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Floating Bilayer drug delivery systems- An Unconventional approach in Conventional Form

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ABSTRACT

Gastric emptying is a complex process and makes in vivo performance of the drug delivery systems uncertain. Floating Bilayer drug delivery system is combined principle of bilayer tablet as well as floating mechanism. Floating drug delivery system provides advantages local delivery to specific region like stomach and proximal small intestine and it's also shows better bioavailability and improved therapeutic activity. Floating Bilayer tablet is suitable for sequential release of two drugs in combination, separate two incompatible substances and also for sustained release tablet in which one Layer is immediate release as initial dose and second layer is maintenance dose. The purpose of this paper is to review the concept of Floating Bilayer drug delivery systems with the recent literature and current technology used in the development of Floating Bilayer drug delivery system as well as summarizes evaluation method and applications of various floating dosage forms.

Key words: - Bilayer Floating drug delivery systems, Gastric residence time, Swelling index, Buoyancy

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INTRODUCTION

The oral route is increasingly being used for the delivery of therapeutic agents because the low cost of the therapy and ease of administration lead to high levels of patient compliance. More than 50% of the drug delivery systems available in the market are oral drug delivery systems[1]. Controlled-release drug delivery systems (CRDDS) provide drug release at a predetermined, predictable, and controlled rate. Controlled-release drug delivery system is capable of achieving the benefits like maintenance of optimum therapeutic drug concentration in blood with predictable and reproducible release rates for extended time period; enhancement of activity of duration for short half-life drugs; elimination of side effects; reducing frequency of dosing and wastage of drugs; optimized therapy and better patient compliances[2,3]. The successful development of oral controlled drug delivery systems requires an understanding of the three aspects of the system, namely.

1. The physiochemical characteristics of the drug
2. Anatomy and physiology of GIT and Characteristics of Dosage forms[4]

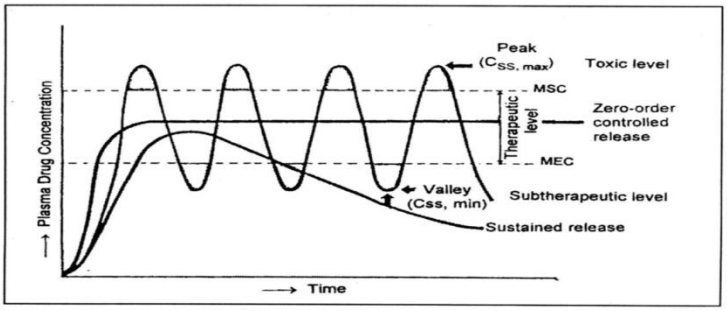

Figure:-1 Drug level verses time profile showing differences between zero order, controlled releases, slow first order sustained release and release from conventional table

Good fundamental understanding of the anatomic and physiological characteristics of the human GIT is required to modulate the gastrointestinal transit time of a drug through FDDS for maximal Gastrointestinal absorption of drugs and site-specific delivery[5].

Gastrointestinal retention

Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients5. To successfully

modulate the gastrointestinal transit time of a drug delivery system through floating drug delivery system (FDDS) For maximal gastrointestinal absorption of drugs and site-specific delivery, one needs to have a good fundamental understanding of the anatomic and physiological characteristics of the human GIT. These are outlined and briefly discussed[1].

Stomach anatomy

The main function of the stomach is to process and transport food. It serves as a short-term storage reservoir, allowing a rather large meal to be consumed quickly. Substantial enzymatic digestion is initiated in stomach, particularly of proteins. Vigorous contractions of gastric smooth muscle mix and grind foodstuffs with gastric secretions, resulting in liquefaction of food. As food is liquefied in the stomach, it is slowly released into the small intestine for further processing[6].

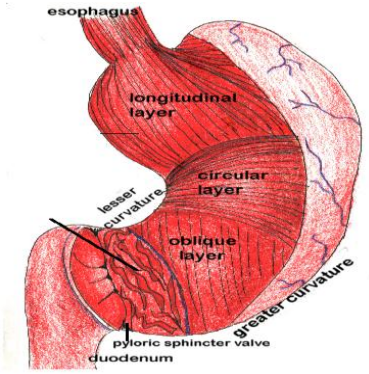

Figure:-2 Anatomy of stomach

Anatomically the stomach is divided into 3 regions: fundus, body, and antrum (pylorus). The proximal part made of fundus and body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions[7]. It has been reported that the mean value of pH in fasted healthy subjects is 1.1± 0.15. But when food comes into the stomach, the pH may rise to levels in the 3.0 to 4.0 level due to the buffering capacity of proteins. However, in fasted state, basal gastric secretion in women is slightly lower than that of men[8]. Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC), which is further divided into following 4 phases

Phase I (Basal phase) lasts from 30 to 60 minutes with rare contractions.

Phase II (Preburst phase) lasts for 20 to 40 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.

Phase III (burst phase) lasts for 10 to 20 minutes. It includes intense and regular contractions for short period. It is due to this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave.

Phase IV lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.

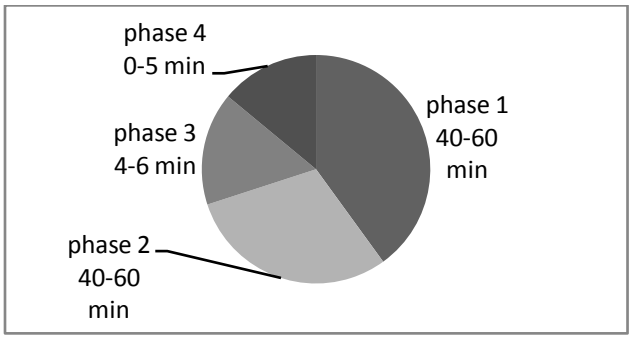

Figure:-3 Phase Diagram of stomach

FACTORS AFFECTING GASTRIC RESIDENCE TIME OF FDDS

a) Formulation factors

Size of tablets

Retention of floating dosage forms in stomach depends on the size of tablets. Small tablets are emptied from the stomach during the digestive phase, but large ones are expelled during the house keeping waves[9]. Floating and nonfloating capsules of 3 different sizes having a diameter of 4.8 mm (small units), 7.5 mm (medium units), and 9.9 mm (large units), were formulated and analyzed for their different properties. It was found that floating dosage units remained buoyant regardless of their sizes on the gastric contents throughout their residence in the gastrointestinal tract, while the nonfloating dosage units sank and remained in the lower part of the stomach. Floating units away from the gastro-duodenal junction were protected from the peristaltic waves during digestive phase while the nonfloating forms stayed close to the pylorus and were subjected to propelling and retropelling waves of the digestive phase[10]. Density of tablets Density is the main factor affecting the gastric residence time of dosage form. A buoyant dosage form having a density less than that of the gastric fluids floats, since it is away from the pyloric sphincter, the dosage unit is retained in the stomach for a prolonged period. A density of less than 1.0g/ml i.e. less than that of gastric contents has been reported. However, the floating force kinetics of such dosage form has shown that the bulk density of a dosage form is not the most appropriate parameter for describing its buoyancy capabilities[11].

Shape of tablets

The shape of dosage form is one of the factors that affect its gastric residence time. Six shapes (ring tetrahedron, cloverleaf, string, pellet, and disk) were screened *in vivo* for their gastric retention potential. The tetrahedron (each leg 2cm long) rings (3.6 cm in diameter) exhibited nearly 100% retention at 24 hr[12].

Viscosity grade of polymer

Drug release and floating properties of FDDS are greatly affected by viscosity of polymers and their interaction. Low viscosity polymers (e.g., HPMC K100 LV) were found to be more beneficial than high viscosity polymers (e.g., HPMC K4M) in improving floating properties. In addition, a decrease in the release rate was observed with an increase in polymer viscosity[13].

b) Idiosyncratic factors

Gender

Women have slower gastric emptying time than do men. Mean ambulatory GRT in meals (3.4±0.4 hours) is less compared with their age and race-matched female counterparts (4.6±1.2 hours), regardless of the weight, height and body surface[4].

Age

Low gastric emptying time is observed in elderly than do in younger subjects. Intrasubject and intersubject variations also are observed in gastric and intestinal transit time. Elderly people, especially those over 70 years have a significantly longer GRT[14].

Posture

i) Upright position

An upright position protects floating forms against postprandial emptying because the floating form remains above the gastric contents irrespective of its size14. Floating dosage forms show prolonged and more reproducible GRTs while the conventional dosage form sink to the lower part of the distal stomach from where they are expelled through the pylorus by antral peristaltic movements[15].

ii) Supine position

This position offers no reliable protection against early and erratic emptying. In supine subjects large dosage forms (both conventional and floating) experience prolonged retention. The gastric retention of floating forms appear to remain buoyant anywhere between the lesser and greater curvature of the stomach. On moving distally, these units may be swept away by the peristaltic movements that propel the gastric contents towards the pylorus, leading to significant reduction in GRT compared with upright subjects[16].

Concomitant intake of drugs

Drugs such as prokinetic agents (e.g., metoclopramide and cisapride), anti Cholinergics (e.g., atropine or propantheline), opiates (e.g., codeine) may affect the performance of FDDS. The coadministration of GI-motility decreasing drugs can increase gastric emptying time[16].

Feeding regimen

Gastric residence time increases in the presence of food, leading to increased drug dissolution of the dosage form at the most favorable site of absorption. A GRT of 4-10 h has been reported after a meal of fats and proteins[17].

SUITABLE DRUGS FOR BILAYE FLAOTING DRUG DELIVERY SYSTEM

Delivery of the Drugs in continuous and controlled manner have a lower level of side effects and provide their effects without the need for repeated dosing or with a low dosage frequency. Sustained release in the stomach is also useful for therapeutic agents that the stomach does not readily absorb, since sustained release prolongs the contact time of the agent in the stomach or in the upper part of the small intestine, from where absorption occurs and contact time is limited. Appropriate candidates for controlled release gastroretentive dosage forms are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of the GIT.

1. Narrow absorption window in GI tract, e.g., riboflavin and Levodopa
2. Basically absorbed from stomach and upper part of GIT, e.g.,chlordiazepoxide an cinnarazine.
3. Drugs that disturb normal colonic bacteria, e.g., amoxicillin trihydrate.
4. Locally active in the stomach, e.g., antacids and misoprostol.
5. Drugs that degrade in the colon, e.g., ranitidine HCl and metronidazole.

Table 1:- Marketed Formulations of Floating Drug Delivery System [18, 19, 20, 21, 22,23]

S.No	Brand Name	Drug	Dosage Form
1	Topalkan	Aluminum -Magnesium antacid	Floating Liquid Alginate Preparation
2	Liquid Gavison	Aluminum hydroxide, Magnesium carbonate	Effervescent Floating Liquid Alginate Preparation
3	Valrelease	Diazepam	Floating Capsule
4	Madopar	Levodopa, Benserazide	Floating Controlled Release Capsule
5	Cifran OD	Ciprofloxacin	Gas-generating Floating Tablets
6	Conviron	Ferrous sulphate	Colloidal Gel Forming FDDS
7	Cytotec	Misoprostal	Bilayer Floating Capsule
8	Amalgate Float Coat	Antacid	Floating Dosage Form

Table 2:- Dosage Forms of FDDS with Examples of Various Drugs [18,20,]

Dosage Forms	Drugs
Floating tablets	Acetaminophen, Acetylsalicylic acid, Ampicillin, Amoxicillin trihydrate, Atenolol, Captopril, Cinnerzine, Diltiazem, Fluorouracil, Isosorbide dinitrate, Isosorbid mononitrate, p- Aminobenzoic acid
Floating capsules	Furosemide, L-DOPA, Benserazide, Nicardipine, Misoprostol, Propranolol, Pepstatin
Floating microspheres	Aspirin, Griseofulvin, p-nitro aniline, Ibuprofen, Terfenadine, Tranilast
Floating granules	Cinnarizine, Diclofenac sodium, Diltiazem, Indomethacin, Fluorouracil, Prednisolone, Isosorbide mononitrate ,Isosorbide dinitrate.
Powders	Several basic drugs-Riboflavin,phosphate, Sotalol, Theophylline.
Films	Cinnerzine, P-Aminobenzoic acid, Piretanide, Prednisolone, Quinidine gluconate
Multiple unit floating Dosage form	Clarithromycin, *p*-aminobenz oic acid)
Bilayer tablet	Misoprostal
Foams/hollow bodies	Ibuprofen
Floating controlled release capsule	Levodopa, Benserazide

Table 3:- Patents on Floated Drug Delivery System for Different Dosage Forms

Sr no	Type of Formulation	Patent No.
1	Bilayer Tablet[24]	EP-002445
2	Multiple Unit Floating Dosage Form[25]	European patent (EP) 10697
3	Gastro Retentive Dosage Form[26]	U.S-7,413,752
4	Floating Tablet[27]	U.S-66,352279
5	Microspheres[28]	U.S-6207197
6	3-layer Tablet[29]	U.S-5780057
7	Foams (or) Hollow Bodies[30]	U.S-5626876
8	Floating Tablet[31]	U.S-5169639
9	Granule[32]	U.S-4844905
10	Floating Capsule[33]	U.S-4814178,-79
11	Tiny Pills[34]	U.S-4434153
12	Floating Capsule[35]	U.S-4126672
13	Floating Device[36]	U.S-4055178
14	Empty Globular Shells[37]	U.S-3976164

INTRODUCTION TO FLOATING BILAYER TABLET

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so 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 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 Floatation of a drug delivery system in the stomach can be achieved by incorporating floating chamber filled with vacuum, air, or inert gas.[38] from the system. After release of drug, the residual system is emptied from the stomach[38]. 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.

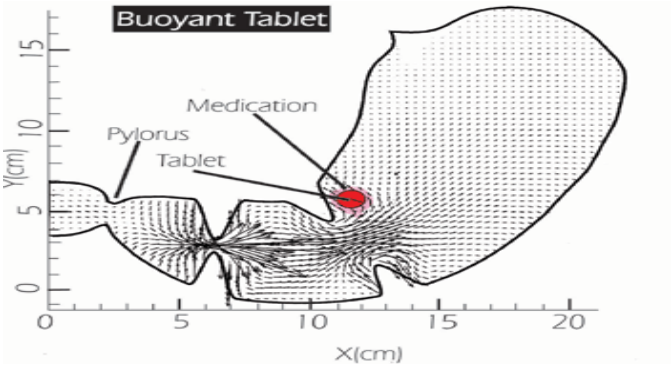

Figure:-4 Buoyant Tablet

Bilayer tablets are composed of two layers of granulation compressed together. They have appearance of a sandwich because the edges of each layer are exposed. They have the appearance of a sandwich because the edges of each layer are exposed. Bi-layer tablets are prepared with one layer of drug for immediate release with second layer design to release drug, later, either as second dose or in an extended release manner. [39]

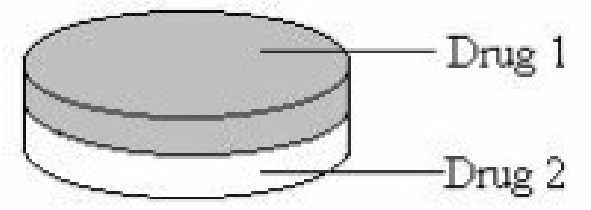

Figure:-5 Bilayer floating Tablet

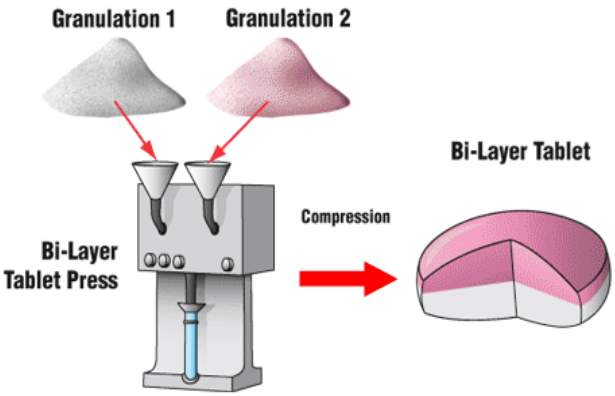

Figure:-6 Bilayer tablet press

Compression cycle for bilayer tablet Bi-layer tablets are tablet, made by compressing two different granulations fed into a die succession, one on top of another, in layers. Each layer comes from a separate feed frame with individual weight control. Rotary tablet press can be set up for two or three layers. More are possible but the design becomes very special. Figure 6 represents compression cycle of bi-layer tablet[39].

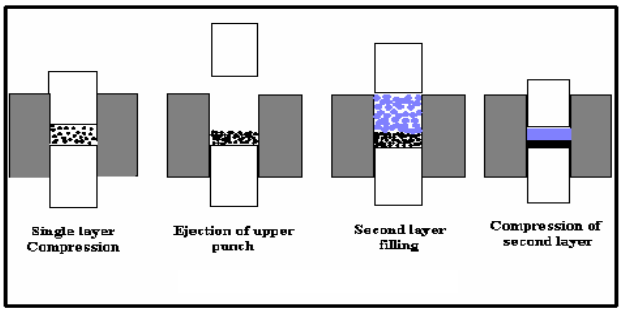

Figure:-7 Compression cycle of bilayer flaoting tablet

Advantages

- This dosage form has the advantage of separating two incompatible substances.
- It makes possible Extended-release preparations with the immediate-release quantity in one and the slow-release portion in the second.
- The weight of each layer can be accurately controlled, in the contrast to putting one drug of a combination product in a sugar coating.
- Two-layer tablet require less material than compression coated tablets, weight less, and may be thinner.
- Analytical work may be simplified by separating of the layer prior to assay.
- Bilayer tablet prepared from two different release pattern containing layer like immediate release layer and sustain release layer shows release like following figure;

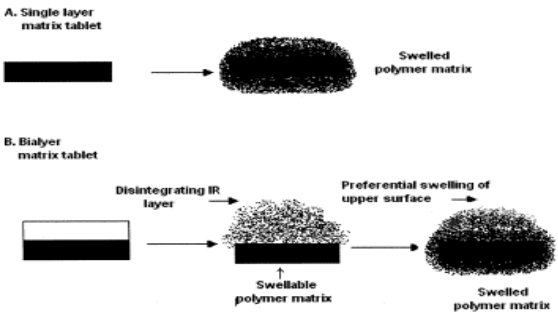

Figure:-8 Release pattern of bilayer floating tablet

Bilayer tablet are prepared by compressing two different blend fed into a die succession, one on the top of another, in layers. Each layer comes from separate fed frame with individual weight control. Rotary tablet press can be set up for two layers.

1) RoTab Bilayer [40]

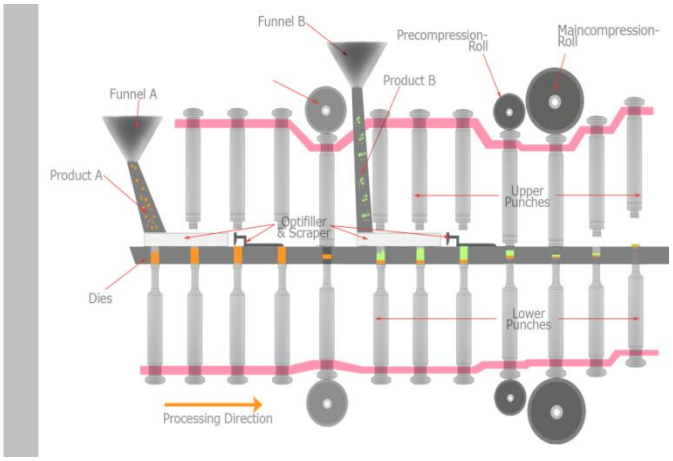

Figure:- 9 RoTab Bilayer

1) Compactest bilayer rotary tablet press on the market with high sophisticated R&D and production functions
2) Noise and vibration reduced for optimum operation in the lab
3) Easy maintenance by automatical punch lubrication with intervall setting
4) Optimized for operation with only one occupied punch station
5) Easy sampling for first layer (weight adjustment)
6) 2 Optifiller for 1st and 2nd tablet layer with special dust extraction rails to minimize cross-contamination
7) A touch screen display allows to operate and control the machine easily by the operator and visualizes all machine parameters, as compaction forces, speeds, tablet production etc.

2)Mini Bi-Layer Press (for compression of double layer tablet)[40]

1) Designed to represent two-layer tablet productions at a small scale.
2) Larger turret diameter & variable speed allow for realistic scale up to large rotary presses .
3) Two forces feeder system helps to maintain uniform die fill and represents production equipment .
4) Pressure compensation hydraulic system.
5) Tablet thinckness & weight adjustment settings are outside the machine.
6) Designed as per cGMP norms.
7) Lower punch seal to avoid jamming of the lower punches.
8) Transparent Guards at compression zone with safety switches.

3)KORSCH XM 12 Bi-Layer Tablet Press[40]

It is a small-scale press which is ideal for product development, scale-up, clinical trials, and midrange production. The bi-layer execution, single-layer conversion kit, and exchangeable turret offer unprecedented flexibility. The XM 12 Bi-Layer Tablet Press offers a new standard in GMP with extreme accessibility to the compression zone and a combination of quick disconnects and smooth surfaces that permit fast cleaning and changeover.

The XM 12 Bi-Layer Tablet Press features a retractable second layer feeder that permits automated first layer sampling at production speeds. The first layer sampling capability also offers a hardening feature, in which the main compression station will automatically compress the first layer tablet for in-process measurement. The two feeders are zero clearance and are configured with an integrated dust extraction manifold, which cleans the die table and completely eliminates any potential for cross-contamination.

4)MODUL™ P rotary tablet press with Bi-layer ECM[40]

GEA Courtoy's MODUL™ P, the smallest tablet press in the MODUL™ range, is now available with an Exchangeable Compression Module (ECM) for bi-layer tablet (bilayer) production.

The MODUL™ P with bi-layer ECM is the first press to enter the market that enables continuous bi-layer tabletting on a small scale. It is the perfect solution to your bi-layer formulation development, clinical trial and other small-scale production needs

Advantages of Floating Bilayer Drug Delivery System

- These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine, e.g., riboflavin and furosemide.
- The fluctuations in plasma drug concentration are minimized, and concentration-dependent adverse effects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index.
- The efficacy of the medicaments administered utilizing the sustained release principle of floating formulation has been found to be independent of the site of particular medicaments.
- Complete absorption of the drug from the floating dosage form is expected even at the alkaline pH of the intestine. The dissolution of the drug in gastric fluid occurs and then the dissolved drug is available for absorption in the small intestine after emptying of the stomach contents.

- Poor absorption is expected when there is vigorous intestinal movement and a shorted transit time as might occur in certain type of diarrhea. Under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.
- 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. A significant increase in the bioavailability of floating dosage forms (42.9%) could be achieved as compared with commercially available LASIX tablets (33.4%) and enteric-coated LASIX-long product (29.5%).

Limitations of Bilayer Floating Drug Delivery Systems

- A high level of fluid in the stomach is required for drug delivery to float and work efficiently.
- Drugs which have stability and solubility problems in GIT are not suitable candidates for these types of systems.
- Drugs such as nifedipine, which under goes first pass metabolism may not be desirable for the preparation of these types of systems. Drugs which are irritant to Gastric mucosa are also not desirable.
- The drug substances that are unstable in the acidic environment of the stomach are not suitable candidates to be incorporated in the systems.

IN VITRO AND IN VIVO EVALUATION PARAMETERS OF STOMACH SPECIFIC BFDDS

Different studies reported in the literature indicate that pharmaceutical dosage forms exhibiting gastric residence in vitro floating behavior show prolonged gastric residence in vivo. Although, in vitro floating behavior alone is not sufficient proof for efficient gastric retention so *in vivo* studies can provide definite proof that prolonged gastric residence is obtained.

1) Hardness, friability, assay, content uniformity (Tablets)

These tests are performed as per described in specified monographs.

2) Floating lag time and total floating time determination

The time between the introduction of the tablet into the medium and its rise to upper one third of the dissolution vessel is termed as floating lag time and the time for which the dosage form floats is termed as the floating or flotation time. These tests are usually performed in simulated gastric

fluid or 0.1 mole.lit-1 HCl maintained at 37o C, by using USP dissolution apparatus containing 900 ml of 0.1 molar HCl as the dissolution medium[41].

3) Drug release

The test for in vitro drug release studies are usually carried out in simulated gastric and intestinal fluids maintained at 370 C. Dissolution tests are performed using the USP dissolution apparatus. Samples are withdrawn periodically from the dissolution medium, replaced with the same volume of fresh medium each time, and then analyzed for their drug contents after an appropriate dilution. Recent methodology as described in USP XXIII states that the dosage unit is allowed to sink to the bottom of the vessel before rotation of blade is started. A small, loose piece of non reactive material such as not more than a few turns of wire helix may be attached to the dosage units that would otherwise float. However, standard dissolution methods based on the USP or British Pharmacopoeia (BP) have been shown to be poor predictors of in vitro performance for floating dosage forms.

4)Drug loading, drug entrapment efficiency, particle size analysis, surface characterization, micromeritics studies and percentage yield (for floating microspheres and beads)

Drug loading is assessed by crushing accurately weighed sample of beads or microspheres in a mortar and added to the appropriate dissolution medium which is then centrifuged, filtered and analyzed by various analytical methods like spectrophotometry. The percentage drug loading is calculated by dividing the amount of drug in the sample by the weight of total beads or microspheres. The particle size and the size distribution of beads or microspheres are determined in the dry state using the optical microscopy method. The external and cross-sectional morphology (surface characterization) is done by scanning electron microscope (SEM). The measured weight of prepared microspheres was divided by total amount of all non-volatile components used for the preparation of microspheres, which will give the total percentage yield of floating microspheres[42, 43].

5) Resultant weight determination

Bulk density and floating duration have been the main parameters to describe the adequacy of a dosage form's buoyancy Although single density determination does not predict the floating force evolution of the dosage form because the dry material of it is made progressively reacts or interacts with in the gastric fluid to release its drug contents. So to calculate real floating capabilities of dosage form as a function of time a novel method has been conceived. It operates by force equivalent to the force F required to keep the object totally submerged in the fluid. This force determines the resultant weight of the object when immersed and may be used to quantify

its floating or non floating capabilities. The magnitude and direction of the force and the resultant weight corresponds to the Victoria sum of buoyancy (Fbuoy) and gravity (Fgrav) forces acting on the objects as shown in the equal

F = Fbuoy – Fgrav

F = dfgV – dsgV = (df-ds) gV

F = (df – M/V) gV

In which the F is total vertical force (resultant weight of the object), g is the acceleration due to gravity, df if the fluid density, ds is the object density is the object mass and V is the volume of the object.

6) Weight gain and water uptake (WU)

Weight gain or water uptake can be studied by considering the swelling behavior of Floating dosage form. The study is done by immersing the dosage form in simulated gastric fluid at 37oC and determining the dimensional changes like tablet diameter and/ or thickness at regular 1-h time intervals until 24 h, the tablets were removed from beaker, and the excess surface liquid was removed carefully using the paper. The swollen tablets were then reweighed and WU is measured in the terms of percent weight gain, as given by equation

WU = (Wt – Wo) X 100 / Wo

In which Wt and Wo are the weights of the dosage form at time t and Initially, respectively[11].

7) X-Ray/Gamma scintigraphy

For *in vivo* studies, X-Ray/Gamma Scintigraphy is the main evaluation parameter for floating dosage form. In each experiment, the animals are allowed to fast overnight with free access to water, and a radiograph is made just before the administration of the floating tablet to ensure the absence of radio-opaque material. Visualization of dosage form by X-ray is due to the inclusion of a radio-opaque material. The formulation is administered by natural swallowing followed by 50 mL of water. The radiographic imaging is taken from each animal in a standing position, and the distance between the source of X-rays and the animal should kept constant for all imaging, so that the tablet movement could be easily noticed. Gastric radiography was done at 30-min time intervals for a period of 5 h using an X-ray machine. Gamma scintigraphy is a technique whereby the transit of a dosage form through its intended site of delivery can be non-invasively imaged *in vivo* via the judicious introduction of an appropriate short lived gamma emitting radioisotope. The inclusion of a γ-emitting radionucleide in a formulation allows indirect external observation using a γ-camera or scintiscanner. But the main drawback of γ- scintigraphy

are the associated ionizing radiation for the patient, the limited topographic information, low resolution inherent to the technique and the complicated and expensive preparation of radiopharmaceutical[44,45].

8) Pharmacokinetic studies

Pharmacokinetic studies include AUC (Area under Curve), Cmax, and time to reach maximum plasma concentration (Tmax) were estimated using a computer. Statistical analyses were performed using a Student t test with p, 0.05 as the minimal level of significance[46].

9) Specific Gravity

Displacement method is used to determine the specific gravity of floating system using benzene as a displacing medium[47].

FUTURE PROSPECTS WITH RESPECT TO HERBAL DRUGS

Herbal drug delivery is the emerging field in the pharmacy. The use of FBDDS for herbal medicament is the novel approach for the better delivery. The drug release profile has been a major focusing area for the pharmaceutical research scientists for the past two decades. The scientists are finding it a great opportunity to work on GI transit profiles. This has given rise to new products with substantial benefits to the patients. Now with the advent of FBDDS the products have been designed which could release drug for upto 12 or 24 hrs. Using bilayer floating approach combination of two herbal drugs can be also given for more therapeutic effect. Bilayer floating also provide the IR and SR concept for herbal drug as well.

Some herbal drugs that can be delivered as bilayer floating drug delivery systems are:

Forskolin: A natural root extract from the Coleus Forskolin, was developed into a gastro retentive floating drug delivery system, using different grades of HPMC. The drug is used as anti-obesity agent reducing fat in body muscles. Forskolin increases cAMP accumulation, and therefore stimulates lipolysis. So, with high concentrations of forskolin, cAMP and lipolysis increases Enhanced lipolysis increases fat degradation and fat usage as a fuel in the body. This may promote fat and weight loss. It is thought that supplementing with forskolin may enhance fat loss without loss of muscle mass.[48]

Black myrobalan: The aqueous extract of black myrobalan (Terminalia chebula Retz) has been shown to have uniform antibacterial activity against ten clinical strains of H. pylori.[29]

Ginger: Ginger root (Zingiber officinale Rosc.) has been used traditionally for the treatment of gastrointestinal ailments such as motion sickness, dyspepsia and hyperemesis gravidarum, and is also reported to have chemopreventative activity in animal models. The gingerols are a group of

structurally related polyphenolic compounds isolated from ginger and known to be the active constituents.[49]

Turmeric: Curcumin, a polyphenolic chemical constituent derived from turmeric (Curcuma longa L.), has been shown to prevent gastric and colon cancers in rodents. Many mechanisms had been proposed for the chemopreventative effects, although the effect of curcumin on the growth of H. pylori has not been reported.[49]

Licorice: In a recent study at the Institute of Medical Microbiology and Virology, Ger-many, researchers found that licorice extract produced a potent effect against strains of H. pylori that are resistant against clarithromycin, one of the antibiotics typically used in the three antibiotic treatment regimens.[49]

Berberine: Berberine is a plant alkaloid isolated from the roots and bark of several plants including golden seal, barberry,Coptis chinensis Franch. And Yerba mansa. Berberine-containing plants have been used medicinally in ayurvedic and Chinese medicine, and are known to have antimicrobial activity against a variety of organisms including bacteria, viruses, fungi, protozoans, helminths, and chlamydia. More recently, berberine had been demonstrated to be effective against H. pylori.[49]

All these herbal drugs can be prepared as gastroretentive floating bilayer drug delivery system.

CONCLUSION

FBDDS approach may be used for various potential active agents with narrow absorption window, e.g. antiviral, antifungal and antibiotic agents (sulphonamides, quinolones, penicillins, cephalosporins, aminoglycosides and tetracyclines) which are absorbed from very specific regions of GI tract and whose development has been halted due to the lack of appropriate pharmaceutical technologies.So Pharmaceutical industries are trying to prepare one of the most economic and convetional dosage form, and Floating bilayer tablet is best then any other approaches. In addition, by continual supplying the drug to its most efficient site of absorption, the dosage form may allow for more effective oral use of peptide and protein drugs such as calcitonin, erythropoetin, vasopressin, insulin, low molecular weight heparin, and LHRH. Some of the unresolved critical issues related to the rational development of FBDDS include, the quantitative efficiency of floating delivery systems in the fasted and fed states and the correlation between prolonged GRT and SR/PK characteristics. However, we are as close as we have ever been to see a greater transition of gastric retention devices from developmental level to the manufacturing and commercial level.

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