

MODIFIED DISSOLUTION APPARATUS FOR FLOATING DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

A gastro retentive drug delivery system with prolonged residence time in the stomach is of particular interest for some drugs. Floating drug delivery systems are of particular interest for drugs that are locally active and have narrow absorption window in stomach or upper small intestine, unstable in the intestinal or colonic environment, and exhibit low solubility at high pH values. The floating formulation is evaluated for various quality control tests. Among all the tests dissolution study is very important evaluation test for any kind of formulation. In vitro dissolution testing is generally carried out for quality control purposes and to establish an in vivo in vitro correlation. Traditional in vitro dissolution methods have been shown to be poor predictors of in vivo performance for floating dosage forms. The currently used in vitro dissolution methods do not mimic the conditions present in the stomach gastric like volume, gastric secretion, gastric emptying to the intestine and intestinal absorption. The present review focused on the several modified dissolution apparatus for the floating drug delivery system.

Keywords: FDDS, Modified Dissolution, Gastric Retention, In vitro-In vivo Correlation

INTRODUCTION

Gastro-retentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Gastro-retentive dosage forms can remain in the gastric region for long periods and hence significantly prolong the gastric retention time (GRT) of drugs.

Physiology of Stomach (Wilson and Washington, 1989; Desai, 1984; Davis et al., 1986)

Food is passed out from stomach to intestine by gastric motility. There is specific motility pattern in fasted condition called as Migrating Myoelectric Complex (MMC) *cycle*. MMC is subdivided into four phases. The whole MMC cycle is repeated every 2-3 hours.

Phase I is basal phase, which is silent period of 30-60 minutes and characterized by lack of secretory, electrical and contractile activity and there is no contractions.

Phase II is pre-burst phase, which exhibit intermittent action for 20-40 minutes. Some bile secretion started and contractile motions increases frequency. Mucus discharge is started during later part of phase II.

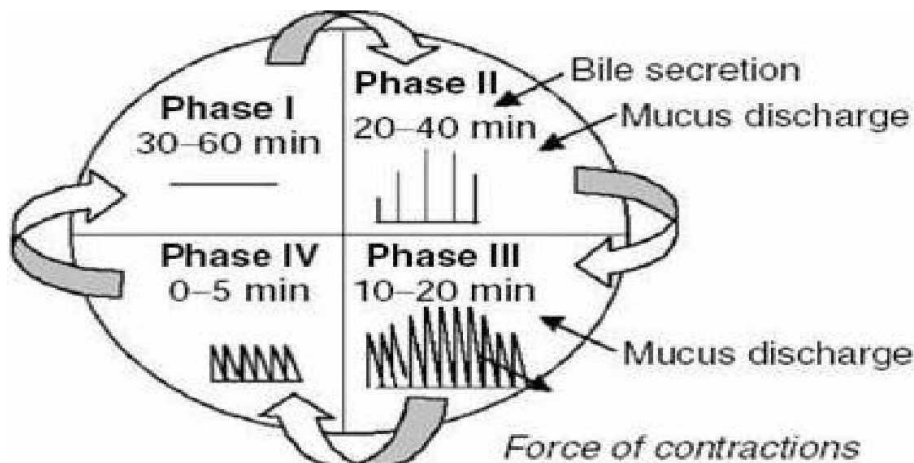


Figure 1: Migrating Myoelectric Complex (MMC) cycle

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Phase III is burst phase, which is characterized by intense and large regular contractions termed as “house keeper waves”. These waves sweep off undigested food by maximizing the pyloric opening and lasts for 10-20 minutes. Thus, this phase enables efficient evacuation of the stomach contents.

Phase IV is transition period up to 5 minute, between phase III & I.

Factors Affecting Gastric Retention Time of the Dosage Form (Patel, 2007; Oth et al., 1992; Timmermans et al., 1989; Gergogiannis et al., 1993; Cargill et al., 1988; Li et al., 2003; Mojaverian et al., 1988; Timmermans and Moes, 1994; Chawla et al., 2003)

1. **Density:** GRT is a function of dosage form buoyancy that is dependent on the density. The density of a dosage form also affects the gastric emptying rate and determines the location of the system in the stomach. Dosage forms having a density lower than the gastric contents can float to the surface, while high density systems sink to bottom of the stomach. A density of $< 1.0 \text{ gm/ cm}^3$ is required to exhibit floating property.

2. **Size & Shape of dosage form:** Shape and size of the dosage forms are important in designing indigestible single unit solid dosage forms. In most cases, the larger the dosage form the greater will be the gastric retention.

3. **Single or multiple unit formulation:** Multiple unit formulations show a more predictable release profile and insignificant impairing of performance 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.

4. **Fed or unfed state:** However, in the fed state, MMC is delayed and GRT is considerably longer.

5. **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.

6. **Caloric content:** GRT can be increased by 4 to 10 hours with a meal that is high in proteins and fats.

7. **Frequency of feed:** the GRT can increase by over 400 minutes, when successive meals are given compared with a single meal due to the low frequency of MMC.

8. **Others:** Same as factors affect the gastric emptying time.

Dissolution Apparatus (Burns et al., 1998; Gohel et al., 2004)

Floating tablets are retained in the stomach and are useful for drugs that are poorly soluble or unstable in intestinal fluids. The draw backs faced by the conventional USP (Apparatus 2) during the testing floating drug delivery systems are, the volume of dissolution medium (900 mL) is very high as compared to stomach content, adherence of dosage form on the shaft, Problems faced during sample collection and the major drawback is the test does not mimic the release of acid from stomach lining and gastric emptying through pylorus opening. The USP (Apparatus 4) also suffers from a set of drawbacks which include the inability in examining the floating ability as the dosage form remains stationary during the test in the cell and the usage of high flow rate (50 mL/min). Traditional in vitro methods suffers from drawbacks such as sticking of the tablet to the agitating device, unable to mimic the in vitro condition and these are poor predictors of in vivo performance of floating dosage forms. To overcome these disadvantages a more reliable method has been proposed.

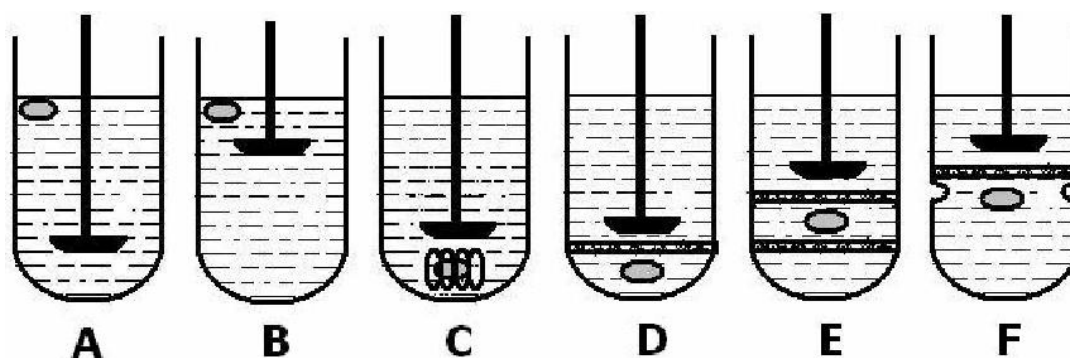


Figure 2: Modified Dissolution apparatus for FDDS

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A. In vitro dissolution test is generally done by using USP apparatus with paddle and GRDDS is placed normally as for other conventional tablets. But sometimes as the vessel is large and paddles are at bottom, there is much lesser paddle force acts on floating dosage form which generally floats on surface. As floating dosage form not rotates may not give proper result and also not reproducible results. Similar problem occur with swellable dosage form, as they are hydrogel may stick to surface of vessel or paddle and gives irreproducible results. In order to prevent such problems, various types of modification in dissolution assembly made are as follows.

B. To prevent sticking at vessel or paddle and to improve movement of dosage form, method suggested is to keep paddle at surface and not too deep inside dissolution medium.

C. Floating unit can be made fully submerged, by attaching some small, loose, non- reacting material, such as few turns of wire helix, around dosage form. However this method can inhibit three dimensional swelling of some dosage form and also affects drug release.

D. Other modification is to make floating unit fully submerged under ring or mesh assembly and paddle is just over ring that gives better force for movement of unit.

E. Other method suggests placing dosage form between 2 ring/meshes.

F. In previous methods unit have very small area, which can inhibit 3D swelling of swellable units, another method suggest the change in dissolution vessel that is indented at some above place from bottom and mesh is place on indented protrusions, this gives more area for dosage form.

G. Modified beaker Dissolution Apparatus

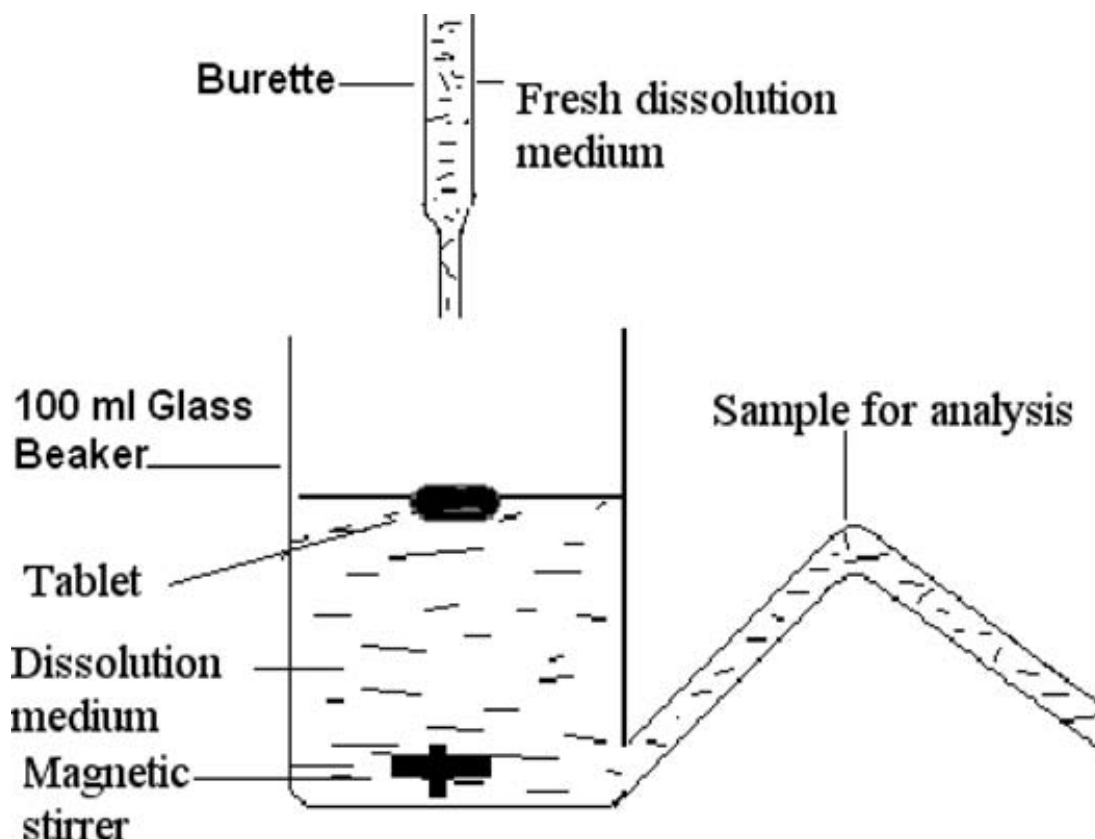


Figure 3: Schematic presentation of the Modified beaker Dissolution apparatus

The modified dissolution (Karande and Yeole, 2006; Hilton and Deasy, 1992; Dave *et al.*, 2004; Yang *et al.*, 1999; Costa, 2001) apparatus delivery system (I) is subjected to conditions similar to those experienced in the GI tract: gastric volume of 70 mL, gastric emptying and gastric secretion rates of 2 mL/min.

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H. Novel Multicompartment Dissolution Apparatus

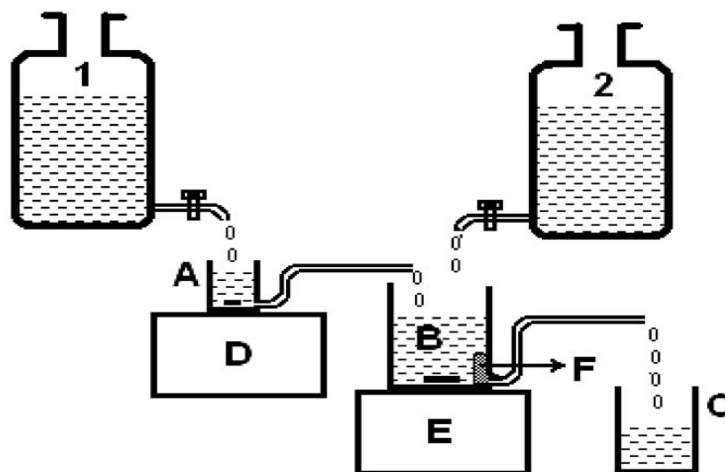


Figure 4: Novel Multicompartment Dissolution Apparatus

1 - Gastric Reservoir, 2 - Intestinal Reservoir, A - Gastric Compartment, B - Intestinal Compartment, C - Absorption Compartment, D and E - Magnetic stirrer with heating facility, F - filter

A novel multicompartment dissolution apparatus (Karande and Yeole, 2006) as shown schematically in Figure 4, comprises a series of three compartments: a gastric compartment, an intestinal compartment and an absorption compartment. A gastric compartment is designed by modification of a glass beaker (100-mL capacity) at the base by adding an S-shaped side arm such that the beaker can hold 70 mL of 0.1 N HCl. An intestinal compartment is designed by similar modification, from a glass beaker (500-mL capacity) such that it can hold 400 mL of intestinal fluid.

A volumetric cylinder is placed as an absorption compartment to collect fluid coming out of the intestinal compartment. A Whatman filter is placed at the bottom output of intestinal compartment to trap undissolved particles before the absorption compartment. Two glass vessels (5-liter capacity) are used as reservoirs using a valve to deliver fluid constantly at flow rate of 2 mL/min from each vessel. Magnetic stirrers with heating facility.

CONCLUSION

USP paddle and basket methods are not the proper methods for evaluation of floating drug delivery system. To avoid problems like floating and sticking to paddle or vessel associated with dissolution study of low density dosage forms, various modifications of USP dissolution apparatus have been tried for better in vivo correlation. However all of these modifications are limited in their ability to mimic in vivo condition. Recently, a novel in vitro dissolution method is required for FDDS.

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