



## International Journal of Current Trends in Pharmaceutical Research

IJCTPR, 2013: Vol. 1(4): 273-276

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# Floating Drug Delivery System: A Novel Approach to Drug Delivery

Saurabh Sharma\*, Alpesh Yadav

Maharishi Arvind Institute of Pharmacy, Jaipur-302020, Rajasthan, India

Available Online 7 November 2013

**Abstract:** The concept behind the development of novel delivery system in certain drawback of conventional dosages form and to overcome the certain aspect related to physicochemical properties of drug molecule and related the formulation development. Several approaches are currently utilized in the prolongation of the gastric residence times, including floating drug delivery systems, swelling and expanding systems, polymeric bioadhesive systems, modified shape systems, high-density systems and other delayed gastric emptying devices. The management of illness through medication is entering a new era in which growing number of novel drug delivery systems are being employed and are available for therapeutic use. Oral sustained release gastro-retentive dosage forms (GRDFs) offer many advantages for drugs with absorption from upper parts of gastrointestinal tract and for those acting locally in the stomach, improving the bioavailability of the medication. Floating Drug Delivery Systems (FDDS) is one amongst the GRDFs used to achieve prolonged gastric residence time. Various types of techniques employed for development of this dosages form. Review focused on formulation aspect of effervescent floating drug delivery system with their evaluation techniques.

**Key words:** Floating Drug Delivery System, Gastroretentive Drug Delivery System, Swelling, Novel Delivery System.

### Introduction

Oral route is the most popular and convenient route for various drugs. Oral route generally consider an ideal drug delivery system that will possess two main properties:

1. It should be in a single dose for prolonging action.
2. It should be deliver the active drug directly to the target site.

These considerations have led to the development of a controlled or sustained delivery system. Sustained delivery describes a drug delivery system with delayed and/or prolonged release of drug. The main purpose for developing these systems is to enhance the safety of a product to extend its duration of action<sup>1</sup>. There are many disadvantages of these systems such as longer time to achieve therapeutic blood levels, more variation in bioavailability, enhanced first pass effect, and dose dumping. These systems are usually more expensive than the conventional systems. Since these products are made for the population at large, and not for an individual, they may result in higher or lower steady state drug level in different individuals. If the therapeutic range of drug is broad enough, it may not cause any problem. In spite of their disadvantages, research is continued in this area, as there is much scope to further improve currently available systems<sup>2,3</sup>. Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. One of such difficulties is the ability to confine the dosage form in the desired area of the gastrointestinal tract. To overcome this physiological problem, several drug delivery systems with prolonged gastric retention time have been investigated. Attempts are being made to develop a controlled drug delivery system that can provide therapeutically effective plasma drug concentration levels for longer durations, thereby reducing the dosing frequency and minimizing fluctuations in plasma drug concentration at steady state by delivering drug in a controlled and reproducible manner<sup>4,5</sup>.

### Advantages of FDDS

Floating dosage systems form important technological drug delivery systems with gastric retentive behavior and offer several advantages in drug delivery. These advantages include:

1. Ease of administration and better patient compliance.

2. Improved drug absorption, because of increased GRT and more time spent by the dosage form at its absorption site.
3. Controlled delivery of drugs.
4. Minimizing the mucosal irritation due to drugs, by drug releasing slowly at controlled rate.
5. Delivery of drugs for local action in the stomach.
6. Site-specific drug delivery.
7. Simple and conventional equipment for manufacture.
8. Treatment of gastrointestinal disorders such as gastro-esophageal reflux.
9. Ease of administration and better patient compliance<sup>6,7</sup>.

#### Disadvantages of FDDS

1. Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.
2. Gastric emptying of floating forms in supine subjects may occur at random and becomes highly dependent on the diameter and size. Therefore patients should not be dosed with floating forms just before going to bed.
3. Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.
4. High variability in gastric emptying time due to its all or non-emptying process<sup>8,9</sup>.

#### Drug Candidates Suitable for floating Drug Delivery

Drugs which have site-specific absorption in the stomach or upper parts of the small intestine (furosemide, riboflavine-5-phosphate), drugs required to exert local therapeutic action in the stomach (antacids, anti-H.pylori agents, misoprostol), drugs unstable in the lower part of Gastro-intestinal tract (captopril), drugs insoluble in intestinal fluids (quinidine, diazepam), drugs with variable bioavailability (sotalol HCl)<sup>10,11</sup>.

#### Factors Affecting Gastric Retention

The gastric retention time (GRT) of dosage form is controlled by several factors, that affect their efficacy as a gastroretentive system.

1. **Size:** Dosage form unit with a diameter of more than 7.5 mm are reported to have an increased GRT compared to those with a diameter of 9.9 mm.
2. **Shape of dosage form:** Tetrahedron and ring-shaped devices with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to have better GRT. 90% to 100% retention at 24 hours compared with other shapes.
3. **Density:** Density of the dosage form should be less than the gastric contents (1.004gm/ml).
4. **Fed or unfed state:** Under fasting conditions, the GI motility is characterized by periods of strong motor activity or the migrating myoelectric complex (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and, if the timing of administration of the formulation coincides with that of the MMC, the GRT of the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer.
5. **Caloric content:** GRT can be increased by four to 10 hours with a meal that is high in proteins and fats.
6. **Single or multiple unit formulation:** Multiple unit formulations show a more predictable due to failure of units, allow co-administration of units with different release profiles or containing incompatible substances and permit a larger margin of safety against dosage form failure compared with single unit dosage forms.
7. **Frequency of feed:** The G R T can increase by over 400 minutes when successive meals are given compared with a single meal due to the low frequency of MMC.
8. **Nature of meal:** Feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging drug release.
9. **Age:** Elderly people, especially those over 70, have a significantly longer GRT.
10. **Gender:** Mean ambulatory GRT in males (3.4 0.6 hours) is less compared with their age and race-matched female counterparts (4.6 1.2 hours), regardless of the weight, height and body surface.
11. **Posture:** GRT can vary between supine and upright ambulatory states of the patient.
12. **Concomitant drug administration:** Anticholinergics like Atropine and Propantheline, Opiates like Codeine and Prokinetic agents like Metoclopramide and Cisapride.
13. **Biological factors:** Diabetes and Crohn's disease. The resting volume of the stomach is 25 to 50 mL. Volume of liquids administered affects the gastric emptying time. When volume is large, the emptying is faster. Fluids taken at body temperature leave the stomach faster than colder or warmer fluids. Studies have revealed that gastric emptying of a dosage form in the fed state can also be influenced by its size. Small-size tablets leave the stomach during the digestive phase while the large-size tablets are emptied during the housekeeping waves. Timmermans and Andre studied the effect of size of floating and nonfloating dosage forms on gastric emptying and concluded that the floating units remained buoyant on gastric fluids. These

are less likely to be expelled from the stomach compared with the nonfloating units, which lie in the antrum region and are propelled by the peristaltic waves<sup>10,12-15</sup>.

### Formulation Aspects

The design of novel controlled release dosage forms should take into account three important criteria, viz., drug, delivery, and destination. Preformulation studies help in studying the physicochemical properties of drugs. These properties include pKa, pH, solubility, and incompatibility. The solubility of a compound affects the choice of a controlled drug delivery system. If the compound has very low solubility (i.e. less than 0.01 mg/ml), it is inherently sustained. A drug has to cross a variety of biological membranes in order to produce a therapeutic effect when it is administered to the gastrointestinal tract. Thus a partition coefficient of a drug is important in determining penetration of these membrane barriers by the drug. Compounds with very low partition coefficients will not easily penetrate these membranes, resulting in poor bioavailability. Acid-base hydrolysis and enzymatic degradation attack orally administered drugs. Compounds such as propantheline are unstable in small intestine. This results in decrease bioavailability when administered in controlled release delivery form. In case of oral drug delivery systems, the first destination is the gastrointestinal tract. From here the drug is absorbed and is taken to the site of action. Thus physiology of the gastrointestinal tract has a direct effect on the design of controlled release delivery systems. In addition, effects of disease conditions and co-administered drugs also affect the design<sup>16,17</sup>.

1. **Absorption window:** site of absorption also favours the development of this formulation.
2. **Shorter biological half-life:** Ranitidine hydrochloride having shorter biological half life's favours for the formulations.
3. **Solubility:** Drug having better solubility in acidic environment and also having specific site of absorption in the upper part of the small intestine. Drug having stability at gastric pH.
4. **Dose:** drugs that are used locally in stomach like Ranitidine hydrochloride, famotidine (H<sub>2</sub>- receptor antagonist). It is widely used/prescribed in duodenal ulcers, gastric ulcers, Zollinger-Ellison's syndrome, gastroesophageal reflux disease and erosive esophagitis.
5. **Others:** due to certain more reasons like: conventional dosage forms having poor patient compliance, increase the chance of missing dose of a drug due to shorter half life of drugs for which frequent administration is necessary<sup>18,19</sup>.

In conventional dosage forms it is very difficult to maintain plasma concentration time profile in steady state manner due to missing of dose. The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the CSS values fall or rise beyond the therapeutic range<sup>9,20</sup>.

### Conclusion

There are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing toward commercializing this technique. It is expected that the FDDS approach may be used for many potentially active agents with narrow absorption window, whose development has been halted due to lack of appropriate pharmaceutical FDDS technologies. Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extends the time for drug absorption. Gastro-retentive floating drug delivery systems have emerged as an efficient means of enhancing the bioavailability and controlled delivery of many drugs.

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