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A REVIEW OF FLOATING DRUG DELIVERY SYSTEM

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ABSTRACT: The principal objective behind the writing of this article on the floating drug delivery system (FDDS) was to systematize the recent literature with the core process of floatation in acquiring gastric retention. Oral administration is the most convenient and preferred means of any drug delivery to the systematic circulation. The different strategies used in the development of FDDS by constructing the effervescent and non-effervescent type of floating tablets basis of which is buoyancy mechanism. FDDS is a method to deliver the drugs that are active locally with a narrow absorption window in the upper gastrointestinal tract, unstable in the lower intestinal environment, and possess low solubility with higher pH values. Floating dosage forms can be delivered in conventional forms like tablets, capsules with the addition of suitable ingredients along with the gas generating agent.

Index Terms: **Gastro retentive system, Floating drug delivery system, Single unit, Multiple units.**

INTRODUCTION:

Oral administration is the most convenient and preferred means of any drug delivery to the systematic circulation. Oral controlled release drug delivery has recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation. The solid oral dosage forms such as capsule, tablets give specific drug concentration in systemic blood circulation without getting any control over drug delivery system and also cause major fluctuations in plasma drug concentrations. Floating drug delivery systems (FDDS) are invented to retain the drug in the stomach and applicable for drugs with poor solubility and low stability in intestinal fluids. The basis behind FDDS is making the dosage form less dense than the gastric fluids to make it float on them. FDDS are hydro-dynamically controlled low-density systems with 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. The residual system is emptied from the stomach with the release of the drug. This results in enhanced gastric residence time and good control over plasma drug concentration fluctuations. The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release [1]. Prolonging the gastric retention of a delivery system is desirable for achieving the greater therapeutic efficacy of the drug substance under certain circumstances. For example, drugs which show better absorption at the proximal part of the gastrointestinal tract and drugs with low solubility and get degraded in alkaline pH found efficient in prolonging gastric retention. In addition, for sustained drug delivery to the stomach and proximal small intestine in treating certain ulcerative conditions, prolong gastric retention of the therapeutic moiety and hence offer numerous advantages including improved bioavailability and therapeutic efficacy with reduction of dosing frequency [2].

BASIC GIT 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, whereas the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions [3]. Gastric emptying occurs in both the fasting and fed states. During the fasting state an inter digestive series of electrical events take place which cycle both through stomach and intestine every 2-3 hrs, which is called as inter digestive 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 [4].

1. Phase 1-(Basic phase)-last from 30-60 minutes with rare contractions.

2. Phase 2-(Pre-burst phase)-last for 20-40 minutes with intermittent action potential and contractions. 3. Phase 3-(Burst phase) - last for 10-20 minutes which includes intense and regular contractions for short period.

4. Phase 4-last for 0-5 minutes and occurs between phase 2 and 1 of 2 consecutive cycles.

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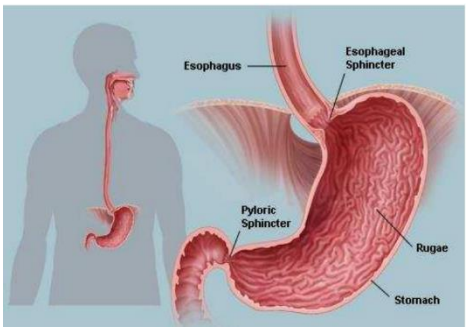

figure 1: anatomy of stomach.

B. ADVANTAGES OF FDDS

1. Floating dosage forms such as tablets or capsules will remains in the solution for prolonged time even at the alkaline pH of the intestine.

2. FDDS are advantageous for drugs meant for local action in the stomach e.g.: Antacids

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

4. Acidic substance like aspirin causes irritation on the stomach wall when come in contact with it hence; HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs.

5. The FDDS are advantageous for drugs absorbed through the stomach e.g.: Ferrous salts, Antacids.

C. DISADVANTAGES OF FDDS

1. Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.

2. 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.

3. One of the disadvantages of floating systems is that they require a sufficiently high level of fluids in the stomach, so that the drug dosages form float therein and work efficiently.

4. These systems also require the presence of food to delay their gastric emptying.

D. CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEMS

Floating drug delivery systems are classified depending up on the two formulations variables Effervescent and Non-effervescent systems.

EFFERVESCENT FLOATING DOSAGE FORMS These are matrix type systems prepared with the help of swellable polymers such as hydroxypropyl methylcellulose or polysaccharides and chitosan and various effervescent components like sodium bicarbonate, calcium carbonate, citric acid or tartaric acid. These dosage forms are developed in such a way that, when they come in contact with gastric juice in the stomach, Carbon dioxide is liberated and is trapped in the swollen hydrocolloids. This provides buoyancy to the dosage form. The liberated carbon dioxide may intimately get mixed within the tablet matrix in case of single layered tablet. The multi-particulate floating reservoir types of delivery systems may contain double or triple layers. The triple layered tablets may be prepared, which contains swellable gas generating layer, sustainable approach was utilized in the development of floating or pulsatile drug delivery system based on the coated effervescent core. [5] The dosage form had two layers, first layer consisted of drug, cellulose acetate or HPMC as a sustained release core and second layer consisted of effervescent agents, PEG 4000 (4%based on the weight of the second layer) and lactose or microcrystalline cellulose as filler. Sodium bicarbonate and citric acid were used as an effervescent agent in a ratio of 1:0. in the concentration of 30-50 % of the w/w of the core. The carbon dioxide is generated upon contact with the medium and gets entrapped in the polymeric matrix, which provides buoyancy to the dosage form. It was observed that addition of 10-20% w/w of HPMC significantly retarded drug release compared to the dosage form without HPMC. Programmable drug delivery systems for oral administration were developed. It was a new prototype model device (3 cm long and 0.9 cm internal diameter) made to comprise of a cylindrical shell in the form of oral capsule. Drug was placed in a cylindrical disc made up of slowly eroding polymer and compressed to zero porosity, a flexible rubber disc, compressible acid resistant spring and a special acid impervious nonpermeable rubber ballooning system containing bicarbonate granules. The device in the form of nondigestible oral capsule containing drug in a slowly eroding matrix was designed to utilize on automatically operated geometric obstruction that keeps the device floating in the stomach and prevents the system from passing through remainder of GIT. The different grades of HPMC were used to develop the eroding matrix. They concluded that duration of action was dependent on erosion rate of the incorporated polymer and the in vitro release of drug from developed device could be maintained up to 20 days.

Sodium alginate beads consisting of gas forming agent were made up of HPMC and sodium alginate (9:1w/w) with gas generating agent in the concentration 0:1 to 1:1(gas forming agent/alginate w/w). The resultant solution was dropped in to 1% (w/v) calcium chloride solution containing 10% (v/v) acetic acid. The suspended beads were stirred with a magnetic stirrer for 10 minutes. The prepared beads were evaluated for the effect of carbon dioxide producing agent on size, floating properties, porosity, morphology and mechanical strength of beads. It was observed that amount of gas forming agent had a significant effect on size, floating ability, porosity, morphology, release rate and mechanical strength. Calcium carbonate formed smaller but stronger beads as compared to sodium bicarbonate. Calcium carbonate was found to be less effective gas generating agent than sodium bicarbonate. But it forms superior quality floating beads with significantly extended drug release.[6] Multiple unit type of floating pills composed of inner effervescent layer containing sodium bicarbonate and tartaric acid and outer swellable polymeric membrane made up of polyvinyl acetate and purified shellac. The inner layer was further divided into two sub layers to avoid physical contact between sodium bicarbonate and tartaric acid. When the pill was immersed in buffer solution at 37 °C, it settled down at the bottom, buffer solution entered in to the effervescent layer through the outer swellable membrane. Carbon dioxide was generated due to reaction between sodium bicarbonate and tartaric acid and formed swollen pills (like balloons) with a density much lesser than 1.0 g/ml. The system was found to float completely within 10 minutes and had a good floating ability independent of pH, viscosity of the medium and drug release in a sustained manner.

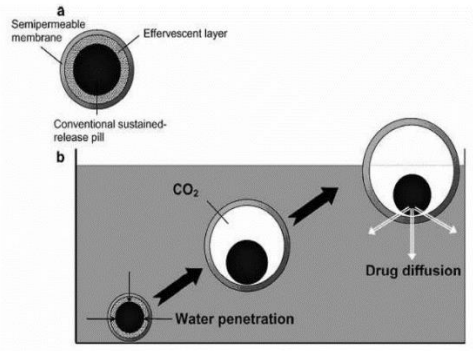

figure 2: floating pills a) The penetration of water into effervescent layer leads to a CO2 generation and makes the system to float (b) Mechanism of floatation.

2. NON-EFFERVESCENT FDDS The non-effervescent FDDS works on the mechanism of polymer swelling, bio adhesion of the polymer to mucosal layer of GI tract. The most commonly used excipients for the preparations of non-effervescent FDDS are gel forming or swellable type hydrocolloids, polysaccharides and matrix forming polymers like polymethacrylates, polycarbonates, polyacrylates polystyrenes and bio adhesion polymers like chitosan and carpools. One of the approaches in the development of such floating dosage forms involves thorough mixing of drug and gel forming hydrocolloids. After oral administration, the dosage form comes in contact with gastric fluids and gets swollen, form a gelatinous barrier at the surface. The swollen dosage form maintains a relative integrity of shapes and bulk density less than 1.0. The air entrapped within the swollen polymer matrix imparts buoyancy to the dosage forms. Hydrodynamically balanced capsules containing mixture of drug and hydrocolloids. Upon contact with gastric fluid, the capsule shell dissolved in gastric fluid followed by swelling of mixtures, formation of a gelatinous barrier and maintains bulk density less than 1.0, which remained buoyant on the gastric fluid for an extended period of time. Intragastric floating drug delivery device. The system composed of a drug reservoir encapsulated in a microporous compartment having pores on top and bottom surfaces. The peripheral walls of the reservoir compartment were completely sealed to prevent any physical contact of the undissolved drug with walls of the stomach.

Novel levodopa gastro retentive dosage form based on unfolding polymeric membranes, that combines extended dimensions with high rigidity. It was folded into a large size gelatine capsule. In vitro studies showed that unfolded form reached within 15 minutes after administration and it was confirmed in vivo in beagle dogs. The unfolded form was maintained for at least 2 hours. It was concluded that this dosage form could improve therapy of different narrow absorption window drugs. However, there are possibilities of the polymeric films to get stuck in the oesophagus causing extreme discomfort to the patient or drug related injuries and repeated administration of rigid dosage form may result in gastric obstruction.

E. FACTORS INFLUENCING GASTRIC RETENTION Gastric residence time of an oral dosage form is influenced by many factors. To pass through the pyloric size should be in the range of 1-2 mm. The pH of the stomach in fasting state and fed state are 1.5-2.0 and 2.0- 6.0 respectively. A large volume of waste administrated in oral dosage form raises the pH of the stomach contents to 6-9. The rate of gastric emptying depends mainly on viscosity, volume and caloric contents of meals. It does not make any difference whether the meal has high protein, fat or carbohydrate contents as long as the caloric content is the same while there is decrease in gastric emptying time by increasing acidity and caloric value [7].

Other factors influence such as biological factors which includes age, body mass, index, gender, posture and diseased states. In case of elderly persons gastric emptying is slowed down. Females have slower gastric emptying rates than that of males. Stress increases the gastric emptying rates whereas depression slows it down. Volume of liquids administered also effects the gastric emptying time. Larger the liquid content, faster the emptying. Several formulations parameters can affect the gastric residence time such as Size, Shape, Density, Diameter etc, of the dosage unit which affects gastric emptying. Out of all ring-shaped devices have better gastric rates when compared to all other shapes. Formulations having a diameter more than 7.5mm shows better gastric residence time compared with formulations having 9.9mm. Density of a dosage form influences the gastric emptying rate. A buoyant dosage form having a density of less than that of the gastric fluids. So, the unit is retained in the stomach for a prolonged period. Out of all the floating drug delivery system formulations are having reliable gastric emptying patterns due to free distribution of the drug throughout the GIT when compare to single unit formulations [8].

F. LIST OF DRUGS EXPLORED FOR VARIOUS FLOATING DOSAGE FORMS

1. Microspheres Tablets /Pills: Chlorpheniramine maleate, Aspirin, griseofulvin, Acetaminophen, nitroaniline, Acetylsalicylic acid, Ibuprofen, Amoxycillin trihydrate, Terfenadine, Ampicillin, Trani-last, Atenolol, Theophylline, Captopril, Isosorbide di nitrate, Sotalol, Isosorbide mononitrate.

2. Films: P-Aminobenzoic acid, Cinnarizine, Piretanide, Prednisolone, Quinidine gluconate.

3. Granules: Cinnarizine, Diclofenac sodium, Diltiazem, Indomethacin, Fluorouracil, Prednisolone, Isosorbide mononitrate, Isosorbide dinitrate.

4. Powders: Riboflavin, phosphate, Sotalol, Theophylline.

5. Capsules: Verapamil HCl, Chlordiazepoxide HCl, Diazepam, Furosemide, L-, opa and benserazide Misoprostol, Propranolol HCl, Ursodeoxycholic acid, Nicardipine [9]. Table 1: Marketed products of FDDS

table 1: Marketed products of FDDS

S.No	Product	Active Ingredients
1	Madopar	Levodopa and benserzide
2	Valrelease	Diazepam
3	Topalkan	Aluminum magnesium Antacid
4	Almagate flatcoat	Antacid
5	Liquid gavi-son	Alginic acid and sodium bicarbonate

G. POLYMERS AND OTHER INGREDIENTS USED TO PREPARATIONS OF FLOATING DRUGS

i) Polymers: The following polymers used to preparations of floating drugs: HPMC K4 M, Calcium alginate, Eudragit S100 Eudragit RL, Propylene foam, Eudragit RS, ethyl cellulose, poly methyl meth acrylate, Methocil K4M, Polyethylene oxide, β cyclodextrin, HPMC 400, 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.

ii) Inert fatty materials (5%-75%): Edible, inert fatty materials having a specific gravity of less than one can be used to decrease the hydrophilic property of formulation and hence increase buoyancy. E.g., Beeswax, fatty acids, long chain fatty alcohols, Gelucires® 39/01 and 43/01.

iii) Effervescent agents: Sodium bicarbonate, citric acid, tartaric acid, Di-SGC (Di-Sodium Glycine Carbonate, CG (Citroglycine).

iv) Release rate accelerants (5%-60%): e.g., lactose, mannitol.

v) Release rate retardants (5%-60%): e.g., Dicalcium phosphate, talc, magnesium stearate.

vi) Buoyancy increasing agents (upto80%): e.g., Ethyl cellulose. vii) Low density material: Polypropylene foam powder (Accrual MP 1000®).

H. APPROACHES TO DESIGN FLOATING DOSAGE FORMS

The following approaches have been used for the design of floating dosage forms of single and multiple unit systems.

1. SINGLE –UNIT DOSAGE FORMS In low density approaches the globular shells apparently having lower density than that of gastric fluid can be used as a carrier like popcorn, poprice, polystrol for the drug for its controlled release. The polymer of choice can be either Ethyl cellulose or HPMC. Depending on 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 in to a micro porous component that houses as a reservoir having apertures present at top and bottom walls through which the gastrointestinal tract fluid enters to dissolve the drug.

HYDRO DYNAMICALLY BALANCED SYSTEMS (HBS)

These systems are designed to prolong the stay of the dosage forms in the gastric intestinal tract and aid in enhancing the absorption. Drugs having a better solubility in acidic environment and also having specific site of absorption in the upper part of small intestine is achieved by these HBS systems. To retain in stomach for a prolonged period of time the dosage form must Have bulk Density of less than one and has to maintain its structural integrity and release drug constantly from the dosage form. Among all the advantages single-unit formulations are associated with some limitations/problems such as sticking together or being obstructed in the GIT which may lead to potential danger of producing irritation

2. MULTIPLE-UNIT DOSAGE FORMS Multi-particulate dosage forms are gaining much favour over single-unit dosage forms. The potential benefits include increased bioavailability; predictable, reproducible and generally short gastric residence time, no risk of dose dumping; reduced risk of local irritation, and the flexibility to blend pellets with different compositions or release patterns. Because of their smaller particle size these systems are capable of passing through the GI tract easily, leading to less inter- and intra-subject variability. However, potential drug loading of a Multiarticulate system is lower because of the proportionally higher need for excipients (e.g., sugar cores). Most Multiparticulate Pulsatile delivery systems are reservoir devices coated with a reputable polymeric layer. Upon water ingress, drug is released from the core after rupturing of the surrounding polymer layer, due to pressure build-up within the system. The pressure necessary to rupture the coating can be achieved with swelling agents, gas producing effervescent excipients or increased osmotic pressure. Water permeation and mechanical resistance of the outer membrane are major factors affecting the lag time. Water soluble drugs are mainly released by diffusion; while for water insoluble drug, the release is dependent on dissolution of drug.

I. EVALUATION OF FLOATING DRUG DELIVERY SYSTEMS Various parameters that need to be evaluated in gastro retentive formulations which includes floating duration, dissolution profiles, specific gravity, content uniformity, hardness and friability in case of solid dosage forms. In case of Multiparticulate drug delivery systems, differential scanning calorimeter (DSC), particle size analysis, flow properties, surface morphology, mechanical properties and x-ray diffraction studies are performed [10]

CHARACTERIZATION PARAMETERS

1. SIZE AND SHAPE EVALUATION The particle size and shape play 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 resistance counting methods, Sedimentation techniques, Laser diffraction methods, ultrasound attenuation spectroscopy, Air Pollution Emissions Measurements etc.

2. FLOATING PROPERTIES Effect of formulation variables on the floating properties of gastric floating drug delivery system was determined by using continuous floating monitoring system and statistical experimental designs.

3. SURFACE TOPOGRAPHY The surface topography and structures were determined using scanning electron microscope operated with an acceleration voltage of 10k.v, Contact angle meter, atomic force microscopy (AFM), Contact profilometer [11].

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

1. Storability 2. Agglomeration in the case of powders 3. Microbiological stability 4. Flow properties, viscosity 5. Dry substance content 6. Concentration or purity 7. Commercial grade (compliance with quality agreements) Thus moisture content of the prepared formulations was determined by Karl fisher titration, vacuum drying, Themo gravimetric methods, Air oven method, Moisture Meters, Freeze drying as well as by physical methods [12].

5. SWELLING STUDIES Swelling studies were performed to calculate molecular parameters of swollen polymers. Swelling studies was determined by using Dissolution apparatus, optical microscopy and other sophisticated techniques which include H1NMRimaging, Confocal laser scanning micro- scope (CLSM), Cryogenic scanning electron microscopy (Cryo-SEM), Light scattering imaging (LSI) etc. The swelling studies by using Dissolution apparatus was calculated as per the following formula (Ferdous Khan et al, 2008, Ziayur Rahman et al, 2006). Swelling ratio = Weight of wet formulation / Weight of formulations

6. DETERMINATION OF THE DRUG CONTENT Percentage drug content provides how much amount of the drug that was present in the formulation. It should not exceed the limits acquired by the standard monographs. Drug content was determined by using HPLC, HPTLC methods, near infrared spectroscopy (NIRS), Micro titrimetric methods, Inductively Coupled Plasma Atomic Emission Spectrometer (ICPAES) and also by using spectroscopy techniques [13].

7. PERCENTAGE ENTRAPMENT EFFICIENCY Percentage entrapment efficiency was reliable for quantifying the phase distribution of drug in the prepared formulations. Entrapment efficiency was determined by using three methods such as Micro dialysis method, Ultra centrifugation, and pressure Ultra filtration.

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 [14]. The in-vitro release studies (suitable drug for medium and method) are discussed the below Table.2

9. POWDER X-RAY DIFFRACTION X-ray powder diffraction) is the predominant tool for the study of polycrystalline materials and is eminently suited for the routine characterization of pharmaceutical solids. Samples were irradiated with α radiation an analysed between 2 ºC and 60 ºC. The voltage and current used were 30KV and 30mA respectively.

10. FOURIER TRANSFORMS INFRARED ANALYSIS Fourier transform infrared spectroscopy is a technique mostly used to identify organic, polymeric, and some inorganic materials as well as for functional group determination. Fourier Transform Infrared Analysis (FT-IR) 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.

11. DIFFERENTIAL SCANNING CALORIMETRY (DSC) DSC are 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 aluminium 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.

J. APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEMS

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.

2. SUSTAINED DRUG DELIVERY oral CR formulations are encountered with problems such as gastric residents time in the GIT these problems can be can be overcome with the HBS systems which can remain in the stomach for longer periods and have a bulk density less than one as a result of which they can float on the gas these systems are relatively larger in size and passing and passing from the pyloric opening is prohibited.

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. E.g.: Furosemide and Riboflavin

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.

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 provides 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 resistance.

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.

CONCLUSION Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extends the time for drug absorption. FDDS promises to be a potential approach for gastric retention. Although there are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing toward commercializing this technique.

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