

Floating Drug Delivery System: An Overview

Azhar Danish Khan*, Meenakshi Bajpai

College of Pharmaceutical Sciences, Raj Kumar Goel Institute of Technology,
5 Km stone Delhi- Meerut Ghaziabad 201003 India

**Corres: Author- azhardk@gmail.com, Ph No. 09891307291*

Abstract: Gastric emptying is a complex process and makes in vivo performance of the drug delivery systems uncertain. In order to avoid this variability, efforts have been made to increase the retention time of the drug-delivery systems for more than 12 hours. The floating or hydrodynamically controlled drug delivery systems are useful in such application. From the formulation and technological point of view, the floating drug delivery system is comparatively easy and logical approach. The present review addresses briefly about the floating drug delivery systems. It also summarizes methods of evaluation of various floating dosage forms and applications of these systems.

Keywords: Floating drug delivery system, single unit, multiple unit, evaluation and applications.

INTRODUCTION

Historically, the oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulation, etc. From immediate release to site-specific delivery, oral dosage forms have really progressed. However, it is a well-accepted fact that it is difficult to predict the real in vivo time of release with solid, oral controlled release dosage forms. Thus, drug absorption in the gastrointestinal (GI) tract may be very less in terms of percentage drug absorbed and highly variable in certain circumstances^[1]

Drug Delivery system is becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biological parameters pertinent to their performances. Controlled Drug Delivery System provides drug release at a predetermined, predictable and controlled rate to achieve high therapeutic efficiency with minimal toxicity. Despite tremendous advancement in drug delivery, oral route remains the preferred route for the administration of therapeutic agents and oral drug delivery is by far the most preferable route of drug delivery because of low cost of therapy and ease of administration leads to high levels of patient compliance as well as the fact that gastrointestinal physiology offers more flexibility in dosage form design than most other routes, consequently much effort has been put into

development of strategies that could improve patient compliance through oral route.^[2]

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. Several difficulties are faced in designing controlled release systems for better absorption and enhanced bioavailability. One of such difficulties is the inability to confine the dosage form in the desired area of the gastrointestinal tract. Drug absorption from the gastrointestinal tract is a complex procedure and is subject to many variables. It is widely acknowledged that the extent of gastrointestinal tract drug absorption is related to contact time with the small intestinal mucosa. Thus small transit time is an important parameter for drugs that are incompletely absorbed^[3] The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion, flotation, sedimentation, expansion modified shape systems or by the simultaneous administration of pharmacological agent that delay gastric emptying. This review focuses on the principal mechanism of flotation to achieve gastric retention.

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. 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.

These considerations have led to the development of oral floating dosage forms possessing gastric retention capabilities. Thus when a drug possesses a narrow 'absorption window' design of sustained release preparation require both prolongation of gastrointestinal transit time of dosage forms and controlled drug release.

Floating dosage form with prolonged residence time in stomach is highly desirable for drug ^[4]

- That are locally active in stomach
- That have absorption window in stomach or in upper small intestine.
- That are unstable in intestinal or colonic environment
- Have low solubility at high pH value.

TABLE 1: List of Drugs Formulated as Single and Multiple Unit Forms of Floating Drug Delivery Systems

Tablets	Chlorpheniramine maleate, Theophylline, Furosemide, Ciprofloxacin, Captopril, Acetylsalicylic acid, Nimodipine, Amoxycillin trihydrate, Verapamil HCl, Isosorbide di nitrate, Sotalol, Isosorbide mononitrate, Aceraminophen, Ampicillin, Cinnarazine, Diltiazem, Flurouracil, Piretanide, Prednisolone,
Capsules	Nicardipine, L-Dopa and benserazide, chlordizepoxide HCl, Furosemide, Misoprostal, Diazepam, Propranolol, Urodeoxycholic acid.
Microspheres	Aspirin, Griseofulvin, and p-nitroaniline, Ketoprofen, Tranilast, Iboprufen, Terfenadine.

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM

The floating drug delivery system can be divided into gas generating and non-effervescent systems.

Gas-Generating Systems: Floatability can be achieved by generation of gas bubbles. CO₂ can be generated in situ by incorporation of carbonates or bicarbonates, which react with acid—either the natural gastric acid or co-formulated as citric or tartaric acid. The optimal stoichiometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76:1. An alternative is to incorporate a matrix with entrapped of liquid, which forms a gas at body temperature. The approach has been used for single and multiple unit systems.

In single unit systems, such as capsules or tablets, effervescent substances are incorporated in the hydrophilic polymer, and CO₂ bubbles are trapped in the swollen matrix. In vitro, the lag time before the unit floats is <1 min and the buoyancy is prolonged for 8 to 10 h. In vivo experiments in fasted dogs showed a mean gastric residence time increased up to 4 h. Bilayer or multilayer systems have also been designed. Drug and excipients can be formulated independently and the gas generating unit can be incorporated in any of the layer. Further refinements involve coating the matrix with a polymer which is permeable to water, but not to CO₂. The main difficulty of such formulation is to find a compromise between elasticity, plasticity and permeability of the polymer.

Sriamornsak et al prepared calcium pectinate beads containing carbonate salt as a gas forming agent. The beads were prepared by dispersing carbonate salt in pectin solution and then extruding into neutral or acidified solution of calcium chloride. Incorporation of carbonate salt results in formation of porous beads which upon reaction with acid caused release of carbon dioxide providing buoyancy to beads.^[5]

Sonar et al prepared bilayered and floating bioadhesive tablets of rosiglitazone maleate. Rosiglitazone maleate bilayer tablets contained two layers, a floating layer and a sustained release (SR) layer. The sustained layer was compressed and granules of the floating layer were added to it then both layers were compressed using a single station rotary press. HPMC and Sodium bicarbonate was added in the floating layer and when immersed in 0.1 N HCl the tablets expanded and rise to the surface.^[6]

Non-Effervescent Systems: 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. Excipients used most commonly in these systems include hydroxypropyl methyl cellulose (HPMC), polyacrylate polymers, polyvinyl acetate, Carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonate.

Kaza et al prepared sustained release floating tablets of Ranitidine Hydrochloride using swellable polymers like HPMC K 100M and HPMC K 15M. The tablets were found buoyant for around 24 hrs^[7]

Nur and Zhang developed floating tablets of captopril using HPMC (4000 and 15 000 cps) and carbopol 934P. In vitro buoyancy studies revealed that tablets of 2 kg/cm² hardness after immersion into the floating media floated immediately and tablets with hardness 4 kg/cm² sank for 3 to 4 minutes and then came to the surface. Tablets in both cases remained floating for 24 hours. The tablet with 8 kg/cm² hardness showed no floating capability. It was concluded that the buoyancy of the tablet is governed by both the swelling of the hydrocolloid particles on the tablet surface when it contacts the gastric fluids and the presence of internal voids in the center of the tablet (porosity). A prolonged release from these floating tablets was observed as compared with the conventional tablets and a 24-hour controlled release from the dosage form of captopril was achieved.^[8]

ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM

1. The Gastroretentive systems are advantageous for drugs absorbed through the stomach. E.g. Ferrous salts, 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. Administration of prolongs release floating dosage forms, tablet or capsules, will result in dissolution of the drug in the gastric fluid. They dissolve in the gastric fluid would be available for absorption in the small intestine after emptying of the stomach contents. It is therefore expected that a drug will be fully absorbed from floating dosage forms if it remains in

the solution form even at the alkaline pH of the intestine.

4. The gastro retentive systems are advantageous for drugs meant for local action in the stomach. E.g. antacids.
5. 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.

DISADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM:

1. Floating system is not feasible for those drugs that have solubility or stability problem in G.I. tract.
2. These systems require a high level of fluid in the stomach for drug delivery to float and work efficiently coat, water.
3. The drugs that are significantly absorbed through out gastrointestinal tract, which undergo significant first pass metabolism, are only desirable candidate.

APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEMS

Floating drug delivery offers several applications for drugs having poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage form at the site of absorption and thus enhances the bioavailability. These are summarized as follows.

Sustained Drug Delivery:

HBS systems can remain in the stomach for long periods and hence can release the drug over a prolonged period of time. The problem of short gastric residence time encountered with an oral CR formulation hence can be overcome with these systems. These systems have a bulk density of < 1 as a result of which they can float on the gastric contents. These systems are relatively large in size and passing from the pyloric opening is prohibited.

Recently sustained release floating capsules of nicardipine hydrochloride were developed and were evaluated in vivo. The formulation compared with commercially available MICARD capsules using rabbits. Plasma concentration time curves showed a longer duration for administration (16 hours) in the sustained release floating capsules as compared with conventional MICARD capsules (8 hours).^[9]

Sidhaye developed sustained release floating drug delivery system of *in-situ* gelling suspension of cinnarizine. Cinnarizine has half life of 3-6 hours and

required dose is 30mg three times a day. Hence sustained drug delivery system for pediatric patient was developed. Different formulations of cinnarizine were prepared, containing different concentration of gelling agent such as sodium alginate and calcium carbonate. Polysorbate 80 was used as wetting agent and methyl paraben was added as preservative. Sodium citrate was used to prevent gelation outside in the gastric environment. The drug release was studied by dissolution rate test with pH 1.2 simulated gastric fluid using the USP 24 type II apparatus at 50rpm to evaluate for the desired release pattern. The suspension showed pseudoplastic behavior, instant gelation, 98.90% release in 12 hours, instant floating ability with duration of floating for more than 24 hours in pH 1.2 buffer. Thus, sustained release floating drug delivery system of *in-situ* gelling suspension of Cinnarizine was formulated having sustained drug action for 12 hours.^[10]

Rajendran et al prepared Nimodipine loaded alginate chitosan beads by ionic gelation using various concentrations of alginate and chitosan. The swelling ability and invitro release behaviour was studied at pH 1.2 and 6.8. It was found that beads loaded with alginate showed poor sustained release whereas modification with chitosan yielded beads with satisfactory sustained effect.^[11]

Goole et al studied the in vitro evaluation and the enhancement of the floating properties of coated sustained release (SR) minitables (MTs). The evaluated system consisted of a 3-mm drug-containing gas-generating core prepared by melt granulation and subsequent compression, which was then coated with a flexible polymeric membrane. Eudragit® RL30D and acetyl triethylcitrate were used as a film former and a plasticizer, respectively. The optimally coated floating MTs floated within 10 min and remained buoyant for more than 13 h, regardless of the pH of the test medium. By evaluating the dissolution profiles of levodopa at different pH, it was found that the release of levodopa was sustained for more than 12 h regardless of the pH, even if the coating did not cancel the effect of pH dependent solubility of the active drug.^[12]

Site-Specific Drug Delivery:

These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine.

Somani et al prepared floating pulsatile delivery system of Acelofenac based on hollow calcium pectinate beads intended for chronopharmacotherapy. This concept was applied to

increase the gastric residence of a dosage form having lag phase followed by a burst release. The lag phase was in acidic medium during floating followed by a burst release in the phosphate buffer. This system provides a time and site specific release of drug as per chronotherapy of disease like Rheumatoid and Osteoarthritis^[13]

Furosemide is primarily absorbed from the stomach followed by the duodenum. Menon et al developed a monolithic floating dosage form with prolonged gastric residence t and the bioavailability was increased. AUC obtained with the floating tablets was approximately 1.8 times those of conventional furosemide tablets.^[14]

Patel et al formulated multiple unit floating beads of Famotidine to provide sustained release of drugs with a view to provide an effective and safe therapy to target peptic ulcer with a reduced frequency of dose with prolonged therapeutic effect. The buoyancy was provided by evolving Carbon dioxide from alginate matrix^[15]

Rajnikanth et al prepared Gellan gum based floating beads containing clarithromycin (FBC) by ionotropic gelation method for stomach-specific drug delivery against *Helicobacter pylori*. Kinetic treatment of the in vitro drug release data with different kinetic equations revealed matrix diffusion mechanism. Prepared beads showed good anti-microbial activity against isolated *H. pylori* strain. The prepared beads have shown good in vivo floating efficiency in rabbit stomach. The stability studies of beads did not show any significant changes after storage of beads at 40 degrees C/75% relative humidity for 6 months. The preliminary results from this study suggest that floating beads of gellan can be used to incorporate antibiotics like clarithromycin and may be effective when administered locally in the stomach against *H. pylori*.^[16]

Shishu et al developed a multiple-unit-type oral floating dosage form (FDF) of 5-fluorouracil (5-FU) to prolong gastric residence time, target stomach cancer, and increase drug bioavailability. The floating bead formulations were prepared by dispersing 5-FU together with calcium carbonate into a mixture of sodium alginate and hydroxypropyl methylcellulose solution and then dripping the dispersion into an acidified solution of calcium chloride. The optimized formulation was subjected to in vivo antitumor studies to check the therapeutic efficacy of the floating dosage forms containing 5-FU against benzo(a)pyrene-induced stomach tumors in albino female mice (Balb/C strain). The multiple-bead FDF was found to reduce

the tumor incidence in mice by 74%, while the conventional tablet dosage form reduced this incidence by only 25%. Results indicate that FDF performed significantly better than the simple tablet dosage form.^[17]

Absorption Enhancement:

Drugs that have poor bioavailability because of site-specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption.

Joseph et al developed a floating type dosage form of piroxicam in hollow polycarbonate microsphere capable of floating on simulated gastric fluid and intestinal fluid using solvent evaporation technique. In vitro release of piroxicam from PC microsphere into simulated gastric fluid at 37 °C showed no significant burst effect. In vivo evaluation in rabbits showed that the bioavailability of piroxicam PC microspheres was 1.4 times than that of free drug. The elimination half life was increased up to six times. Thus it produced both sustained delivery and enhanced bioavailability^[18]

Yang et al developed a swellable asymmetric triple-layer tablet with floating ability to prolong the gastric residence time of triple drug regimen (tetracycline, metronidazole, clarithromycin) of *Helicobacter pylori*-associated peptic ulcers using HPMC and PEO as the rate-controlling polymeric membrane excipients. Results demonstrated that sustained delivery of tetracycline and metronidazole over 6 to 8 hours could be achieved while the tablets remained floating. It was concluded that the developed delivery system had the potential to increase the efficacy of the therapy and improve patient compliance.^[19]

Sato and Kawashima developed microballoons of riboflavin, which could float in JP XIII no 1 solution (simulated gastric fluid). These were prepared by an emulsion solvent technique. To assess the usefulness of the intragastric floating property of the developed microballoons of riboflavin, riboflavin powder, nonfloating microspheres of riboflavin, and floating microballoons of riboflavin were administered to 3 volunteers. Riboflavin pharmacokinetics was assessed by urinary excretion data. It could be concluded that although excretion of riboflavin following administration of floating microballoons was not sustained in fasted state, it was significantly sustained in comparison to riboflavin powder and nonfloating microspheres in the fed state. This could

be due to the reason that the nonfloating formulation passes through the proximal small intestine at once from where riboflavin is mostly absorbed, while the floating microballoons gradually sank in the stomach and then arrived in the proximal small intestine in a sustained manner. Total urinary excretion (%) of riboflavin from the floating microballoons was lower than that of riboflavin powder. This was attributed to incomplete release of riboflavin from microballoons at the site of absorption.^[20]

Shimpi et al studied the application of hydrophobic lipid, Gelucire 43/01 for the design of multi-unit floating systems of a highly water-soluble drug, diltiazem HCl. Diltiazem HCl-Gelucire 43/01 granules were prepared by the melt granulation technique. The granules were evaluated for in vitro and in vivo floating ability, surface topography, and in vitro drug release. In vivo floating ability was studied by γ -scintigraphy in 6 healthy human volunteers and the results showed that the formulation remained in the stomach for 6 hours. It could be concluded that Gelucire 43/01 can be considered as an effective carrier for design of a multi-unit FDDS of highly water-soluble drugs such as diltiazem HCl.^[21]

In a recent work by Sriamornsak et al, a new emulsion-gelation method was used to prepare oil-entrapped calcium pectinate gel (CaPG) beads as a carrier for intragastric floating drug delivery. The gel beads containing edible oil were prepared by gently mixing or homogenizing an oil phase and water phase containing pectin, and then extruded into calcium chloride solution with gentle agitation at room temperature. The oil-entrapped calcium pectinate gel beads floated if a sufficient amount of oil was used. Scanning electron photomicrographs demonstrated very small pores, ranging between 5 and 40 μ m, dispersed all over the beads. The type and percentage of oil played an important role in controlling the floating of oil-entrapped CaPG beads. The oil-entrapped CaPG beads were a good choice as a carrier for intragastric floating drug delivery.^[22]

Floating drug delivery is associated with certain limitations. Drugs that irritate the mucosa, those that have multiple absorption sites in the gastrointestinal tract, and those that are not stable at gastric pH are not suitable candidates to be formulated as floating dosage forms.

Floation as a retention mechanism requires the presence of liquid on which the dosage form can float on the gastric contents. To overcome this limitation, a bioadhesive polymer can be used to coat the dosage so that it adheres to gastric mucosa, or the dosage form can be administered with a full glass of

water to provide the initial fluid for buoyancy. Also single unit floating capsules or tablets are associated with an “all or none concept,” but this can be overcome by formulating multiple unit systems like floating microspheres, microballoons and beads.

DESIGN OF FLOATING DOSAGE FORM

Single Unit Dosage Form: In these forms a low density approach is required in which the globular shells apparently having lower density than that of gastric fluid can be used as a carrier for drug for its controlled release. A buoyant dosage form can also be obtained by using a fluid-filled system that floats in the stomach. In coated shells popcorn, poprice, and polystyrol have been exploited as drug carriers. Sugar polymeric materials such as methacrylic polymer and cellulose acetate phthalate have been used to undercoat these shells. These are further coated with a drug-polymer mixture. The polymer of choice can be either ethylcellulose or hydroxypropyl cellulose depending on the type of release desired. Finally, the product floats on the gastric fluid while releasing the drug gradually over a prolonged duration. Fluid-filled floating chamber type of dosage forms includes incorporation of a gas-filled floatation chamber into a microporous component that houses a drug reservoir. Apertures or openings are present along the top and bottom walls through which the gastrointestinal tract fluid enters to dissolve the drug. The other two walls in contact with the fluid are sealed so that the undissolved drug remains therein. Hydrodynamically balanced systems (HBS) are designed to prolong the stay of the dosage form in the gastro intestinal tract and aid in enhancing the absorption. Such systems are best suited for drugs having a better solubility in acidic environment and also for the drugs having specific site of absorption in the upper part of the small intestine. To remain in the stomach for a prolonged period of time the dosage form must have a bulk density of less than 1. It should stay in the stomach, maintain its structural integrity, and release drug constantly from the dosage form. Various types of tablets (bilayered and matrix) have been shown to have floatable characteristics. Some of the polymers used are hydroxypropyl cellulose, hydroxypropyl methylcellulose, cross povidone, sodium carboxy methylcellulose, and ethyl cellulose

Patel et al developed intra gastric floating system for Cefuroxime Axetil. The effect of polymers like hydroxypropyl methyl cellulose (HPMC) K4M / HPMC K 100 LV ratio (polymer blend) and Sodium lauryl sulfate on drug release from HPMC matrices. Tablets were prepared using direct compression

technique. Formulations were evaluated for in vitro buoyancy and drug release. It was concluded that HPMC and SLS imparted hydrophilic environment and wettability to molecules of drug leads to more uniform drug release^[23]

Li et al designed a floating delivery system for oral controlled delivery of Calcium. Polymers used were HPMC, citric acid and Magnesium stearate. All the polymers were blended and filled in a hard gelatin capsule. These capsules were studied for floating ability and drug release. Using Statistical Optimization procedures a floating delivery system for oral controlled delivery of calcium was developed.^[24]

Patel et al developed intragastric floating tablets of Verapamil hydrochloride. HPMC, Carbopol and Xanthum gum were incorporated for gel forming properties. Buoyancy was achieved by adding an effervescent mixture of Sodium bicarbonate and Anhydrous citric acid.^[25]

Desai et al formulated novel floating controlled-release drug delivery system in an effort increase the gastric retention time of the dosage form and to control drug release. The buoyancy was attributed to air and oil entrapped in the agar gel network. A floating controlled-release 300-mg theophylline tablet having a density of 0.67 was prepared and compared *in vitro* and *in vivo*. The *in vitro* release rate of the floating tablet was slower. *In vivo* scintigraphic studies for a floating and a heavy nonfloating tablet, under fasting and nonfasting conditions, showed that the presence of food significantly increased the gastric retention time for both tablets, and tablet density did not appear to make a difference in the gastric retention time. However, the positions of the floating and nonfloating tablets in the stomach were very different.^[26]

Single-unit formulations are associated with problems such as sticking together or being obstructed in the gastrointestinal tract, which may have a potential danger of producing irritation. Due to unpredictable gastric emptying associated with Migrating Myoelectric complex motility pattern, multiparticulate systems are more advantageous than the single unit systems, as the later ones experience “all or none” emptying pattern from the stomach. Multiple unit dosage forms are claimed to reduce intersubject variability in absorption and lower the probability of dose dumping.

Multiple-Unit Dosage Forms: The purpose of designing multiple-unit dosage form is to develop a reliable formulation that has all the advantages of a single-unit form and also is devoid of any of the

above-mentioned disadvantages of single-unit formulations. In pursuit of this endeavor many multiple-unit floatable dosage forms have been designed. There are various types of multiple unit dosage forms e.g. floating microspheres, pellets and beads. Multiple unit dosage forms provide various advantages like uniform drug release, decreased intersubject variability and minimum risk of dose dumping.

Elmowafy et al (2009) prepared floating famotidine loaded mineral oil entrapped emulsion gel beads (MOEG) by emulsion gelation method. Different polysaccharides (sodium alginate, pectin) and oil concentration (10%, 20% and 30%/w/w) and drug polymer ratio (1:1, 2:1 and 3:1) were used and their influence on bead uniformity, drug entrapment efficiency and in vitro drug release was studied.^[28]

Patel et al (2006) studied the effect of drug concentration and curing time on processing and properties of calcium alginate beads containing Metronidazole by response surface methodology. Curing time was kept as low as possible to improve entrapment with increasing drug concentration. Beads formed were spherical with size range b/w 1.4 and 1.9 mm. Scanning Electron Microscope photomicrographs revealed increase in leaching of drug crystals with increase in curing time and high drug concentration.²⁸ Roy et al (2009) studied a new approach known as floating pulsatile delivery. especially the multiparticulate pulsatile approaches have gained a great importance in the recent years. Various approaches have been studied e.g. swelling or rupturing, dissolution or erosion, changed permeability of the membrane.^[29]

Nath et al (2009) designed a sustained release floating microspheres of metformin HCl, using two polymers of different permeability characteristics, Cellulose acetate butyrate (M.W. of 16000) and Eudragit RL 100 (M.W. of 150,000) using oil in oil emulsion solvent evaporation method. The prepared microspheres were studied for drug release behavior. Polymers were used separately or in combination. Results revealed that microspheres prepared from a single polymer or combination exhibit Higuchi Spherical matrix release, followed by first order and zero order kinetics.^[30]

Sato et al (2004) prepared microballons with floating properties by emulsion solvent diffusion method utilizing enteric acrylic polymer codissolved with drug in a mixture of dichloromethane and ethanol. The release properties of five different drugs exhibiting distinct water solubilities (Aspirin, Salicylic

acid, Ethoxybenzamide, Indomethacin and Riboflavin) entrapped within microballons were investigated.^[31]

EVALUATION OF FLOATING DOSAGE FORM

A. For Single Unit Dosage Forms (ex: tablets) :

(i) Floating lag time: It is the time taken by the tablet to emerge onto the surface of dissolution medium and is expressed in seconds or minutes.

(ii) In vitro drug release and duration of floating: This is determined by using USP II apparatus (paddle) stirring at a speed of 50 or 100 rpm at $37 \pm 0.2^\circ\text{C}$ in Simulated gastric fluid (pH 1.2 without pepsin). Aliquots of the samples are collected and analyzed for the drug content.

The time (hrs) for which the tablets remain buoyant on the surface of the dissolution medium is the duration of floating and is visually observed.

(iii) In vivo evaluation for gastro-retention: This is carried out by means of X-ray or Gamma scintigraphic monitoring of the dosage form transition in the GIT. The tablets are also evaluated for hardness, weight variation, etc.

B. For Multiple Unit Dosage Forms (ex: floating beads):

Apart from the In vitro release, duration of floating and in vivo gastro-retention tests, the multiple unit dosage forms are also evaluated for –

(i) Morphological and dimensional analysis with the aid of scanning electron microscopy (SEM). The size can also be measured using an optical microscope.

(ii) % yield of beads: This is calculated from

$$\frac{\text{Weight of beads obtained}}{\text{Total weight of drug and polymer}} \times 100$$

(iii) Entrapment efficiency: The drug is extracted by a suitable method, analyzed and is calculated from

$$\frac{\text{Practical amount of drug present}}{\text{Theoretical drug content}} \times 100$$

(iv) In vitro floating ability (Buoyancy %): A known quantity of microspheres are spread over the surface of a USP (Type II) dissolution apparatus filled with 900 ml of 0.1 N HCl containing 0.002% v/v Tween 80 and agitated at 100 rpm for 12 hours. After 12 hours, the floating and settled layers are separated, dried in a dessicator and weighed. The buoyancy is calculated from the following formula.

Buoyancy (%) = $W_f / (W_f + W_s) * 100$

Where W_f and W_s are the weights of floating and settled microspheres respectively.

(v) Drug-excipient (DE) interactions: This is done using FTIR. Appearance of a new peak, and/or disappearance of original drug or excipient peak indicates the DE interaction.

Apart from the above mentioned evaluation parameters, granules (ex: Gelucire 43/01) are also evaluated for the effect of ageing with the help of

Differential Scanning Calorimeter or Hot stage polarizing microscopy.

CONCLUSION

Drug absorption in the stomach is a variable process which depends upon gastric emptying and other physiological factors. Floating Delivery system can provide sufficient gastric retention which may help to provide sustained release dosage form with enhanced absorption. In spite of its various limitations serious efforts are being done to commercialize this delivery system.

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