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A REVIEW ON FLOATING POLYMERS

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ABSTRACT :

The most popular method of administering medication is through an oral drug delivery mechanism. Numerous components are crucial to the creation of the medication delivery system. Among the parts of the drug delivery system that have changed over time are polymers. The macromolecule compound known as a polymer is made up of many monomer units bound together by bonds. For medications that are mostly absorbed in the upper parts of the gastrointestinal (GI) tract—the stomach, duodenum, and jejunum—drug delivery systems (FDDS) provide an extra benefit. The goal of producing this review on floating drug delivery systems (FDDS) was to concentrate on the many kinds of FDDS, the flotation principle and mechanism for achieving gastric retention, and the polymers utilized in FDDS.

Based on where they come from, the polymers utilized in the drug delivery system are classified as either synthetic or natural. Each variety of polymer possesses certain benefits and drawbacks. The various natural and synthetic polymer types utilized in the medication delivery system are discussed in this specific article. The article mentions a number of polymers, including sodium alginate, guar gum, chitosan, and xanthan gum. The synthetic polymers HPMC, Eudragit, and Ethylcellulose are mentioned.

Keywords: Floating polymers, Natural gums, HPMC, buoyancy, floating drug delivery systems.

INTRODUCTION :

Recently, oral controlled release medication delivery has of growing interest in the pharmaceutical industry to obtain better therapeutic benefits, namely patient compliance, simplicity in dosage administration, and formulation flexibility. Medications with brief half-lives and easy absorption from the gastrointestinal tract (GIT) are rapidly removed from the bloodstream. 1 For these medications to have an appropriate therapeutic effect, frequent administration is necessary. In an effort to get around this restriction, oral sustained-controlled release formulations have been developed. 5 Such a drug delivery would remain in the stomach after oral administration and release the medication in a regulated way, allowing the drug to be delivered constantly to the gastrointestinal tract's (GIT) 1 absorption sites. A longer stomach residence time is preferred for the drug delivery in order to create an oral controlled release dosage form that is site-specific. Extended stomach retention enhances the solubility of drugs that are less soluble in high pH environments, decreases drug waste, lengthens the time of drug release, and increases bioavailability. 2.

Additionally, a longer stomach gastric retention time (GRT) may be beneficial for local action in the upper portion of the small intestine, such as the management of peptic ulcers.

An technique called gastroretentive drug delivery aims to target site-specific medication release in the upper gastrointestinal tract (GIT) for either local or systemic effects by extending the stomach residence period. More advantages of this extended retention ability include: extending the duration of action for medications with short half-lives; increasing the bioavailability of medications; eliminating side effects; decreasing the frequency of dosages; preserving medications due to prior benefits; enhancing the solubility of medications that are less soluble in high pH environments; optimizing therapy; and, finally, facilitating patient compliance. 3, 4.
The limited absorption window in the upper gastrointestinal system of medications with low bioavailability can be addressed by floating drug delivery in a number of ways. By keeping the dosage form where it is absorbed, it increases the bioavailability. Here is a summary of them. 7

Sustained Drug Delivery

Because HBS systems can stay in the stomach for extended periods of time, they can release the medication gradually. These approaches can thereby solve the issue of the short gastric residence time that arises with an oral CR formulation. These systems can float on the contents of the stomach since their bulk density is less than 1. These systems are really big, and it's not allowed to pass via the pyloric aperture. Nicardipine hydrochloride sustained

release floating capsules were recently created and tested in vivo. The formulation was tested on rabbits and compared with MICARD capsules that are sold commercially. 4

2. Site-Specific Drug Delivery

This is why they are so effective for drugs like riboflavin and furosemide that are specifically absorbed in the stomach and the proximal part of the small intestine. From the stomach, Furosemide is mainly absorbed through the duodenum. It was reported that a monolithic floating dosage form with prolonged gastric residence time was developed and bioavailability increased..Thus, if misoprostol could be selectively given to the stomach slowly, it would have ensured optimal blood levels required for therapy while minimizing waste .18

3. Absorption Enhancement

Potential candidates for inclusion in floating drug delivery systems are drugs that have low bioavailability due to site-specific absorption in the upper gastrointestinal tract thereby maximizing their absorption/Laboratory data on optimization of formulation parameters were presented as well . The bioavailability of these dosage forms can be significantly raised up to 42.9% when compared to that achieved by commercially available LASIX tablets (33.4%) or enteric coated LASIX-long preparations (29.5%). 11

FLOATING DRUG DELIVERY SYSTEM :

Floating drug delivery systems (FDDS) are less dense than gastric fluids and can float in the stomach for considerable length of time without modifying the rate of gastric emptying. Meanwhile, as long as it is afloat on the contents of the stomach, slowly release the drug at desired rate from system. 9

After drug has been released, what remains of the system is emptied out of the stomach. This results in increased GRT and a better way to control plasma drug concentration oscillations. 6

However, besides minimal gastric content necessary to attain proper buoyancy retention principle some minimum level floating force (F) is also required to guarantee that dosage forms keep floating steadily on top of meal. To determine floating force kinetics, researchers have introduced an innovative apparatus for calculation of resultant weight. The apparatus works by continuously determining the amount equivalent to F; being a function of time that is needed to retain the object submerged. 9

If F is largely positive upward, then it will enable an object float better. In order to eliminate unexpected intra-gastric buoyancy capacity variances problems with stability and durability of produced floating forces have been taken into account during optimization process via this machine on FDDS. 18

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM

1. Single Unit Floating Dosage Systems
    a) Effervescent Systems (Gas-generating Systems)
    b) Non-effervescent Systems
2. Multiple Unit Floating Dosage Systems

a) Non-effervescent Systems
b) Effervescent Systems (Gas-generating Systems)
c) Hollow Microspheres
d) Raft Forming Systems. 17
e)

POLYMERS USED IN FLOATING DRUG DELIVERY SYSTEM :

Polymers used in the floating system are designed to target the drug delivery at specific areas of GIT i.e. stomach. Floating drug delivery uses both synthetic and natural polymers. In natural systems, Guar gum, Chitosan, xanthan gum, Gellan gum, Sodium alginate etc are used as natural polymers for the floating system. For synthetic polymers employed in the floating drug delivery include HPMC, Eudragit, ethyl cellulose among others.3

Natural Polymers

Natural gums which are plant extracts are hydrophilic carbohydrate polymer having high molecular weight (molecular mass). They are generally insoluble in organic solvents such as hydrocarbons and ethers. However some of them may be converted into water-soluble products or form swellable gels on contact with cold water. 6

Synthetic polymer has disadvantages over natural polymer.

It has advantages over other synthetic polymer that are:

- Biodegradable
- Biocompatible
- Non-toxic
- Economical (low cost)
- Environmental friendly
- Locally available sources. 10

1. Guar gum

Guar gum is a galactomannan polymer that occurs naturally. By hydrating and swelling in cold water, guar gum creates thick colloidal dispersions or sols. This gelation property slows down the release of drugs and is an elastic medium for extended release forms. In making floating drug delivery systems, disintegrant and polymers are used as guar gums in the pharmaceutical industry. 11

Properties of guar gum:

- It is soluble in water but insoluble in organic solvents.
- Strong hydrogen bond property.
- Excellent thickening, emulsion, film forming property.
- Ability to control rheology.

Benefits of guar gum in floating drug delivery system:

It has been shown that polymer swelling influences drug release patterns and amounts. Moreover, it was observed that during in vitro dissolution testing of drugs with guar gum formulation were not much affected by stirring speeds while dissolved profiles were unaffected to great extent . 17

Chitosan

Being non-toxic, biodegradable and biocompatible; it has favorable biological properties. Because it adheres to biological tissues well and inhibits bacterial adhesion on it, this bioadhesive polymer can be used for site-specific targeting. Chitosan is high molecular weight polycationic weak base with pka value of 6.2-7. On addition to acidic pH of 1.2 or neutral media it become buoyant in nature and provide control release 26. By increasing thickness of chitosan film release rate can be decreased .

Advantages of chitosan:

- It forms film that reduces effect of gastrointestinal transit time.
- Hallow microcapsule tend to float on gastric fluid for about 12hrs.
- Release rate of drug followed zero order kinetics . 18

3. Xanthan gum

Gum also has an excellent solubility and stability under acidic and alkaline conditions and in the presence of salts and resists common enzymes.

Advantages of Xanthan gum:

- It is used to increase or decrease rate of release of drug from formulation
- Soluble in water
- High viscosity at low concentration
- It has potential advantage of drug release at zero order kinetics. Some tablet containing xanthan gum and citric acid show buoyancy for more than 24hrs.19

Gellan gum

Gellan gum is a high molecular weight, extracellular, linear polysaccharide that is deacetylated and anionic. This gum offers excellent release of flavor, high gel strength, excellent stability, strong film forming, process flexibility, high clarity, and gel properties that are thermally reversible 26. Spingomonas elodea produces gellan gum as a byproduct of fermentation. 23

Benefits of gum called gellan

It offers outstanding stability, high gel strength, and taste release.
When positively charged ions are introduced, it gels.
It serves as a stabilizing or thickening agent in food products.
The primary component of sodium alginate is the sodium salt of alginic acid, a blend of polyuronic acids made up of leftovers from d'mannuronic and L guluronic acids. Investigations have been done on the molecular weight and block structure of sodium alginate samples.
Typical Characteristics: pH-7.2 (1% w/v aqueous solution) is the acidity/alkalinity.
Practically insoluble in 95% ethanol, ether, chloroform, and ethanol/water combinations with a minimum of 30% ethanol content. Additionally, practically insoluble in aqueous acidic solutions with a pH of less than three and other organic solvents. slowly soluble in water, creating a colloidal solution that is viscous.
Viscosity (dynamic): A range of commercially available grades of sodium alginate produce aqueous solutions with different viscosities. 21

Artificial Polymers

In the pharmaceutical industry, synthetic polymers are becoming more and more significant. Synthetic polymers are used as film coating agents, binder, etc. Polymers are massive macromolecules with a wide range of functional groups. Synthetic polymers come in two varieties: fully synthetic and semi-synthetic, which are modified versions of natural polymers. The following is a list of synthetic polymers used:

1. Methyl hydroxypropyl cellulose
2. Eudragit
3. Ethyl cellulose

The following are some drawbacks of synthetic polymers.
High expense, toxicity, and environmental contamination; both short-term and long-term negative effects,Low biocompatibility Local and inflammatory reaction.25

Methyl hydroxypropyl cellulose

The ethers of hydroxypropyl methylcellulose are a large family of odorless, white to off-white, water-soluble polymers that thicken, bind, hold water, create films, and lubricate. This semi-synthetic, inert, viscoelastic polymer is utilized in several commercial goods as an excipient and controlled-delivery ingredient in oral medications.
Function: bioadhesive material; coating agent; extended-release agent; emulsifying agent; emulsion stabilizer; film-forming agent; foaming agent; granulation aid; modified-release agent; mucoadhesive; release-modifying agent; solubilizing agent; stabilizing agent; suspending agent; sustained release agent; tablet binder; thickening agent; viscosity-increasing agent. 4
It is practically insoluble in hot water, chloroform, ether, and 95% ethanol; nevertheless, it is soluble in methanol and dichloromethane mixtures, water and alcohol mixtures, and ethanol and dichloromethane mixtures. Aqueous acetone solutions, dichloromethane and propan-2-ol combinations, and other organic solvents can dissolve some grades of HPMC. There are grades that can swell in ethanol. 22
Applications: HPMC is mainly utilized in oral goods as a matrix for prolonged release tablet formulations, as well as a tablet binder and film-coating agent. Wet or dry granulation techniques can use binder concentrations ranging from 2% to 5% w/w. In tablets and capsules, high viscosity grades can be utilized to delay the release of medication from a matrix at values of 10–80% w/w.12
Hypromellose is additionally utilized in liquid oral dosage forms at concentrations between 0.25 and 5.0% as a thickening and/or suspending agent. Film-forming solutions are used to film-coat tablets at concentrations of 2–20% w/w, depending on the viscosity grade. Higher viscosity grades are employed with organic solvents, whereas lower viscosity grades are used in aqueous film-coating solutions. 7

2 .The Eudragit

Names that are not proprietary: BP: Methacrylas polymerisatum et methylum methacrylicum 1:1 USPNF: Copolymer of methylic acid
Alternative terms: Methacrylates with polymers.
Category of function: Tablet diluent, tablet binder, and film formerSynopsis:
Methacrylic acid, methacrylic acid esters, and dimethylaminoethyl methacrylates are synthesized cationic and anionic polymers that come in different ratios to form polymethacrylates. Commercially, there are a number of varieties that can be purchased as an organic solution, an aqueous dispersion, or a dry powder. Most frequently, an acetone and propan-2-ol (60:40) mixture is utilized as the organic solvent. The powdered form of Eudragit S 100 is marketed under the name Enteric Coating Material, and the solvents used in its production are 95% acetone and alcohols, which dissolve in intestinal fluid at pH 7. 15

Methacrylic acid and methyl methacrylate undergo anionic copolymerization to produce Eudragit L and S, which are also known as methacrylic acid copolymers in the USPNF 23 monograph. In Eudragit L (Type A), the ratio of free carboxyl groups to the ester is roughly 1:1, while in Eudragit S (Type B), it is roughly 1:2. Both polymers are easily soluble in neutral to slightly alkaline environments (pH 6–7) and combine with alkalis to create salts, which results in film coatings that are soluble in intestinal fluid but resistant to gastric media. Eudragit L-100 and Eudragit S-100 are powders that are white and freely flow, containing a minimum of 95% dry polymers. 17

Applications:

Oral capsule and tablet formulations employ polymethacrylates (Eudragit) mainly as film-coating agents.

Different films with varying solubility characteristics can be generated, depending on the type of polymer utilized.Eudragit S 100 dissolves in 1N NaOH, acetone, and alcohols. On the other hand, because Eudragit L, S, and FS kinds are resistant to stomach fluid, they are employed as enteric coating agents.

3.Ethyl cellulose

For more than 50 years, ethocel (ethylcellulose polymers) has been extensively utilized in the pharmaceutical sector. Pharmaceutical formulations have chosen to use ethylcellulose for a variety of reasons, including moisture protection, extrusion granulation, micro-encapsulation of actives, extended release binder in inert matrix systems, solvent, and taste-masking of bitter actives. 11

Solubility: Ethylcellulose, a partially O ethylated cellulose with an ethoxy concentration (-OC2H5) ranging from 44 to 51%, is a water-insoluble cellulose ether. It swells when stomach juice is present, but it is insoluble at any pH that an organism experiences. After that, it allows for prolonged, customized drug release and is water permeable. It is hence appropriate for increased patient compliance. 8

Applications:

Since EC possesses significant elastic qualities, its usage in wet extrusion procedures is limited. However, it can be effectively used as a matrix former when combined with certain plasticizing agents. Water is adequate to make a wet granulation product when utilizing fine particle ethylcellulose (FPEC) and coarse particle ethylcellulose (CPEC) as diluents with high molecular weight polyethylene oxide (PEO), which was employed as a binder and extrusion aid. In order to add its flexibility to the wetted mass during extrusion and to the extrudate during spheronization, MCC was added to formulations.

The perfect polymer for creating goods with customized medication release is ethylene glycol. A limited quantity of ethylcellulose polymers are utilized in prolonged release solid dose formulations and have received approval for usage in general pharmaceutical applications. Ethocel 4 and Ethocel 10 are three different forms of Ethylcellulose that vary in terms of the length of the polymer chains, the rate of dissolution, and the viscosity of their solution. It is acceptable to make MR coatings with ethylcell 33 .
The force that causes items to float in a fluid medium like water is called buoyancy. The upward force that an object experiences when submerged in a liquid is known as the buoyant force.It is necessary to comprehend the variables influencing buoyancy in order to comprehend it. This section will cover the variables that impact buoyancy.

1. Fluid Density: The buoyant force is contingent upon the fluid density in which the object is submerged. The buoyant force increases with fluid density. For instance, because saltwater is denser than freshwater, an object will float in saltwater more readily than in freshwater.
2. Object Volume: The buoyant force is also influenced by the object's volume. The buoyant force of an object increases with its volume. For instance, due to its larger capacity, a large boat will float more easily than a small toy boat.
3. Weight of the Object: The buoyant force is negatively impacted by the object's weight.An object will feel less buoyant force the heavier it is. For instance, a large rock . 5

CONCLUSION :

For medications that are mostly absorbed in the upper regions of the gastrointestinal tract, the FDDS provide an extra benefit. The jejunum, duodenum, and stomach, or digestive system.
Drugs are released from dosage forms under controlled conditions thanks to the usage of polymers. Polymers are compounds that are employed in formulations for a variety of purposes, such as emulsifying, gelling, increasing viscosity, and retarding pace.
Consequently, understanding polymers is crucial in the realm of medication delivery. To produce more effective dose forms, however, a great deal of effort still needs to be done to overcome various physiological and pharmacological limitations.

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