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The Quick Review on Floating Drug Delivery System

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ABSTRACT

One major limitation of the oral controlled drug delivery system is that not all drug candidates are absorbed uniformly throughout the GIT. Some drugs are absorbed only in one segment of the GIT or are absorbed to varying degrees in different segments of the GIT, reducing their bioavailability. Floating drug delivery systems have a lower bulk density than gastric fluids and thus remain buoyant in the stomach for a longer period of time, releasing the drug slowly at the desired rate from the system and increasing the bioavailability of drugs with a narrow absorption window. This review covers, in addition to the background, formulation evaluationand recent developments.

Keywords: - Floating drug delivery, bioavailability, Hydrodynamically Balanced System, Microspheres.

INTRODUCTION

A drug delivery system's goal is to deliver a therapeutic amount of drug to the appropriate location in the body in order to achieve and then maintain desired drug concentrations. Becauseof the low cost of therapy and ease of administration, the oral route is increasingly used to deliver therapeutic agents, resulting in high levels of patient compliance. Oral drug delivery systems account for more than half of all drug delivery systems on the market [1,2,3].The ability to extend and control the emptying time of dosage forms that remain in the stomach for a longerperiod of time than conventional dosage forms is a valuable asset for dosage forms that remainin the stomach for a longer period of time than conventional dosage forms. . Several challengesarise when designing controlled release systems for improved absorption and bioavailability.

One of these challenges is the inability to limit the dosage form to a specific region of the gastrointestinal tract. In humans, the relatively short gastric emptying time (GET), which normally takes an average of 2-3 hours across the main absorption zone, i.e. the stomach and upper intestine, can result in incomplete drug release from the drug delivery system, resultingin reduced efficacy of the administered dose. Sustained-release dosage forms deliver the medication over a longer period of time. Controlled release indicates that the system can provide some therapeutic control [4].

Controlled release (modified release) dosage forms are becoming increasingly popular. These more sophisticated systems can be used to change the pharmacokinetic behaviour of drugs in order to provide a twice-daily or once-daily dose. This is accomplished by achieving zero-orderrelease from the dosage form[5]. Drug release from a dosage form that is independent of the amount of drug in the delivery system is referred to as zero-order release. Mucoadhesion, flotation, sedimentation, expansion, modified form systems, or simultaneous administration of pharmacological agents that slow gastric emptying can all be used to achieve controlled gastricretention of solid drug forms.

Oral controlled-release dosage forms should not be developed unless the recommended dosinginterval for the controlled-release dosage form is longer than that for the immediate-release dosage form or significant clinical benefits, such as reduced side effects, can be justified. Whencompared to immediate-release or conventional dosage forms, the controlled-release formulation has a lower Cmax. Researchers have discussed in vivo/in vitro evaluation of FDDS to assess the efficacy and use of such systems. Several recent examples have been reported that demonstrate the efficacy of such systems for drugs with bioavailability issues[6,7].

Basic Physiology

Anatomy

The stomach is well known for serving as a "depot" for sustained release (SR) dosage forms. The stomach is an organ that has the ability to store and mix food. The stomach is divided anatomically into three parts: the fundus (above the esophageal opening into the stomach), thebody (the central part), and the antrum (or pylorus).

The fundus and body of the Oblasti form the proximal stomach, which serves as a reservoir for ingested materials, while the distal region(antrum) is the main site of mixing movements that act as a pump to empty the stomach. Whenfasting, the stomach is a folded bag with a residual volume of 50 ml and a small amount of gastric juice(pH 1–3) and air [8,9].

Most drugs have insignificant gastric absorption under physiological conditions due to their small surface area (0.1-0.2 m^2) covered by a thick layer of mucous membrane, lack of villi onthe mucosal surface, and short residence time in the stomach.

Dynamics
The process of emptying the stomach occurs both when fasting and when satiated; however, the motility pattern in the two cases is significantly different. It is characterised by an interdigestive series of electrical events that cycle through the stomach and small intestine every 2-3 hours when fasting[7]. This activity is known as the interdigestive myoelectric cycle or migrating myoelectric complex (MMC), and it is frequently divided into four stages[8].

Phase I (basal phase) : Period of no contraction lasting from 40 to 60 minutes
Phase II (Preburst phase): Period of intermittent contraction and of similar duration. As the phase progresses, the intensity and frequency also increases gradually
Phase III (burst phase) : Period of regular contraction at the maximal frequency lastingfrom 4 to 6 minutes.
Phase IV: Period of transition between Phase III and Phase I and lasts from 0 to 5 minutes

A complete cycle of these four phases lasts 90-120 minutes on average. Phase III serves as acleaning phase, removing all indigestible materials from the stomach and small intestine. As a result, any CR gastrointestinal drug delivery system (GIDS) designed to remain fasted shouldbe able to withstand a phase III scavenging event if GI retention time is to be increased.

The contraction pattern shifts from fasting to satiation after consuming a mixed meal. This pattern, also known as the digestive motility pattern, is characterized by continuous contraction,as in phase II fasting.

Various approaches have been pursued over the last three decades to increase gastric retention of an oral dosage form, which are discussed below [9,10,11].

Hydrodynamically balanced system or floating drug delivery system
Because FDDS or Hydrodynamically Balanced System (HBS) has a lower bulk density than gastric fluids, it remains buoyant in the stomach for extended periods of time without affectingthe rate of gastric emptying. The drug is slowly released from the system at the desired rate while the system floats on the stomach contents.

The residual system is emptied from the stomach after the drug is released. This results in an increase in GRT and better control of fluctuations in plasma drug concentrations in some cases.

Swelling systems
When these products are swallowed, they swell to the point where they obstruct their exit fromthe stomach through the pylorus. As a result, the dosage form is retained in the stomach for anextended period of time. Because they tend to remain stuck at the pyloric sphincter, these systems are known as "plug-type systems." When the polymer comes into contact with gastricfluid, it absorbs water and swells.

High density formulation
Coated pellets with a density greater than that of stomach contents (1.004 g/cm^3) are used in high density formulations. These systems, which have a density of 3 g/cm^3, are kept in the gastric cavity.

This is accomplished by coating the drug with heavy inert material such as barium sulphate, zinc oxide, titanium dioxide, iron powder, and so on. The only significant disadvantage of suchsystems is that they are technically difficult to manufacture with a large amount of drug (>50%)and at the required density of 2.4-2.8 g/cm^3.

Modified Shape System
Shape-modified systems are non-disintegrating geometries moulded from silastic elastomer or extruded from polyethylene blends that extend the GRT depending on the drug delivery device's size, shape, and flexural modulus.

Bioadhesive System
These systems are used to pinpoint the location of a delivery device within the environment. drug absorption through the body's lumen and cavities process in a site-specific manner The method entails the use of bioadhesive polymer capable of adhering to the epithelial surface ofthe GI tract The proposed bioadhesion mechanism is the formation of hydrogen and electrostatic bonding at the mucus-polymer interface boundary.

Rapid hydration in contact with the muco-epithelial Surface appears to favour adhesion, especially if water can be applied, excluded at the reactive surfaces

Types of Floating Drug Delivery System

Based on the mechanism of buoyancy, two distinctly different technologies have been utilizedin development of FDDS that are:

1. Effervescent systems
2. Non- Effervescent System

Effervescent FDDS

Volatile liquid containing system: The GRT of a drug delivery system can be maintained by incorporating an inflatable chamber containing a liquid, such as ether or cyclopentane, which gasifies at body temperature to cause the chamber in the stomach to inflate. The device may also include a bioerodible plug made of polyvinyl alcohol, polyethylene, or other materials thatgradually dissolves, causing the inflatable chamber to release gas and collapse after a predetermined time, allowing the inflatable systems to be ejected spontaneously from the stomach[12].

Gas-Generating Systems: These buoyant delivery systems use effervescent reactions between carbonate/bicarbonate salts and citric/tartaric acid to liberate CO2, which is entrapped in the system's jellified hydrocolloid layer, lowering its specific gravity and causing it to float over gastric content[13].

Non-Effervescent FDDS:

Non-effervescent FDDS is based on the mechanism of the polymer swelling or bioadhesion tothe mucosal layer of GI tract. The commonly used excipients in non-effervescent FDDS are gel forming or highly swellable cellulose type hydrocolloids, hydrophilic gums, and matrix forming materials such as polycarbonate, polyacrylate, polymethacrylate, and bioadhesive polymers such as Chitosan and carbopol.

The various types of this system are as follows:

Single Layer Floating Tablets: They are made by intimately mixing the drug with a gel- forming hydrocolloid, which swells when it comes in contact with gastric fluid and maintains a bulk density of less than one. They are made by combining the drug with a low-density entericmaterials like HPMC.

Bi-layer Floating Tablets: A bi-layer tablet has two layers: one immediate release layer that releases the initial dose from the system and another sustained release layer that absorbs gastric fluid, forming an impermeable colloidal gel barrier on its surface and maintaining a bulk density less than unity, allowing it to float in the stomach.

Alginate Beads: By freeze dried calcium alginate, multi-unit floating dosage forms were created. Dropping sodium alginate solution into aqueous solution in calcium chloride causes calcium alginate to precipitate, resulting in the formation of porous system which can maintaina floating force for more than 12 hours. In comparison to solid beads, which had a one-hour residence time, these floating beads had a more than 5.5-hour residence time.

Hollow Microspheres: A novel emulsion-solvent diffusion method is used to create hollow microspheres (micro balloons) with drug loaded outer polymer shells. The drug's ethanol: dichloromethane solution and an enteric acrylic polymer are poured into an agitated aqueous PVA solution that is thermally controlled at 40 °C. The gas phase formed in a dispersed polymer droplet by evaporation of dichloromethane forms an internal cavity in a polymer microsphere containing drug. For more than 12 hours, the microballoons float continuously onthe surface of acidic dissolution media containing surfactant [14, 15].

Advantages of Fdds

1. Even at the alkaline pH of the intestine, floating dosage forms such as tablets or capsules will remain in the solution for extended periods of time.
2. FDDS are useful for drugs with local action in the stomach, such as antacids.
3. FDDS dosage forms are useful in cases of vigorous intestinal movement and diarrhoea because they keep the drug in a floating state in the stomach, resulting in a relatively better response.
4. Because acidic substances, such as aspirin, irritate the stomach wall when they come into contact with it, HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs.
5. FDDS are useful for drugs that are absorbed through the stomach, such as ferrous salts andantacids [16].

Disadvantage of Fdds

1. Floating systems are impractical for drugs with poor solubility or stability in gastric fluids.
2. Drugs that are well absorbed throughout the GI tract and undergo significant first-pass metabolism, such as nifedipine, may not be suitable candidates for FDDS because slow gastricemptying may result in reduced systemic

bioavailability. There are also limitations to the use of FDDS for drugs that are irritating to the gastric mucosa.

3. One disadvantage of floating systems is that they require a sufficient amount of fluid in the stomach in order for the drug dosages to float and work efficiently.
4. These systems also need food to delay gastric emptying.
5. Floating DDS with a single unit [17].

APPLICATION OF FLOATING DRUG DELIVERY SYSTEM

Sustained Drug Delivery

Continuous Drug Delivery Because the HBS system can remain in the stomach for extended periods of time, can release the drug over time time. The issue of short gastric residence time encountered with an oral controlled release As a result, formulation can be overcome using these systems. These systems have a bulk density of one as a result of which they can float on the gastric contents. Recently sustained release floating Nicardipine capsules were developed tested in vivo When compared to commercially available MICARD capsules rabbits. Plasma concentration time curves revealed a longer administration period (16 hours) in the in comparison to sustained release floating capsules with standard MICARD cap (8 hours)[18].

Site-specific drug delivery systems

These are especially beneficial for drugs that are specifically absorbed from the stomach or the proximal part of the small intestine, such as riboflavin, furosemide, and misoprostal. A bilayer floating capsule was developed for local delivery of misoprostol, a synthetic analogue of prostaglandin E used to protect against gastric ulcers caused by NSAID administration. The desired therapeutic level could be achieved and drug waste reduced by targeting slow delivery of misoprostol to the stomach[19].

Absorption Enhancement

Drugs with poor bioavailability due to site specific absorption from the upper part of the GIT are potential cardidates for formulation as floating drug delivery systems, thereby maximizing their absorption. When compared to commercially available LASIX tablets (33.4%) and enteric coated LASIX-long product (29.5%), floating dosage forms achieved a significant increase in bioavailability (42.9%)[20].

Constant Blood Level Maintenance

These systems make it simple to maintain a constant blood level while also making administration easier and improving patient compliance.

CONCLUSION

In the field of gastric retention. A noval controlled release drug delivery system was developed in order to increase the dosage form's gastric retention and control the release. Because these floating tablets provide a stable and sustained release dosage form. FDDS has the potential to be a viable approach for gastric retention. Despite the fact that there are a number of challenges to overcome in order to achieve prolonged gastric retention, a large number of companies are working to commercialise this technique.

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