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RECENT ADVANCES IN CONTROLLED RELEASE GASTRO-RETENTIVE DRUG DELIVERY SYSTEMS: A COMPREHENSIVE REVIEW

Hari Krishna Mohan*[1], Niranjan Babu Mudduluru[2], Diwakar Surakani[3]

[1]Department of Pharmaceutics, Seven Hills College of Pharmacy, Tirupati, A.P., India
[2]Department of Pharmacognosy, Seven Hills College of Pharmacy, Tirupati, A.P., India
[3]Department of Pharmaceutics, Seven Hills College of Pharmacy, Tirupati, A.P., India

Corresponding Author
Hari Krishna Mohan
Associate Professor, Department of Pharmaceutics Seven Hills College of Pharmacy, Tirupati, A.P., India – 517561 Contact: 7730084513, Email: harikrishnam@shcptirupati.edu.in

ABSTRACT

The oral route is widely preferred for drug administration due to its simplicity, patient adherence, and formulation flexibility. However, this method faces challenges such as limited gastric residence time (GRT) for drugs absorbed in specific regions of the gastrointestinal tract (GIT) and for sustained drug delivery systems. Various strategies have been proposed to prolong the gastric retention of delivery systems in the upper GIT to overcome these limitations. Gastroretentive dosage forms (GRDFs) aim to achieve site-specific drug release in the upper GIT, thereby extending GRT. They enhance the bioavailability of drugs with narrow therapeutic windows and enable continuous, prolonged drug release, thereby increasing dosing intervals. This article aims to provide an overview of several gastroretentive methods developed to date. It discusses key factors influencing gastric retention to address the physiological challenges associated with achieving prolonged drug release in the stomach. Furthermore, the review evaluates criteria for gastroretentive drug delivery systems, summarizing various technologies including magnetic systems, high-density (sinking), floating, bio- or mucoadhesive, expandable, unfoldable, ultra-porous hydrogel, and other emerging approaches. This comprehensive study offers insights into the current landscape of gastroretentive drug delivery technologies, highlighting their potential in enhancing drug efficacy and patient outcomes.

KEYWORDS: Floating Delivery, Gastro retentive system, Gastric retention time, Gastric emptying time.

INTRODUCTION

Despite significant advancements in drug delivery, oral administration remains the primary method due to its cost-effectiveness and ease of use among patients1,2. Controlled-release drug delivery systems (CRDDS) ensure consistent and regulated drug release3,4. For oral CRDDS to be effective, drugs must be well absorbed throughout the gastrointestinal tract (GIT)5. While conventional oral dosage forms provide precise drug concentrations in the bloodstream, they often exhibit variability in plasma drug levels and lack control over drug release timing6[1].

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Gastro-retentive drug delivery systems (GRDDS) aim to target site-specific drug release in the upper GIT by prolonging gastric residence time7. Several methods are employed to retain drugs in the stomach. Floating systems use low-density components that generate gas to float on the gastric fluid8. Swelling systems involve dosage forms that expand in size to float in the gastric fluid, owing to their lower density compared to stomach contents8[2].

Bioadhesive systems adhere to the mucosal surface of the stomach, utilizing various mechanisms for adhesion. High-density systems remain in the distal stomach due to their mass exceeding that of gastric fluid. Superporous hydrogel systems swell upon water absorption through capillary wetting of porous materials. Raft-forming systems contain polymers that float on stomach contents and swell to form a gel layer. Expandable systems swell and unfold through diffusion processes9. These diverse approaches illustrate the efforts to enhance drug efficacy and patient compliance through innovative gastro-retentive technologies[3].

Anatomy and Physiology of the Stomach:

The stomach, located between the esophagus and the small intestine, represents the most expanded segment of the digestive tract. The pyloric sphincter regulates the opening from the stomach into the duodenum. Anatomically, the stomach consists of four main parts: the fundus, body, antrum, and pylorus.

Stomach Function:

The fundus constitutes the principal part of the stomach, with the body and antrum comprising the larger portion. The antrum grinds and filters food, while the fundus and body are involved in storage. The stomach's mucosa lacks gastric pits. Refer to Figure 1 for an illustration of stomach physiology.

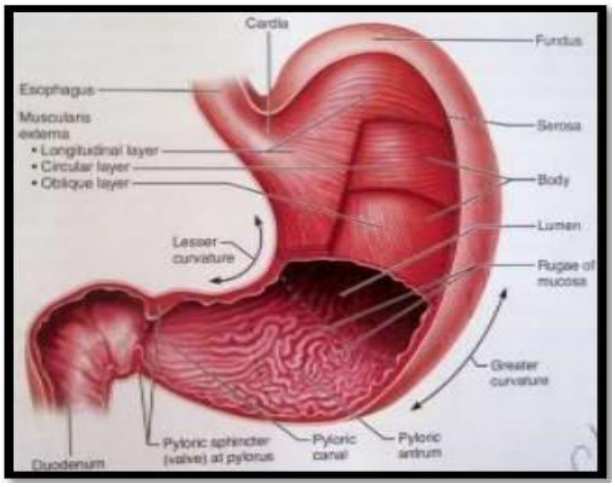

Fig no: 1 Physiology of stomach

Gastric Motility and Gastric Emptying Rate:

There are distinct patterns of gastrointestinal motility and secretion during the fed and fasting states. Refer to Figure 2 for an illustration of the phases of gastric motility and gastric emptying rate[4].

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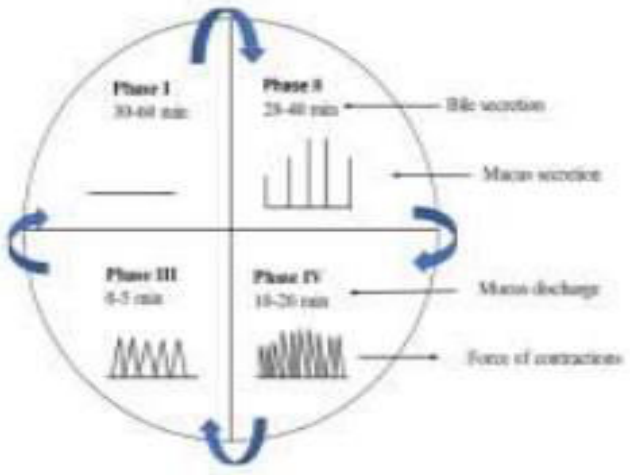

Fig no: 2 Phases of Gastric motility and gastric emptying rate

The feeding status significantly impacts the bioavailability of oral medications. The fasting state is characterized by an inter-digestive electrical event known as the inter-digestive myoelectric cycle or migrating motor complex (MMC), which consists of four stages. These stages include:

a) Phase I (basal phase), lasting 40–60 minutes with occasional contractions.

b) Phase II (pre-burst period), also lasting 40–60 minutes, marked by sporadic contractions.

c) Phase III (burst phase), lasting 4–6 minutes, featuring strong and frequent contractions that propel undigested food from the stomach to the intestine.

d) Phase IV, a brief period of 0–5 minutes occurring between cycles III and I.

Following the ingestion of a mixed meal, the motility pattern shifts from fed to fasting state. During this digestive motility pattern, contractions break down food particles to less than 1 mm in size, suspending them for passage through the pylorus. Delayed initiation of MMC in the fed state slows down gastric emptying rates.

Gastroretentive Techniques:

Several techniques are employed for achieving gastroretention. Figure 3 illustrates various gastroretentive techniques [5].

Fig No:3 Schematic Representation of different Gastro retentive Techniques

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EVALUATION OF FLOATING TABLETS

Pharmacopeial Tests:

Hardness

Tablet hardness was determined using a Monsanto Hardness Tester, applying diametric compression. Mechanical stability is typically achieved with a tablet hardness of 2-4 kg/cm².

Friability

Friability of the tablets was assessed using a Roche Friabilator. Initially, the weight (W0) of 20 tablets was recorded. The tablets were then dedusted in a drum for a specified duration (100 freefalls in a Roche Friabilator), and their final weight (W1) was measured. The percentage friability was calculated using the formula:

Percentage Friability = [(W0 - W1) / W0] * 100
weight loss of slightly more than 1% is considered acceptable.

Gellan Gum

Gellan gum acts as a crosslinking agent in the presence of Ca2+ ions, facilitating the formation of in-situ gels. This property makes it useful in pharmaceutical applications where gellan gum is employed as a crosslinker for in-situ gel formation.

Xanthan Gum

Xanthan gum finds applications in food, cosmetics, and both topical and oral pharmaceutical formulations due to its non-toxic and non-irritating characteristics. It is widely used for its beneficial properties in various industries.

Poly (ethylene oxide) (PEO)

High molecular weight PEO is recognized for its effectiveness in controlled-release dosage forms, mainly due to its ability to sustain the release of active pharmaceutical ingredients (APIs) by controlling the rate of polymer swelling and erosion. In aqueous environments, high molecular weight PEO can form dense polymeric networks, giving it viscoelastic properties when swollen. This characteristic makes it particularly suitable for enhancing the mechanical strength of matrix tablets that require high swellability and robustness[6].

Drug Content Uniformity Test

To determine drug content uniformity, twenty tablets were randomly selected, and their drug content percentage was analyzed [7]. The tablets were considered to pass the test if they contained between 85% and 115% (100±15%) of the specified amount of drug [8]. This test ensures consistency in the dosage form's drug content [9].

CONCLUSION

Enhanced bioavailability and controlled drug delivery are key advantages of gastroretentive drug delivery systems. These systems aim to prolong gastric retention, thereby improving the absorption of drugs that exhibit regional variability in absorption within the gastrointestinal

tract (GIT). As our understanding of GIT physiology grows, more sophisticated delivery systems are being developed to optimize the distribution of molecules. These advancements are particularly beneficial for drugs with long half-lives, low bioavailability, or extensive first-pass metabolism. Through our literature review, we have identified several potential benefits of gastroretentive drug delivery systems, especially for drugs with poor absorption profiles. These systems maximize therapeutic efficacy by extending the duration of gastric retention. Various methods have been devised to achieve this, including modified shape systems, high-density formulations, polymer bioadhesive systems, swelling and expanding systems, floating drug delivery systems (hydrodynamically balanced systems), and other devices that delay gastric emptying.

REFERENCES

[1]. Chawla, G., & Bansal, A. (2003). A means to address regional variability in intestinal drug absorption. Pharm tech, 27(2), 50-68.

[2]. Pandey, A., Kumar, G., Kothiyal, P., &Barshiliya, Y. (2012). A review on current approaches in gastro retentive drug delivery system. Asian Journal of Pharmacy and Medical Science. Vol, 2(4).

[3]. Chien, Y. W. (1990). Controlled and modulated-release drug delivery systems. Encyclopedia of pharmaceutical technology, 280, 313.

[4]. Ritschel, W. A. (1976). Handbook of basic pharmacokinetics.

[5]. Jain, N. K. (2002). Controlled novel drug delivery, Ist Eds.

[6]. Rouge, N., Allémann, E., Gex-Fabry, M.,Balant, L., Cole, E. T., Buri, P., &Doelker, E. (1998). Comparative pharmacokinetic study of a floating multiple-unit capsule, a high-density multiple-unit capsule and an immediaterelease tablet containing 25 mg atenolol. PharmaceuticaActaHelvetiae, 73(
2), 81-87.

[7]. Pund, A. U., Shendge, R. S., &Pote, A. K. 2020). Current approaches on gastroretentivedrug delivery systems. Journal of Drug Delivery and Therapeutics, 10(1), 139-146.

[8]. Pund, A. U., Shendge, R. S., &Pote, A. K. (2020). Current approaches on gastroretentive drug delivery systems. Journal of Drug Delivery and Therapeutics, 10(1), 139-146.

[9]. More, S., Gavali, K., Doke, O., &Kasgawade, P. (2018). Gastroretentive drug delivery system. Journal of drug delivery and therapeutics, 8(4), 24-35.