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A Novel of Floating Tablet Delivery System as A Tool to Enhance Absorbtion of Drug: A Review

Iyan Sopyan[1,2], Amelia P. Pertiwi[2], M. N. Mu'tashim[2], Kiara P. Dhirgantara[2], Ega Megawati[2], Zara F. Herlian[2]

1. Pusat Studi Penghantaran dan Disposisi Obat, Faculty of Pharmacy, Universitas Padjadjaran Jl. Raya Bandung Sumedang KM 21 Jatinangor, 45363.
2. Undergraduate Program, Faculty of Pharmacy, Universitas Padjadjaran, Jl. Raya Bandung Sumedang KM 21 Jatinangor, 45363

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ABSTRACT

This assessment of a floating drug for a novel of new drug delivery system (NDDS) is written to elucidate FDDS based on existing literature. The most recent progresses of FDDS include the formulation and physiological variables that could affect gastric retention and formulations are discussed in detail. This review also summarizes method assessments for FDDS pharmaceutical dosage form and its classification. FDDS. FDDS is made to increase the absorption of the drug that is expected to dissolve in the stomach so that the drug enters the intestine in a dissolved state and the fraction of the absorbed drug increases. FDDS approach is the best way to deal with drugs with low solubility in the digestive tract.

Keywords: Floating Tablet, Evaluation, Gastric Retentive

1. Introduction

Unique of the target drug delivery systems is to reach a therapeutic concentration of medicine to the fix target and to ensure the optimum drug level. Drugs that absorbed in the gastrointestinal route easily will dissolve quickly from the systemic circulation. If an inadequate drug release prepartion of drug and the residence time at the upper gastrointestinal (a prominent place for the absorption of many drugs) very fast will make bioavailability become low. Thus, prolonged gastric maintenance is very important at the control of gastroprotection time to formulate a system of controlled release in the stomach for elongated periods of time and could be estimated (1). The anticipation depend on the state of the subject and design of formulations itself, the maintenance activity can last from a several minutes until hours (usually 12 hours). The scheme of the drug delivery system is controlled oral (DDS) is usually referred to to get bioavailability of the drug that is more probale and repaired (2). The typical drug has the development of oral drug-delivery systems that consist of the optimization of dosage form and GI physiology habits. (3). Floating drug delivery system (FDDs) is a gastro retentive pharmaceutical preparation that could delay the gastric residence time to get adequate bioavailability of a drug (4). The system is floating in the gastric fluid for a low substance density than the aqueous medium (5).

2. Methods

This review was made by looking at international journal 2000-2019, the journal taken was an international journal both indexed and not indexed scopus, with due regard to important aspects of the method of making FDDT, characterization and evaluation.

3. Discussion

3.1 Definition

Floating systems are low-density systems that have sufficient resistance to float on the stomach and stay afloat in the gastric without creat an effect on the gastric emptying rate for long period times. While the system floats on the gastric contents, the drug will be released slowly at the desired concentration of the system. thus, the residue will be cleared from the stomach. These results will conduct to GRT

*Corresponding author,
e-mail : i.sopyan@unpad.ac.id (I. Sopyan)

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elevation and be better control of fluxes in plasma drug concentrations. Even so, furthermore to the content of the stomach minimally required to enable the achievement of the right of retention of the principle of buoyancy, floating style minimal level (F) also required to give a reliable dosage form floats on the surface of foods (6). It also useful for proximal gastrointestinal (GI) tracts local drugs, for example, antibiotics for Helicobacter pylori on the manage for a peptic ulcer (7), and for drugs that difficult to dissolve or not stable in intestinal fluids (8).

3.2 Anatomy and physiology the stomach

Topographically, the stomach has five regions (Fig. 1): (1) the cardia and gastroesophageal (GE) junction, (2) the fundus, (3) the antrum, (4), the corpus and (5) the pylorus (9).

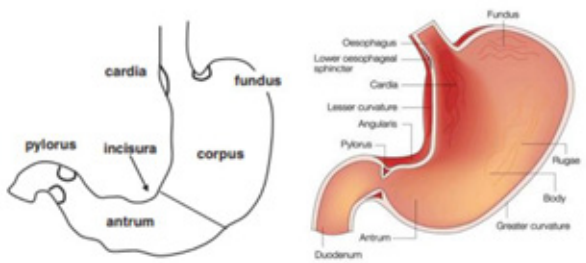

Figure 1. Structure of gastric (9)

In the stomach, part of the proximal made by fundus. The body acts as a reservoir for undigested materials and the antrum is the main site for mixing gestures and acts as a pump for gastric emptying by propelling actions (10). Gastric emptying occurs in both the fasting and fed states' time. During the fasting state, the inner digestive myoelectric cycle or migrating myoelectric cycle (MMC) occurs during 2-3 hours, which is further divided into four phases (11)

a. Stage 1 (Basic phase)
   Last from 30-60 minutes with infrequent contractions.
b. Stage 2 (Preburst phase)
   Last for 20-40 minutes with reccurent action potential and contractions.
c. Stage 3 (Burst phase)
   Last for 10-20 minutes which includes powerful and regular contractions for quick period.
d. Stage 4
   Last for 0-5 minutes and happens between stage 2 and 1 of 2 repeated cycles (Fig.2).

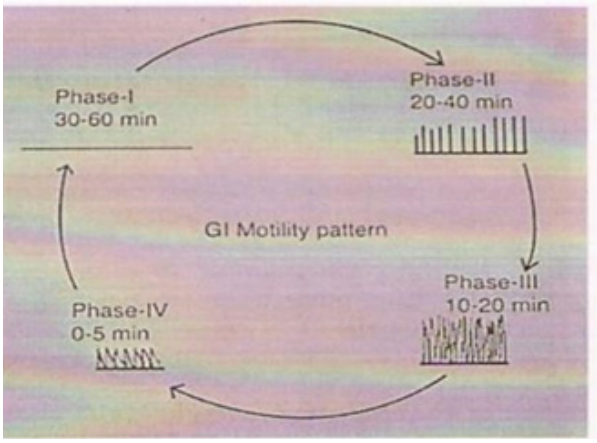

Figure 2. Gastrointestinal motility model (11)

The stomach has three layers of muscular: an inside circular layer, a mid longitudinal layer, and an outside but incomplete oblique layer. Motor functions in the stomach are separated by region. The fundus relaxes as fluids and solids enter the esophagus, a response known as accesible relaxation, and further as food enters the funds, a process is known as adaptive relaxation (12). This response permits the liquid to pool in the fundus bag while the solid components of the meal remain in the mainstream of flow to the pylorus. After the ingestion of a mixed meal, the pattern of contractions variation from fast to that of the fed state which is also termed as digestive motility pattern.

3.3 Advantages of floating drug delivery systems

1. Tablets or capsules in the floating tablet forms will remain in the liquid for a prolonged time even at the high pH of the intestine region.
2. In the stomach, Floating Drug Systems are advantageous for local action, ex: Antacids
3. Floating drugs delivery systems dosage forms are advantageous in the case essential of intestinal movement and in diarrhea to keep the drug in the floating state in the stomach to obtain a relatively better response.
4. Acidic stuffs like aspirin cause annoyance on the stomach barrier when coming in contact

with it hence; HBS/FDDS formulations may be valuable for the administration of aspirin and other similar drugs.

5. The Floating Drug Delivery Systems are advantageous for drugs absorbed by the stomach ex: Antacids and Ferrous salts (13).

3.4 Disadvantages of Floating Drug Delivery Systems

1. Floating systems are not viable for those drugs that have solubility or stability problems in gastric fluids.
2. Nifedipine, which is well absorbed along the entire GI tract and which undertake significant first-pass metabolism, may not be appropriate candidates for Floating Drug Delivery Systems since the slow gastric clearing may cause reduced systemic bioavailability (BA). Also, there are limitations to the applicability of FDDS for drugs that are irritant to the gastric mucosa.
3. Floating Drug Delivery Systems need a sufficiently high level of fluids in the stomach so that the drug dosages form float within and work efficiently.
4. These systems also involve the presence of food to delay their gastric emptying. (14).

3.5 Clasification of floating mechanism

Floating drug delivery systems (NDDS) are characterized based on two varieties of preparation variables: effervescent and Non-effervescent system (15,16) such as Fig. 3.

Non-effervescent System

The non-effervescent FDDS primarily based on the system of swelling of polymer or the adhesion to the mucosal layer in the gastrointestinal tract. Two of the most common excipient for non-effervescent FDDS are gel-forming or highly swellable cellulose type of hydrocolloid, polysaccharides and also matrix-forming material such as polycarbonate, polyacrylate, polystyrene, polymethacrylate as well as a bio-adhesive polymer such as chitosan and Carbopol (17).

Colloidal gel barrier system

Sheth and Tossounian first design the Hydrodynamically Balanced System (HBS) that contains drugs with gel-forming hydrocolloid, back in 1975. The system corporate a high level of gel-forming around 20-75% w/w, highly swellable, cellulose type hydrocolloids, polysaccharides and also matrix-forming polymers. When coming in contact with gastric fluid, these hydrocolloids in the system will hydrate and forming a colloidal gel barrier around the surface, these gel barriers control the rate of penetration of the fluid to the device and the release of the drug (18).

Bilayer floating tablet

Bilayer floating tablet contain of two-layer of immediate-release tablet that release the first dose of the system while the sustained release layer absorb the gastric fluid and form a colloidal gel barrier on the superficial, it preserves the bulk density to less than one and will remain floating in the stomach (18).

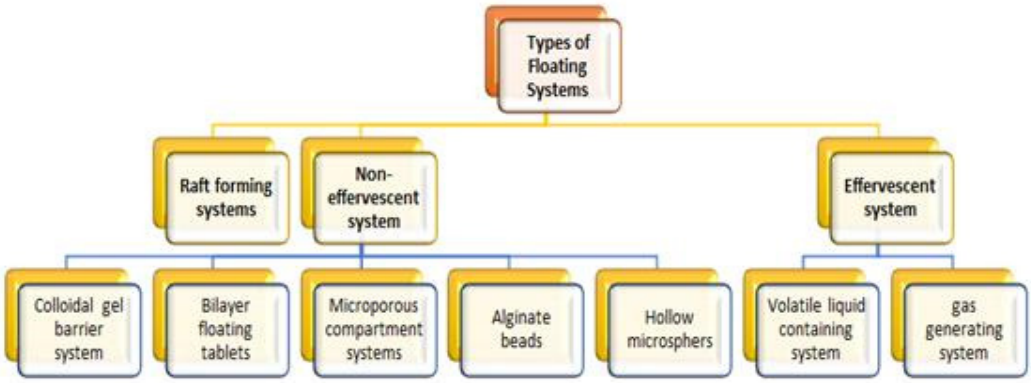

Figure 3. Classification of floating system (15)

Micro-porous compartment system

A Microporous section has pores placed on the top and bottom of the wall containing a packed medicine reservoir. The peripheral wall drug reservoir is completely sealed to seal the insoluble drug with the stomach surface. The entrapped in the room will be used to float the system on the stomach contents and into the fluid hole that will dissolve the drug to be absorbed in the intestine (20).

Alginate beads

Multi-unit floating dosage forms are made from freeze-dried calcium alginate. Round beads with 2.5 mm diameter can be equipped with dripping sodium alginate soluble to a calcium chloride solution, this process will result in precipitation of calcium alginate which can form a porous system that can reinforce the capacity to float for more than 12 hours and have some more time long (21).

Hollow microspheres

Hollow microspheres are micro balloons occupied with medication in the outer shell of the polymer and used by the emulsion solvent diffusion method. Ethanol solution: aqueous dichloromethane and enteric solution of a PVA of a turn temperature of 400^{o}C. The resulting gas phase is spread into polymer droplets by vaporization of dichloromethane forming an internal holow in a polymeric microsphere with the drug formed an internal cavity in the microsphere of polymer with the drug. The micro-balloons will float constantly over the surface of acidic dissolution media that hold a surfactant for more than 12 hours (*in vitro*) (22).

Effervescent system

In an effervescent system, preparation are designed to produce carbon dioxide gas. Among them are carbonates, generating gases, and other organic acids. The design of the formulation aims to decrease the density system that can be floating in the gastric fluid (23). The free CO_2 gas can mix rapidly in the tablet matrix in the case of single-layered tablets (24). The other way is trough combining a matrix that contains a part of liquid, where later from the fusion will produce gas that will evaporate at body temperature (25). This effervescent system can be categorized into two groups, gas producing system and volatile liquid containing the system.

Volatile liquid

The volatile liquid containing systems Inflatable chamber with a liquid can be incorporated which provides sustained gastric retention of the drug delivery system (26). Liquids in this system include cyclopentane, either that gasifies at body temperature which can lead to inflammation of the chamber in the stomach. They contain a hollow deformable unit which is osmotically controlled floating systems. The system is differed into two compartments the first section contains a drug and there is volatile liquid in the second compartment (27). Gas generating systems, It contains polymers that gasify at body temperatures effervescent compounds such as swellable polymers like methodical and polysaccharides tartaric acid, sodium bicarbonate, and citric acid. Resin beads loaded with bicarbonate and coated with ethylcellulose is the most common approach for the preparation of these systems. The ethylcellulose coating is permeable to water which releases CO_2 due to which it floats (28).

Raft forming systems

Raft forming systems consume a foundamental mechanism by forming a thick interconected gel in contact with gastric fluid, in which apiece part of the portion of the liquid forms a continuous layer called a raft. The formation of carbon dioxide gas can make this raft afloat. Also, carbon dioxide can prevent the discharge of gastric fluid into the esophagus (29). This system usually contains a gelling agent, a carbonate or a bicarbonate base to make a less dense system and can make it float in the gastric solution (30).

3.6 Factors affecting gastric retention time of the preparation

1. Density-should be lower than that of the gastric contents (1.004 g/ml)
2. Size- the diameter of more than 7.5 mm (31).
3. Incidence of feeding- GRT can rise by more than 400 min when consecutive foods are

dispense compared to a single meal due to low-frequency MMC.

4. Caloric content- can be increased by 4-10 with foods high in protein and fat.
5. Gender- average outpatient GRT in men (3.4 h) less than age and race matching with women (4.6 hours) regardless of height, body weight and surface (32).

3.7 Evaluation of floating tablet

Hardness

Tablets are sited between two anvils of hardness tester and the force (kg) is gradually increased to get a proper reading. Readings on a noticeable scale are recorded for the pressure, which is required to break the tablet (33).

Drug content

Five tablets for each group were taken and ground. The powder equal to 100 mg of the drug was weighed and moved to a beaker glass and then 0.01 N HCl was added and then shaken for 5 minutes and added 0.01 N HCl to make up to 100 ml and the solution was then produced for 15 min and filtered through the filter paper Whatman. Finally, a solution was diluted appropriately and then measured spectrophotometrically at 203 nanometers using UV-Visible spectrophotometer (Jasco V530 with 0.01N HCl blank). (34).

Determination of the drug content uniformity

The portion of drug content provides how much volume of drug is in the formulation. It should not exceed the limits obtained by standard monographs. The drug content is determined using HPLC, NIRS, HPTLC, Microtitrimetric method, and ICPAES (35).

Swelling index

The swelling behavior of the measuring unit is determined by the weight assignment. The tablet swelling index corresponds to the tablet site in the dissolution tool basket (type 1) using a pH 6.8 buffer dissolution medium at 37 ± 0.5ºC. The trials were conducted in triplicate for each time point, the swelling index was calculated using the following formula (36).

$$\text{Swelling index} = \frac{W_s - W_d}{W_d} \quad \text{.....Eq. 1}$$

Disintegration test

The time of tablet disintegration was carried out by using a therminate tablet disintegration test device (37).

Floating properties

The effect of formulation variables on the floating properties of gastric drug delivery systems is determined by using a continuous floating monitoring system and statistical trial design (38).

***In-vitro* dissolution studies**

The rate of release of Ondansetron Hydrochloride from floating tablets is determined using the USP Dissolution Testing Apparatus 2 (paddle method). The dissolution test was done using 900 ml 0.1 N HCl for 12 hours. The sample (5 ml) of the solution was quite from the dissolution apparatus every hour and the sample were changed with a new dissolution medium. The sample was filtered through a 0.45µm membrane filter and diluted to a concentration corresponding to 0.1 N HCl for 12 hours. The transmitan or absorbance of this solution was quantified at 310 nm (37).

4. Conclusion

Drugs that are removed quickly from the blood stream can be surmounted by Floating drug delivery system (FDDs) that can delay gastric retention of the dosage form and the enhance of drug absorption.

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