

REVIEW ARTICLE

Floating Drug Delivery System: An OutlookLalmalsawmi Renthlei¹, Manjima Dewan¹, Nabin Thapa Magar², Sushil Regmi², Himal Barakoti^{1,2*}¹Faculty of Pharmaceutical Science, Assam Down Town University, Guwahati, Assam, India, ²Department of Pharmacy, College of Medical and Allied Sciences, Purbanchal University, Gothgaun, Morang, Nepal**Received: 10 November 2019; Revised: 15 December 2019; Accepted: 20 January 2020****ABSTRACT**

Floating drug delivery approach uses low-density systems that have sufficient buoyancy to flow over the gastric contents and remains buoyant in the stomach without affecting the stomachic emptying rate for a chronic period of time. This result is increased gastric retention time and better control of the fluctuations in plasma drug concentration with a low risk of toxicity. Drugs, which are locally active in the stomach, drugs having narrow absorption window and unstable in the intestine, and colonic environment, are the potential drug candidates. The approach not only improves drug absorption but also minimizes the mucosal irritation of drugs. As the approach requires a high fluid level in the stomach to float and work efficiently, it makes the approach limited up to some extent. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films, and hollow microspheres and few formulations have been commercialized in the market at the present time. This review gives an overview of the approach of floating drug delivery at present with sequential demystification thus enabling a greater understanding of their role in medicine and drug delivery.

Keywords: Drug delivery, floating, gastric residence**INTRODUCTION**

Oral drug delivery system is the most common and prominent method for administration of drugs compared to the other delivery system. It has subsequent advantages of ease of administration thus generating better patient compliance.^[1,2] The therapeutic effectiveness depends on factors as gastric emptying time, gastric pH, drug release from the dosage form, extent of absorption, etc. The approach of drug delivery also plays an important role in the drug-releasing capability in the systemic circulation.^[3,4] It is widely acknowledged that the extent of GI drug absorption is associated with the time content of drug with the small intestinal mucosa.

Oral drug delivery system, although being the most prominent method, it also has demerits for certain peculiar drugs which have to be absorbed in the upper gastrointestinal (GI) part. This leads to a narrow absorption window and thus short absorption phase for a drug is achieved.^[5] This decrease in the absorption phase can further lead to decrease bioavailability of the drug in the system. Conventional oral drug delivery systems may also have a problem on the dissolution and diffusion efficiency of the drug to release it in the GI tract (GIT) in a controlled manner.^[6] This may occur as conventional oral delivery cannot localize the drug at the required site for a period of time. Thus, the conventional oral drug delivery system has some drawbacks relating to the bioavailability of the drug, rate of drug release, and retention duration in the GIT.^[7] To overcome these drawbacks, controlled-release drug delivery system is employed to get the better therapeutic activity of the drug by releasing

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at specified intervals of time and retaining the drugs in the GIT.^[8-10] Various approaches with a notable emphasis on the floating drug delivery system (FDDS) are extensively considered to produce gastro retentive drug delivery system and overcome the demerits of conventional oral drug delivery as given in Figure 1.^[11]

FDDS or dynamically controlled system is the low-density system which has sufficient buoyancy to float over the gastric content and remains buoyant in the stomach without affecting the stomachal evacuation rate for extended period of time. This results in increased gastric retention time and better control of the fluctuation in plasma drug concentration.^[12,13] Many buoyant systems can be developed based on granules, powders, capsules, tablet, laminated films, and hollow microspheres. FDDS is useful for drug which may act locally on stomach such as antacids, antibiotics, and drugs that are absorbed in stomach such as albuterol, chlordiazepoxide, and drug rapidly absorbed from GIT such as amoxicillin, and drugs that have narrow absorption window, for example, ofloxacin, levodopa, and theophylline, drugs having low bioavailability, for example, ranitidine, misoprostol, and drugs which are poorly soluble in intestinal pH, for example, diazepam

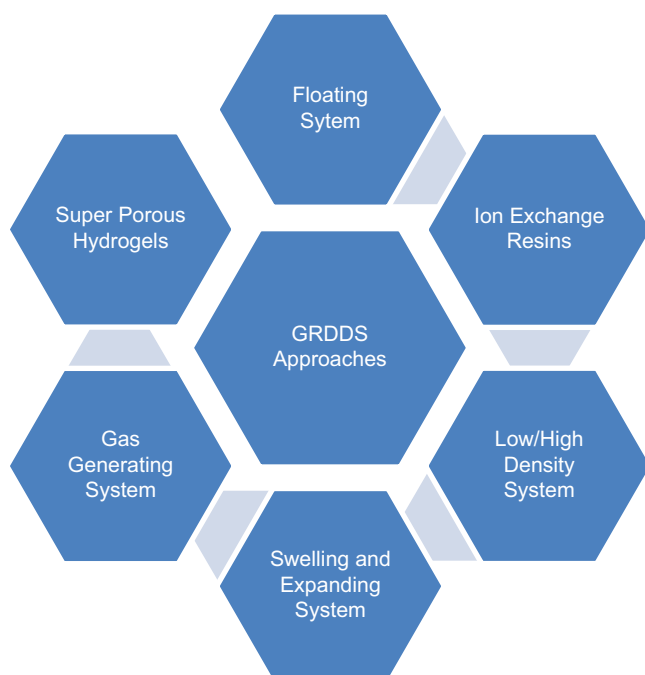


Figure 1: Various techniques of gastroretentive drug delivery system

and dipyridamole. Floating drug delivery offers many applications for the drug having poor bioavailability due to the slim absorption window within the upper part of the GIT.^[14] It relaxes the dosage form at the site of absorption and thus enhanced bioavailability. Table 1 show case the pros and cons of Floating drug delivery system in regards to the conventional formulation techniques.

Nowadays, different kinds of drugs are formulated into the FDDS and other methods to increase their gastric retention. Tables 2 and 3 gives sight on few examples of commercially available floating tablets and capsules and few patents filed under floating formulation respectively. Although the production of FDDS is quite large now, many researches are still done to improve this drug delivery system. Many projects works and researches are performed so as to make FDDS a better choice for the formulation of certain drugs.

Table 1: Advantages and disadvantages of FDDS^[13]

Advantages	
1.	FDDS enhances bioavailability. Bioavailability is increased of control release GRDF as compared to non-retentive.
2.	FDDS minimizes the adverse activity of drugs at the colon. The drug in GRDF at the stomach minimizes the amount of drug that reaches the colon and as a result, prevents the degradation of the drug.
3.	FDDS also reduces the counter activity of the body leading to higher drug efficacy.
4.	The FDDS is helpful for the drugs which are absorbed in the proximal part of the small intestine.
5.	FDDS is advantageous for local action in the stomach.
6.	FDDS improves drug absorption. It also improves the gastric residence time of the dosage form.
Disadvantages	
1.	FDDS required a high amount of fluid in the stomach for a specific activity.
2.	The drug which undergoes the first-pass metabolism may not be desirable such as nifedipine.
3.	The dosage has to be administered with a high amount of water to float and work efficiently.
4.	Gastric mucosa irritating drugs are not suitable or desirable.
5.	Floating system is not feasible for those drugs that have solubility or stability problem in the GIT.
6.	The drug substances that are unstable in the acidic environment of the stomach are not suitable candidates to be incorporated into the systems.

FDDS: Floating drug delivery system, GRDF: Gastroretentive dosage form, GI: Gastrointestinal

Table 2: FEW commercially available FDDS formulation

Brand name	Delivery system	Drug	Company
Valrelease [®]	Floating capsule	Diazepam	Hoffmann-LaRoche
Madopar [®] HBS (Prolopa [®] HBS)	Floating, CR capsule	Benserazide and L-Dopa	Roche Products, USA
Liquid Gaviscon [®]	Effervescent floating liquid alginate preparations	Al hydroxide, Mg carbonate	GlaxoSmithKline, India
Cifran OD [®]	Gas-generating floating form	Ciprofloxacin	Ranbaxy, India
Convicon [®]	The colloidal gel-forming FDDS	Ferrous sulfate	Ranbaxy, India
Topalkan [®]	Floating liquid alginate preparation	Al-Mg antacid	Pierre Fabre Drug, France
Cytotec [®]	Bilayer floating capsule	Misoprostol	Pharmacia, USA

Table 3: Few patents on FDDS

Title	Patent number	Date	Inventors	References
Gastric Floating System	WO 02/102415 A1	December 27, 2002	Avachat MK, Dhamne AG.	[44]
Floating drug delivery composition	WO 01/58424 A1	August 16, 2001	Watts PJ, Smith A, Bond JR and Lafferty WCI	[45]
Gastroretentive drug delivery system comprising an extruded hydratable polymer	WO 03/105812 A1	December 24, 2003	Hassan M	[46]
Gastroretentive drug delivery system	WO 2014/014348 A1	January 23, 2014	Meijerink HJC, Changoer L, Blom W, Visser MR, Frijlink HW and Eissens AC	[47]
Gastroretentive drug formulation and delivery systems and their method of preparation using functionalized calcium carbonate	WO 2014/057026 A1	April 17, 2014	Gerard DE., Schoelkopf J, Gane PA.C, Eberle VA, Alles R, Puchkov M and Huwyler J	[48]

TYPES OF FDDS

On the basis of the mechanism of buoyancy, FDDS can be divided into two distinct types:

1. Effervescent system
2. Non-effervescent system.

Effervescent system

The effervescent system can also be called the gas generating system. Gas generating agents are used along with carbonates (sodium bicarbonate), and organic acids (citric acid, and tartaric acid) to generate carbon dioxide gas.^[15,16] This generation of carbon dioxide reduces the density of the drug and makes it floatable in the stomach thus increasing their retention. This system is further classified into two types – volatile liquid containing system and gas generating system.

Volatile liquid containing system

This system involves the use of liquids such as ether and cyclopentane, which is volatile. This system provides gastric retention by incorporating

an inflatable chamber with a liquid. The system contains two compartments: First compartment consist of the drugs and the second compartment contains volatile liquids.

Gas generating system

This system mainly involves the use of agents which release carbon dioxide for drug retention. Agents such as sodium bicarbonate, citric acid, tartaric acid, and chitosan are mainly used to generate carbon dioxide and thus reducing the density of the drug and make them float in the stomach. This floating helps the drug to be retained for a longer duration of time.

Non-effervescent system

This system mainly depends on the mechanism of swelling of polymers and their adhesion to the GIT as agents causing effervescence are not used. Excipients, normally used in this system, consist of gel-forming or extremely swellable polysaccharide sort hydrocolloids, polysaccharides, and matrix-forming materials such as polycarbonate, polyacrylate, polystyrene, and bio-adhesive materials such as chitosan and

carbopol.^[17,18] This system is again classified into various types, such as:

Colloidal gel barrier system

This system is designed by Sheth and Tossounian. To enhance the gastric residence time (GRT), gel-forming hydrocolloids are used for buoyancy and this increases the amount of drugs in the absorption site. Hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, polysaccharides, and polystyrenes are various gel-forming agents used.

Bilayer floating tablet

A bilayer floating tablet consists of two immediate release layers. The first one releases the initial dose while the other one layer sustained releases the drug. The sustained release of drugs is achieved by absorbing gastric fluid and forming an impermeable gel barrier on the surface thereby enhancing the buoyancy.

Microporous compartment system

This system contains an encapsulated drug reservoir which has pores on the top and bottom wall. Through these pores, entrapment of air is possible. Floating of the system over the gastric content is stimulated by the presence of entrapped air in the floating chamber. The gastric fluid enters through an aperture which dissolves the drug for absorption in the intestine.

Alginate beads

Alginate beads are multi-unit floating dosage forms. They are developed from freeze-dried calcium alginate. They are spherical beads with pair around of 2.5 mm diameter and are prepared by dropping sodium alginate solution into an aqueous solution of calcium chloride causing precipitation of calcium alginate. This precipitation leads to the formation of a porous system which can maintain a floating force for over 12 h.

Hollow microspheres

Hollow microspheres or microballoons are prepared by novel emulsion solvent diffusion

method loaded with the drug in their outer polymer shells. The microballoons floating continuously over the surface of acidic dissolution media contains surfactant for more than 12 h *in vitro*.

PHYSIOLOGY OF STOMACH

The main function of the stomach is to store, process, and transport food and other substances administered orally. The stomach is mainly divided into three regions: Fundus, body, and antrum. The process of storing and digestion of food occur within these regions. The gastric emptying occurs both during fasting state and fed state, but the pattern of motility differs in both of these states.^[16,19]

The GI motility of the stomach consists of two modes; they are inter-digestive motility pattern and digestive motility pattern. In the fasted state, the inter-digestive motility pattern is dominated. In a fasting state, a series of electrical events take place which cycle in the stomach and small intestine in every 2–3 h. This cycle is called an inter-digestive myoelectric cycle (IMC) or migrating myoelectric cycle (MMC).^[20] Each cycle lasts for 90–120 min and consists of four phases, as described by Wilson and Washington.^[21] A full cycle begins in the lower esophageal sphincter and finished in the ileum. The phases of the cycle are as follows:

- a) Phase 1: In this phase, the gastric emptying rate is slow as the onset of MMC is delayed. This phase usually lasts for 30–60 min. Contraction does not occur in this phase. It is also known as the basal phase.
- b) Phase 2: In this phase, bile secretion and mucus discharge take place and intermediate contraction occurs. It lasts from 20 to 40 min. It is also known as the pre-burst phase. The intensity and frequency increase gradually as the phase progresses.
- c) Phase 3: In this phase, regular and intense contraction takes place for a short time. It last usually for 10–20 min. This phase is also called a housekeeper wave as it tends to empty the fasting contents of the stomach. Large objectives remain in the stomach in the fed state but passed down to the small intestine during this phase.

d) Phase 4: This is the intermediate state between phases 3 and 1. It lasts from 0 to 5 min.

FACTORS AFFECTING GRT OF FDDS

There are various factors that affect gastric emptying time.^[16] Some of these are as follows:

Effects of dosage form size and shape

Small size tablets are expelled from the stomach during the digestive phase while the large size tablets are expelled during the housekeeping wave phase. Particle size should be within the range of 1–2 mm. It is found that floating units have large GRT than the non-floating unit. Ring-shaped and tetrahedron have a better GRT as compared with other shapes.^[22]

Gender, posture, and age

Rate of emptying of stomach is lower in female than in male. In the case of an elderly person, gastric emptying time is slowed down, especially in the case of man above 70 years.^[22]

Effect of food and specific gravity

To float in the stomach, the density of FDDS should be less than gastric content, i.e. 1.0 g/cm³. Various studies show that the intake of food is the main determinant of gastric emptying than food. Food is the most important factor than buoyancy in GRT. GT is increased in fed condition as the onset of MMC is delayed. GRT is faster in the fasted state (<2 h) and long after the meal (around 4 h).^[23]

Nature of meal and frequency of food

The rate of the gastric emptying time mainly depends on the volume, viscosity, and the caloric content of meals. Feeding of indigestible polymer or fatty acid can change the motility pattern of the stomach. It can increase the gastric emptying rate and prolong the release of the drug. A protein-rich diet can increase GRT by 4–10 h.^[23]

Diseases

Diseases such as diabetes and Crohn's disease can alter the gastric emptying time. This also depends on the type of food consumed by such patients. Depression slows the gastric emptying time while stress increases the rate.

Effect of drugs

Drugs such as atropine, glycopyrrolate, metoclopramide, and domperidone increase the gastric emptying time while anti-cholinesterase drug-like neostigmine decreases the gastric emptying rate.

State of the drug

A demonstration using radiolabeled technique shows that the rate of gastric emptying time differs between liquid, digestible solid, and indigestible solid.

Formulation parameters

Multi-particulate formulations show better gastric emptying pattern than the single unit formulations.

COMPONENTS OF FDDS

The following components are used in the formulation of FDDS.

Hydrocolloids

Hydrocolloids are synthetic, anionic, non-ionic like modified cellulose derivatives, and hydrophilic gum, for example, acacia, pectin, agar, gelatin, and bentonite. Hydrocolloids must be hydrated in the gastric medium, i.e., the gastric fluid having pH 1.2. The bulk density of the formulation may be more than 1 initially, but after entering the gastric fluid, it should be hydrodynamically balanced to get a bulk density <1 to assure buoyancy.^[24]

Polymers

Polymers used in the preparation of floating tablets are – HPMC K4M, HPMC K15M, HPMC

K100M, polyethylene glycol, polycarbonate, sodium alginate, PVA, PVP, Eudragit, carbopol, methyl methacrylate, acrylic polymer, HPC-H, and HPC-M. They are mainly used to hold the drug and other ingredients together.^[25,26]

Effervescent agent

Sodium bicarbonate, citric acid, tartaric acid, nitroglycerin, and Di-sodium glycine carbonate are used as an effervescent agent to release carbon dioxide gases.^[27]

Inert fatty materials

Fatty materials have a specific gravity less than one, which decrease the hydrophilic property and hence increased buoyancy, for example, beeswax, fatty acid, long-chain alcohol, and mineral oil.^[27]

Release rate accelerants

Release rate of the formulation can be modified and increased by using excipients such as lactose and mannitol. It may present by 5–60% of total weight.^[18,27]

Release rate retardants

They decrease the solubility hence retard the release rate of medicaments, for example, dicalcium phosphate, talc, and Mg-stearate.^[18]

Buoyancy increasing agent

Materials like ethyl cellulose, which have a low bulk density less than one, can be used for increasing the buoyancy of the formulation. It may be present with 80% of the weight.^[18]

Low-density material

They are used if necessary to decrease the weight of the formulation for them to float, for example, polypropylene foam powder.

Miscellaneous

Adjuvant such as preservatives, stabilizers, lubricants, binders can be used in the formulation as per requirements.

FORMULATION OF FDDS

Method for single layer floating tablet

In general, single layer floating tablets are prepared using compression methods. Normally, three basic compression methods are used.^[24] They are as follows:

Direct compression method

The direct compression method is the process by which tablets are directly prepared from powdered materials without modifying the physical nature of the materials. This method is used for crystalline chemicals having good compressible characteristics and flow properties such as potassium salt (chloride, bromide), ammonium chloride, sodium chloride, and methenamine. For the preparation of tablets, first all the powder ingredients are mixed together then grind in a mortar and pestle to get a fine powder. Now a quantity of powdered material is poured into a die, the upper and lower punches of the tablet machine compress the material under high pressure.

Dry granulation method

It is the process by which tablets are prepared without a liquid solution. This method is used for the ingredients that are sensitive to moisture or unable to withstand elevated temperature during drying. In this process, the powdered materials are aggregated under high pressure.

Wet granulation method

In the wet granulation method, the active ingredients are mixed with a liquid granulation to form a granule in a rapid mixer granulator (RMG). The RMG is a chopper used for various purpose that consists of an associate blade and a chopper. It is used for high-speed dispersion of dry powders

and solvent granulations. Moist materials from wet edge steps are placed on giant trays and placed in drying chambers with constantly moving air current and thermostable heat controller. Commonly used dryers are tray dryer and fluidized bed dryer. After drying, the granules are reduced in particle size by passing through a smaller mesh screen. The lubricant is then added as a fine powder to promote the flow of granules. These granules are then compressed to develop a pill. Dry granulation has a shorter, more cost-effective manufacturing process than wet granulation. Because it does not need heat or wetness, dry granulation is especially suitable for active ingredients that are sensitive to solvents or labile to moisture and elevated temperatures.

Methods for bilayer floating tablet^[17,28]

Oros® push-pull technology

It is a two- or three-layer systems, where a drug layer and push layer are present. Drug layer contains drug with other products, and due to this drug is less soluble. Sometimes with the drug suspending agent and osmotic agent are also added. The tablet core is surrounded by a semi-permeable membrane.

L-OROS Tm technology

L-OROS system is developed by Alza due to the solubility problem. In this system, a drug is present in a dissolved state in a lipid soft gel product. The liquid gel is produced first and then barrier membrane, after which osmotic membrane and semi-permeable membrane coat are applied and it is then drilled out through an external orifice.

DUROS technology

This technology is also known as miniature drug dispensing system which works like a miniature syringe and releases a small quantity of drug consistently over a period of time. It avoids exposure to high initial drug concentration. There is an associate outer cylindrical titanium alloy reservoir that has high impact strength by which drug molecules inside it are protected and shielded from enzymes.

Élan drug technologies' dual release drug delivery system

DUREDASTM Technology provides a different release pattern of a single drug or combines release of the drug. It means it provides sustained release as well as immediate release. This technology also provides various advantages such as two drug components that provide changing the site of drug release or drug absorption. It another benefit is that it also consists of bilayered tablet technology in which it contains modified as well as immediate drug release pattern in one tablet.

EN SO TROL technology

An integrated approach is employed by Shire Laboratory for the drug delivery system. In this technology, first identification and then the inclusion of enhancer are done which is identified to form an optimized dosage form in a controlled release system. By this system, enhancement in solubility is achieved.

RoTab bilayer

RoTab bilayer is used for the formulation of mono and bilayer tablets. In this technique, dose and the compression force are automatically regulated by adjusting the filling speed and die table. Hardness is also regulated if required.

Geminex technology

In this drug delivery system at different times more than one drug can be delivered at different times. This technology increases the therapeutic efficacy of the drug and also decreasing its side effects. As it provides delivery of drugs at different rates in a single tablet, so it is useful in both industry and for the patient.

CHARACTERIZATION

Pre-compression study

Compatibility studies between drugs and excipients

The physical compatibility of the drug with various excipients is carried out and select suitable excipients for a stable and good formulation. The

compatibility studies are performed using Fourier-transform infrared (FTIR) spectrometer. The FTIR spectrum of the pure drug and physical mixture of the drug and excipients are studied.^[29]

Angle of repose

Angle of repose is the maximum angle possible between the surface of the pile of the powder and the horizontal plane. The flow property of granules is defined by the following method.^[30]

$$\tan \theta = \frac{h}{r}$$

$$\theta = \tan^{-1} \frac{h}{r}$$

Where

θ = angle of repose

h = height in cm

r = radius in cm.

Bulk density

Bulk density can be determined using a known amount of sample into a graduated measuring cylinder than measuring the weight and volume.^[31] It is determined using the following formula:

$$\text{Bulk density} = \frac{\text{Mass of the powder}}{\text{Volume of the powder}}$$

Tapped density

Tapped density can be determined by placing a graduated cylinder containing a known amount of sample in a mechanical tapping apparatus.^[31] It can be determined using the following formula:

$$\text{Tapped density} = \frac{\text{Mass of powder}}{\text{Volume of powder after tapping}}$$

Powder flow properties: The flow properties are determined by

a. Carr's index (I)

The compressibility index (CI) can be measured from the bulk and tapped densities.

According to this theory, the less compressible material is more Flowable.^[32] A material having values <20–30% is defined as the free-flowing material, and based on the apparent bulk density and tapped density, the percentage compressibility of the bulk drug can be determined using the following formula. It is expressed in percentage:

$$I = \frac{D_t - D_b}{D_t} \times 100$$

Where D_t is the tapped density of the powder and D_b is the bulk density of the powder.

b. Hausner ratio

Hausner ratio can be calculated by the formula:

Hausner ratio = Tapped density/Bulk density.

Post-compression parameters

The prepared tablets can be evaluated for quality control tests such as weight variation, hardness, thickness, friability, and content uniformity.

Weight variation

For this test, ten tablets are taken randomly from each batch and weighed individually. Calculate the average weight and compare the individual weight to the average. From this percentage, weight difference can be calculated.^[33]

Hardness and friability test

The hardness of tablet can be determined by Monsanto hardness tester. Ten tablets are randomly picked from each batch. The tablets are then placed between two anvils of hardness tester and the force is gradually increased and the reading from the scale is recorded for the pressure which is required for breaking the tablet.

Friability test can be done by Roche friabilator. For this test, ten tablets are weighed and placed in the Roche friabilator. It rotates for 4 min at 25 rpm. After 4 min tablets are reweighed and the percentage of weight loss is calculated.^[9] The obtained value should not be more than 1%. Friability test can be done using the following formula:

$$\text{Friability (\%)} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Tablet dimensions

Thickness and diameter of tablets can be measured using a Vernier caliper. Three tablets of each formulation are picked randomly and the dimension is determined. It is expressed in mm and the standard deviation is also calculated.^[34]

Content uniformity test

The floating tablets are tested for their drug content. Five tablets are finely powdered; than the powder is accurately weighed. The quantities of the powder should be equivalent to 15 mg of drug. Now transfer the powder to 100 ml of volumetric flask. The flask is filled with 0.1N HCl (pH 1.2 buffers) solution and mixed thoroughly. The solution is made up to volume and filtered. Dilute 10 ml of the resulting solution to 100 ml of 0.1N HCl and measure the absorbance of the resulting solution at a suitable wavelength using UV-visible spectrophotometer. The linearity equation obtained from the calibration curve is used for estimation of the drug in the tablet formulations.^[34,35]

In vitro buoyancy studies

The *in vitro* buoyancy can be determined by floating lag time (FLT), as per the method. The tablets are placed in a 250 ml beaker, containing 200 ml of 0.1 N HCl. The time required for the tablet to rise to the surface and float is determined as FLT, and the time period up to which the tablet remained buoyant is determined as FLT.^[36]

Swelling study

The swelling index (SI) can be determined by placing the tablets separately in a glass beaker containing pH 1.2 HCl buffer and incubated at regular 1-h time intervals until 24 h. The floating tablets are removed from beaker, and the excess surface liquid is removed carefully using the % SI and is calculated using the following formula:^[36,37]

$$\text{Swelling index (SI \%)} = \frac{W_t - W_0}{W_n} \times 100$$

In vitro dissolution studies

The *in vitro* dissolution study may be performed using a United States Pharmacopoeia type II (paddle) apparatus at a rotational speed of 100 rpm. The dissolution test is performed using 900 ml of 0.1 N HCl at 37°C ± 0.5°C. A sample (10 ml) of the solution is withdrawn from the dissolution apparatus at predetermined time intervals for 24 h, and the samples are replaced with pre-warmed fresh dissolution media. The samples are filtered through a Whatman filter paper and diluted to a suitable concentration with 0.1 N HCl as a blank. The absorbance of the solution is measured at a suitable wavelength using a UV spectrophotometer.^[6,38]

Drug content

A total number of 10 tablets can be weighed and taken into a mortar and crushed into a fine powder. An accurately weighed about 10 mg of the drug is dispersed in 100 ml of pH 1.2 HCl buffer, filtered, diluted, and analyzed for drug content at a suitable wavelength using a UV visible spectrophotometer.^[34,39]

Stability study

The stability studies can be carried out by sealing the formulation in an aluminum foil and stored in different temperatures 4°C, 25°C/60% RH, and 40°C/75% RH, respectively, for 3 months. After 3 months, the samples are withdrawn and retested for drug content, buoyancy lag-time, and buoyancy time. The amount of drugs is detected using UV spectrophotometer at a suitable wavelength against the blank. The results indicate that this formulation remained stable for 3 months.^[38,39]

Disintegration time

In vitro disintegration time can be determined using the disintegration test apparatus. For this, tablet is placed in each of the six tubes of the apparatus and one disc is added to each tube. The time taken for the complete disintegration of the tablet is measured.

Evaluation of prepared floating microspheres

Percentage yield (%)

The percentage yield of floating microspheres is calculated by dividing the actual weight of the product to the total amount of all non-volatile components and is represented by the following formula:

$$\% \text{ yield} = \frac{\text{Weight of floating microsphere}}{\text{Weight of drug and polymer}} \times 100$$

Particle size

Particle size and shape of the microspheres are determined by optical microscopy. The freshly prepared microspheres are examined on an optical microscope, and the size of microspheres is measured by precalibrated ocular micrometer and stage micrometer. About 100 particles of each formulation are observed and measured.

Micrometric properties

The prepared microspheres are characterized by micrometric properties such as microsphere size, Bulk density, tapped density, Carr's CI, Hauser's ratio, and angle of repose.^[40]

Bulk and tapped density

Bulk and tapped densities are measured using 50 ml of the graduated cylinder. 5g of accurately weighed sample is passed through a glass funnel. The sample is poured in the cylinder and tapped mechanically 3 times and 100 times for calculating bulk volume (V_b) and tapped volume (V_t), respectively. Then tapped volume is noted down and bulk density and tapped density is calculated.

$$\text{Bulk density} = \frac{\text{Mass of microsphere}}{\text{Volume of microsphere after tapping}}$$

Carr's compressibility

CI or Carr's index value of microspheres is calculated by the following equations:

$$\% \text{ Compressibility index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Hausner's ratio

Hausner's ratio of microspheres is determined by comparing the tapped density to bulk density using the equation:

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \times 100$$

Floating time

It is defined as the time taken by the floating microspheres to remain buoyant in the medium. The floating microspheres are placed in a beaker containing 200 ml of 0.1N HCl and examined for the duration of time of float.

Drug content

The floating microspheres are weighed accurately and crushed. The powdered microspheres are placed in a 100 ml of volumetric flask, and the volume is made up using pH 6.8 phosphate buffers and kept for 24 h. The solution is then filtered through Whatman paper and diluted with fresh solvent. Absorbance is measured at a suitable wavelength using UV spectrophotometer, and the percent drug content is calculated.^[41]

Drug entrapment efficiency

The percent of drug entrapped is calculated as follows:

$$\text{Entrapment efficiency} = \frac{\text{Calculated drug content}}{\text{Theoretical drug content}} \times 100$$

Surface morphology

The surface morphology is measured using a scanning electron microscope.

In vitro drug release study

The *in vitro* drug release is carried out in 0.1 N HCl (pH 1.2) for 2 h and in pH 6.8 buffer for 10 h. The drug release rate from floating microspheres is determined using paddle type eight-station dissolution test apparatus. A weighed amount of 100 mg of floating microspheres equivalent to the

drug is kept in 0.1 N HCl (1.2 pH) maintained at $37 \pm 0.5^\circ\text{C}$ at a rotation speed of 100 r/min. 5 ml sample is withdrawn at 60 min time interval, the initial volume of the dissolution fluid is maintained by adding 5 ml of fresh dissolution fluid after each withdrawal and passed through 5 m membrane filter and analyzed spectrophotometrically.^[42]

FUTURE PERSPECTIVE OF FDDS

Floating drug delivery is a potential approach which is evident from recent study and publications. Several narrow absorption window drugs may benefit from compounding into a FDDS. Replacing the parenteral administration of drugs to oral pharmacotherapy would substantially improve treatment. Some of the unresolved essential problem associated with the rational development of FDDS embody the quantitative potency of floating delivery systems within the fasted and fed states and also correlation between prolonged gastroretentive and sustained release pharmacokinetic characteristics.^[43] The buoyant delivery system considered a beneficial strategy for the treatment of gastric and duodenal cancers. Drugs that have poor bioavailability due to their restricted absorption to the upper GIT can be delivered into FDDS with efficiency. Thereby increasing their absorption and rising their absolute bioavailability. The FDDS reduces fluctuations in the plasma level of drug results from delayed gastric emptying. The floating concept can also be utilized in the development of various anti-reflux formulations, and these are potential to treat the Parkinson's disease. Combination therapy to treat *Helicobacter pylori* infection in a single FDDS needs to be developed. The investigations will be concentrated on the concept of the design of novel polymers according to clinical and pharmaceutical needs. However, the study is close as the process is seeing the greater transition of gastric retention devices from a developmental level to the manufacturing and commercial level.

CONCLUSION

FDDS extents the bioavailability and control the delivery of the drug to the system and also optimize

the delivery of drug molecules, which exhibit the absorption window and lowers the first-pass metabolism of certain drugs. Future research work in FDDS should be aimed at discovering means to control accurately the drug input rate into the GI tract for the optimization of the pharmacokinetic and toxicological profiles of medicinal agents. This drug delivery approach will certainly help patients to increase compliance with betterment in the process of drug delivery and can be an ideal approach with industrial applicability and feasibility.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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