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An Overview on Gastroretentive Drug Delivery System: Current Approaches and Advancements

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ABSTRACT

Gastroretentive Drug Delivery System (GRDDS) can elevate the controlled delivery of drugs that have an absorption window by continuously releasing the drug for a constant period of time before it extends its absorption site. This includes floating system, dilation and expanding system, muco - adhesive system, high density system and other postponed gastric emptying devices. The present article briefly about the formulation consideration for GRDDS, factors controlling gastric retention time, advantages, disadvantages and evaluation of GRDDS.

Key words: Gastroretentive drug delivery system; floating system; non floating system.

1. INTRODUCTION

Oral route of drug administration is the most commonly and convenient used method of drug delivery systems. 90% drugs are used to administration by this oral route. During the past two-decade, oral drug delivery systems have been developed to act as drug reservoirs from which the active substance can be released over a defined period of time at a premeditated and controlled rate.[1] Yet, this route has a several physiological problems. Including an unpredictable gastric emptying rate that varies from person to person, a brief gastrointestinal transit time (8-12h). These difficulties have convinced researchers to draw a drug delivery system which can stay in the stomach for prolonged and expected period. Tablets are most common type of solid dosage form and tablets are classified based upon the drug release pattern, i.e. immediate release and modified release pattern. Trial are being made to develop a drug delivery system which can provide therapeutically effective plasma drug concentration for a longer period, with compressing the dosing frequency and reduce fluctuation in plasma drug concentration at steady state by distribute the drug in a controlled and reproducible manner.[2]

1.1 Factors Affecting Gastric Retention Time of the Dosage Form

Many factors affect the gastric retention process, which vigorously change the release of damage and its absorption; it is desirable to develop a drug delivery system that extended gastric residence and a drug release profile separate of patient related variables. The factors that affect the gastric emptying and the gastric retention of the drugs include density of dosage form, size, shape, fasting, state etc. [3]

1.1.1 Density

Density of a dosage form also influences the gastric emptying rate and regulates the location of t a stomach. Dosage forms having a density lower than the gastric contents can drift to the surface density systems drill to bottom of the stomach.[4] A density of < 1.0 gm/ cm^3 is appropriate to property.

1.1.2 Size

Size should be greater than 7.5 mm in diameter.[5]

1.1.3 Shape of the dosage form

A tetra hedron shaped or rings shaped consist in the stomach for sustained period than the other of similar size.[5] Individual and multiple units of formulation showing a more predictable release profile and in consequential impairing the performance due to failure of the unit.[6]

1.1.4 Fed or unfed state

In a fasting condition, the GI motility is defined by the periods of strong motor activity that occur every 1.5-2 hrs. Food intake, viscosity and volume of food, caloric value and frequency of feeding have an intellectual effect on the gastric retention of dosage forms. The presence or absence of the food in the gastrointestinal tract (GIT) effects the gastric retention time (GRT) of the dosage form. The presence of a food in gastrointestinal tract (GIT) improves the gastric retention time (GRT) of the dosage form and so, the drugs absorption rises by aits allowing stay at an absorption site for a longer duration.[7] Over, increase in acidity and caloric value shows down gastric emptying time (GET) that can enhance the gastric retention of dosage forms.

1.1.5 Nature of meal

Feeding an indigestible polymers or fatty acids can change the motility arrangement so, stomach in a fed state decreasing gastric emptying rate and prolonging drug release.[8]

1.2 Advantages of GRDDS

There are various advantages of GRDDS such as

1. For drugs with comparatively short half-life, sustained release may result in a flip-flop pharmacokinetics and allow reducing frequency of dosing with improved patient compliance.[9]

2. Gastroretentive drug delivery can be provided prolong and sustain release of drugs from dosage forms which employ local therapy in the stomach and small intestine. Consequently, they are useful in the treatment of disorders connected to the stomach and small intestine.[10]

3. The constraint, slow delivery of drug form Gastroretentive dosage form provides sufficient local action at the diseased practically e.g., antacids, anti-ulcer drug, antibacterial for H. Pylori infection. This site-specific drug delivery reduces the undesirable side effects.[11]

4. Gastroretantive drug delivery system is suitable PH dependent absorption from stomach e.g. furosemide, captopril, diazepam, verapamil, cefpodoxime proxetil.[12]

5. Gastroretentive dosage forms reduce the fluctuation of drug concentrations and effects. Then, concentration adverse effects that are associated with peak concentrations can be presented. This characteristic is importance for drug with narrow therapeutic index.[11]

6. Gastroretentive drug delivery decreases the counter activity of the body most significant to higher drug efficiency.[13]

7. Drug movement is not observed and maintains the appropriate therapeutic plasma and tissue concentrations over prolonged time period. This avoids the sub-therapeutics as well as toxic concentration and minimizes the risk of failure of the medical treatment and undesirable side effects.[11]

8. The continuing mode of drug release from Gastroretentive doses form delegate extension of the time over a critical concentration and thus increase the pharmacological effects and improves the chemical effects.[14]

1.3 Limitation of GRDDS [15]

1. GRDDS is not acceptable for the drugs which are not enduring in acidic environment.

2. It is not appropriate for the drugs which are absorbed better in the inferior part of GIT.

3. Difficulty to attain the appropriate result and problem of the dose dumping.

4. Gastric retention is impact by the many factors like gastric motility, pH and existence of food. Thus, the dosage form should be able to hold the grinding and churning force of peristaltic wag of stomach.

5. Poor in vitro and in vivo correlation.

6. Cost of formulation is higher.

2. PROSPECTIVE DRUG CONTESTANT FOR GRDDS

1. Those Drugs which locally action in the stomach e.g. misroprostol, antacids etc.

2. Drugs that have small absorption window in gastrointestinal tract (GIT) e.g. L-DOPA, paraaminobenzoic acid, furosemide, riboflavin etc.
3. Drugs those are unsteady in the intestinal or colonic conditions e.g. captopril, ranitidine HCl, metronidazole.
4. Drugs that interfere usual colonic microbes e.g. antibiotics against Helicobacter pylori.
5. Drugs that express low solubility at high pH values e.g. diazepam, chlordiazepoxide, Verapamil hydrochloride.

3. DIFFERENT APPROACHES OF GDDS

Different approaches have been used to increase the retention time of oral dosage forms in the stomach. Some are formulated as single component or as multi-component dosage forms. GRDDS can be broadly categorized into non-floating system and floating.

3.1 Non-floating Drug Delivery System

These GDDS do not float in the stomach however they remain retained there by different mechanisms. Non-floating system is further divided into:

a. High density (sinking) drug delivery system
b. Bioadhsive or mucoadhesive system
c. Magnetic system
d. Un-foldable system

3.1.1 High Density (Sinking) Drug Delivery System

This approach involves formulation of coating drug on a heavy core or mixed with inert materials such as iron powder, barium sulfate, zinc oxide and titanium oxide so that the density of the formulations exceed the density of the normal gastric content. These materials rise the density up to 1.5-2.4 gm/cm. Based on the density, the GI transit time of pellets can be prolonged from an average of 5.8 to 25 hours. Although success of this system in human beings was not observed and no formulation has been promoted.[16]

3.1.2 Bioadhsive or Mucoadhesive System

The gastric retention time is stretched by adhering the bioadhesive system to gastric mucosa membrane. Original adhesive material derived from fimbria of bacteria or its synthetic equivalents have also been tried for the attachment to the gut. The adherence of the delivery system to the gastric wall rises residence time there by improving bioabailability. The chemicals used for the mucoadhesion purpose include carbopol, polycarbophil, carboxymethyl celluloselectin, chitosan, gliadin etc. Although gastric mucoadhesive power does not incline to be strong enough to resist the propulsion force of stomach wall. Other drawback of this type of system is incessant production of mucus and dilution of the gastric content.[17]

3.1.3 Magnetic System

This system involves introduction of a small magnet and another magnet on the abdomen over the position of the stomach. The outward magnet should be placed with a degree of accuracy which may decline the patient submission.[18]

3.1.4 Un-foldable System

Un-foldable drug delivery system explains and increases in size and it remains lodged at sphincter evading its exit from the stomach. It requires system to be small enough to be swallowed but disclose itself when it encounters gastric fluid.[19] And after certain duration its size should become small so that it will be easily banished. The un-foldable systems are composed of different biodegradable polymers.

3.2 Floating Drug Delivery System (FDDS)

In contrast to the high-density drug delivery system, floating systems have density less than the gastric content, so the system remain in the stomach for a prolonged period of time without affecting the gastric contents.[6] Floating drug delivery systems are also known as a low-density system. Floating drug delivery system can be divided into:

a. Effervescent system
b. Non-effervescent system
1. Hydrodynamically balanced system
2. Microbaloons or hollow microspheres
3. Alginate beads
4. Microporous compartment

3.2.1 Effervescent System

Effervescent System comprises of the swellable polymers like chitosan and effervescent substance like sodium bicarbonate, disodium glycine carbonate, cytroglycine, citric acid and tartaric acid. The ideal ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76:1. When the system encounters gastric fluid, it releases carbon dioxide instigating the formulation to float in the stomach.[20] This system can be classified as single unit matrix tablets or multiple unit pills. Single unit matrix tablet can be single or multilayer type.

3.2.2 Non-effervescent System

This system involves, gel forming or highly swellable cellulose type hydrocolloids, polysaccharides, and matrix forming

polymers such as polycarbonate, polyacrylate, polymethacrylate and polystyrene. Later to oral direction, this dosage form surges in contact with gastric fluids and achieves a bulk density of less than 1. The air captured within the swollen matrix imparts buoyancy to the dosage form. Swollen gel-like structure behaves as a reservoir and permits sustained release of drug through the gelatinous mass. Excellent example of this approach is super porous hydrogels.[21] The dosage form swells significantly to numerous times of original volume upon contact with gastric fluid. The gastric contraction thrusts the dosage form to the pylorus but due to larger size of the dosage form, the contractions slip over the surface of the system. Because of this the dosage form pushes back into the stomach.[22]

Non-effervescent system can be further classified as below:

1. Hydrodynamically Balanced System

The Hydrodynamically Balanced System (HBS) was designed by sheth and tossounian. HBS includes drug with gel-forming hydrocolloids meant to remain buoyant on the stomach content. This system comprises one or more gel forming cellulose type hydrocolloid like hydroxypropyl methyl cellulose, ethyl cellulose, hydroxypropyl cellulose, agar, carrageen or alginic acid. It also contains a matrix forming polymers such as polyacrylate, polycarbophil and polystyrene. When this system meets gastric fluid, the hydrocolloid in the system hydrates and this forms a colloid gel barrier around its surface.[23]

2. Microbaloons or Hollow Microspheres

This system is formed by emulsion-solvent diffusion method. Ethanol or dichloromethane solution (1:1) and an acrylic polymer are poured into an agitated aqueous solution of polyvinyl alcohol at 40°C. The gas phase generated in the isolated polymer droplet by the evaporation of dichloromethane form an internal cavity in the microsphere of the polymer with the drug.[24] The microballoons continuously over the surface of acidic dissolution media containing surfactant for more than 12 hours.

3. Alginate Beads

Calcium alginates have been used to forming multi-unit floating dosage forms. By dropping sodium alginate solution into the aqueous solution of calcium chloride spherical beads of about 2.5 mm diameter can be prepared. These beads are detached and air dried.[25] This results in the formation of a porous system which remains buoyant in the stomach.

4. Microporous Compartment

It involves drug reservoir encapsulated inside a micro porous compartment having pores along its top and bottom walls. The floatation chamber contained the entrapped air causes the delivery system to float over the gastric content. Gastric fluid enters through the aperture, dissolves the drug and transfers the dissolved drug in stomach and proximal part of the small intestine for absorption.[26]

4. CONCLUSION

Gastroretentive drug delivery systems have highly explored in recent years. GRDDS current approaches of enhancing bioavailability and controlled delivery of drugs that exhibit an absorption window. Gastroretentive drug delivery approaches comprised mainly of floating, bioadhesive, swelling, magnetic, and high systems. These systems not only provide controlled release of the drug but also present the drug in an absorbable form at the regions of optimal absorption. All these drug delivery systems have their own advantages and disadvantages. For designing a successful GRDDS, it is necessary to take into consideration the physiological events in the GIT, physicochemical properties of the drug, formulation strategies, and correct combination of drug and excipients.

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