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# Overview Article: - Floating Drug Delivery System

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**A B S T R A C T**

Scientific and technical developments in the research and development of new drug delivery systems have taken place in the past year to address physiological disturbances such as short gastric residence times and unpredictable gastric emptying times. Several approaches are currently used to increase gastric residence time (GRT), including floating drug delivery systems (FDDS), also known as hydrodynamically balanced system (HBS), swelling and expanding systems, polymeric bioadhesive system, modified shape system, high density system and other delayed gastric emptying devices. Floating Drug Delivery Systems (FDDS) is one of the gastroretentive dosage forms used to achieve a prolonged residence time in the stomach. The aim of writing this review on floating drug delivery system (FDDS) was to collect the current literature with a particular focus on the main floating mechanism to achieve gastric retention. Sustained oral release gastrointestinal dosage forms provide many advantages for drugs with absorption from the upper gastrointestinal tract and for drugs that act locally in the stomach. This review includes physiological factors, factors governing gastric retention time, excipient variables affecting gastric retention, approaches to the design of single-unit hydrodynamically balanced systems and multi-unit floating structures, and aspects of their classification, formulation, and evaluation are discussed in detail, and advantages and disadvantages with a small application these systems.

**Keywords**: Gastro retention system, Gastrointestinal tract, Floating drug delivery system, Classification, Methods, Evaluation.

## 1. INTRODUCTION

A drug delivery system represents the pure raw form of drugs either in solid, liquid or semi-solid form, which should be therapeutically effective, safe and stable enough to deliver the required amount of drug to the intended site in the body, so that it reaches the correct concentration immediately and then to maintain the adjusted concentration. [1] Due to the low cost of treatment, increased patient compliance and easy application of oral drug administration are mostly preferred. Despite its many advantages, the frequency of drug dosing should be increased because it is easily emptied from the stomach. [2] To overcome these obstacles, drug administration must ensure a prolonged residence time in the stomach. Gastro retention contributes to increasing bioavailability, prolonging drug release time, minimizing drug wastage, and improving drug solubility, which is less soluble in a high pH environment. [3] Many drugs released in the stomach have the greatest therapeutic impact because they are continuously delayed and controlled release. This type of drug delivery route would have comparatively fewer side effects and would eliminate the need for repeated doses. [4] In pharmaceutical dosing, formulation of drugs in multi-layered/bi-layered tablets is an innovative approach to deliver the initial dose and maintain the dose in the tablet. This design allows for a sustained-release preparation with an immediate release amount of drug in one layer and a sustained-release portion in the other, thereby maintaining a sustained blood level. The immediate-release section breaks down rapidly after absorption by delivering an initial dose of drug for an immediate effect, where the matrix layer remains intact as it passes through the gut most of the time, gradually dissolving from the exposed phases along the way, helping to maintain the blood level initially achieved. [5]

Common controlled-release dosage forms typically prolong the release of drugs and do not have a rapid onset of action after oral administration. Thus, coated tablets provide a pharmacokinetic benefit over conventional controlled-release dosage forms because the drug is rapidly released from the rapid-release layer, resulting in a rapid increase in plasma drug concentration accompanied by continued drug release from the sustained-release layer. [6]

### *1.1 Drug suitable for gastroretentive drug delivery system: [7]*

- Drugs that are locally active in the stomach, such as antacids, misoprostol, etc.
- Medicines showing a narrow absorption window in the gastrointestinal tract, e.g. Riboflavin, Furosemide, etc.
- Medicines showing instability in the colonic environment, e.g. Ranitidine HCl, Captopril, etc.

- Medicines that are effective against normal gut microbes, eg antibiotics against Helicobacter pylori.
- Drugs that have low solubility at high pH values, e.g. Chlordiazepoxide, Diazepam, etc.

***1.2 Drug unsuitable for the gastroretentive system of drug administration: [7]***

- Medicines that have very limited solubility in an acidic environment, e.g. Phenytoin etc.
- Medicines with persistent instability in the conditions of the stomach environment, e.g. Erythromycin, etc.
- Drugs that are mainly used for their selective release in the colon, e.g. 5-amino
- salicylic acid and corticosteroids etc.

***1.3 GRDDS CLASSIFICATION: [8-12]***

Dosage forms that can be retained in the stomach are called gastroretentive dosage forms (GRDFs).

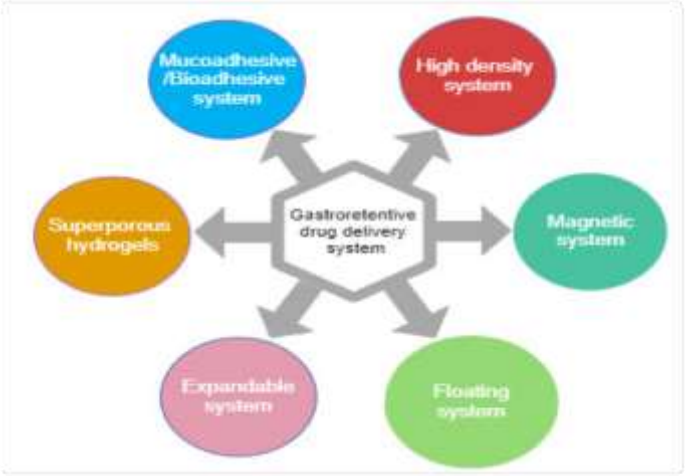


**Figure 1 :- Types of Gastro Retentive Dosage Forms. [30]**

***1.3.1. High density system:***

These types of GRDF have a density of -3 g/cm3 and are retained in the stomach cavity. These systems can be maintained in the lower part of the stomach above a maximum threshold density of 2.4-2.8 g/cm3. The main limitation is that they are technically difficult to produce with large amounts of drug product.

***1.3.2. Swelling and expanding system:***

Expandable GRDF is typically based on three configurations, a small configuration that allows easy oral administration; an expanded form which is carried out in the stomach and thus prevents its passage through the pyloric sphincter and finally another small form which is achieved in the stomach when retention is no longer necessary. Swelling usually occurs due to osmosis and unwrapping is due to mechanical shape memory.

***1.3.3. Mucoadhesive or bioadhesive system:***

These systems allow incorporation with bioadhesive agents that allow the system to adhere to the stomach walls, thereby preventing gastric emptying. Bio/mucoadhesive systems bind to the gastric epithelial cell surface or mucin and prolong GRT by increasing the intimacy and duration of contact between the dose type and the biological membrane.

***1.3.4. Superporous hydrogel:***

These are swellable systems with an average pore size > 100 μm, swelling to equilibrium within a minute due to the rapid absorption of water by capillary wetting through multiple interconnected open pores. They swell to a large size and are expected to provide sufficient mechanical strength to withstand the pressure caused by gastric contraction.

### *1.3.5. Magnetic system:*

Magnetic dosage forms contain an extracorporeal magnet and a small internal magnet that guides the gastrointestinal passage of the dosage form. From formulation and from a technological point of view, the Floating Drug Delivery System (FDDS) is a very easy and logical approach in the development of GRDF. [8,9,11]

## 2. FLOATING DRUG DELIVERY SYSTEM: [3,8]

FDDS or hydrodynamically balanced systems (HBS) are low-density systems that have sufficient tendency to float above the stomach contents and remain in the stomach for a longer period of time, which releases the drug component at the desired rate while floating above the stomach. content contributes to an increase in gastroretention time and a decrease in fluctuation. FDDS is a mechanism of a gastro-retention drug delivery system that controls the pharmacokinetic rate of drug release to a specific site to achieve its pharmacological effect.

### *2.1. Basic physiology of the gastrointestinal tract: [11]*

The stomach is anatomically divided into 3 regions: fundus, body and antrum (pylorus).

**Fundus:** proximal part.

**Body:** functions as a reservoir of undigested material,

**Pylorus:** it is the site for mixing the contents and acts as a pump to empty the stomach by propulsive actions.

### *2.2. Stomach Physiology:*

The stomach is the enlarged part of the alimentary canal between the esophagus and the small intestine. The stomach is retracted when empty, and the mucosa and submucosa are thrown into distinct folds called rugae.

Below are the four main types of secretory epithelial cells that cover the surface of the stomach and line the gastric pits and glands.

**Mucous cells:** secrete an alkaline fluid.

**Parietal cells:** secrete an acid which is hydrochloric acid.

**Principal cells:** secrete pepsin, a proteolytic enzyme.

**G cells:** secrete the hormone gastrin.

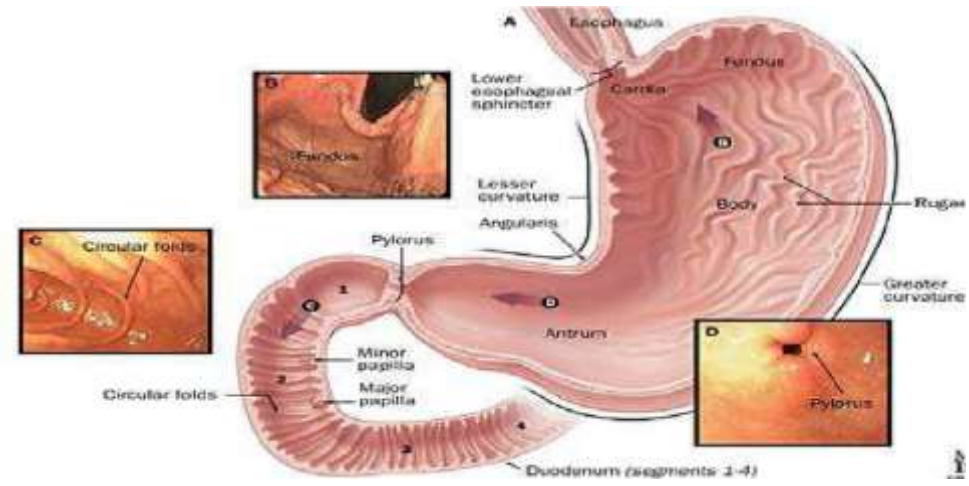


**Figure 2: Physiology of the stomach. [31]**

### *2.3 Stomach motility:*

Gastric motility is controlled by a complex set of neural and hormonal signals.

***2.4 Empty stomach rate:***

Stomach emptying occurs both during fasting and when satiated. During the fasting process, an interdigestive sequence of electrical events takes place every 2 to 3 hours in both the stomach and intestines.

It is called the interdigestive myoelectric cycle or the myoelectric migratory cycle (MMC), which is further divided into 4 phases.

**1. Phase I (Basal phase):** lasts from 40 to 60 minutes with rare contractions.

**2. Phase II (pre-burst phase):** lasts 40 to 60 minutes with intermittent action potentials and contractions.

**3. Phase III (burst phase):** lasts 4 to 6 minutes, which includes intense and regular contractions for a short time.

**4. Phase IV:** lasts 0 to 5 minutes and occurs between Phases III and I of 2 consecutive cycles. [11]

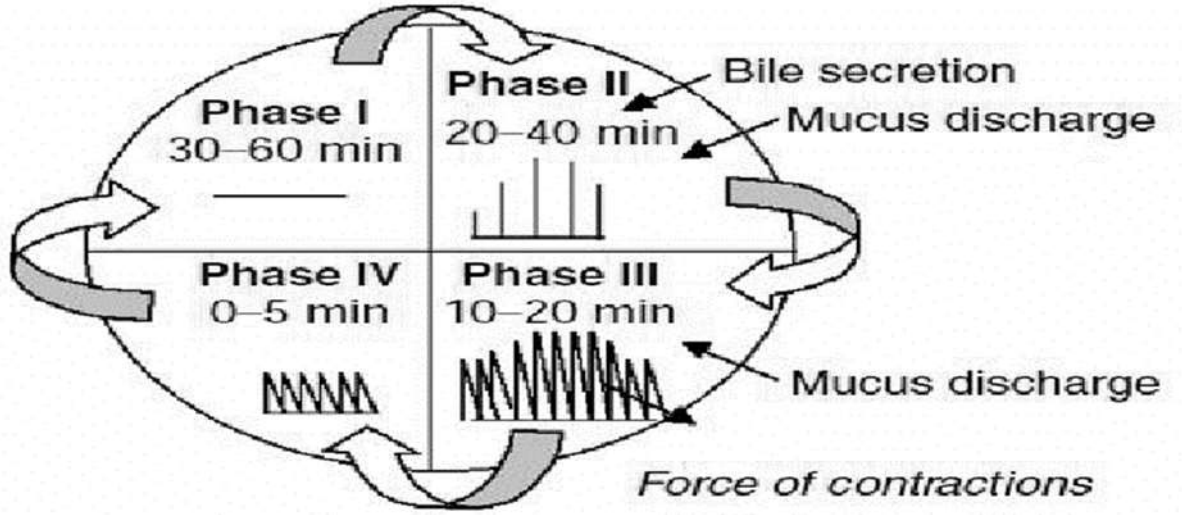


**Figure 3: Motility pattern in the GIT. [32]**

***2.5 Factors controlling the retention time in the stomach of the dosage form: [13]***

• The nature of the food

• Fed or Unfed State

• Age

• Frequency of administration

• Simultaneous administration of drugs

• Density

• Size and shape

• Calorie content

• Gender

• Deportment

## 3. CLASSIFICATION: [1]

**A. Effervescent FDDS**

1. Gas production system

2. A system containing a volatile liquid

**B. Non-Effervescent FDDS**

1. Colloidal gel barrier system

2. Two-layer floating tablets

3. Microporous compartment system

4. Floating beads/alginate beads

5. Micro balloons/hollow microspheres

**C. Raft forming system**

### *3.1. Effervescent FDDS*

This system uses a floating chamber filled with water, vacuum, air or inert gas. CO2 can be introduced into the floatation chamber, which is produced as a result of the effervescent reaction between an organic acid (citric acid) and carbonate/bicarbonate salts. Such a system uses a matrix prepared with swelling polymers such as chitosan-like polysaccharides, effervescent materials such as citric acid, sodium bicarbonate, and tartaric acid, or chambers containing a liquid that gasifies at body temperature.

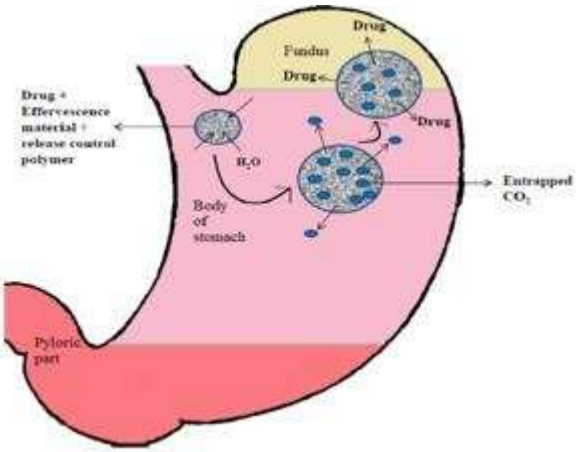


**Figure 4: Effervescence-based GRDDS.[33]**

### *3.2 Non-effervescent FDDS*

In the GI tract, non-effervescent FDDS is based on the mechanism of polymer swelling or bioadhesion to the mucosal layer. The most commonly used excipients in non-foaming FDDS are:

• hydrophilic gums,

• Gel-forming or highly swellable cellulose-type hydrocolloids

• Polysaccharides and matrix forming materials such as polymethacrylate, polycarbonate, polystyrene, polyacrylate as well as bioadhesive polymers such as Carbopol and Chitosan**.**

### *3.3 Raft forming system*

Raft-forming systems are mostly considered for the delivery of antacids and other drugs for gastro-infection and gastrointestinal disorders. On contact with gastric fluid, the gel-forming solution swells and forms a viscous compact gel containing captured CO2 bubbles forming a raft layer on the gastric fluid, which gradually releases the medicinal substance into the stomach.

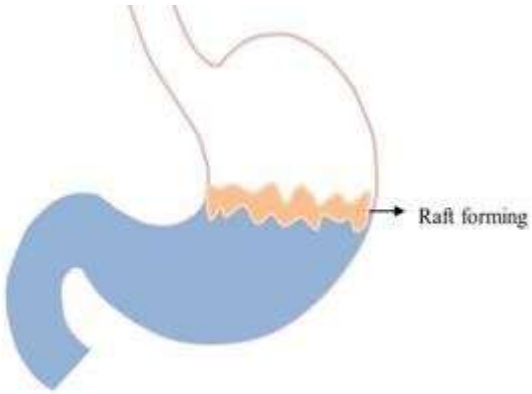


**Figure 5: GRDDS based on Raft Forming System.[34]**

## 4. POLYMERS USED IN FLOATING DRUG DELIVERY SYSTEM:-

Polymers are used in a floating system to target drug delivery to a specific region in the GI tract, i.e. the stomach. Both synthetic and natural polymers are used in floating drug application. Natural polymers used in floating system are guar gum, chitosan, xanthan gum, gellan gum, sodium alginate, etc. Synthetic polymers used for floating drug delivery are HPMC, Eudragit, ethyl cellulose, etc. [35]

### *4.1.1 A natural polymer has advantages over a synthetic polymer.*

They are as follows:

• Biodegradable

• Biocompatible and non-toxic.

• Low cost.

•Environmentally friendly

• Local availability.

### *4.1.2 Natural polymer has some disadvantages.*

They are as follows:

• Microbial contamination

• Batch-to-batch variation

• Uncontrolled rate of hydration

• Reduced viscosity during storage. [36]

### *4.2 Natural polymers.*

Natural gums (obtained from plants) are high molecular weight hydrophilic carbohydrate polymers. They are generally insoluble in organic solvents such as hydrocarbon, ether. Gums are either soluble in water or absorb water and swell or disperse in cold water to form a viscous solution or jelly.

1 Guar gum Endosperm of the seed of cynopsis tetragonolobus

2 Xanthum gum Fermentation of glucose by Xanthomonas compestris

3 Sodium alginate Laminaria hyperboria

4 Chitosan Shell of marine invertebrates

5 Pseudomonas elodea gellan gum

### *4.2.1. Guar gum*

Guar gum is a naturally occurring galactomannan polysaccharide. Guar gum hydrates and swells in cold water to form viscous colloidal dispersions or salts. This gelling property slows drug release and makes it a flexible carrier for sustained-release dosage forms.38 In the pharmaceutical industry, guar gum is used as a disintegrate and as a polymer in a floating drug delivery system.

Features of guar gum:

• It is soluble in water but insoluble in organic solvents.

• Strong hydrogen bonding property.

• Excellent thickening, emulsifying, film-forming properties.

• Ability to control rheology.

***Advantages of guar gum in a floating drug delivery system:***

Polymer swelling has been reported to play an important role in the pattern and amount of drug release. Guar gum formulations were found to be relatively insensitive to stirring speed during in vitro drug dissolution testing and the dissolution profile was not significantly affected. [37]

### *4.2.2. Xanthan gum*

Xanthan gum is a high molecular weight extracellular polysaccharide produced by pure culture aerobic fermentation of carbohydrates. Xanthan is a long-chain polysaccharide with a large number of trisaccharide side chains. The rubber also has excellent solubility and stability in acidic and alkaline conditions and in the presence of salts and resists common enzymes.

***Benefits of xanthan gum:***

• Used to increase or decrease the rate of drug release from a formulation

• Soluble in water

• High viscosity at low concentration

• Has the potential advantage of drug release with zero-order kinetics.

Some tablets containing xanthan gum and citric acid show buoyancy for more than 24 hours.

### *4.2.3. Sodium alginate*

Sodium alginate consists primarily of the sodium salt of alginic acid, which is a mixture of polyuronic acids composed of residues of d'mannuronic acid and L guluronic acid. The block structure and molecular weight of sodium alginate samples were investigated.

• **Typical properties:** Acidity/alkalinity ph-7.2 (1% w/v aqueous solution).

• **Solubility:** Practically insoluble in ethanol (95%), ether, chloroform and ethanol/water mixtures in which the ethanol content is higher than 30%. It is also practically insoluble in other organic solvents and aqueous acidic solutions in which the pH is lower than 3. Slowly soluble in water, forming a viscous colloidal solution.

• **Viscosity (dynamic):** Different types of sodium alginate are commercially available, which provide aqueous solutions with different viscosities. A 1% w/v aqueous solution at 208 °C will typically have a viscosity of 20–400 mpa s (20–400 cp). Viscosity can vary depending on concentration, pH, temperature or the presence of metal ions. Above pH 10, the viscosity decreases. [38]

### *4.2.4. Chitosan :-*

Chitosan is a natural polymer obtained by deacetylation of chitin. It has favorable biological properties such as non-toxic, biodegradable, biocompatible. It is a bioadhesive polymer and has antibacterial properties, making it suitable for site-specific application. Chitosan is a high molecular polycationic weak base with a pka value of 6.2-7. In addition to acidic pH 1.2 or neutral media, it naturally floats and provides controlled release.38 By increasing the thickness of the chitosan film, the release rate can be reduced. [39]

***Benefits of chitosan:***

• Forms a film that reduces the effect of transit time through the gastrointestinal tract.

• Hallow microcapsules tend to float on gastric fluid for about 12 hours.

• The drug release rate followed zero-order kinetics. [39]

### *4.2.5. Gellan gum*

Gellan gum is an anionic, high molecular weight, deacetylated extracellular linear polysaccharide. This gum has excellent flavor release, high gel strength, excellent stability, process flexibility, high clarity, good film formation, and thermally reversible gel properties.38 Gellan gum is produced as a fermentation product from spingomonas elodea.

***Advantages of Gellan gum:***

• Has excellent flavor release, high gel strength and excellent stability.

• When positively charged ions are added, it forms a gel

• It is used in a food product as a thickener or stabilizing agent. [37]

### *4.3 Synthetic polymers*

Synthetic polymers are increasingly important in pharmaceuticals. Synthetic polymer is used as a binder, film coating agent, etc. Polymers are macromolecules that are very large in number and contain various functional groups. Synthetic polymers are either purely synthetic or are a modified form of a natural polymer known as semi-synthetic. The list of synthetic polymers used is as follows:

1. Hydroxypropylmethylcellulose.

2. Eudragit.

3. Ethyl cellulose.

The disadvantages of synthetic polymer are as follows

• High toxicity of environmental pollution

• Acute and chronic side effects

• Poor biocompatibility

• Inflammatory reaction and local reaction. [39]

### *4.3.1. Hydroxypropylmethylcellulose*

Hydroxypropyl methylcellulose ethers belong to a large family of white to off-white, water-soluble, odorless polymers that bind, retain water, thicken, film, and lubricate. It is a semi-synthetic, inert, viscoelastic polymer, used as an excipient and controlled-release ingredient in oral drugs, found in a number of commercial products.

***Synonyms:*** Hypromellose, Methocel, Metolose, Pharmacoat, Benecel MHPC, E464, etc.

***Functional category:***

Bioadhesive Material, Coating Agent, Controlled Release Agent, Dispersing Agent, Solubility Enhancer, Emulsifier, Emulsion Stabilizer, Extended-release agent, film-forming agent, foaming agent, granulating agent, modified-release agent, mucoadhesive agent, release-modifying agent, solubilizing agent, stabilizing agent, suspending agent, extended-release agent, tablet binder, thickening agent, viscosity-increasing agent. [42]

General properties common to Hypremellose are listed below.

Individual types exhibit these properties to varying degrees and may have other properties that are desirable for specific applications.

• Apparent density: 0.25~0.70g/cm3

• Refractive index = 1.336

• Surface tension: 42 to 56 mn/m

***Solubility:***

Soluble in cold water, forming a viscous colloidal solution; practically insoluble in hot water, chloroform, ethanol (95%) and ether, but soluble in mixtures of ethanol and dichloromethane, mixtures of methanol and dichloromethane and mixtures of water and alcohol. Some types of HPMC are soluble in aqueous acetone solutions, mixtures of dichloromethane and propan-2-ol, and other organic solvents. Some species are swellable in ethanol. [43]

***Application:***

In oral products, HPMC is primarily used as a tablet binder, in film coating, and as a matrix for use in extended-release tablet formulations. Concentrations between 2% and 5% w/w they can be used as a binder in wet or dry granulation processes. High degrees of viscosity can be used to slow the release of drugs from the matrix at levels of 10–80% w/w in tablets and capsules. [40]

Hypromellose is also used in liquid oral dosage forms as a suspending and/or thickening agent in concentrations ranging from 0.25-5.0%. Depending on the degree of viscosity, concentrations of 2-20% w/w are used for film-forming solutions up to coated tablets. Lower viscosity grades are used in aqueous film coating solutions, while higher viscosity grades are used with organic solvents. Examples of commercially available coating materials include Any Coat C, Spectracel, Pharmacoat, and the Methocel E Premium LV series.

Hypromellose is also used as a suspending and thickening agent in topical formulations.

Hypromellose in concentrations between 0.45-1.0% by weight can be added as a thickener to eye drop vehicles and artificial tear solutions. It is also used commercially in liquid nasal formulations at a concentration of 0.1%.

Hypromellose is used as an emulsifier, suspending agent, and stabilizing agent in topical gels and ointments.

***Advantages :-***

• Water-soluble and the most widespread polymer in nature

• Used as a thickener, film former and water retention agent

• Hydrophilic matrix is the simplest sustained release technology for oral dosage form. [41]

### *4.3.2. Eudragit.*

Unproprietary names: BP: Acidum methacrylicum et methylis methacrylas polymerisatum 1:2 USPNF: methacrylic acid copolymer

***Synonyms:*** Polymer methacrylates.

***Functional category:*** Film forming agent; tablet binder; tablet diluent

***Description:***

Polymethacrylates are synthetic cationic and anionic polymers of dimethylaminoethyl methacrylate, methacrylic acid and methacrylic acid esters in various proportions. Several different types are commercially available and can be obtained as a dry powder, as an aqueous dispersion, or as an organic solution. A mixture of acetone and propan-2-ol (60:40) is most often used as an organic solvent. Eudragit S 100 is available in powder form and the solvent for this purpose is 95% acetone and alcohols, which are soluble in intestinal fluid from pH 7 and are used as an enteric coating material. Eudragit L and S, also referred to as methacrylic acid copolymers in USPNF monograph 23, are products of anionic copolymerization of methacrylic acid and methyl methacrylate. The ratio of free carboxyl groups to ester is approximately 1:1 in Eudragit L (type A) and approximately 1:2 in Eudragit S (type B). Both polymers are readily soluble in neutral to slightly alkaline conditions (pH 6–7) and form salts with alkalis to form film coatings that are resistant to gastric media but soluble in intestinal fluid. Eudragit L100 and Eudragit S-100 are white loose powders with a minimum of 95% dry polymers.

***Incompatibilities:***

Incompatibility occurs with certain polymethacrylate dispersions depending on the ionic and physical properties of the polymer and solvent. For example, soluble electrolytes, pH changes, some organic solvents and extreme temperatures can cause coagulation; Interactions between polymethacrylates and some drugs may occur, although solid polymethacrylates and organic solutions are generally more compatible than aqueous dispersions.

***Application:***

Polymethacrylates (Eudragit) are primarily used in oral capsule and tablet formulations as film coating agents. Depending on the type of polymer used, films with different solubility characteristics can be produced. Eudragit S 100 is soluble in acetone and alcohols and 1N NaOH.

In contrast, Eudragit L, S and FS types are used as enteric coating agents because they are resistant to gastric fluid.

Different types of enteric coatings are soluble at different pH values: e.g. Eudragit L is soluble at pH >6, while Eudragit S and FS are soluble at pH >7. Class S is generally used for tablet coating, while the flexible dispersion FS 30 D is preferred for particle coating.

Eudragit RL, RS, NE 30D, NE 40D and NM30D are used to form water-insoluble film coatings for sustained release products. Eudragit RL films are more permeable than Eudragit RS films, and films of different permeability can be obtained by mixing the two types together. Polymethacrylates are also used as binders in both aqueous and organic wet granulation processes. A larger amount (5-20%) of dry polymer is used to control the release of the active ingredient from the tablet matrix. Solid polymers can be used in direct compression processes in amounts of 10-50%.

Polymethacrylate polymers can further be used to form the matrix layers of transdermal delivery systems and have also been used to prepare new gel formulations for rectal administration. [41]

***4.3.3. Ethyl cellulose.***

Ethocel (ethylcellulose polymers) has been widely used in the pharmaceutical industry for over 50 years. Ethyl cellulose is used in pharmaceutical formulations for a variety of purposes such as taste masking of bitter actives, moisture protection, stabilizer, sustained release multiparticulate coating, microencapsulation of actives, sustained release binder in inert matrix systems, solvent, and extrusion granulation.

***Solubility:***

Ethyl cellulose is a water-insoluble cellulose ether that is prepared from cellulose, it is partially O-ethylated cellulose, its content of ethoxy groups (-OC2H5) varies between 44-51%. . It is insoluble at any pH found in the body, but swells in the presence of gastric juice. It is then permeable to water and allows prolonged modified release of the drug. This makes it suitable for better patient cooperation.

***Application:***

The use of EC in wet extrusion processes is limited, because the polymer has considerable elastic properties, but it can be successfully used as a forming matrix in combination with some plasticizers. The potential of coarse ethyl cellulose (CPEC) and fine particle ethyl cellulose (FPEC) as a diluent with high molecular weight polyethylene oxide (PEO) used as an extrusion aid and binder showed that water is sufficient to prepare a wet granulation product when using FPEC. MCC was included in the formulations to contribute its plasticity to the wetted mass during extrusion and to the extrudate during spheronization.

Ethyl cellulose is an ideal polymer for the creation of products enabling modified drug release. A small number of ethyl cellulose polymers have been approved for general pharmaceutical application and are used in sustained-release solid dosage formulations. There are several types of such ethyl cellulose, eg Ethocel 4, Ethocel 10 and Ethocel 45, which differ in the length of the polymer chains, dissolution rate and viscosity of their solution. Ethyl cellulose is suitable for the preparation of MR coatings. [42]

## 5. Approaches to the design of a floating drug delivery system: [11]

For individual dosage forms (e.g. tablets):

**A) Floating Lag Time:** The time required for the tablet to rise to the surface of the dissolution medium and is measured in seconds or minutes.

**B) In-vitro drug release and swimming time:** This is calculated using a USP II apparatus (scoop) stirring in simulated gastric fluid (pH 1.2 without pepsin) at 50 or 100 rpm at 37 ± 0.20°C . samples are then often taken and analyzed for drug content. The time (hours) during which the tablets remain floating on the surface of the dissolution medium is the floating time and is observed visually.

**(C) Gastro-retention assessment in vivo:** Performed by x-ray or gamma-scintigraphic testing of the transition of the drug form in the GIT. Tablets are also tested for hardness, weight changes, etc

## 6. Methodology. [18 – 21]

***5.1. Direct compression technique:***

It means pressing tablets directly from the powder content without changing the physical structure of the substance itself. Dicalcium trihydrate phosphate, tricalcium phosphate, etc. are the most commonly used carriers.

***5.2. Effervescent technology:***

The effervescent reaction between the organic acid (citric acid) and bicarbonate salts fills the floating chamber of the drug delivery system with an inert gas (CO2).

***5.3. Wet granulation technique:***

It involves massaging the wet powder, grinding or drying. Wet granulation shapes the granules by binding the powders together with an adhesive rather than compacting them.

***5.4. Ionotropic gelation technique:***

Gelation of the anionic polysaccharide sodium alginate, a primary polymer of natural origin, was performed with oppositely charged calcium ions (counterions) to create instant microparticles.

***5.5. Solvent evaporation technique:***

The capacity of the continuous phase is insufficient to remove the entire amount of liquid dispersion solvent. The solvent evaporates from the surface of the dispersion and receives the cured microspheres.

***5.6. Spray drying technique:***

It involves dispersing the core layer into the liquefied contents of the coating and spraying the core coating mixture into the environment so that the coating solidifies by rapid evaporation in which the coating material is solubilized.

***5.7. Melt solidification technique:***

This method involves emulsifying the molten mass in an aqueous phase followed by cooling to solidify. Carriers used for this technique are lipids, waxes, polyethylene glycol, etc.

***5.8. Melt granulation technique:***

This is a method that agglomerates pharmaceutical powders using a fusible binder and does not use water or organic solvents for granulation.

## 7. EXCIPIENTS INCORPORATED IN VARIOUS FLOATING DOSAGE FORMS: [22]

**1. Effervescent substances**: E.g. citric acid, tartaric acid, sodium bicarbonate, Di-SGC (Disodium glycine carbonate), CG (Citroglycine).

**2. Release rate retarders:** Certain substances such as talc, calcium phosphate, magnesium stearate are used to slow down the release rate.

**3. Inert fatty materials:** E.g. Long-chain fatty alcohols, beeswax, fatty acids, geluccirs 39/01 and 43/01.

**4. Release rate Accelerators:** E.g. Mannitol, lactose, etc. • Hydrocolloids: E.g. Acacia, β-cyclodextrin, gelatin, alginates, pectin, HPMC, carbopol, etc.

**5.Buoyancy-increasing agents:** E.g. Ethyl cellulose and polypropylene powder (Accurel MP 1000)

## 8. ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM: [23]

• FDDS can remain in the stomach for several hours and thereby increase the gastric retention time of various drugs.

• Advantageous for drugs that are intended for local action in the stomach, e.g. antacids.

• FDDS formulations are useful in bowel movement and diarrhea to keep the drug floating in the stomach for a comparatively better response.

• By reducing dosing frequency, FDDS improves patient compliance.

• Treatment of gastrointestinal disorders such as gastroesophageal reflux.

• Despite the first-pass bioavailability effect, because plasma drug concentration is excluded.

• HBS/FDDS formulations can be useful for the administration of aspirin and other similar drugs, as these drugs are acidic and cause irritation of the stomach wall.

• Beneficial for drugs that are absorbed through the stomach, eg iron salts, antacids.

• Delivery of the drug to a specific location.

## 9. DISADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM: [23]

• Medicinal substances that are unstable in the acidic environment of the stomach are not suitable candidates for integration into systems.

• In these systems, the presence of food is usually required to prolong their gastric emptying.

• Not suitable for drugs that have a problem with stability or solubility in the GIT.

• Drugs that are subject to the first-pass effect of the liver and drugs that are significantly absorbed in the gastrointestinal tract they are only desirable candidates.

• The tendency to float depends on the hydration state of the dosage form. Intermittent administration of water is helpful to keep the tablets moving.

## 10. EVALUATION OF A FLOATING DRUG DELIVERY SYSTEM [24-27]

### *10.1. Bulk density:*

It is the ratio of the total weight of the powder (m) to the bulk volume (Vo) of the powder.

**Db=m/Vo**

### *10.2. Tapped Density:*

It is the ratio of the total weight of the powder (m) to the wiped volume (Vi) of the powder.

**Dt = m/Vi**

### *10.3. Compressibility Index:*

The flowability of a powder can be evaluated by evaluating the bulk density (ρo) and tapped density (ρt) of the powder and the rate at which it packed. Compressibility index calculated using

**Compressibility Index = 100 × [(VO – Vf)/VO]**

Where,

Vo = bulk density g/ml,

Vt = Tapped density g/ml.

### *10.4. Hausner ratio:*

It is evaluated by subtracting the tapped density and dividing by the bulk density using the following formula.

**Hausner's ratio = Tapped density / bulk weight**

### *10.5. Angle of repose:*

Frictional forces in loose powder or granules can be measured using the angle of deposit. This is the maximum possible angle between the surface of the pile of powder or granules and the horizontal plane. The granules are allowed to flow through a funnel attached to a stand at a fixed height (h). The angle of repose is then calculated by measuring the height and radius of the pile of granules formed.

**Tan θ = (h/r)**

θ= tan-1 (h/r)

θ = Angle of repose

h = height of the heap

r = radius of the heap

### *10.6. Tablet dimensions:*

Thickness and diameter were measured using a calibrated Vernier calliper. Three tablets of each formulation were randomly selected and the thickness was measured separately.

### *10.7. Hardness:*

Hardness shows the tablet's ability to withstand mechanical shocks during handling. Tablet hardness was evaluated using a Monsanto hardness tester. It was expressed in kg/cm2. Three tablets were randomly selected and the hardness of the tablets was decided.

### *10.8. Friability test:*

The friability of the tablets was evaluated using a Roche Friabilator. It was expressed as a percentage (%). Ten tablets were initially weighed (W) and transferred to the fribilator. The friabilator was run at 25 rpm for 4 min or run up to 100 rpm. The tablets were reweighed (Wo). The % friability was then calculated using the formula –

**%F = 100 (1-WO/W)**

A tablet friability of less than **1%** was considered desirable.

### *10.9. Tablet density:*

Tablet density was an excellent parameter for floating tablets. The tablet could float most efficiently when its density became much less than that of gastric fluid (1.004). Density was determined using the following formula.

**V = лr 2h**

**d = m/v**

Where,

v = tablet volume (cc)

r = radius of tablet (cm)

h = tablet crown thickness (g/cc)

m = mass of the tablet

### *10.10. Determining the buoyancy delay (Lag) time:*

Buoyancy delay is the time required for the tablet to reach the surface and float. The buoyancy of the tablets was studied at 37±0.5ºC in 900 ml of simulated gastric fluid. Buoyancy lag time was determined using a stopwatch and total floating time was observed visually.

### *10.11. Floating time:*

Floating time was measured using a USP dissolution apparatus-II at 50 rpm using 900 mL of 0.1N HCl and the temperature was set at 37±0.5 °C throughout the study. Floating time (floating time) is the time for which the tablet floats in the dissolution medium (including floating lag time, which is the time required for the tablet to rise to the surface), is measured by visual observation.

### *10.12. Swelling Index:*

A swelling study was performed for the floating extended-release tablets. Accurately weighed tablets were placed in a USP Dissolving Apparatus II containing 900 mL of 0.1N HCl maintained at 37±2°C and allowed to swell to constant weight. The tablets were removed, dried with filter paper and weight changes were determined. Experiments were performed in triplicate. The degree of swelling (swelling index) was then determined from the formula.

**Swelling index = (Ws-Wd)/Wd**

Where, Wd is the initial weight of the tablet and

Ws is the weight of the tablet at equilibrium swelling in the medium.

### *10.13. Drug content:*

Five tablets were randomly selected from the lot, weighed and crushed to a powder in a mortar. An accurately weighed amount of powdered tablets equivalent to 100 mg was taken into a standard flask and made up to the mark with 0.1 N HCL; the solution was filtered through 0.45 µm membrane paper. The analysis was carried out by the spectrophotometric method.

### *10.14. In vitro dissolution studies:*

The release rate of the floating tablets was determined using a USP Dissolution Tester II (scoop type). The dissolution test was performed using 900 ml of 0.1N HCl, at 37 ± 0.5 °C. A sample (5 mL) of the solution was withdrawn from the dissolution device every hour for 12 h and the samples were replaced with fresh dissolution medium. The samples were passed through Whatman filter paper and the absorbance of these solutions was measured.

## 11. APPLICATION OF FLOATING DRUG DELIVERY SYSTEM: [28]

**1. Increased Bioavailability:** The bioavailability of CR-GRDF riboflavin is substantially increased compared to administration of CR polymer formulations without GRDF.

**2. Sustained drug delivery:** Oral CR formulations showed GIT problems such as gastric residence time. HBS systems that can remain in the stomach for extended periods and have a bulk density of less than 1 and can float on the stomach contents can usually overcome these problems.

**3. Site-Specific Drug Delivery Systems:** Controlled, gradual delivery of drug to the stomach provides appropriate local therapeutic rates and reduces systemic drug exposure. Dosing frequency may be reduced by increased gastric availability from a locally controlled drug delivery system. E.g. Furosemide and Riboflavin.

**4. Improved absorption:**

Drugs with low bioavailability due to site-specific absorption from the upper GIT are possible candidates for development as floating drug delivery systems by optimizing their absorption.

**5. Minimal adverse reactions in the large intestine:**

Retention of drug in the stomach in HBS minimizes the amount of drug entering the colon. In this way, the unwanted activity of the drug in the area of the large intestine can be prevented.

**6. Reduced drug concentration fluctuation:**

Continuous drug administration after CR-GRDF administration produces blood drug concentrations in a narrower range compared to immediate-release types of dosage forms.

## 12. CONCLUSION:

The development of an effective gastroretentive dosage form for the transport of stomach-specific drugs is a current project. Accordingly, several strategies have been used to create advantageous gastroretention, of which the floating drug delivery system has emerged as a very promising approach. These systems offer the benefit of improved absorption of drugs that are absorbed from the upper stomach, increasing the bioavailability and controlled delivery of many drugs with new and vital therapeutic options. This leads to less frequent dosing and more favorable treatment efficacy. Good stability and better drug release compared to other conventional dosage forms make such a system more reliable. Drug absorption in the GIT is an extremely variable system, and prolonging the GI retention of the drug form increases the time of drug absorption. The floating drug delivery system ensures that it is a gastric retention technique. Although there is a wide range of complications that must be incurred in order to obtain prolonged GI retention, many companies are focusing on commercializing this approach. This is evidenced by the wide range of industrial products and patents issued in this area.

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