope, electro resistance counting methods.

Floating properties: Effect of formulation variables on the floating properties of gastric floating drug delivery system was determined by using continuous floating monitoring system and statistical experimental design.

Surface topography: The surface topography and structures were determined using scanning electron microscope operated with an acceleration voltage of 10kv, contact angle meter, contact profilometer.

Determination of moisture content: It shows whether a product intendedfor trade and production has standard properties.

Swelling studies: Swelling studies were performed to calculate molecular parameters of swollen polymers. Swelling studies were determined by using dissolution apparatus, optical microscopy and other sophisticated techniques which include cryogenic scanning electron microscopy, light scattering imaging, etc.

In-Vivo methods include

- ✓ γ- Scintigraphy
- ✓ Radiology
- ✓ Gastroscopy
- ✓ Ultrasonography
- ✓ Magnetic resonance imaging (MRI)

APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEMS

1. **Sustained drug release:** HBS system can remain in the stomach for long periods and hence can release the drug over a prolonged period of time. These systems have a bulk density of <1 as a result of which they can float on the gastric contents.
2. **Enhanced bioavailability:**The enhanced bioavailability of riboflavin CR-GDRF is significantly enhanced incomparision to the administration of non-GRDF CR polymeric formulations.
3. **Site specific drug delivery:** Furosemide is primarily absorbed from the stomach followed by the duodenum. It has been reported that a monolithic floating dosage form with prolonged gastric residence time was developed and the bioavailability was increased.
4. **Absorption enhancement:** Drugs that have poor bioavailability because of site-specific absorption from the upper part of the GIT are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption.
5. **Minimized adverse activity at the colon:**Retention of the drug in the HBS systems at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in the colon may be prevented, which leads to the development of microorganism's resistance.

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6. **Reduced fluctuations of drug concentration:** Fluctuations in drug effects are minimized and concentration dependent adverse effects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index.
7. **Enhanced first-pass metabolism:**The pre-systemic metabolism of the tested compound may be considerably increased when the drug is presented to the metabolic enzymes (cytochrome P450, in particular CYP3A4) in a sustained manner, rather than by a bolus input.
8. **Improved selectivity in receptor activation:** Minimization of fluctuations in drug concentration also makes it possible to obtain certain selectivity in the elicited pharmacological effect of drugs that activate different types of receptors at different concentrations.
9. **Reduced counter-activity of the body:** Slow input of the drug into the body was shown to minimize the counter activity leading to higher drug efficiency.
10. **Extended time over critical (effective) concentration:** The sustained mode of administration enables extension of the time over a critical concentration and thus enhances the pharmacological effects and improves the clinical outcomes[37].

LIST OF DRUGS EXPLORED FOR VARIOUS FLOATING DOSAGE FORMS

- ✓ **Microspheres Tablets/Pills:** Chlorpheniramine maleate, Aspirin, Griseofulvin, Acetaminophen, P-nitroaniline, Acetylsalicylic acid, Ibuprofen, Amoxycillin trihydrate, Terfenadine, Ampicillin, Atenolol, Theophylline, Captopril, Isosorbide dinitrate, Sotalol, Isosorbide mononitrate.
- ✓ **Films:** P-Aminobenzoic acid, Cinnarizine, Piretanide, Prednisolone, Quinidine gluconate.
- ✓ **Granules:** Cinnarizine, Diclofenac sodium, Diltiazem, Indomethacin, Fluorouracil, Prednisolone, Isosorbide mononitrate, Isosorbide dinitrate.
- ✓ **Powders:** Riboflavin, Sotalol, Theophylline.
- ✓ **Capsules:** Verapamil HCl, Chlordiazepoxide HCl, Diazepam, Furosemide, L-dopa, Misoprostol, Propranolol HCl, URSO Deoxy-Cholic acid, Nicardipine.

II. CONCLUSION

Recently many drugs have been formulated as floating delivery systems with an objective of sustained release and restricting the region of drug release to stomach. The advancement in delivery technology will lead to the development of large number of floating delivery system to optimize the delivery of molecules that exhibit absorption window, low bioavailability and extensive first pass metabolism. It is also evident that the maximum number of commercial products and patents of gastro retentive systems belong to the class of floating drug delivery systems. So, with an improved knowledge of formulation aspects and physiochemical and pharmacological prospects of drugs someone can design an optimum system for drug delivery in the gastric cavity.

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