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## REVIEW ARTICLE

**BILAYER AND FLOATING-BIOADHESIVE TABLETS: INNOVATIVE APPROACH TO GASTRORETENSION****\*Pranjal Kumar Singh<sup>1</sup>, Sanjoo Kumar<sup>1</sup>, VK Shukla<sup>1</sup>, Guru Sharan<sup>1</sup>, Pankaj Verma<sup>1</sup>, Samiran Dey<sup>2</sup>**<sup>1</sup>Department of Pharmaceutics, IIMT College of Medical Sciences, Meerut, Uttar Pradesh, India<sup>2</sup>Department of Pharmacy, Innovative College of Pharmacy, Greater Noida, Uttar Pradesh, IndiaCorresponding author's Email- [Parthalwaysforu@gmail.com](mailto:Parthalwaysforu@gmail.com)**ABSTRACT**

A bilayer and floating-bioadhesive drug delivery system exhibiting a unique combination of floatation and bioadhesion to prolong residence in the stomach. Bilayer tablet is new era for the successful development of controlled release formulation along with various features to provide a way of successful drug delivery system. Controlled release (CR) dosage forms have been extensively used to improve therapy with several important drugs. Incorporation of the drug in a controlled release gastro-retentive dosage forms (CR-GRDF) which can remain in the gastric region for several hours would significantly prolong the gastric residence time of drugs and improve bioavailability, reduce drug waste, and enhance the solubility of drugs that are less soluble in high pH environment. Several approaches are currently utilized in the prolongation of the GRT, including floating drug delivery systems (FDDS), swelling and expanding systems, polymeric bioadhesive systems, high-density systems, modified-shape systems and other delayed gastric emptying devices. The floating and bioadhesive drug delivery systems are considerably easy and logical approach. An attempt has been made in this review article to introduce the society to the current technological developments in bilayer and floating- bioadhesive drug delivery system.

**Keywords:** Gastric retention time. mucoadhesive tablets. floating drug delivery systems. bilayer tablet**INTRODUCTION**

A gastroretentive dosage form will release the drug over an extended period in the stomach and upper gastrointestinal tract (GIT) thus enhancing the opportunity for absorption. Various approaches have been proposed to control the gastric residence of drug delivery systems in the upper part of the GIT including floating drug delivery systems (FDDS)<sup>1,2</sup> high density DDS, mucoadhesive systems<sup>3-5</sup>, swelling and expanding DDS<sup>6</sup>, modified shape systems<sup>7</sup> and other delayed gastric devices<sup>8</sup>. FDDS is a gastroretentive dosage form (GRDF), which can prolong the gastric residence time (GRT) to produce an acceptable drug bioavailability<sup>9,10</sup>. FDDS is suitable for drugs with an absorption window in the stomach or the upper small intestine<sup>11</sup>, for drugs which act locally in the stomach<sup>12</sup> and for drugs that are poorly soluble or unstable in the intestinal fluid.

Normal gastric residence times usually range between 5 minutes and 2 hours. Migrating myoelectric complex (MMC) is characterized by four phases: Phase I—Period of no contraction (40-60 minutes), phase II—Period of intermittent contractions (20-40 minutes), phase III—Period of regular contractions at the maximal frequency that travel distally also known as housekeeper wave. (10-20 minutes) and phase IV Period of transition between phase III and phase I (0-5 minutes)<sup>13</sup>.

**FLOATING DRUG DELIVERY SYSTEM:**

Floating systems or Hydrodynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the

stomach without affecting the gastric emptying rate for a prolonged period of time. 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<sup>14</sup>. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres<sup>15</sup>.

**CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM<sup>16</sup>:**

Floating drug delivery systems are classified depending on the use of two formulation variables: effervescent and non-effervescent systems.

**Effervescent Floating Dosage Forms:**

These are matrix types of systems prepared with the help of swellable polymers such as methylcellulose and chitosan and various effervescent compounds, eg, sodium bicarbonate, tartaric acid, and citric acid. They are formulated in such a way that when in contact with the acidic gastric contents, CO<sub>2</sub> is liberated and gas entrapped in swollen hydrocolloids which provides buoyancy to the dosage forms.

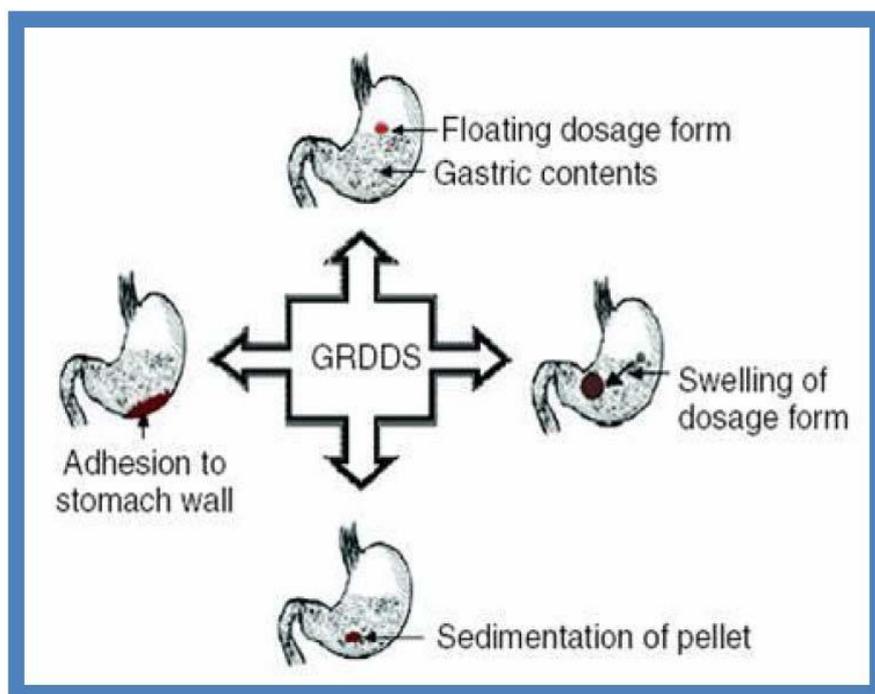


Figure 1: Different approaches of gastric retention

### Non-effervescent Floating Dosage Forms:

Non-effervescent floating dosage forms use a gel forming or swellable cellulose type hydrocolloids, polysaccharides, and matrix-forming polymers like polycarbonate, polyacrylate, polymethacrylate, and polystyrene. The formulation method includes a simple approach of thoroughly mixing the drug and the gel-forming hydrocolloid. After oral administration this dosage form swells in contact with gastric fluids and attains a bulk density of  $< 1$ . The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so formed swollen gel-like structure acts as a reservoir and allows sustained release of drug through the gelatinous mass.

### BIOADHESIVES SYSTEMS:

Another approach to increase gastric residence time of the dosage forms is to bind them to gastric mucosa or epithelial cell surfaces. Scientists studied a broad spectrum of polymers for their bioadhesive properties<sup>17</sup>. They concluded that anionic polymers have better binding capacity than neutral or cationic polymers. In case of bioadhesive systems, the mechanism of adhesion is thought to be the formation of electrostatic and hydrogen bonding at the mucus-polymer boundary. The adhesion is favored by rapid hydration. These bioadhesive systems do not seem to be a very feasible solution as this bond formation is prevented by the acidic environment and thick mucus present in the stomach<sup>18</sup>. High turnover of mucus adds to the difficulties in retaining a bioadhesive system at the site.

Mucoadhesive tablets, in general, have the potential to be used for controlled release drug delivery, but coupling of mucoadhesive properties to tablet has additional advantages, e.g. efficient absorption and enhanced bioavailability of the drugs due to a high surface to volume ratio, a much more intimate contact with the mucus layer. Mucoadhesive tablets can be tailored to adhere to any mucosal tissue including those found in stomach<sup>19</sup>, thus offering the possibilities of localized as well as systemic controlled release of drugs. The application of mucoadhesive tablets to the mucosal tissues of gastric epithelium is used for administration of drugs for localized action. Mucoadhesive tablets are widely used because they release the drug for prolong period, reduce frequency of drug administration and improve the patient compliance.

### ADVANTAGES OF GASTRORETENTION SYSTEM<sup>20, 21</sup>:

1. The gastroretentive systems are advantageous for drugs meant for local action in the stomach. e.g. antacids.

2. Acidic substances like aspirin cause irritation on the stomach wall when come in contact with it. Hence HBS formulation may be useful for the administration of aspirin and other similar drugs.
3. When there is a vigorous intestinal movement and a short transit time as might occur in certain type of diarrhea, poor absorption is expected. Under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.
4. The gastroretentive systems are advantageous for drugs absorbed through the stomach. e.g. Ferrous salts, antacids.

### DISADVANTAGES OF GASTRORETENTION SYSTEM<sup>22</sup>:

Such systems cannot be used in the case of drugs like aspirin and other nonsteroidal anti-inflammatory drugs like aspirin and other nonsteroidal anti-inflammatory drugs that induce gastric lesions or for drugs that are unstable in the acidic environment of stomach.

Many times it is difficult to incorporate a drug in such gastric retention systems. The retention of these systems depends on many factors such as gastric motility, pH, and presence of food. It is not easy to design and fabricate a system that can overcome all these difficulties.

### BILAYER AND FLOATING- BIOADHESIVE DRUG DELIVERY SYSTEMS:

Various approaches have been worked out to improve the retention of oral dosage form in the stomach, e.g. floating systems, swelling and expanding systems, bioadhesive systems, high density systems. Floating systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach for a

prolonged period. While the system floats over the gastric contents, the drug is released slowly at the desired rate, which results in increased gastro-retention time and reduces fluctuation in plasma drug concentration, Bioadhesive delivery systems are capable to adhere to mucous membrane that prevents their passage through the pylorus; as a result, the dosage form is retained in the stomach for a longer period of time.

In this article, an effervescent floating system and a bioadhesion system will be in combination. Floating dosage forms are meant to remain floating on the gastric fluid when the stomach is full after a meal. However, as the stomach empties and the tablet reaches the pylorus, the buoyancy of the dosage form may be reduced. It may be that the dosage form will then pass through the pylorus into the small intestine. Thus, the buoyancy of an FDDS in the stomach may be limited to only 3–4 h. Furthermore, floating systems do not always release the drug at the intended site. In a bioadhesive drug delivery system, it is quite likely that the system becomes dislodged from the stomach mucosa wall when the system is full and the semi-liquid contents are churning around due to the effect of peristalsis<sup>23</sup>. A floating-bioadhesive system would overcome these drawbacks of floating and bioadhesive systems and would have a significant effect on improving the therapeutic effect of the drug involved<sup>24</sup>. The purpose of this paper is to develop a novel sustained release tablet with a unique combination of bioadhesion and floatation to prolong the gastric residence time of active pharmaceutical ingredients (API), which is absorbed from the gastrointestinal tract while its solubility decreases with increasing pH over the physiological range.

Bilayer tablets have some key advantages compared to conventional monolayer tablets. For instance, such tablets are commonly used to avoid chemical incompatibilities of formulation components by physical separation. In addition, bilayer tablets have enabled the development of controlled delivery of active pharmaceutical ingredients with pre-determined release profiles by combining layers with various release patterns, or by combining slow-release with immediate-release layers.

#### **NEED OF BILAYER TABLETS**<sup>25, 26</sup>:

1. For the administration of fixed dose combinations of different APIs 13, prolong the drug product life cycle, buccal/ mucoadhesive delivery systems 15, fabricate novel drug delivery systems such as chewing device and floating tablets for gastro-retentive drug delivery.
2. Controlling the delivery rate of either single or two different active pharmaceutical ingredient(s)
3. To modify the total surface area available for API layer either by sandwiching with one or two inactive layers in order to achieve swellable/erodible barriers for modified release.

4. To separate incompatible Active pharmaceutical ingredient (APIs) from each other, to control the release of API from one layer by utilizing the functional property of the other layer (such as, osmotic property).

#### **ADVANTAGES OF THE BI-LAYER TABLET DOSAGE FORM:**

1. Bi-Layer execution with optional single-layer conversion kit.
2. Cost is lower compared to all other oral dosage form.
3. Greatest chemical and microbial stability over all oral dosage form.
4. Objectionable odor and bitter taste can be masked by coating technique.
5. Flexible Concept.
6. They are unit dosage form and offer the greatest capabilities of all oral dosage form for the greatest dose precision and the least content variability.
7. Easy to swallowing with least tendency for hang-up.
8. Suitable for large scale production.

#### **DISADVANTAGES OF BI-LAYER TABLET DOSAGE FORM ARE:**

1. Some drugs resist compression into dense compacts, owing to amorphous nature, low density character.
2. Bitter tasting drugs, drugs with an objectionable odor or drugs that are sensitive to oxygen may require encapsulation or coating.
3. Difficult to swallow in case of children and unconscious patients.
4. Drugs with poor wetting, slow dissolution properties, optimum absorption high in GIT may be difficult to formulate or manufacture as a tablet that will still provide adequate or full drug bioavailability.

#### **CONCLUSION:**

Bilayer and floating-bioadhesive dosage forms exhibit a unique combination of floatation and adhesion for prolonged residence in the stomach. Bi-layer tablets provide one of the important design approaches where incompatible drugs, with different indication, and same drug with different release rate (e.g. IR and ER) can be incorporated in a single unit. Many different types of presses are being used to produce bi-layer tablets, ranging from simple single-sided presses to highly sophisticated machines such as the Courtoy-R292F. The preparation of tablets in the form of bi-layers is used to provide systems for the administration of drugs, which are incompatible and to provide controlled release tablet preparations by providing surrounding or multiple swelling layers.

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