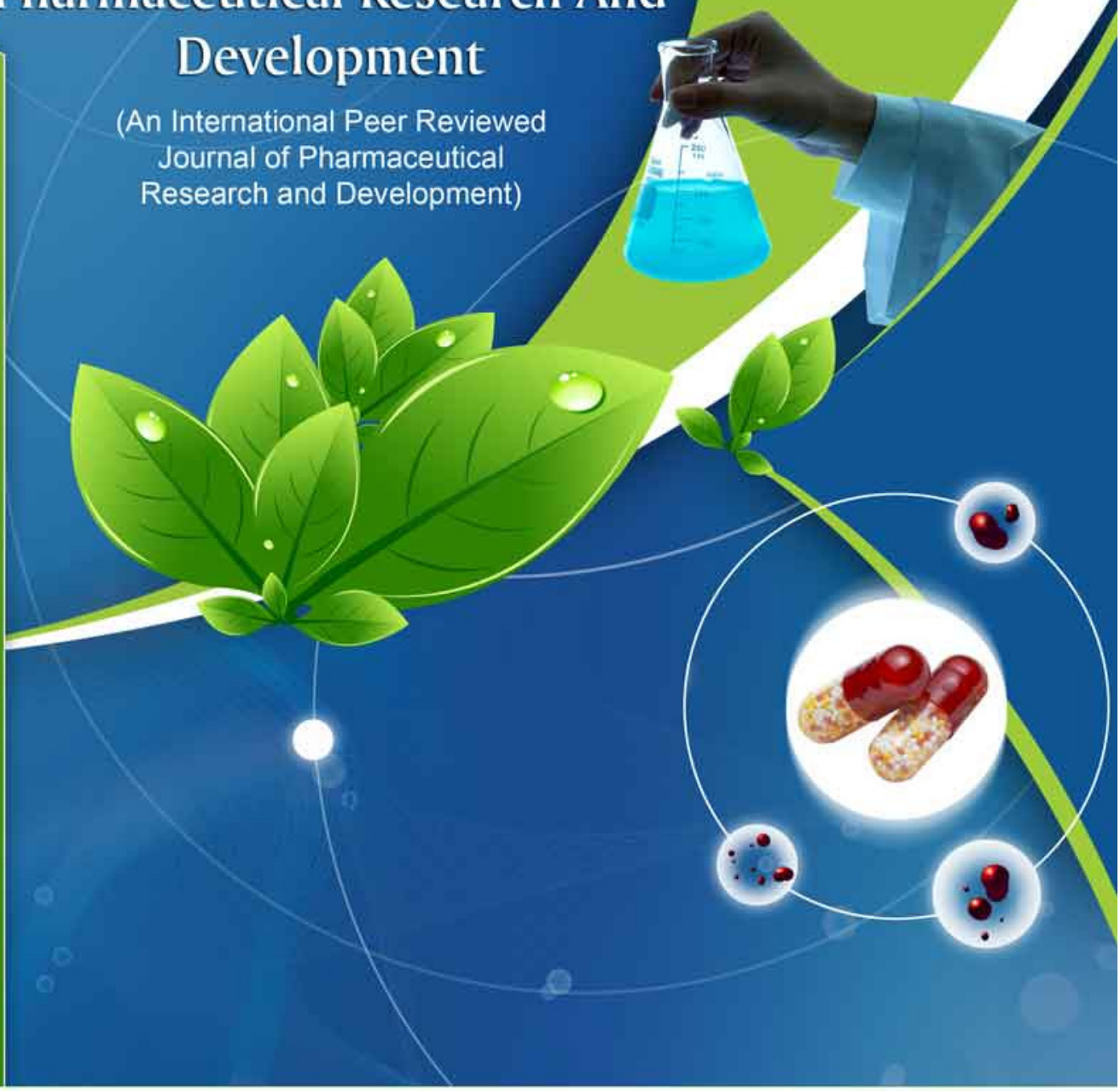
ISSN : 2320 4850

BI MONTHLY

Asian Journal of Pharmaceutical Research And Development

(An International Peer Reviewed Journal of Pharmaceutical Research and Development)

AJPRD



Volume - 01 Issue - 04 JULY-AUG 2013

website: www.ajprd.com
editor@ajprd.com

Asian Journal of Pharmaceutical Research and Development
(An International Peer-Reviewed Journal of Pharmaceutical Research and Development)
www.ajprd.com
ISSN 2320-4850

Review Article

A REVIEW ON CURRENT APPROACHES IN FLOATING DRUG DELIVERY SYSTEM

Gupta Akanksha*, Natasha Sharma, M.P. Khinchi, Dilip Agrawal

Department of Pharmaceutics, Kota College of Pharmacy, Kota

Received: 26 June 2013, ***Revised and Accepted: 5 August 2013***

ABSTRACT

Floating drug delivery system provides local delivery to specific region like stomach and proximal small intestine and it's also shows better bioavailability and improved therapeutic activity and substantial benefits to patients. The objective of our review is to compile the recent advancements and literatures regarding the novel do form i.e. the floating drug delivery systems (FDDS) that can be retained in the stomach for a prolonged period of time and gives therapeutic action in a predetermined manner. Gastric emptying is a complex process and makes in vivo performance of the drug delivery systems uncertain. The floating drug delivery systems are useful approach to avoid this variability with increase the retention time of the drug delivery systems for more than 12 hours. Effervescent and non-effervescent are two class of floating system and can formulate either in single unit dosage form or in multiple unit dosage form. The methodologies used in the development of FDDS by formulating effervescent and non effervescent floating tablets based on buoyancy mechanism. By utilizing above feasible approaches it is possible to deliver drugs which have narrow therapeutic window. Our review article suggests that how the gastro retentive dosage forms (GRDFs) help to improve patient compliance and robustness.

Key words: *Floating drug delivery system, Floating tablet*

INTRODUCTION

Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. One of such difficulties is the ability to confine the dosage form in the desired area of the gastrointestinal tract. To overcome this physiological problem, several drug delivery systems with prolonged gastric retention time have been investigated. Attempts are being made to develop a con-trolled drug delivery system that can provide therapeutically effective plasma drug concentration levels for longer durations, there by reducing the dosing frequency and minimizing fluctuations in plasma drug concentration at steady state by delivering drug in a controlled and reproducible manner. 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 of drugs that are less soluble in high pH environment. Gastric retention to provide new therapeutic possibilities and substantial benefits from patients. The controlled gastric retention of solid dosage forms may be achieved by the mechanism of mucoadhesion, floatation, sedimentation, expansion, modified shape systems or by the administration of pharmacological agents, that delaying gastric emptying. Based on these approaches, floating

*For Correspondence:
Akanksha Gupta
Kota College of Pharmacy
Sp-1 RIICO Industrial Area, Ranpur, Kota
Mail id: akankshagupta1@yahoo.in

drug delivery systems seems to be the promising delivery systems for control release of drugs [1].Floating drug delivery systems (FDDS) are aimed to retain the drug in the stomach and are useful for drugs that are poorly soluble or unstable in intestinal fluids. The underlying principle is very simple i.e., to make the dosage form less dense than the gastric fluids so that it can float on them. The density of the system can be reduced by incorporating a number of low density fillers into the systems such as hydroxyl cellulose, lactates or microcrystalline cellulose. However, this system is not ideal because its performance is highly dependent on the presence of food and fluid in the stomach. The basic idea behind the development of such a system was to maintain a constant level of drug in the blood plasma inspire of the fact that the drug dose not undergoes disintegration. The drug usually keeps floating in the gastric fluid and slowly dissolves at a pre-determined rate to release the drug from the dosage form and maintain constant drug levels in the blood. The concept of floating tablets is mainly based on the matrix type drug delivery system such that the drug remains embedded in the matrix which after coming in contact with the gastric fluid swells up and the slow erosion of the drug without disintegration of the tablet takes place. Sometimes for generating a floating system we even need to add some effervescent or gas generating agent which will also ultimately reduce the density of the system and serve the goal of achieving a floating system. These systems have a particular advantage that they can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the GIT. These systems continuously release the drug before it reaches the absorption window, thus ensuring optimal bioavailability [2].

MECHANISM OF FLOATING SYSTEMS

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. 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 from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. 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. The object floats better if F is on the higher positive side [2, 3].

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

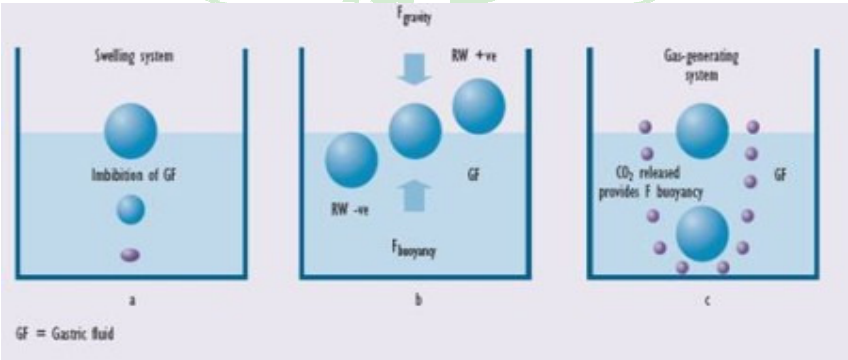


Fig.1. Mechanism of floating drug delivery system

ADVANTAGES OF FDDS

FDDS is highly advantageous in the treatment of the disorders related to the stomach. As the prime objective of such systems is to produce a gastro retentive product or a product which has an enhanced retention time in the stomach [2].

- Drugs with considerably short half life can be administered in this manner to get an appreciable therapeutic activity.
- Enhancement of the bioavailability for drugs which can metabolized in the upper GIT.
- They also have an advantage over the conventional system as it can be used to overcome the adversities of gastric retention time as well as the gastric emptying time.
- The duration of treatment through a single dose, which releases the an active ingredient over an extended period of time
- The active entity is delivered specifically to the site of action, thus minimizing or eliminating the side effects.

DISADVANTAGES OF FDDS [2, 4]

- The major disadvantage of floating system is requirement of a sufficient high level of fluids in the stomach for the drug delivery to float. However this limitation can be overcome by coating the dosage form with the help of bioadhesive polymers that easily adhere to the mucosal lining of the stomach
- Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.
- Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.
- High variability in gastric emptying time due to its all (or) non-emptying process.
- Patients should not be dosed with floating forms just before going to bed.
- Floating system is not feasible for those drugs that have solubility (or) stability problem in gastric fluids.

DRUG CANDIDATES SUITABLE FOR GASTRORETENTIVE DRUG DELIVERY SYSTEM [2, 5]

- Drugs which act primarily in the stomach. E.g. antacids.
- Drugs that are primarily absorbed from the stomach. E.g. amoxicillin
- Drugs those are poorly soluble at alkaline pH. E.g. verapamil, diazepam, etc.
- Drugs with a narrow window of absorption. E.g. levodopa, cyclosporine, etc.
- Drugs which are rapidly absorbed from the GIT. E.g. tetracycline
- Drugs that degrade in the colon. E.g. ranitidine, metformin, etc.
- Drugs that disturb normal colonic microbes. E.g. Antibiotics against Helicobacter pylori.

DRUG CANDIDATES UNSUITABLE FOR GASTRORETENTIVE DRUG DELIVERY SYSTEM [2, 5]

- Drugs that have very limited acid solubility E.g. phenytoin etc.
- Drugs that suffer instability in the gastric environment E.g. erythromycin etc.
- Drugs intended for selective release in the colon E.g. 5- amino salicylic acid and corticosteroids etc.

LIST OF DRUGS EXPLORED FOR VARIOUS FLOATING DOSAGE FORMS

Microspheres Tablets /Pills:

Chlorpheniramine maleate, Aspirin, griseofulvin, Acetaminophen, p-nitroaniline, Acetylsalicylic acid, Ibuprofen, Amoxycillin trihydrate, Terfenadine, Ampicillin, Trani-last,Atenolol, Theophylline, Captopril, Isosorbide di nitrate, Sotalol, Isosorbide mononitrate.

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

Granules: Cinnarizine, Diclofenac sodium , Diltiazem, Indomethacin ,Fluorouracil,

Prednisolone , Isosorbide mononitrate ,Isosorbide dinitrate.

Powders: Riboflavin phosphate, Sotalol, Theophylline.

Capsules: Verapamil HCl, Chlordiazepoxide HCl, Diazepam, Furosemide, benserazide Misoprostol, Propranolol HCl, Nicardipine [1]

POLYMERS AND OTHER INGREDIENTS USED TO PREPARATIONS OF FLOATING DRUGS [1, 7]

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 methacrylate, 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%):

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.

Effervescent agents:

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

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

Release rate retardants (5%-60%): E.g. Dicalcium phosphate, talc, magnesium stearate. ***Buoyancy increasing agents (upto80%):*** E.g. Ethyl cellulose.

Low density material: Polypropylene foam powder (Accurel MP 1000®).

FACTORS CONTROLLING GASTRIC RETENTION OF DRUGS [2-7]

The factors which are to be considered during the development of gastro retentive drugs are-

Physiological factors

Size of dosage form:

Dosage forms having greater diameter than the diameter of pyloric sphincter remain in the gastric region as these cannot move away along with the gastric contents into intestine nor they can be affected by the gastric emptying.

Shape of dosage form:

Round or spherical or ring shaped dosage forms are considered to be better in comparison to other shapes.

Density:

The density of a dosage form also affects the gastric emptying rate and determines the location of the system in the stomach. Dosage forms having a density lower than the gastric contents can float to the surface, while high density systems sink to bottom of the stomach. Dosage form with density lesser than 1.0 gm/ cm3 is required to exhibit floating property.

Biological factors

Age:

Gastric retention time is longer in geriatric patients, while it is lower in neonates and children when compared to normal adults.

Gender:

Gastric retention time in male (3-4 hours) is less than the female (4-6 hours).

Fed or unfed state:

Gastric retention time is less during fasting conditions as the gastric motility increases during fasting conditions.

Feed frequency:

Higher the frequency of taking food, longer will be the gastro retention time.

Nature of meal:

Higher the amount of fatty acids and other indigestible polymers lesser the gastric retention time due to alteration in gastric motility.

Concomitant drug administration:

Administration of certain drugs along with gastric motility enhancers or depressants, greatly affect gastric retention time and hence absorption of stomach specific absorbing drugs.

Disease state:

Gastric disease conditions like diabetes, Crohn's disease etc alters the Gastric retention time

PHARMACOKINETIC AND PHARMACODYNAMIC ASPECTS OF FDDS [2]

The aim of this section is to delineate these aspects in order to suggest rational selection of drugs for which FDDS would be a beneficial strategy.

Pharmacokinetic aspects

Absorption window:

Validation that the drug is within the category of narrow absorption window agents currently various experimental techniques are available that permit us to verify the absorption properties of the tested molecule, to determine the mechanism of intestinal absorption and to elucidate the permeability at different regions of the GI tract. In the case of absorption by active transporters that are capacity limited, the efficacy of the transport activity may increase following sustained presentation of the drug to the transporting enzymes in comparison to non-control release mode of administration.

Enhanced bioavailability:

Once it has been ascertained that the compound in question is defined as narrow absorption window, the possibility of improving bioavailability by continuous administration of the compound to the specific site should be tested. For example, we have found that certain bisphosphonates, including alendronate, are absorbed directly from the stomach. However, the magnitude of this pathway remains modest even in the case where the prolonged gastric retention of the bisphosphonate in rats is produced by experimental/surgical means. On the other hand, the bioavailability of control release (CR) floating systems of Riboflavin and Levodopa are significantly enhanced in comparison to administration of simple CR polymeric formulations. It may be concluded that several different processes, related to absorption and transit of the drug in the gastrointestinal tract, act concomitantly and influence the magnitude of drug absorption. Therefore, *in vivo* studies are necessary to determine the release profile of the drug from the dosage form that will provide enhanced bioavailability.

Enhanced first pass biotransformation:

In a similar fashion to increased efficacy of active transporters exhibiting capacity limited activity, the pre-systemic metabolism of the tested compound may be considerably increased when the drug is presented to the metabolic enzymes (cytochrome P450, in particular CYP3A4) in a sustained manner, rather than by a bolus input

Improved bioavailability due to reduced P-glycoprotein (P-gp) activity in the duodenum:

In apparent contrast to the higher density of CYP3A4 at the upper part of the intestine, P-gp mRNA levels increase longitudinally along the intestine such that the highest levels are located in the colon. Therefore, for drugs that are P-gp substrate and do not undergo oxidative metabolism, such as Digoxin, floating systems may elevate absorption compared to the immediate and CR dosage forms.

Reduced frequency of dosing:

For drugs with relatively short biological half-life, sustained and slow input from control release floating system may result in a flip-flop pharmacokinetics and enable reduced dosing frequency. This feature is associated with improved patient compliance, and thereby improves therapy.

Targeted therapy for local ailments in the upper GIT:

The prolonged and sustained administration of the drug from the floating systems to the stomach may be advantageous for local therapy in the stomach and the small intestine.

Pharmacodynamic aspects of FDDS:

Reduced fluctuations of drug concentration:

Continuous input of the drug following floating system 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. Improved selectivity in receptor activation: Minimization of fluctuations in drug concentration also makes it possible to obtain certain selectivity in the elicited pharmacological effect of drugs that activate different types of receptors at different concentrations. Reduced counter-activity of the body: In many cases, the pharmacological response, which intervenes with the natural physiologic processes, provokes a rebound activity of the body that minimizes drug activity. Slow input of the drug into the body was shown to minimize the counter activity leading to higher drug efficiency.

Minimized adverse activity at the colon:

Retention of the drug in the GRDF 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 floating formulation for beta-lactam antibiotics that are absorbed only from the small intestine and presence in the colon leads to development of microorganisms

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM

Based on the buoyancy mechanism floating systems are classified as follows

- Effervescent systems
- Non effervescent systems

EFFERVESCENT SYSTEMS

These dosage forms are developed in such a way that, when they come incontact with gastric juices in the stomach , carbon dioxide gas is released due the reaction between sodium bicarbonate, citric acid and tartaric acid and is trapped in the swollen hydrocolloids. This provides buoyancy to the dosage form there by making it to float on the gastric fluids. These systems may also contain liquids which gasify and evaporates at body temperature by which the specific gravity decreases and causes the dosage form to float. These effervescent systems have been further classified into different types [5]

Volatile liquid containing systems

These are further classified as-

Intragastric floating gastrointestinal drug delivery systems

These systems are made to float in the stomach because of the floating chamber, which may be filled with air or vaccum or harmless gas, and the drug reservoir is encapsulated inside a micro porous compartment. This micro porous compartment has pores on the top and bottom surfaces, where as the peripheral walls of the reservoir compartment were completely sealed to prevent any physical contact of the undissolved drug with the walls of the stomach [5].

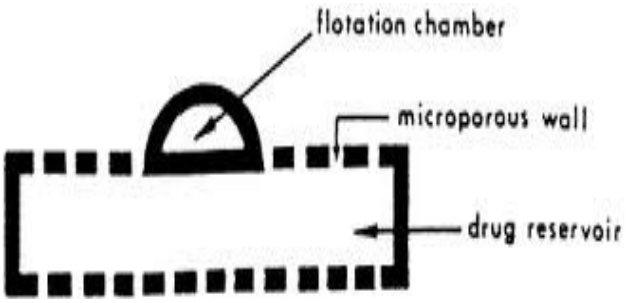


Fig. 2.Intragastric floating gastrointestinal drug delivery system

Inflatable gastrointestinal drug delivery system

These systems consist of inflatable chamber with liquid ether that gasifies at body temperature making the chamber to inflate in the stomach. This inflatable chamber contains a drug reservoir which is encapsulated in a gelatin capsule. After oral administration, the capsule dissolves and releases the drug reservoir together with the inflatable [7]

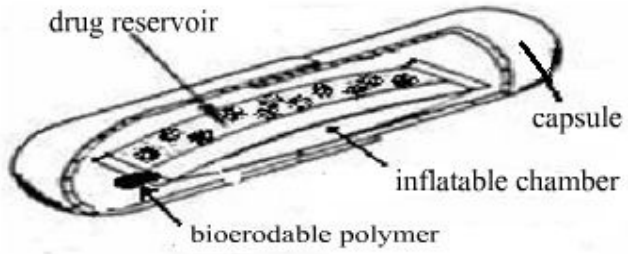


Fig.3. Inflatable gastrointestinal delivery system

Intragastric osmotically controlled drug delivery system

It consists of osmotic pressure controlled drug delivery device and an inflatable support in a biodegradable capsule. On reaching the stomach, inflatable capsule disintegrates and releases the osmotically controlled drug delivery. The inflatable support inside forms a deformable hollow polymeric bag that contains a liquid that gasifies at body temperature to inflate the bag. Osmotic pressure controlled drug delivery device consists of two components i.e. drug reservoir compartment and osmotically active compartment. The drug reservoir compartment is enclosed in a pressure responsive collapsible bag, which is impermeable to vapour and liquid and it contains a delivery orifice. The osmotically active compartment consists of a semi permeable membrane which encloses osmotically active salt. This device on reaching the stomach absorbs water from the gastro intestinal fluids through the semi permeable membrane into the osmotically active compartment and dissolves the osmotically active salt and creates the osmotic pressure. The pressure developed acts on the collapsible bag which forces the drug reservoir compartment to activate the release of drug in the solution form through the delivery orifice. After the predetermined period of time the biodegradable plug in the floating support erodes and deflates the support, which is then emptied from the stomach [9]

.

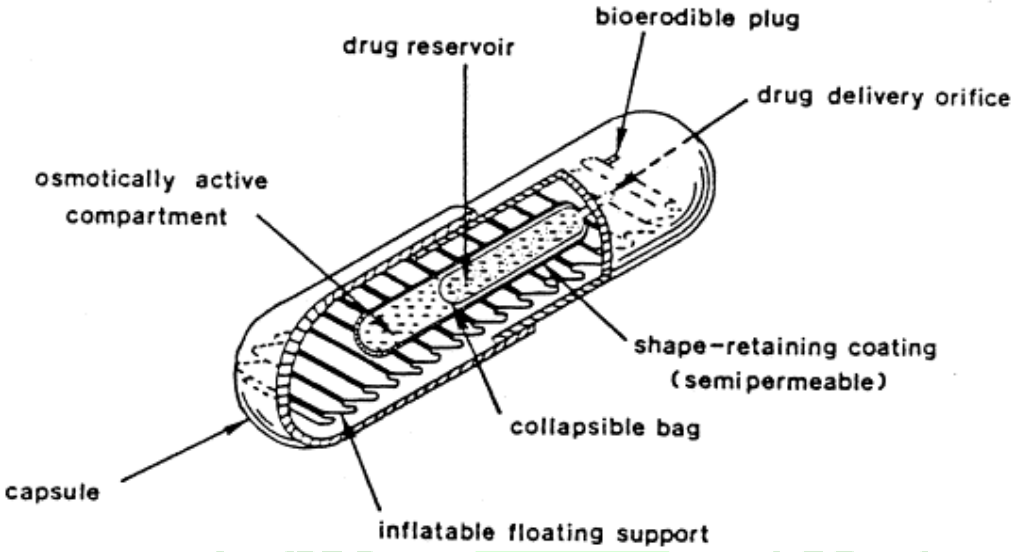


Fig.4 Intragastric osmotically controlled drug delivery system

Gas generating systems

In these systems floatability is achieved by generation of gas bubbles. Carbon dioxide is generated in situ by incorporation of carbonates or bicarbonates, which react with acid, either the natural gastric acid or co-formulated as citric or tartaric acids. The gas generated makes the systems to float on the gastric fluids and releases the drug at a predetermined rate. These are of different types [9-12]

Floating capsules

Floating capsules are prepared by filling a mixture of sodium alginate and sodium bicarbonate,

these float due to the generation of carbon dioxide which gets trapped in the

hydrating gel network on exposure to an acidic environment [12]

Floating pills

These systems consist of two layers, inner effervescent layer containing sodium bicarbonate and tartaric acid and the outer swellable polymeric membrane. The inner layer is further divided into two sub layers to avoid physical contact between sodium bicarbonate and tartaric acid. When this pill is immersed in buffer solution at 37 °C, it settles down at the bottom and buffer solution enters into the effervescent layer through the outer swellable membrane. Swollen pills or balloons are formed due the generation of carbon dioxide as a result of reaction between sodium bicarbonates and tartaric acid. The carbon dioxide generated is entrapped within the delivery system making the device to float. These systems were found to float completely within 10 minutes and have good floating ability independent of pH, viscosity of the medium and the drug is released in a controlled manner

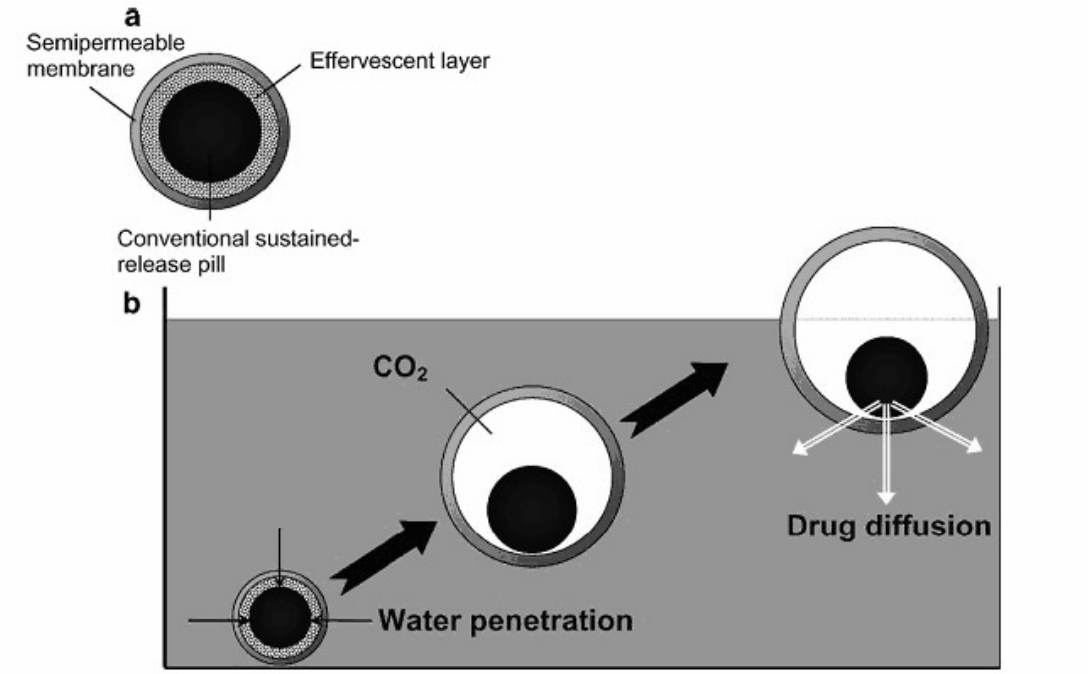


Fig. 5 Floating pills (a) The penetration of water into effervescent layer leads to a CO2 generation and makes the system to float (b) Mechanism of floatation

Floating systems with ion exchange resins

These systems are formulated by using ion exchange resin that is loaded with bicarbonate by mixing the beads with sodium bicarbonate solution .These loaded beads were then surrounded by a semi permeable membrane to avoid the sudden loss of carbon dioxide. Upon coming in contact with gastric contents there is an exchange of chloride and bicarbonate ions resulting in generation of carbon dioxide thereby carrying beads toward the top of gastric contents and producing a floating layer of resin beads, which releases the drug at a predetermined [12-14]

.

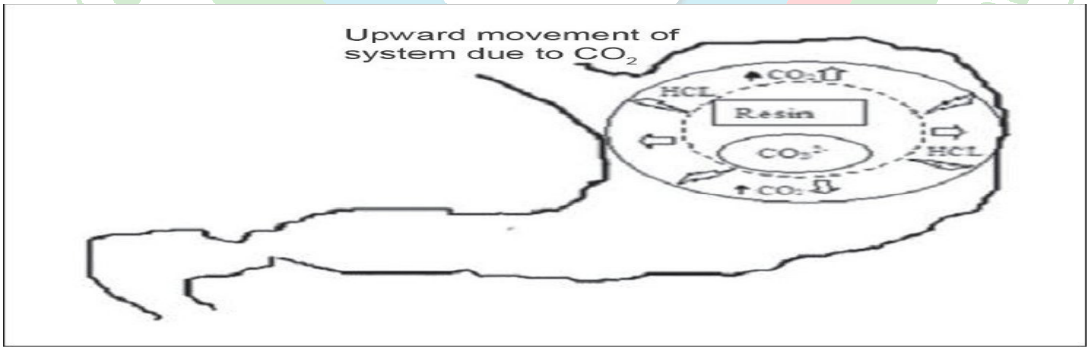


Fig. 6 Floating systems with ion exchange resins

NON EFFERVESCENT SYSTEMS

Non effervescent drug delivery systems are those which upon swallowing swells via imbibitions of gastric fluids to an extent that it prevents their exit from the stomach. These systems may also be referred to as 'plug-type systems' since they have the tendency to remain lodged near the pyloric sphincter. Different types of non effervescent systems are-

Hydrodynamically balanced systems (HBS)

HBS are also called as 'colloidal barrier systems' these systems contains drug along with the gel forming hydrocolloids. When the capsules containing the drug hydrocolloid

mixture comes in contact with the gastric fluids, the capsule shell dissolves and the mixture swells to form a gelatinous barrier, which imparts buoyancy in gastric fluids for a prolonged period of time due to the continuous erosion of the surface. This allows water penetration in to the inner layers maintaining surface hydration and buoyancy to the dosage form. This gel barrier controls the rate of fluid penetration into the device and consequent release of drug from the system [14,15]

.

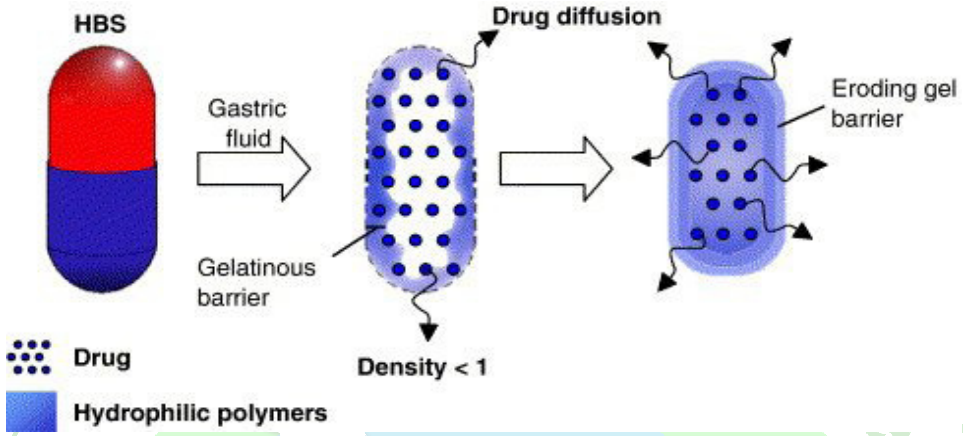


Fig.7 Hydrodynamically balanced systems

Micro porous compartment systems

This technology is based on the encapsulation of a drug reservoir inside a micro porous compartment with apertures along its top and bottom walls. The peripheral walls of the drug reservoir compartment are completely sealed to prevent any direct contact of the gastric mucosal surface with the undissolved drug. Gastric fluid enters through the aperture, dissolves the drug for continuous transport across the intestine for drug absorption [15]

.Micro balloons / hollow Microspheres

Micro balloons/ hollow microspheres are the low density systems that have sufficient

buoyancy to float over gastric contents and remain in stomach for prolonged period. These systems contain outer polymer shell loaded with drug. When they come in contact with gastric fluid the gel formers, and polymers hydrate to form a colloidal gel barrier that controls the rate of fluid penetration into the device and consequent drug release. As the exterior surface of the dosage form dissolves, the gel layer is maintained by the hydration of the adjacent hydrocolloid layer. The air trapped by the swollen polymer lowers the density and confers buoyancy to the microspheres. These are considered as one of the most promising buoyant systems as they possess the unique advantage of multiple unit system as well as better floating properties because of central hollow space inside the microspheres [15]

.Alginate beads

These are the freeze-dried calcium alginate beads of approximately 2.5 mm diameter prepared by dropping sodium alginate solution into aqueous solution of calcium chloride, causing precipitation of calcium alginate leading to formation of porous system, which helps in floating of the system on the gastric contents. Due to the porous nature these can maintain a floating force for over 12 hours. When compared with solid beads, which gave a short residence time of 1 hour, and these floating beads shows a prolonged residence time of more than 5.5 hours [15]

.Matrix layered tablets

These are the dosage forms which contain gel forming hydrocolloids which make the delivery system to float on the gastric contents. These may be single layered, bi layered and tri layered [9, 14]

- Single layered matrix tablets are obtained by intimate mixing of drug with gel forming hydrocolloids which swells in contact with gastric fluids and maintains bulk density less than gastric fluids
- Bi layered tablets contain one immediate release layer and one sustained release layer. Immediate release layer releases the initial dose of drug and the sustain release layer absorbs the gastric fluids and produces the bulk density of less than that of GI fluids and remain in stomach for an extended period of time.
- Tri layered tablets consists of immediate release layer, sustained release layer and the gas generating layer, which helps the system to float

.

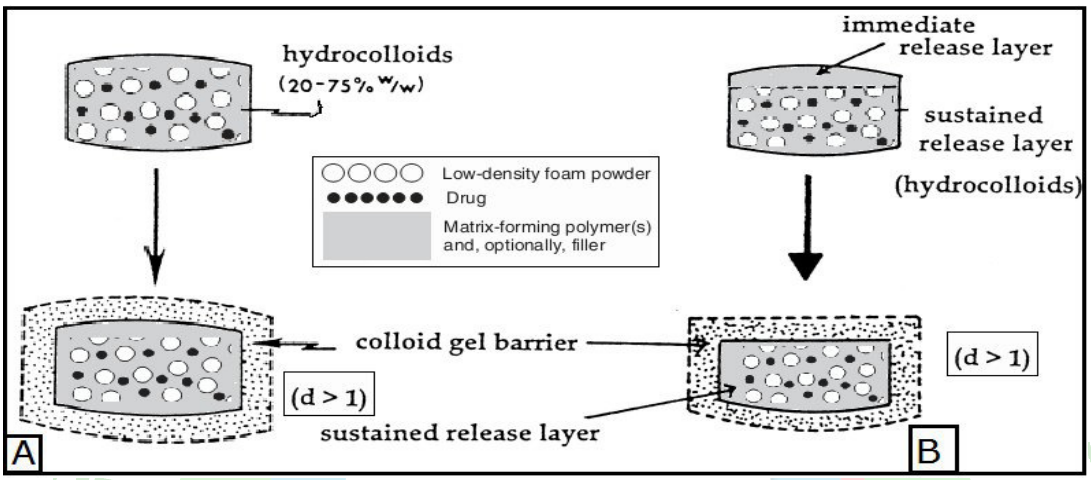


Fig.8 (A) Single layer floating tablet; (B) Bilayer floating tablet

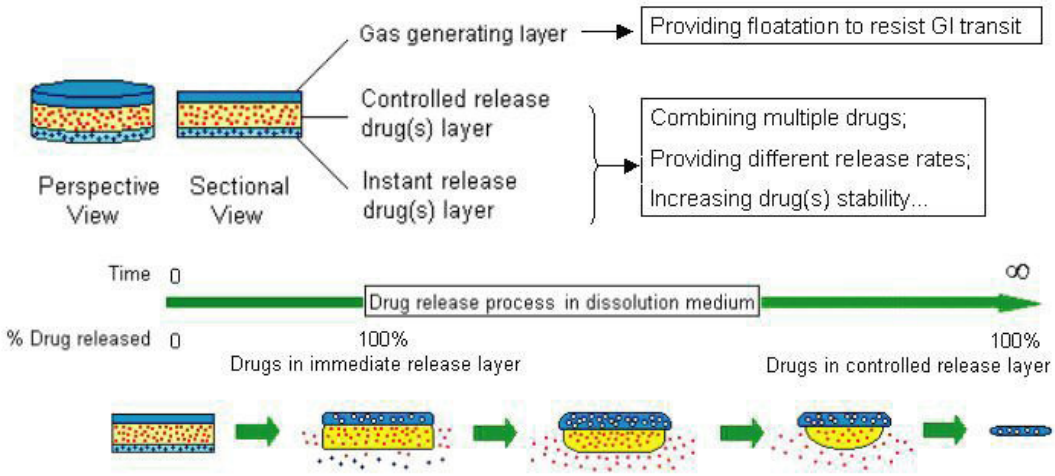


Fig. 9 Tri layer floating tablet

Raft forming systems:

These systems contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of carbon dioxide to make the system less dense and float on the gastric fluid. The mechanism involved in the raft formation includes the formation of viscous cohesive gel on contact with gastric fluids, where in each portion of the liquid swells forming a continuous layer called as raft. This raft floats on gastric fluids and prevent the reflux of the gastric contents into esophagus by acting as a barrier between stomach and esophagus, thus these systems have received much attention for the delivery of antacids and drug delivery for gastrointestinal infections and disorders [17, 18]

.

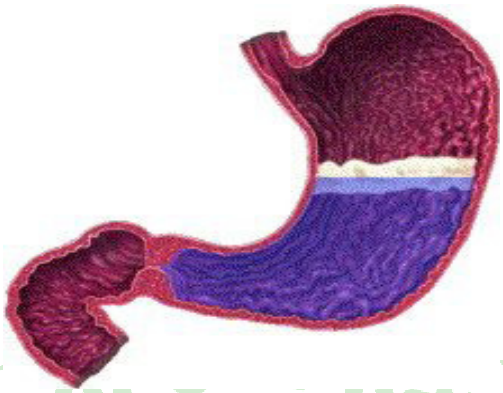


Fig.10. Barrier formed by the raft forming system

EVALUATION

Various parameters that need to be evaluated in gastro retentive formulations include

Buoyancy lag time:

It is determined in order to assess the time taken by the dosage form to float on the top of the dissolution medium, after it is placed in the medium. This parameter can be measured as a part of the dissolution test. The maximum buoyancy lag time for floating dosage form is 5 min.

Total floating time:

Test for floatation is usually performed in SGF-Simulated Gastric fluid maintained at 37˚C. The time for which the dosage form continuously floats on the dissolution media is termed as total floating time.

Specific gravity/density:

It can be determined by the displacement method using Benzene as displacement medium.

Resultant weight:

Now we know that bulk density and floating time are the main parameters for describing buoyancy. But only single determination of density is not sufficient to describe the buoyancy because density changes with change in resultant weight as a function of time. For example a matrix tablet with bicarbonate and matrixing polymer floats initially by gas generation and entrapment but after some time, some drug is released and simultaneously some outer part of matrixing polymer may erode out leading to change in resultant weight of dosage form. The magnitude and direction of force/resultant weight (up/down) is corresponding to its buoyancy force (Fbuoy) and gravity force (Fgrav) acting on dosage form.

$F = Fbuoy – Fgrav$,

$F = Df\ g\ V – Ds\ g\ V$,

$F = (Df – Ds)\ g\ V$,

$F = (Df – M/V)\ g\ V$

Where F = Resultant weight of object; Df= Density of fluid; Ds = Density of solid object; g = Gravitational force; M = Mass of dosage form; V = Volume of dosage form So when Ds, density of dosage form is lower, F force is positive gives buoyancy and when it is Ds is higher, F will negative shows sinking.

Water uptake:

It is an indirect measurement of swelling property of swellable matrix. Here dosage form is removed out at regular interval and weight changes are determined with respect to time. So it is also termed as weight gain,

Water uptake = $WU = (Wt – Wo)*100/Wo$

Where, Wt = weight of dosage form at time t

Wo = initial weight of dosage form

In Vitro Dissolution Tests:

In vitro dissolution test is generally done by using USP apparatus with paddle The in vitro release of drug from different formulations was examined by using simulated gastric fluid(PH 1.2, without enzymes) 900 ml as the dissolution medium and maintained at 37˚C at a rotation speed of 50-100 rpm. An aliquot of 5 ml of the solution was withdrawn at predetermined time intervals and replaced by 5ml of fresh dissolution medium. Samples were assayed spectrometrically at maximum wave length [14-20]

APPLICATIONS

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.

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.

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.

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.

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.

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 plasma drug concentration [21-24]

CONCLUSION

Recently many drugs have been formulated as floating drug delivery systems with an objective of sustained release and restricting the region of drug release to stomach. 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. The currently available polymer-mediated non effervescent and effervescent FDDS, designed on the basis of delayed gastric emptying and buoyancy principles, appear to be a very much effective approach to the modulation of controlled oral drug delivery.

The most important criteria which has to be looked into for the productions of a floating drug delivery system is that the density of the dosage form should be less than that of gastric fluid. And hence, it can be concluded that these dosage forms serve the best in the treatment of diseases related to the GIT and for extracting a prolonged action from a drug with a short half life.

REFERENCE-

1. *Arunachalam A, Karthikeyan M, Konam Kishore, Prasad Pottabathula Hari. Review on: Floating drug delivery system. International Journal of Research in Pharmaceutical Sciences, 2011; 2(1): 76-83.*
2. *Geetha A, kumar J. Rajendra , Mohan CH. Krishna. Review on: Floating drug delivery systems. International journal of pharmaceutical research and biomedical analysis, 2012; (1): 1-13.*
3. *Hardenia Shiv Shankar, Jain Ankit, Patel Ritesh, kaushal Anu. Review on: Floating Drug Delivery Systems. Asian Journal of Pharmacy and Life Science, 2011; 1 (3): 284-293.*
4. *Narang Neha. Review on: floating drug delivery system. International journal of applied pharmaceutics, 2011; 3 (1): 1-7.*
5. *Reddy B, Navaneetha K, Sandeep P , Deepthi A. Review on: Gastroretentive drug delivery system. Journal of Global Trends in Pharmaceutical Sciences, 2013; 4 (1): 1018-1033.*
6. *Jain Amit. Review on: New Concept of Floating Drug Delivery System. Indian Journal of Novel Drug delivery, 2011; 3(3): 162-169.*
7. *Kadam Shashikant M, Kadam SR, Patil U, Ratan S. Review on: Floating drug delivery system: An approach to oral controlled drug delivery via gastric retention. International journal of Research in Ayurveda and Pharmacy, 2011; 2(6): 1752-1755.*
8. *Tripathi Purnima, Ubaidulla U, Khar RK. Review on: Floating drug delivery system. International Journal of Research and Development in Pharmacy and Life Sciences, 2012; 1(1): 1-10.*
9. *Pandey A, Kumar G, Kothiyal P, Barshiliya Y. Review on: Current approaches in Gastro-retentive drug delivery system. Asian Journal of Pharmacy and Medical Science, 2012; 2(4):60-77.*
10. *Nadigoti Jagadeesh, Shayeda. Review on: Floating drug delivery system. International journal of Pharmaceutical Science and Nanotechnology, 2009; 2(3): 595-604*
11. *Chowdhury Roy, Verma Santanu. Review on: Floating drug delivery system a new era in novel drug delivery system. International journal of Pharmaceutical Research and Bio-science, 2012; 1(5): 91-107.*
12. *Pal Pallavi, Sharma Vijay, Singh Lalit. Review on: Floating type Gastroretentive Drug delivery system. International research journal of pharmacy, 2012; 3(4): 37-43.*
13. *Sharma Natasha, Agarwal Dilip, Gupta MK, Khinchi MP. Review on: Floating Drug Delivery System. International Journal of Research in Pharmaceutical and Biomedical Sciences, 2011; 2(2): 428-440.*
14. *Vinod KR, Gangadhar M, Sandhya S. Review on: Critical assessment pertaining to Gastric Floating Drug Delivery Systems. Hygeia journal for drugs and medicines, 2013; 5(1): 41-58.*
15. *Vadaliya SK, Desai HT, Patel JK, Vadaliya KR. Review on: Gastro-Retentive Floating Drug Delivery System Containing Anti-Diabetic Drug. International journal of pharmaceutical and chemical sciences, 2012; 1(4): 1322-1335.*
16. *Kumar Neeraj. Review on: Novel Floating Drug Delivery System. International Research Journal of Pharmacy, 2012; 3(8): 29-33.*
17. *Kunal. P. Nayak. Review on: Gastro retentive Drug Delivery System. Journal of Pharmaceutical Research and Opinion, 2012; 2(1): 1-8.*
18. *Nayak Amit Kumar. Review on: Gastroretentive drug delivery systems. Asian Journal of Pharmaceutical and Clinical Research, 2010; 3(1): 2-10.*
19. *Sharma Saurabh, Nanda Arun. Review on: Gastroretentive Drug Delivery System. International Journal of Research in Pharmaceutical and Biomedical Sciences, 2011; 2(3): 954-958.*
20. *Foda NH, Ali SM. Review on: Gastroretentive drug delivery systems as a potential tool for enhancing the efficacy of antibiotics. International Journal of Pharma and Bio Sciences, 2011; 2(2): 94-104*
21. *Soni RP, Patel AV, Patel RB, Review on: Gastroretentive drug delivery systems. International journal of Pharma world Research, 2011; 2(1): 1-24.*
22. *Mayavanshi AV, Gajjar SS. Review on: Floating drug delivery systems to increase gastric retention of drugs. Research Journal of Pharmacy and Technology, 2008; 1(4): 345-348.*
23. *Patel Nirav, Nagesh C, Chandrashekhar S, Patel Jinal. Review on: Floating drug delivery system: An innovative acceptable approach in Gastro retentive drug delivery. Asian Journal of Pharmaceutical Research, 2012; 2(1): 7-18.*
24. *Shep Santosh, Lahoti Sandeep. Review on: Swelling System: A Novel Approach Towards Gastroretentive Drug Delivery System. Indo-Global Journal of Pharmaceutical Sciences, 2011; 1(3): 234-242.*