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A REVIEW ON FLOATING DRUG DELIVERY SYSTEM

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ABSTRACT

Floating drug delivery systems improves the drug bioavailability and patient compliance by increasing the gastric residence time and controlling the drug release. In recent decades, there have been numerous attempts to overcome the barriers like short gastric residence times and unpredictable gastric emptying times. In this review, the technological and research advancements made in floating systems are discussed.

Oral drug delivery system is the most preferred route of administration for drug delivery. In the development of the drug delivery system many components play important role. Polymers are amongst those components which have evolved with the drug delivery system. Polymers are the macromolecule compound containing many monomer units joined to each other by bonds. The floating drug delivery systems (FDDS) become an additional advantage for drugs that are absorbed primarily in the upper segments of gastrointestinal (GI) tract, i.e., the stomach, duodenum and jejunum. The purpose of writing this review on floating drug delivery systems (FDDS) was to focus on the types of floating drug delivery systems, principal and mechanism of floatation to achieve gastric retention and polymers used in floating Drug delivery systems. Polymers used in the drug delivery system are of two types Natural and Synthetic based on their origin. Both types of the polymers have some advantages and disadvantages. This particular article gives information about the different types of natural and synthetic polymer used in the drug delivery system. Natural polymers like guar gum, chitosan, xanthan gum, Gellan gum and sodium alginate are mentioned in the article. Synthetic polymers mentioned are HPMC, Eudragit, and Ethyl cellulose.

Keywords: Floating drug delivery system, Dosages form, Technology for preparation

INTRODUCTION-

Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, low cost of therapy, patient compliance and flexibility in formulation etc. **[1]**. Oral sustained drug delivery formulations show some limitations connected with the gastric emptying time. Variable and too rapid gastrointestinal transit could result in incomplete drug release from the device into the absorption window leading to diminished efficacy of the administered dose **[2]**. It is evident from the recent research and patent literature that an increased interest in novel dosage forms that are retained in the stomach for a prolonged and predictable period of time exists today.

Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms **[3]**. One of such difficulties is the ability to confine the dosage form in the desired area of the gastrointestinal tract. To overcome this physiological problem, several drug delivery systems with prolonged gastric retention time have been investigated **[3]**. Attempts are being made to develop a controlled drug delivery system that can provide therapeutically effective plasma drug concentration levels for longer durations, thereby reducing the dosing frequency and minimizing fluctuations in plasma drug concentration at steady state by delivering drug in a controlled and reproducible manner. That are less soluble in high pH environment. Gastric retention to provide new therapeutic possibilities and substantial benefits from patients **[4]**. The controlled gastric retention of solid dosage forms may be achieved by the mechanism of mucous adhesion, sedimentation or by the administration of pharmacological agents that delaying gastric emptying. Based on these approaches, floating drug delivery systems seems to be the promising delivery systems for control release of drugs **[5]**.

- **TYPES OF FLOATING DRUG DELIVERY SYSTEMS- [6]**

Various approaches have been pursued to increase the retention of an oral dosage form in the stomach. These systems include:

A. Floating systems

B. Bio adhesive systems

C. Swelling and expanding systems

D. High density systems and

E. Modified systems

A. Floating drug delivery systems:

Floating drug delivery system is also called the hydrodynamically balanced system (HBS). Floating drug delivery systems

(FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time **[7]**. While the system is floating on the gastric contents; the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. This delivery system is further divided into in to no effervescent and effervescent (Gas-generating system).

Non-effervescent systems

The Non-effervescent FDDS is based on mechanism of swelling of polymer or bio adhesion to mucosal layer in GI tract. The most commonly used excipients in non-effervescent **[8]**. FDDS are gel forming or highly swellable cellulose type hydrocolloids, hydrophilic gums, polysaccharides and matrix forming materials such as polycarbonate, polyacrylate, polymethacrylate, polystyrene as well as bio adhesive polymers such as Chitosan and Carbopol.

The various types of this system are as:

I. Colloidal gel barrier systems / Single Layer Floating Tablets:

Hydrodynamically balanced system (HBS), which contains drugs with gel forming hydrocolloids, was first designed by Shethand Tossounian in 1975. These systems incorporate a high level(20-75%w/w) of one or more gel forming, highly swellable, cellulose type hydrocolloids, polysaccharides and matrix forming polymers **[9]**. On coming in contact with gastric fluid, the hydrocolloids in the system hydrate and form a colloidal gel barrier around its surface. This gel barrier controls the rate of fluid penetration into the device and consequent release of the drug

II. Bi-layer floating tablet:

A bi-layer tablet contains two-layer one immediate release layer which releases initial dose from system while another sustained release layer absorbs gastric fluid, forming an impermeable colloidal gel barrier on its surface, and maintain a bulk density of less than unity and thereby it remains buoyant in the stomach **[10]**.

III. Micro porous compartment systems

This technology is based on the encapsulation of a drug reservoir inside a micro porous compartment with apertures along its top and bottom walls. The peripheral walls of the drug reservoir compartment are completely sealed to prevent any direct contact of the gastric mucosal surface with the un dissolved drug **[11]**.

IV. Multi particulate system: Floating Beads / Alginate Beads

Multi-particulate drug delivery systems are mainly oral dosage forms consisting of a

multiplicity of small discrete units, each exhibiting some desired characteristics. In these systems, the dosage of the drug substances is divided on a plurality of subunit, typically consisting of thousands of spherical particles with diameter of 0.05-2.00mm. Multi-unit floating dosage forms were developed from freeze- dried calcium alginate. Spherical beads can be prepared by dropping sodium alginate solution into aqueous solution of calcium chloride, causing precipitation of calcium alginate leading to formation of porous system, **[12]** which can maintain a floating force for over 12 hours. When compared with solid beads, which gave a short residence time of 1 hour, and these floating beads gave a prolonged residence time of more than 5.5 hours. Thus, multi particulate dosage forms are pharmaceutical formulations in which the active substance is present as a number of small independent subunits. To deliver the recommended total dose, these subunits are filled into a sachet. Multiple unit type of floating pills and it's floating behavior.

V. Micro balloons / Hollow Microspheres:

There are various approaches in delivering substances to the target site in a controlled release fashion. One such approach is using polymeric micro balloons as carrier for drugs. Hollow microspheres a r e known a s t h e micro balloon. Micro balloons were floatable in vitro for 12 hrs., when immersed in aqueous media. Radio graphical studies proved that micro balloons orally administered to human were dispersed in the upper part of stomach and retained there for three hrs. against peristaltic movements **[13]**.

Effervescent systems:

A drug delivery system can be made to float in the stomach by incorporating a floating chamber, which may be filled with vacuum, air or inert gas

1. Volatile liquid containing systems

These have an inflatable chamber which contains a liquid cyclopentane, that gasifies at body temperature to cause the inflation of the chamber in the stomach. These systems are osmotically controlled floating systems containing a hollow deformable unit **[14]**. There are two chambers in the system first contains the drug and the second chamber contains the volatile liquid.

II. Gas generating systems

These buoyant delivery systems utilizes effervesced action between carbonate/bicarbonate salts and citric/tartaric acid to liberate CO_2, which gets entrapped in the jellified hydrocolloid layer of the system, thus decreasing its specific gravity and making it float over chime. A multiple unit type of floating pills, which generate CO_2, have also been developed. The system consists of a sustained release (SR) pill as seed, surrounded by double layers. The inner

layer is an effervescent layer containing sodium bicarbonate and tartaric acid. The outer layer is of a swell able membrane layer containing PVA, shellac etc. **[15]**. Another effervescent system consisting of a collapsible spring, which controls the release of drug from the polymer matrix, has also been developed. The common approach for preparing these systems involves resin beads loaded with bicarbonate and coated with ethyl cellulose. The coating which is insoluble but permeable, allows permeation of water. Thus, carbon-dioxide is released, causing the beads to float in the stomach.

- **List of Drugs Explored for Various Floating Dosage Forms**

1- **Microspheres Tablets /Pills: [16]**

Chlorpheniramine maleate, Aspirin, griseofulvin, Acetaminophen, p-nitroaniline, Acetylsalicylic acid, Ibuprofen, Amoxycillin trihydrate, Terfenadine, Ampicillin, Trialist, Atenolol, Theophylline, Captopril, Isosorbide di nitrate, Sotalol, Isosorbide mononitrate.

2-**Films:** P-Aminobenzoic acid, Cinnarizine, Piretanide, Prednisolone, Quinidine gluconate **[17]**.

3-**Granules:** Cinnarizine, Diclofenac sodium, Diltiazem, Indomethacin, Fluorouracil, Prednisolone, Isosorbide mononitrate, Isosorbide dinitrate **[18]**.

4-**Powders:** Riboflavin, phosphate, Sotalol, Theophylline.

5-**Capsules:** Verapamil HCl, Chlordiazepoxide**,** Diazepam**,** Furosemide**,** and benderizine Misoprostol**,** Propranolol HCl**,** Ursodeoxycholic acid**,** Nicardipine **[19]**.

- **ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEMS**

Floating dosage systems form important technological drug delivery systems with gastric retentive behavior and offer several advantages in drug delivery. These advantages include:

1. Floating dosage forms such as tablets or capsules will remains in the solution for prolonged time even at the alkaline pH of the intestine.

2. FDDS are advantageous for drugs meant for local action in the stomach eg: Antacids

3. FDDS dosage forms are advantageous in case of vigorous intestinal movement and in diarrhea to keep the drug in floating condition in stomach to get a relatively better response.

4. Acidic substance like aspirin causes irritation on the stomach wall when come in contact with it hence; HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs.

5. The FDDS are advantageous for drugs absorbed through the stomach eg: Ferrous salts, Antacids. Improved drug absorption, because of increased GRT and more time

spent by the dosage form at its absorption site.

6. Controlled delivery of drugs. Minimizing the mucosal irritation due to drugs, by drug releasing slowly at controlled rate.

7. Treatment of gastrointestinal disorders such as gastroesophageal reflux.

8. Ease of administration and better patient compliance.

9. Site-specific drug delivery.

- **DISADVANTAGES OF FLOATING DRUG DELIVERY SYSTEMS**

1. Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.

2. Drugs such as Nifedipine, which is well absorbed along the entire GI tract and which undergo significant first-pass metabolism, may not be suitable candidates for FDDS since the slow gastric emptying may lead to reduced systemic bioavailability. Also, there are limitations to the applicability of FDDS for drugs that are irritant to gastric mucosa.

3. One of the disadvantages of floating systems is that they require a sufficiently high level of fluids in the stomach, so that the drug dosages form float therein and work efficiently.

4. These systems also require the presence of food to delay their gastric emptying.

5. Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.

6. Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.

7. Gastric emptying of floating forms in supine subjects

may occur at random and becomes highly dependent on the diameter and size. Therefore, patients should not be dosed with floating forms just before going to bed.

- **APPLICATION OF FLOATING DRUG DELIEVERY SYSTEM: [20]**

1. Enhanced Bioavailability:

The bioavailability of riboflavin CR-GRDF is significantly enhanced in comparison to the administration of non-GRDF CR polymeric formulations. There are several different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act concomitantly to influence the magnitude of drug absorption.

2. Sustained drug delivery:

Oral CR formulations are encountered with problems such as gastric residence time in the GIT. These problems can be overcome with the HBS systems which can remain in the stomach for long periods and have a bulk density <1 as a result of which they can float on the gastric contents. These systems are relatively larger in size and

passing from the pyloric opening is prohibited.)

3. Site specific drug delivery systems:

These systems are particularly advantageous for drugs that are specifically absorbed from the stomach or the proximal part of the small intestine. The controlled, slow delivery of drug to the stomach provides sufficient local therapeutic levels and limits the systemic exposure to the drug. This reduces side effects that are caused by the drug in the blood circulation. In addition, the prolonged gastric availability from a site directed delivery system may also reduce the dosing frequency. Eg: Furosemide and Riboflavin.

4. Absorption enhancement:

Drugs which are having 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, there by 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 colon may be prevented. This Pharmacodynamic aspect provides the rationale for GRDF formulation for beta lactam antibiotics that are absorbed only from the small intestine, and whose presence in the colon leads to the development of microorganism's resistance.

6. Reduced fluctuations of drug concentration:

Continuous input of the drug following CRGRDF administration produces blood drug concentrations Within a narrower range compared to the immediate release dosage forms. Thus, 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.

➢ CONCLUSION

Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extends the time for drug absorption. Gastro-retentive floating drug delivery systems have emerged as an efficient means of enhancing the bioavailability and controlled delivery of many drugs. The increasing sophistication of delivery technology will ensure the development of increase number of gastroprotective drug delivery to optimize the delivery of molecules that exhibit absorption window, low bioavailability and extensive first pass metabolism. FDDS promises to be a potential approach for gastric retention. Although there are number of difficulties to be worked out to achieve prolonged gastric

retention, a large number of companies are focusing toward commercializing this technique.

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