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A Review on Gastro - Retentive Drug Delivery System

Sakshi Saxena 1, Archana Rautela 2, Reetu Papola 3, Praveen Kumar Ashok 4

Gyani Inder Singh Institute of Professional Studies, Dehradun, Uttarakhand

ABSTRACT

One of the cutting-edge strategies used in the pharmaceutical sector to produce superior therapeutic benefits, such as simple dosage administration, patient compliance, and formulation flexibility, is known as GRDDS. This evaluation is based on a GRDDS, an oral drug delivery system that releases drugs in a regulated manner over a predetermined period of time and functions as a drug reservoir. Gastro retentive medication delivery systems' primary goal is to increase a medicine's bioavailability. The basic anatomy and physiology of the gastrointestinal tract, the requirements for gastroretentive drugs, the need for gastro retention, factors affecting gastro retentive time, the benefits and drawbacks of GRDDS, and recent developments in GRDDS.

Introduction

A form of oral medication delivery system called gastroretentive drug delivery aims to extend the duration that pharmaceuticals spend in the stomach's gastric cavity in order to increase their bioavailability and therapeutic effectiveness. These drug delivery methods employ diverse strategies, such as floating, swelling, or mucoadhesion, to stay in the stomach for a longer period of time. Drugs with a limited window of absorption, low bioavailability, or quick metabolism in the body benefit most from gastroretentive drug delivery methods. Additionally, they can increase patient compliance and lessen the number of times that medications are administered. [1]

NEED FOR GRDDS

• Traditional oral administration is widely used in the pharmaceutical industry to treat diseases. However, conventional delivery has many drawbacks, the most significant of which is non-site specificity.

• Some drugs are only absorbed at specific sites. They require either a specific site release or a release in which the maximum amount of drug reaches the specific site.

• The pharmaceutical industry is now concentrating on such drugs that require site-specificity.

• Gastro-retentive delivery is one of the site-specific drug delivery methods for either the stomach or the intestine.

• It is obtained by holding the dosage form in the stomach. The drug is delivered to a specific site in the stomach, duodenum, or intestine in a controlled manner.

Drugs that are good candidates for gastroretentive drug delivery systems include:

• Drugs that act locally in the stomach, such as antacids and H. Pylori medications, such as Misoprostol.

• Amoxicillin and other drugs that are primarily absorbed in the stomach.

• Drugs that are poorly soluble at alkaline pH, such as furosemide, diazepam, and verapamil, among others.

• Drugs with a narrow absorption window, such as cyclosporine, methotrexate, levodopa, and others.

• Drugs that degrade in the intestine.

• Antibiotics that disrupt normal colonic microbes, such as those used to treat Helicobacter pylori.

• Ranitidine and Metformin HCl are also mentioned as potential drugs for gastroretentive drug delivery systems. [2,3]

Advantages of gastroretentive drug delivery systems include:

• Enhanced patient compliance by reducing dosing frequency.

• Improved bioavailability despite first-pass effect because fluctuations in plasma drug concentration are avoided, and continuous drug release maintains a desirable plasma drug concentration.

• Longer gastric retention time due to buoyancy.

• Improved absorption of drugs that dissolve only in the stomach.

• Prolonged drug release under controlled conditions.

• Drug delivery to the stomach can be site-specific.

• Better than single unit floating dosage forms because microspheres release the drug uniformly with no risk of dose dumping.

• Gastric irritation is avoided due to the sustained release effect.

• Short half-life drugs can have a better therapeutic effect.[4,5,6]

Some of the limitations are:

• Enhanced patient compliance by reducing dosing frequency.

• Improved bioavailability despite first-pass effect because fluctuations in plasma drug concentration are avoided, and continuous drug release maintains a desirable plasma drug concentration.

• Longer gastric retention time due to buoyancy.

• Improved absorption of drugs that dissolve only in the stomach.

• Prolonged drug release under controlled conditions.

• Drug delivery to the stomach can be site-specific.

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• Gastric irritation is avoided due to the sustained release effect.

• Short half-life drugs can have a better therapeutic effect. [7,8]

DIFFERENT APPROACHES OF THE GRDDS

1. Floating Drug Delivery System

Sir Davis first introduced the floating drug delivery system in 1968. The bulk density of the floating drug delivery system is lower than that of gastric fluid, so it stays in the stomach or targeted site for a longer period of time and releases the drug in a controlled manner. Over time, floating drug delivery has no effect on the rate of gastric emptying.

The drug is released in the stomach after the residual system's gastric emptying. As a result, improved bioavailability and control over plasma drug concentrations, as well as increased gastric retention time.[9]

Properties for FDDS

¬ Slow drug release

¬ Act as drug reservoir

¬ Bulk density should be lower than gastric fluid (Approximately 1.004 – 1.0 gm/cm).

¬ Must form a cohesive gel barrier

Effervescent System

The effervescent system matrix is composed of swellable polymers such as tartaric acid, HPMC, and chitosan, as well as effervescent compounds such as sodium bicarbonate, citric acid, and others. Effervescent preparations may improve absorption and gastric pH in the GI tract. The bioavailability of effervescent tablets is higher than that of regular tablets.

Effervescent dosage form (Tablet) containing sodium bicarbonate or citric acid produces carbon dioxide during stomach reaction, resulting in effervescent development. The effervescent reduces the density of the tablet dosage form, allowing it to float in the stomach's gastric fluid. To produce effervescent (carbon dioxide), sodium bicarbonate is mixed with citric acid in a 0:76:1 ratio. When effervescent is produced in gastric fluid, the drug is stored in a reservoir and released in a controlled or sustained manner. [10]

(a) Gas Generating System

The effervescent system includes the gas generation system. As a result, this system uses the effervescent reaction to liberate carbon dioxide by reacting sodium bicarbonate and citric acid. The drug entrapped in the hydrocolloid layer reduces its specific gravity and density, causing it to float over the gastric content after gas release, gas generation, or carbon dioxide production (effervescent).

(b) Volatile Liquid or Vacuum system

Recent approaches in gastro retentive drug delivery system include volatile liquid and vacuum systems. This system consists of an inflatable chamber filled with volatile oils like ether and cyclopentane, which gasify at body temperature. The drug is released after the volatile liquid. The inflatable chamber may also be filled with a bio erodible polymer plug made of polyvinyl alcohol, polyethylene, and other materials.

i) Non – Effervescent System

Matrix forming polymers such as polymethacrylate, polyacrylate, polystyrene, and highly swellable and gel forming substances such as polysaccharide and hydrocolloids are used in the preparation of non-effervescent systems. When a non-effervescent drug (dosage form tablet, capsule, pellets) is administered orally and comes into contact with gastric fluid present in the stomach, the pH ranges to 1 - 3 pH, the drug swells and becomes bulky, and its density decreases to less than 1.As a result, the gastric concentration of the stomach pushes the dosage form to the pylorus, but due to swelling, the pressure through it returns to the surface. As a result, the dosage form floats on the surface of the gastric fluid with slow drug release and high absorption.[11,12,13]

ii) Raft Forming

The raft forming system is primarily used to treat GERD (gastric esophageal reflux disease). When raft forming system comes into contact with gastric fluid, viscous cohesive gel is formed. As a result, the overall portion of the liquid gel swells and forms a continuous layer known as a raft on the surface of the gastric fluid. Raft forming system contains carbonate / bicarbonate, which causes dosage forms to become bulky and is responsible for releasing carbon dioxide, making the system less dense. The gel forming

agent in raft forming systems is sodium alginate, which converts to raft after reacting with gastric fluid and prevents reflux of gastric content into the esophagus.

2. Non – Floating Drug Delivery System

In non – floating drug delivery system the dosage form of gastro retentive drug delivery system dose not float in the stomach but stays remain in the stomach by different mechanism. The drug may settle down in stomach showing bioadhesive and mucoadhesive properties, in this system dosage form release drug in sustain manner it also releases it drug at targeted site it is also pH dependent drug delivery system it gets dissolve at a certain pH [14,15].

Factors which affect Gastric Retention Time of Dosage Form

- The gastric retention time (GRT) of the dosage form is controlled by several factors that affect their efficacy as a gastro retentive system.
    - Density: GRT is a function of dosage from buoyancy, which is density dependent.
    - Size: Dosage form units with a diameter greater than 9.5mm are said to have a higher GRT.
    - Dosage form shape: Tetrahedron and ring-shaped devices with flexural moduli of 48 and 22.5 kilo pounds per square inch (KSI) are said to have better GRT. When compared to other shapes, retention ranges from 90% to 100% after 24 hours.
    - Single or multiple unit formulation: Multiple unit formulations exhibit a more predictable release profile and insignificant impairment of performance due to unit failure, allow co-administration of units with different release profiles or containing incompatible substances, and provide a greater margin of safety against dosage form failure than single unit dosage forms.
    - Fed or unfed state: GI motility is characterized by periods of solid motor activity or the migrating myoelectric complex (MMC) that occur every 1.5 to 2 hours when fasting. The MMC clears the stomach of undigested material. If the timing of the formulation administration coincides with that of the MMC, the GRT of the unit should be very short. In the fed state, however, MMC is delayed and GRT is significantly longer.
    - Meal type: Feeding indigestible polymers or fatty acid salts can shift the stomach's motility pattern to a fed state, slowing gastric emptying and prolonging drug release.
- Age: The GRT of the elderly, particularly those over the age of 70, is significantly longer.
- Concomitant drug administration: Anticholinergic like Atropine and Propantheline, Opiates like Codeine and prokinetic agents like Metoclopramide and Cisapride.
- Biological factors: Diabetes and Crohn’s disease. [16,17]

CONCLUSION

Gastro retention drug delivery system is an excellent starting point for oral drug delivery systems because it has the potential to improve bioavailability, absorption, and other factors. GRDDS approaches improve drug bioavailability.

GRDDS can be used to control the solubility and absorption of oral administered dosage forms. This can increase the bioavailability of drugs with site-specific absorption.

Based on the various literature reviews, we conclude that GRDDS has a specific scope in the pharmaceutical field, and that the market for GRDDS products would be vast with increased patient compliance.

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