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A Typical Review On Floating Drug Delivery System

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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. Several approaches are currently utilized in the prolongation of the GRT, including floating drug delivery systems (FDDS), also known as hydro dynamically balanced systems (HBS), swelling and expanding systems, polymeric bioadhesive systems, modified-shape systems, high-density systems, and other delayed gastric emptying devices. The recent developments of FDDS including the physiological and formulation variables affecting gastric retention, approaches to design single-unit and multiple-unit floating systems, and their classification and formulation aspects are covered in detail. This review also summarizes the in- vitro techniques, in- vivo studies to evaluate the performance and application of floating systems, and applications of these systems.

Keywords: *Floating drug delivery systems, gastroretensive system, in- vitro & in- vivo studies to evaluation of FDDS*

1.Introduction

It is a type of Gastro retentive system where drug can remain in the gastric region for several hours and significantly prolong the gastric residence time of drug. Prolonged gastric retention improves bioavailability, reduces drug waste. Improve solubility for drugs that are less soluble in high pH environments. It has application for local drug delivery to the stomach and proximal small intestines. It helps to provide better availability of new products with new therapeutic possibilities and substantial benefit for patients. The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion[1], flotation[2], sedimentation[3], expansion modified shape systems[4] or by the simultaneous administration of pharmacological agent[5-6] that delay gastric emptying. Based on these approaches, classification of floating drug delivery systems (FDDS) has been described in detail. *In-vivo/in-vitro* evaluation of FDDS has been discussed by scientists to assess the efficiency and application of such systems.

2.Basic Gastrointestinal Tract Physiology

Anatomically the stomach is divided in to three regions fundus, body and antrum (pylorus).The proximal part made of fundus and body acts as a reservoir for undigested materials, where as the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions [7]. Gastric emptying occurs in both the fasting and fed states. During the fasting state an interdigestive series of electrical events take place which cycle both through stomach and intestine every 2-3 hrs, which is called as interdigestive myloelectric cycle or Migrating Myloelectric Cycle (MMC) which is further divided in to four phases. After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state which is also termed as digestive motility pattern (Figure1, 2, 3).

- Phase 1-(Basic phase)-last from 30-60 minutes with rare contractions.
- Phase 2-(Preburst phase)-last for 20-40 minutes with intermittent action potential and contractions.
- Phase 3-(Burst phase)-last for 10-20 minutes which includes intense and regular contractions for short period.
- Phase 4-last for 0-5 minutes and occurs between phase 2 and 1 of 2 consecutive cycles.

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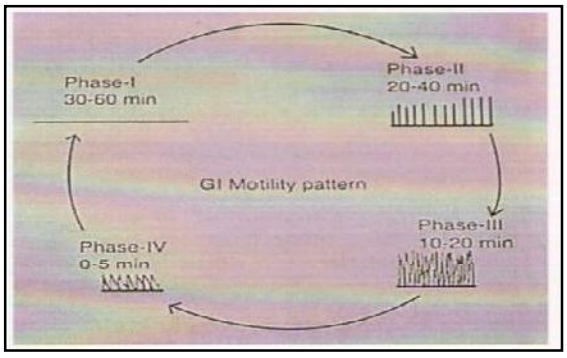


Figure 1: Shows Gastrointestinal motility pattern

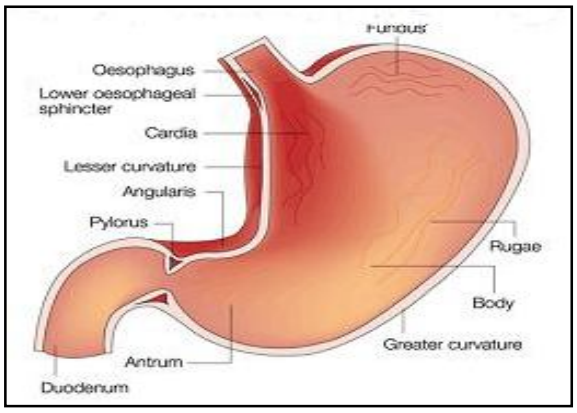


Figure 2: Shows basic structure of stomach

3.Advantages Of Floating Drug Delivery System[8,9]

- The gastroretensive systems are advantageous for drugs absorbed through the stomach, eg. Ferrous salts, antacids.
- Floating dosage forms such as tablets or capsules will remains in the solution prolonged time even at the alkaline pH of the intestine.
- FDDS are advantageous for drugs meant for local action in the stomach, eg: Antacids
- 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.

- FDDS dosage forms are advantageous in case of vigorous intestinal movement and in diarrhea to keep the drug in floating condition in stomach to get a relatively better response.

4.Disadvantages Of Floating Drug Delivery System[8,9]

- The drugs that are significantly absorbed through out gastrointestinal tract, which undergo significant first pass metabolism, are only desirable candidate.
- Drugs such as Nifedipine, which is well absorbed along the entire GI tract and which undergo significant first-pass metabolism, may not be suitable candidates for FDDS since the slow gastric emptying may lead to reduced systemic bioavailability. Also there are limitations to the applicability of FDDS for drugs that are irritant to gastric mucosa.
- Some drugs present in the floating system causes irritation to gastric mucosa.

5.Classification/ Various Approaches To Design Fdds

5.1.Single Unit Floating Dosage Systems

- Effervescent Systems (Gas-generating System)
- Non-effervescent Systems

5.2.Multiple Unit Floating Dosage Systems

- Non-effervescent Systems
- Effervescent Systems (Gas-generating System)
- Hollow Microspheres

5.3.Raft Forming Systems

5.3.1.Single Unit Floating Dosage Systems

5.3.1.1.Effervescent systems (gas-generating systems)

These buoyant systems utilized matrices prepared with swellable polymers like HPMC, polysaccharides like chitosan, effervescent components like sodium bicarbonate, citric acid and tartaric acid or chambers containing a liquid that gasifies at body temperature. The optimal stoichiometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76:1. The common approach for preparing these systems involves resin beads loaded with bicarbonate and coated with ethyl cellulose. The coating, which is insoluble but permeable, allows permeation of water. Thus, carbon dioxide is released, causing the beads to float in the stomach [10]. eg: HPMC, polyacrylate polymers, polyvinyl acetate, polycarbonates sodium alginate, Carbopol®, agar, calcium chloride and polyethylene oxide

5.3.1.2.Non-effervescent systems

This type of system, after swallowing, swells unrestrained via imbibition of gastric fluid to an extent that it prevents their exit from the stomach. These systems may be referred to as the 'plug-type systems' since they have a tendency to remain lodged near the pyloric sphincter. One of the formulation methods of such dosage forms involves the mixing of drug with a gel, which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of less than one within the outer gelatinous barrier. The air trapped by the swollen polymer confers buoyancy to these dosage forms. Examples of this type of FDDS include colloidal gel barrier [11], micro porous compartment system , alginate beads , and hollow microspheres[12] . Another type is a Fluid- filled floating chamber which includes incorporation of a gas-filled floatation chamber into a micro porous component that houses a drug reservoir[13] . 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 un dissolved drug remains therein. The fluid present could be air, under partial vacuum or any other suitable gas, liquid, or solid having an appropriate specific gravity and an inert behavior. The device is of swallowable

size, remains afloat within the stomach for a prolonged time and after the complete release the shell disintegrates, passes off to the intestine, and is eliminated. This particular characteristic would be applicable to drugs that have pH-dependent solubility, a narrow window of absorption, and are absorbed by active transport from either the proximal or distal portion of the small intestine.

5.4.Multiple Unit Floating Systems

Drawback in the area of HBS and other floating tablets are that high variability of gastrointestinal transit time, when orally administered, because of their all-or-nothing gastric emptying nature. In order to overcome the above problem, multiple unit floating systems were developed, which reduce the inter-subject variability in absorption and lower the probability of dose-dumping. Reports have been found on the development of both non-effervescent and effervescent multiple unit systems[14] . Much research has been focused and the scientists are still exploring the field of hollow microspheres, capable of floating on the gastric fluid and having improved gastric retention properties.

5.4.1.Non-Effervescent Systems

There was no much literatures report found in on non-effervescent multiple unit systems, as compared to the effervescent systems. However, few workers have been reported the possibility of developing such system containing indomethacin, using chitosan as the polymeric excipient[14]. A multiple unit HBS containing indomethacin as a model drug prepared by extrusion process is reported. A mixture of drug, chitosan and acetic acid is extruded through a needle, and the extrudate is cut and dried. Chitosan hydrates and floats in the acidic media, and the required drug release could be obtained by modifying the drug-polymer ratio.

5.4.2.Effervescent Systems (Gas-Generating Systems)

Reports was found for sustained release floating granules containing tetracycline hydrochloride, prepared by mixture of drug granulates of two stages A and B, of which A contains 60 parts of HPMC, 40 parts of polyacrylic acid and 20 parts of drug and B contains 70 parts of sodium bicarbonate and 30 parts of tartaric acid. 60 parts by weight of granules of stage A and 30 parts by weight of granules of stage B are mixed along with a lubricant and filled into capsule. In dissolution media,

the capsule shell dissolves and liberates the granules, which showed a floating time of more than 8 hours and sustained drug release of 80% in about6.5 hours. Floating mini capsules of pepstatin having a diameter of 0.1-0.2 mm has been reported by These minicapsule contain a central core and a coating. The central core consists of a granule composed of sodium bicarbonate, lactose and a binder, which is coated with HPMC. Pepstatin is coated on the top of the HPMC layer. The system floats because of the CO_2 release in gastric fluid and the pepstatin resides in the stomach for prolonged period. Alginates have received much attention in the development of multiple unit systems. A multiple unit system was prepared [15] comprises of calcium alginate core and calcium alginate/PVA membrane, both separated by an air compartment. In presence of water, the PVA leaches out and increases the membrane permeability, maintaining the integrity of the air compartment. Increase in molecular weight and concentration of PVA, resulted in enhancement of the floating properties of the system. Freeze-drying technique is also reported for the preparation of floating calcium alginate beads, in that sodium alginate solution is added drop wise into the aqueous solution containing calcium chloride, causing the instant gelation of the droplet surface, due to the formation of calcium alginate.

A new multiple type of floating dosage system had developed having a pill in the core, composed of effervescent layers and swellable membrane layers coated on sustained release pills . The inner layer of effervescent agents containing sodium bicarbonate and tartaric acid was divided into 2 sub layers to avoid direct contact between the 2 agents. These sub-layers were surrounded by a swellable polymer membrane containing polyvinyl acetate and purified shellac. When this system was immersed in the buffer at 37°C, it settled down and the solution permeated into the effervescent layer through the outer swellable membrane. CO_2 was generated by the neutralization reaction between the 2 effervescent agents, producing swollen pills (like balloons) with a density less than 1.0 g/ml [16]

Table 1 . Shows the list of drugs formulated as single and multiple unit forms of floating drug delivery systems

5.4.3.Hollow microspheres

The general techniques are used in this preparation include simple solvent evaporation and solvent diffusion and evaporation. The drug release and better floating properties mainly depend on the type of polymer, plasticizer and the

Tablets	Cholrpheniramine maleate, Theophylline, Furosemide, Ciprofloxacin, Captopril, Acetylsalicylic acid, Nimodipine, Amoxycillin trihydrate, Verapamil HCI, Isosorbide di nitrate, Sotalol, Isosorbide mononitrate, Aceraminophen, Ampicillin, Cinnarazine, Dilitiazem, Florouracil, Piretanide, Prednisolone,Riboflavin- 5`Phosphate.
Capsules	Nicardipine, L-Dopa and benserazide, chlordizepoxide HCI, Furosemide, Misoprostal, Diazepam,Propranlol, Urodeoxycholic acid.
Microspheres	Verapamil, Aspirin, Griseofulvin, and p-nitroanilline, Ketoprofen, Tranilast, Iboprufen, Terfenadine.
Granules .	Indomethacin, Diclofenac sodium, Prednisolone.
Films	Drug delivery device. Cinnarizine
Powders	Several basic drugs.

Table 1: The list of drugs formulated as single and multiple unit forms of floating drug delivery systems

solvents employed for the preparation. Polymers such as polycarbonate, Eudragit® Sand cellulose acetate were used in the preparation of hollow microspheres, and the drug release can be modulated by optimizing the polymer quantity and the polymer-plasticizer ratio. Sustained release floating microspheres using polycarbonate were developed by employing solvent evaporation technique. Aspirin, griseofulvin and p-nitro aniline were used as model drugs [17]. Dispersed phase containing polycarbonate solution in dichloromethane, and micronized drug, was added to the dispersion medium containing sodium chloride, polyvinyl alcohol and methanol. The dispersion was stirred for 3-4h to assure the complete solvent evaporation, and the microspheres obtained were filtered, washed with coldwater and dried. The spherical and hollow nature of the microspheres was confirmed by Scanning electron microscopic studies. The microspheres showed a drug payload of more than 50%, and the amount of drug incorporated is found to influence the particle size

distribution and drug release. The larger proportion of bigger particles was seen at high drug loading, which can be attributed to the increased viscosity of the dispersed phase.

5.5.Raft forming systems

Raft forming systems have received much attention for the delivery of antacids and drug delivery for gastrointestinal infections and disorders. The basic mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft. The raft floats because of the buoyancy created by the formation of CO_2 and act as a barrier to prevent the reflux of gastric Contents like HCl and enzymes into the esophagus. Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of to make the system less dense and float on the gastric fluids[18].

6.Mechanism Of Floating Systems

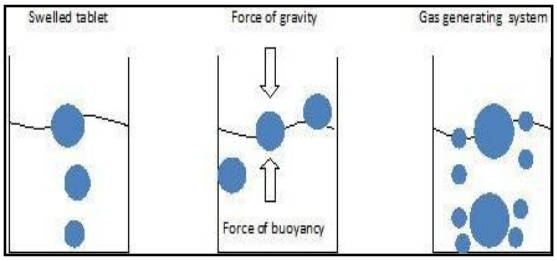
Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT 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. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to maintain the submerged object. This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intra gastric buoyancy capability variations[19].

F = F buoyancy - F gravity = (Df - Ds) gv

Where, F= total vertical force

Df = fluid density, Ds = object density,

v = volume and, g = acceleration due to gravity



(a) *(b)* *(c)*

Figure 3: Shows Different Mechanisms Of Floating Systems.

Microspheres Tablets /Pills	Chlorpheniramine maleate, Aspirin, griseofulvin, Acetaminophen, p-nitroaniline, Acetylsalicylic acid,
Films	P-Aminobenzoic acid, Cinnarizine, Piretanide, Prednisolone, Quinidine gluconate.
Granules	Cinnarizine, Diclofenac sodium , Diltiazem, Indomethacin , Fluorouracil.
Powders	Riboflavin, phosphate, Sotalol, Theophylline.
Capsules	Verapamil HCl, Chlordiazepoxide HCl, Diazepam, Furosemide, L-Dopa and benserazide Misoprostol, Propranolol HCl, Nicardipine [20].

Table 2: List Of Drugs Explored For Various Floating Dosage Forms

7.Polymers And Other Ingredients Used To Preparations Of Floating Drugs

- Polymers: HPMC K4 M, Calcium alginate, Eudragit S100 Eudragit RL, Propylene foam, Eudragit RS, ethyl cellulose, poly methyl metacrylate, Methocel K4M, Polyethylene oxide, β Cyclodextrin, HPMC 4000, HPMC 100, CMC, Polyethylene glycol, polycarbonate, PVA, Polycarbonate, Sodium alginate, HPC-L, CP 934P, HPC, Eudragit S, HPMC, Metolose S.M. 100, PVP, HPC-H, HPC-M, HPMC K15, Polyox, HPMC K4, Acrylic polymer, E4 M and Carbopol.

- Inert fatty materials (5%-75%): Beeswax, fatty acids, long chain fatty alcohols, Gelucires® 39/01 and 43/01.
- Effervescent agents: Sodium bicarbonate, citric acid, tartaric acid, Di-SGC (Di-Sodium Glycine Carbonate, CG (Citroglycine).
- Release rate accelerants (5%-60%): eg. Lactose, mannitol.
- Release rate retardants (5%-60%): eg. Dicalcium phosphate, talc,
- Buoyancy increasing agents (upto80%): eg. Ethyl cellulose.
- Low density material: Polypropylene foam powder (Accurel MP 1000®).

8.Characterization Parameters

8.1.Size And Shape Evaluation

The particle size and shape plays a major role in determining solubility rate of the drugs and thus potentially its bioavailability. The particle size of the formulation was determined using Sieve analysis, Air elutriation analysis, Photo analysis, Optical microscope , Electro résistance counting methods,Sedimentation techniques, Laser diffraction methods, ultrasound attenuation spectroscopy, Air Pollution Emissions Measurements etc [22].

8.2.Floating Properties

Effect of formulation variables on the floating proper-ties of gastric floating drug delivery system was determined by using continuous floating monitoring system and statistical experimental design[23] .

8.3.Surface Topography

The surface topography and structures were deter-mined using scanning electron microscope (SEM) operated with an acceleration voltage of 10k.v, Contact angle meter, Atomic force microscopy (AFM), Contact profiliometer [24].

8.4.Determination Of Moisture Content

The water content per se is seldom of interest. Rather, it shows whether a product intended for trade and production has standard properties such as storability, agglomeration in the case of powders, microbiological stability, flow properties,

viscosity, dry substance content, concentration or purity ,commercial grade (compliance with quality agreements).Thus moisture content of the prepared formulations was determined by Karl fisher titration, vacuum drying, Thermo gravimetric methods, Air oven method, Moisture Meters, Freeze drying as well as by physical methods [25].

8.5.Swelling Studies

Swelling studies were performed to calculate molecular parameters of swollen polymers and determine by using Dissolution apparatus, optical microscopy. The swelling studies calculated by using following formula [26].

- Swelling ratio = Weight of wet formulation / Weight of formulations

8.6.Determination Of The Drug Content

HPLC, HPTLC methods are used to determine the drug content in the system, also can determine by using Near infrared spectroscopy (NIRS), Microtitrimetric methods, Inductively Coupled Plasma Atomic Emission Spectrometer (ICPAES) and spectroscopy techniques [27] .

8.7.Percentage Entrapment Efficiency

Entrapment efficiency was deter-mined by using three methods such as Micro dialysis method, Ultra centrifugation, and pressure Ultra filtration [28] .

8.8.In-Vitro Release Studies

In vitro release studies were performed to provide the amount of the drug that is released at a definite time period. Release studies were performed by using Franz diffusion cell system and synthetic membrane as well as different types of dissolution apparatus[29].

8.9.Powder X-Ray Diffraction (XRD)

X-ray powder diffraction is the predominant tool for the study of poly-crystalline materials and is eminently suited for the routine characterization of pharmaceutical solids. Samples were irradiated with α radiation and analyzed between 2 ºC and 60 ºC .The voltage and current used were 30KV and 30mA respectively [30].

8.10.Fourier Transforms Infrared Analysis (FTIR)

Fourier transform infrared spectroscopy is a technique mostly used to identify organic, polymeric, and some inorganic materials as well as for functional group determination and thereby identify any chemical interaction involved in between drugs and excipients. Fourier Transform Infrared Analysis measurements of pure drug, polymer and drug-loaded polymer formulations were obtained on *FT-IR*. The pellets were prepared on KBr-press under hydraulic pressure of 150kg/cm2; the spectra were scanned over the wave number range of 3600 to 400 cm-1 at the ambient temperature[30].

8.11.Differential Scanning Calorimetry (DSC)

DSC is used to characterize water of hydration of pharmaceuticals. Thermo-grams of formulated preparations were obtained using DSC instrument equipped with an intercooler. Indium/Zinc standards were used to calibrate the DSC temperature and enthalpy scale. The sample preparations were hermitically sealed in an aluminum pan and heated at a constant rate of 10°C/min; over a temperature range of 25° C – 65°C. Inert atmosphere was maintained by purging nitrogen gas at the flow rate of 50ml/min[30] .

9.Evaluation Parameters Of Stomach Specific Fdds

9.1.Measurement Of Buoyancy Capabilities Of The FDDS

The floating behaviour was evaluated with resultant weight measurements. The experiment was carried out in two different media, deionised water in order to monitor possible difference. The results showed that higher molecular weight polymers with slower rate of hydration had enhanced floating behaviour and it was observed more in simulated meal medium compared to de-ionized water.

9.2.Floating Time And Dissolution

The test for floating time measurement is usually performed in stimulated gastric fluid or 0.1 mole/ lit HCl maintained at 37°C. It is determined by using USP dissolution apparatus containing 900 ml of 0.1m/l HCl as the dissolution medium at 37°C. The time taken by the dosage form to float is termed as floating lag time and the time for which the dosage form floats is termed as the floating or flotation

time[31] . A more relevant in-vitro dissolution method pro-posed to evaluate a floating drug delivery system (for tablet dosage form)[32]. A 100 ml glass beaker was modified by adding a side arm at the bottom of the beaker so that the beaker can hold 70 ml of 0.1 mol/lit HCl dissolution medium and allow collection of samples. A burette was mounted above the beaker to deliver the dissolution medium at a flow rate of 2 ml/min to mimic gastric acid secretion rate. The performance of the modified dissolution apparatus was compared with USP dissolution. Apparatus 2 (Paddle): The problem of adherence of the tablet to the shaft of the paddle was observed with the USP dissolution apparatus. The tablet did not stick to the agitating device in the proposed dissolution method.

9.3.Drug Release

Dissolution tests are performed using the dissolution apparatus. Samples are withdrawn periodically from the dissolution medium with replacement and then analyzed for their drug content after an appropriate dilution.

9.4.Content Uniformity, Hardness, Friability (For Tablets)

Drug Loading, Drug Entrapment Efficiency, Particle Size Analysis, Surface Characterization (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 and simulated meal, total beads or microspheres[33]**.**

9.5.X-Ray/Gamma Scintigraphy

X-Ray/Gamma scintigraphy is a very popular evaluation parameter for floating dosage form now a day [34] . It helps to locate dosage form in the GIT [35] and by which one can predict and correlate the gastric emptying time and the passage of dosage form in the GIT[36].

9.6.Pharmacokinetic Studies

Pharmacokinetic studies are the integral part of the *in-vivo* studies and several works has been reported on that. The pharmacokinetics studies of verapamil, from the loading pellets containing drug, filled into a capsule, and compared with the conventional verapamil tablets of similar dose (40 mg). The t_{max} and AUC (0-infinity) values (3.75h and 364.65 ng/mlh, respectively) for floating pellets were comparatively higher than those obtained for the conventional verapamil tablets (t max value 1.21h, and AUC value 224.22ng/mlh)[37] . No much difference was found between the C max values of both the formulations, suggesting the improved bioavailability of the floating pellets compared to the conventional tablets. An improvement in bioavailability has also been observed with piroxicam in hollow polycarbonate microspheres administered in rabbits. The microspheres showed about 1.4 times more bioavailability, and the elimination half-life was increased by about three times than the free drug.

10.Factors Controlling Gastric Retention Of Dosage Forms

10.1.Density Of Dosage Form

Dosage forms having a density lower than that of gastric fluid experience floating behavior and hence gastric retention. A density of <1.0 gm/cm^3 is required to exhibit floating property. However, the floating tendency of the dosage form usually decreases as a function of time, as the dosage form gets immersed into the fluid, as a result of the development of hydrodynamic equilibrium [38] .

10.2.Size Of Dosage Form

The mean gastric residence times of non-floating dosage forms are highly variable and greatly dependent on their size, which may be small, medium, and large units. In most cases, the larger the size of the dosage form, the greater will be the gastric retention time because the larger size would not allow the dosage form to quickly pass through the pyloric antrum into the intestine [39]. Thus the size of the dosage form appears to be an important factor affecting gastric retention.

10.3.Food Intake And Nature Of Food

Food intakes, the nature of the food, caloric content, and frequency of feeding have a profound effect on the gastric retention of dosage forms. The presence or absence of food in the stomach influences the GRT of the dosage form. Usually, the presence of food increases the GRT of the dosage form and increases drug absorption by allowing it to stay at the absorption site for a longer time. In a gamma scintigraphic study of a bilayer floating capsule of misoprostol[40]. the mean gastric residence time was 199 ± 69 minutes; after a light breakfast, a remarkable enhancement of average GRT to 618 ± 208 minutes was observed.

10.4.Effect Of Gender, Posture And Age

A studyfound that females showed comparatively shorter mean ambulatory GRT than males, and the gastric emptying in women was slower than in men[41]. The authors also studied the effect of posture on GRT, and found no significant difference in the mean GRT for individuals in upright, ambulatory and supine state. On the other hand, in a comparative study in humans, the floating and non-floating systems behaved differently[42-43].

11.Applications Of Floating Drug Delivery Systems

11.1.Enhanced Bioavailability

The bioavailability of riboflavin CR-GRDF is significantly enhanced in comparison to the administration of non-GRDF CR polymeric formulations. There are several different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act concomitantly to influence the magnitude of drug absorption.

11.2.Sustained Drug Delivery

Oral CR formulations are encountered with problems such as gastric residence time in the GIT. These problems can be overcome with the HBS systems which can remain in the stomach for long periods and have a bulk density <1 as a result of which they can float on the gastric contents. These systems are relatively larger in size and passing from the pyloric opening is prohibited.

11.3.Site –specific drug delivery systems

These systems are particularly advantageous for drugs that are specifically absorbed from the stomach or the proximal part of the small intestine .The controlled, slow delivery of drug to the stomach provides sufficient local therapeutic levels and limits the systemic exposure to the drug. This reduces side effects that are caused by the drug in the blood circulation. In addition, the prolonged gastric availability from a site directed delivery system may also reduce the dosing frequency.

Eg: Furosemide and Riboflavin.

11.4.Absorption Enhancement

Drugs which are having poor bioavailability because of site specific absorption from the upper part of the GIT are potential candidates to be formulated as floating drug delivery systems, there by maximizing their absorption.

11.5.Minimized Adverse Activity At The Colon

Retention of the drug in the HBS systems at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented. This Pharmacodynamic aspect pro-vides the rationale for GRDF formulation for beta lactam antibiotics that are absorbed only from the small intestine, and whose presence in the colon leads to the development of microorganism's resistance.

11.6.Reduced Fluctuations Of Drug Concentration

Continuous input of the drug following CRGRDF administration produces blood drug concentrations within a narrower range compared to the immediate release dosage forms. Thus, fluctuations in drug effects 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 [21].

12.Conclusion

Current Gastro-retentive floating drug delivery systems designed on the basis of delayed emptying time and buoyancy principles. From the number of commercial and patent issued evident that it is much effective approach to controlled oral drug delivery system.

FDDS promises to be a potential approach for gastric retention. The increasing sophistication of delivery technology will ensure the development of increase number of gastro-retentive drug delivery to optimize the delivery of molecules that exhibit absorption window, low bioavailability and extensive first pass metabolism. It seems that to formulate an efficient FDDS is sort of a challenge and the work will go on and on until an ideal approach with industrial applicability and feasibility arrives.

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