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A REVIEW: GASTRO RETENTIVE DRUG DELIVERY SYSTEM

***Suresh Choudhary, Santosh Waghmare and Hemant Kamble**

Loknete Shri Dadapatil Pharate College of Pharamcy, Mandavgoan Pharat Tal-shirur, Dist-Pune, Maharashtra.

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***Corresponding Author**
Suresh Choudhary
Loknete Shri Dadapatil Pharate College of Pharamcy, Mandavgoan Pharat Tal-shirur, Dist-Pune, Maharashtra.

ABSTRACT

The goal of this review on gastroretentive drug delivery systems (GRDDS) was to compile the current literature with a focus on a few gastroretentive approaches that have recently emerged as important methodologies in the field of site-specific orally administered sustained/controlled release drug delivery. To overcome physiological challenges such as short gastric residence times (GRT) and unpredictable gastric emptying times, technological efforts have been made in the study and development of rate-controlled oral drug delivery systems (GET). GRDDS is a method for extending the GRT and targeting site-specific drug release in the upper gastrointestinal tract (GIT) for a local or systemic effect. Because of the fast gastric transition from the stomach, conventional oral dose forms have low bioavailability issues, especially for medications that are less soluble at an alkaline pH of the intestine. Additionally, medications that have a local action in the stomach are quickly emptied and do not spend enough time in the stomach. To lower the frequency of dose administration, several efforts have been made to extend the retention duration of drug delivery systems. GRDFs not only extend dosing intervals, but they also improve patient compliance beyond what is currently possible with controlled release dosage forms. The benefits, drawbacks, and characterisation of gastroretentive drug delivery devices are discussed in this article. This study contains patents and commercially marketed gastroretentive products.

KEYWORDS: Gastroretentive drug delivery system; approach; floating system; Evaluation.

INTRODUCTION

The oral delivery of drugs is the most favoured route of administration because of ease of administration. The bioavailability of drugs in oral dose forms is affected by a variety of

circumstances. The gastric residence time (GRT) of these dose forms is one of the most important factors. Gastric retention has gotten a lot of attention in recent years because many traditional oral delivery systems have limitations due to fast gastric emptying times. Gastroretentive dosage forms are a type of innovative drug delivery device that can stay in the stomach for an extended amount of time, increasing medication GRT. Gastro-retention aids in improving medication absorption.

The conventional drug delivery system achieves and also maintained the drug concentration in the therapeutically effective range desired for treatment, only when taken numerous times a day. A medication with a narrow absorption window in the GI tract may be poorly absorbed. GRDDS has the advantage of extending the stomach emptying time for these medications.

Preparing controlled release systems for enhanced absorption and bioavailability presents a number of challenges. Drug absorption from the gastrointestinal tract is a complicated process that is influenced by a number of factors. It is broadly recognized that the extent of GIT drug absorption is correlated to contact time with small intestinal mucosa. GRDDS can stay in the GI tract for several hours, considerably extending the GRT of medicines. Extended stomach retention improves bioavailability, reduces drug waste, and enhances the solubility of drugs that are less soluble in a high-pH environment.

Numerous techniques, such as hydrodynamically balanced systems (HBS)/floating drug delivery systems, low density systems, raft systems incorporating alginate gels, mucoadhesive or bioadhesive systems, high density systems, super porous hydrogels, and magnetic systems, are currently used to prepare a successful stomach specific or gastroretentive Drug delivery system. Current technological advancements have created feasible dose alternatives that can be taken via many routes such as oral, topical, parenteral, rectal, nasal, ophthalmic, vaginal, and so on. However, out of all of these routes, the oral route is the most commonly used and favored method of drug delivery for the following reasons:

- Ease of administration
- Ease of production
- Greater design flexibility
- Low cost

Many medications taken by mouth are absorbed primarily through the gastrointestinal tract (GIT), with the stomach and intestines accounting for the majority of absorption. Drugs that are absorbed from the stomach or have a local effect should be kept in the stomach for a long time. Due to stomach emptying, this is extremely difficult to achieve with conventional dosage forms such as capsules and tablets. The temperature and viscosity of the meal, the volume and content of the meal, the emotional state of the individual, the pH of the stomach, body posture, and other factors all affect the gastric emptying of dosage forms. The following conditions necessitate prolonged medication retention in the stomach:

- The stomach is the optimum place for the drug to be absorbed. E.g., Aspirin, Phenylbutazone, etc.
- Drugs that take a long time to dissolve.
- Food aids in the dissolution and absorption of drugs. For example-Griseofulvin
- Drugs have local effects in the stomach.
- Gastric juices aid in the disintegration and dissolving of the medication.

Various methods of regulated medication delivery have been established to achieve all of these circumstances. GRDDS is one of these types of procedures that ensures that a specific drug/dosage form remains in the stomach for a longer period of time.

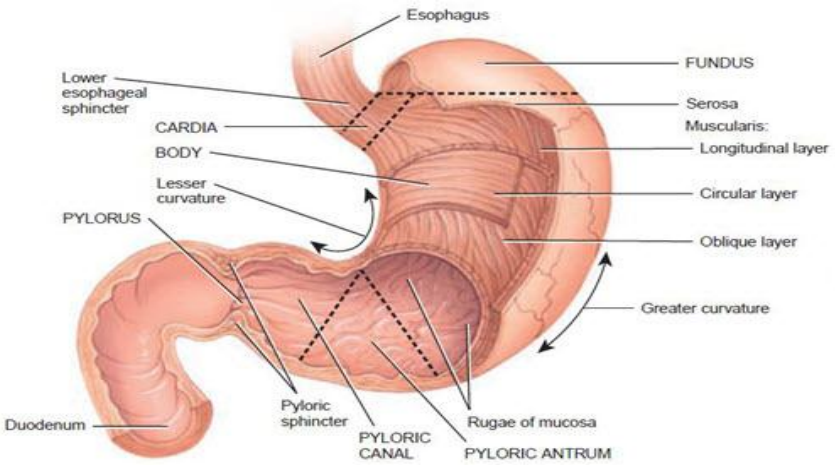
However, in following condition gastroretention is considered undesirable:

- For medications that irritate the stomach.
- E.g., Diclofenac sodium, Ibuprofen, Acetylsalicylic acid, etc.
- For acid labile drugs that are stable at gastric pH.
- E.g., Macrolide antibiotics
- Drugs that are evenly absorbed throughout the GIT.

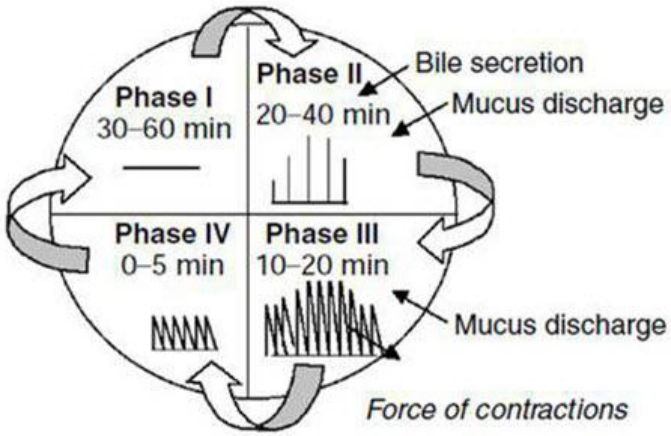
Stomach Physiology

Anatomically the stomach is divided into three regions Fundus, Body and Antrum (pylorus) The fundus and body of the proximal section act as a reservoir for undigested materials, whereas the antrum is the primary site for mixing motions and serves as a pump for stomach emptying by thrusting. Gastric emptying occurs in both the fasting and fed states. The inter digestive myloelectric cycle, also known as the migrating myoelectric cycle (MMC), is a sequence of electrical events that occur during the fasting state and cycle through the stomach and intestine every 2-3 hours. It is divided into four phases. The pattern of contractions varies

from fasted to fed after consuming a mixed meal, which is also known as the digestive motility pattern.



1. **Phase 1**- (Basic phase) last from 30-60 minutes with rare contractions.
2. **Phase 2**- (Preburst 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 cycle.



Factors affecting gastric retention time of the dosage form

- Density- the density of the dosage form should be less than that of the gastric contents (1.004g/ml)
- Size- dosage forms with a diameter greater than 7.5mm had a longer gastric residence period than dosage forms with a diameter of 9.9mm.

- The shape of the dosage form—the tetra hedron stayed in the stomach for longer than other similar-sized devices. Formulation using a single or several units When compared to single unit dosage forms, multiple unit formulations have a more predictable release profile and insignificant performance impairment due to unit failure. They also allow coadministration of units with different release profiles or containing incompatible substances, as well as a larger margin of safety against dosage form failure.
- Fed or unfed state- under fasting conditions, the GI motility is characterized by periods of strong motar activity that occurs every 1.5-2 hrs. The MMC sweeps undigested material from the stomach and if the timing of the formulation coincides with that of MMC, the GRT of the unit can be very short however in fast state MMC is delayed and GRT is longer.
- Nature of meal- feeding of indigestible polymers or fatty acids can change the motility pattern of the stomach to a fed state,thus decreasing gastric emptying rate and prolonging drug release.
- Caloric content-GRT can be increased by 4-10 with a meal that is high in protein and fat.
- Frequency of feed- The GRT can be increase over 400 min when successive meals given are compared with the single meal due to low frequency of MMC.
- Gender- mean ambulatory GRT in male (3.4hrs) is less compared with the age and race matched female counterparts (4.6hrs) regardless of height, weight and body surface.
- Age- people with age more than 70 have a significant longer GRT.
- Concomitant drug administration- anticholinergic like atropine and propetheline, opiates like codeine can prolong GRT

Gastroretentive Drug Delivery Systems Advantages

- Maintenance of constant therapeutic level over longer period of time.
- E.g. Beta lactams antibiotics.
- Increased drug bioavailability.
- E.g. Enhancement of bioavailability of controlled release gastroretentive dosage forms (CR-GRDF) of riboflavin in comparison of non CR-GRDF polymeric formulation.
- By reducing dosing frequency, the gastroretentive dosage form enhances patient compliance.
- Minimizing mucosal irritation of drugs, by releasing drug slowly at a controlled rate.
- E.g. NSAIDs - Treatment of GI disorders like GERD, Helicobacter pylori infection, etc.

- Floating drug delivery system is a feasible approach for the drugs that have limited absorption in the intestine.
- The floating drug delivery system can reduce the counter activity of body, leading to higher drug efficiency.
- For drugs that have comparatively short half-life, sustained release may result in a flip-flop pharmacokinetics.
- The floating drug delivery systems are beneficial for drugs that are absorbed through stomach.

  E.g. Antacids, Ferrous salts, etc.
- Sustained release drug delivery system reduces dosing frequency of drugs with short half-life.
- Bioavailability enhances despite the first pass effect as a result of variations in plasma drug concentration are escaped; a required plasma drug concentration is retained by the continuous drug release.
- Controlled drug delivery of drugs.

Disadvantages of gastro-retentive drug deliverysystems

- Unsuitable for drugs with limited acidsolubility. E.g. Phenytoin.
- Unsuitable for drugs those are unstable inacidic environment. E.g. Erythromycin.
- Drugs that irritates or causes gastric lesions on slow release. E.g. Aspirin &NSAID's. Drugs that absorb selectively in colon E.g. Corticosteroid.
- Drugs that absorb equally well through GIT. E.g. Isosorbide, dinitrate, Nifidipine.
- Floating drug delivery systems require high fluid level in stomach to float and work effectively.

Gastroretentive Drug Delivery Systems Are Required

Because of the rapid gastric transition from the stomach, oral dose forms have low bioavailability, especially for drugs that are less soluble at an alkaline pH of the intestine. Drugs that have a local action in the stomach are also swiftly eliminated and do not have enough time to stay in the stomach. As a result, in such a situation, the frequency of dose administration is increased. A floating drug delivery device has been designed to circumvent such an issue.

Strategies for delaying drug transit through GIT

• Pharmacological approach

It involves the co-administration or incorporation of a drug into the dosage form. This drug delays gastrointestinal emptying. Examples include antimuscarinics, e.g. propantheline.

• Physiological approach

Types of Gastroretentive Dosage Form

• High density system

Mucoadhesive bioadhesive system Magnetic system laying drug transit through GIT administration or incorporation of a drug delays gastrointestinal emptying. Examples include antimuscarinics, e.g. It is the use of natural materials or fat derivatives such as triethanolamine myristate, which stimulate the duodenal or jejunal receptors to slow gastric emptying.

• Pharmaceutical approach

First two approaches are not used due to toxicity problems. The various pharmaceutical approaches are TYPES OF GASTRORETENTIVE DOSAGE FORM This approach involves formulation of dosage forms with density that must exceed density of normal stomach content.

Types of Gastroretentive Dosage Form

High density system Floating system Expandable system Superporous hydrogels 85 It is the use of natural materials or fat derivatives such as triethanolamine myristate, which stimulate the duodenal or w gastric emptying.

Pharmaceutical approach First two approaches are not used due to toxicity problems. The various pharmaceutical approaches are:

High density system

This approach involves formulation of dosage forms with density that must exceed density of normal stomach content (1.004g/ml). These formulations are prepared by coating drug on a heavy core or mixed with heavy inert material such as iron powder, zinc oxide, titanium dioxide, barium sulphate. The resultant pellets can be coated with diffusion controlled Membrane.[18] These systems have some drawbacks like they are technically difficult to manufacture with a large amount of drug because the dry material interacts within the gastric

fluid to release its drug contents. One other problem is that no such system is available in the market.

• Floating or low density system

By virtue of their low densities, FDDS remain afloat above the gastric contents for prolonged periods of time and provide continuous release of the drug. These systems in particular have been extensively studied because they do not adversely affect the mobility of the GIT Their dominance over the other types of GRDDS is also evident from the large number of floating dosage forms being commercialized and marketed world wide.

Non-effervescent Systems

Non-effervescent floating drug delivery systems are normally prepared from gel-forming or highly swellable cellulose type hydrocolloids, polysaccharides or matrix forming polymers like polyacrylate, polycarbonate, polystyrene and polymethacrylate. In one approach, intimate mixing of drug with a gel forming hydrocolloid which results in contact with gastric fluid after oral administration and maintain a relative integrity of shape and a bulk density less than unity within the gastric environment. The air trapped by the swollen polymer confers buoyancy to these dosage forms. Excipients used most commonly in these systems include hydroxypropyl methylcellulose (HPMC) polyacrylates, polyvinyl acetate, carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates. This system can be further divided into the sub-types:

Hydrodynamically balanced systems: Sheth and Tossounian first designated these 'hydrodynamically balanced systems'. These systems contains drug with gel-forming hydrocolloids meant to remain buoyant on the stomach content. These are single-unit dosage form, containing one or more gel-forming hydrophilic polymers. Hydroxypropyl methylcellulose (HPMC), hydroxethyl cellulose (HEC), hydroxypropyl cellulose (HPC), sodium carboxymethyl cellulose (NaCMC), polycarbophil, polyacrylate, polystyrene, agar, carrageenans or alginic acid are commonly used excipients to develop these systems. The polymer is mixed with drugs and usually administered in hydrodynamically balanced system capsule. The capsule shell dissolves in contact with water and mixture swells to form a gelatinous barrier, which imparts buoyancy to dosage form in gastric juice for a long period. Because, continuous erosion of the surface allows water penetration to the inner layers maintaining surface hydration and buoyancy to dosage form.[36] Incorporation of fatty excipients gives low-density formulations reducing the erosion. Madopar LP® , based on the

system was marketed during the 1980's . Effective drug deliveries depend on the balance of drug loading and the effect of polymer on its release profile.

Several strategies have been tried and investigated to improve efficiencies of the floating hydrodynamically balanced systems.

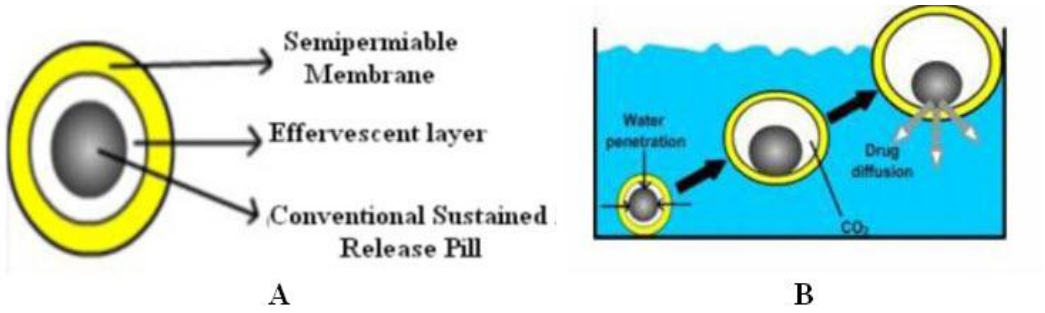
Microballoons / Hollow microspheres: Microballoons / hollow microspheres loaded with drugs in their other polymer shelf were prepared by simple solvent evaporation or solvent diffusion / evaporation methods to prolong the gastric retention time (GRT) of the dosage form. Commonly used polymers to develop these systems are polycarbonate, cellulose acetate, calcium alginate, Eudragit S, agar and low methoxylated pectin etc. Buoyancy and drug release from dosage form are dependent on quantity of polymers, the plasticizer polymer ratio and the solvent used for formulation. The microballoons floated continuously over the surface of an acidic dissolution media containing surfactant for >12 hours. At present hollow microspheres are considered to be one of the most promising buoyant systems because they combine the advantages of multiple-unit system and good floating.

Alginate beads: Talukdar and Fassihi recently developed a multiple-unit floating system based on cross-linked beads. They were made by using Ca2+ and low methoxylated pectin (anionic polysaccharide) or Ca2+ low methoxylated pectin and sodium alginate. In this approach, generally sodium alginate solution is dropped into aqueous solution of calcium chloride and causes the precipitation of calcium alginate. These beads are then separated and dried by air convection and freeze drying, leading to the formulation of a porous system, which can maintain a floating force for over 12 hrs. These beads improve gastric retention time (GRT) more than 5.5 hrs

Microporous compartment system: This approachis based on the principle of the encapsulation of a drug reservoir inside a microporous compartment with pores along its top and bottom walls. The peripheral walls of the device were completely sealed to present any direct contact of the gastric surface with the undissolved drug. In the stomach the floatation chamber containing entrapped air causes the delivery system to float in the gastric fluid . Gastric fluid enters through the aperture, dissolves the drug and causes the dissolved drug for continuous transport across the intestine for drug absorption.

Effervescent (gas generating) systems

Floatability can be achieved by generation of gas bubbles. These buoyant systems utilize matrices prepared with swellable polymers such as polysaccharides (e.g. chitosan), effervescent components (e.g. sodium bicarbonate, citric acid or tartaric acid). The optimal stoicheometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76: 1. In this system carbon dioxide is released and causes the formulation to float in the stomach.



A B

Other approaches and materials that have been reported are a mixture of sodium alginate and sodium bicarbonate, multiple unit floating dosage forms that generate gas (carbon dioxide) when ingested, floating mini capsules with a core of sodium bicarbonate, lactose and polyvinyl pyrrolidone (PVP) coated with hydroxypropyl methylcellulose (HPMC), and floating system based on ion exchange resin technology etc. Bilayer or multilayer system has also been designed. Drugs and excipients can be formulated independently and the gas generating material can be incorporated in to any of the layers. Further modifications involve coating of the matrix with a polymer which is permeable to water, but not to carbon dioxide. The main difficulty of these formulations is finding a good compromise between elasticity, plasticity and permeability of the polymers.

Bioadhesive or Mucoadhesive drug delivery systems

Bioadhesive drug delivery systems are used as adelivery device within the human to enhance drug absorption in a site-specific manner. In this approach, bio adhesive polymers are used and they can adhere to the epithelial surface in the stomach. Thus, they improve the prolongation of gastric retention. The basis of adhesion in that a dosage form can stick to the mucosal surface by different mechanism. These mechanisms are:

1) The wetting theory, which is based on the ability of bioadhesive polymers to spread and develop intimate contact with the mucous layers.

2) The diffusion theory, which proposes physical entanglement of mucin strands the flexible polymer chains, or an interpenetration of mucin strands into the porous structure of the polymer substrate.
3) The absorption theory, suggests that bioadhesion is due to secondary forces such as Vander Waal forces and hydrogen bonding.
4) The electron theory, which proposes attractive electrostatic forces between the glycoprotein mucin net work and the bio adhesive material. Materials commonly used for bioadhesion are poly acrylic acid, chitosan, cholestyramine, sodium alginate, hydroxypropyl methylcellulose (HPMC), sucralfate, tragacanth, dextrin, polyethylene glycol) and polylactic acids etc. Even though some of these polymers are effective at producing bioadhesive, it is very difficult to maintain it effectively because of the rapid turnover of mucus in the gastrointestinal tract

Expandable, unfoldable and swellable systems

A dosage form in the stomach will withstand gastric transit if it bigger than pyloric sphincter. However, the dosage form must be small enough to be swallowed, and must not cause gastric obstruction either singly or by accumulation. Thus, their configurations are required to develop an expandable system to prolong gastric retention time (GRT):

1) A small configuration for oral intake,

2) An expanded gastroretentive form, and

3) A final small form enabling evacuation following drug release from the device. Thus, gastroretentivity is improved by the combination of substantial dimension with high rigidity of dosage form to withstand peristalsis and mechanical contractility of the stomach. Unfoldable and swellable systems have been investigated and recently tried to develop an effective gastroretentive drug delivery. Unfoldable systems are made of biodegradable polymers. They are available in different geometric forms like tetrahedron, ring or planner membrane (4 - label disc or 4 - limbed cross form) of bioerodible polymer compressed within a capsule which extends in the stomach . Swellable systems are also retained in the gastro intestinal tract (GIT) due to their mechanical properties. The swelling is usually results from osmotic absorption of water and the dosage form is small enough to be swallowed by the gastric fluid (Figure 4). Expandable systems have some drawbacks like problematical storage of much easily hydrolysable, biodegradable polymers relatively short-lived mechanical shape memory for the unfolding system most difficult to industrialize and not cost effective. Again,

permanent retention of rigid, large single-unit expandable drug delivery dosage forms may cause brief obstruction, intestinal.

Super porous hydrogel systems

These swellable systems differ sufficiently from the conventional types to warrant separate classification. In this approach to improve gastric retention time (GRT) super porous hydrogels of average pore size >100 micro miter, swell to equilibrium size within a minute due to rapid water uptake by capillary wetting through numerous interconnected open pores . They swell to a large size (swelling ratio: 100 or more) and are intended to have sufficient mechanical strength to withstand pressure by gastric contraction. This is advised by co-formulation of hydrophilic particulate material.

Magnetic Systems

This approach to enhance the gastric retention time (GRT) is based on the simple principle that the dosage form contains a small internal magnet, and a magnet placed on the abdomen over the position of the stomach. Although magnetic system seems to wok, the external magnet must be positioned with a degree of precision that might compromise patient compliance.

Evaluation of Floating Drug delivery system

1**) Evaluation of powder blend**

a) Angle of Repose

b) Bulk Density

c) Percentage porosity

2) Evaluation of tablets

a) Buoyancy capabilities

b) In vitro floating and dissolution behaviour

c) Weight variation

d) Hardness & friability

e) Particle size analysis, surface characterization (for floating microspheres and beads):

f) X-Ray/Gamma Scintigraphy

g) Pharmacokinetic studies

1) Evaluation of powder blend

a) Angle of repose Angle of repose is defined as "the maximum angle possible between the surface of the pile of powder and the horizontal plane." Lower the angle of repose, better the flow properties. The angle of repose may be calculated by measuring the height (h) of the pile and the radius of the base(r) with ruler. Tan θ = h/r

1) b) Bulk density Bulk density denotes the total density of the material. It includes the true volume of interparticle spaces and intraparticle pores. The packing of particles is mainly responsible for bulk.

Bulk density is defined as: Bulk density = Weight of the powder / Bulk volume of powder...

2) When particles are packed, it is possible that a large amount of gaps may be present between the particles. Therefore, trapping of powder allows the particles to shift and remove the voids to minimum volume. The volume occupied by the powder in this condition represents the bulk volume. Substituting this volume for a given weight of powder in equation (2) gives the bulk density.

c) Percentage porosity Whether the powder is porous or nonporous, the total porosity expression for the calculation remains the same. Porosity provides information about hardness, disintegration, total porosity etc. % porosity, € = void volume x100 Bulk volume % porosity, € = (bulk volumetrue volume) x100 True density

2) Evaluation of floating tablets

a) Measurement of buoyancy capabilities of the FDDS: The floating behaviour is evaluated with resultant weight measurements. The experiment is carried out in two different media, deionised water and simulated meal. 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 deionised water.

b) In Vitro floating and dissolution behaviour: The dissolution tests are generally performed on various drugs using USP dissolution apparatus. USP 28 states "the dosage unit is allowed to sink to the bottom of the vessel before rotation of the blade is started". A small, loose piece of nonreactive material with not more than a few turns of a wire helix may be attached to the dosage units that would otherwise float. However, standard USP or BP methods have not been shown to be reliable predictors of in vitro performance of floating dosage forms. Pillay et al applied a helical wire sinker to the swellable floating system of theophylline, which is sparingly soluble in water and concluded that the swelling of the system was inhibited by the wire helix and the drug release also slowed down. To overcome this limitation, a method was

developed in which the floating drug delivery system was fully submerged under a ring or mesh assembly, and an increase in drug release was observed. Also, it was shown that the method was more reproducible and consistent. However, no significant change in the drug release was observed when the proposed method was applied to a swellable floating system of diltiazem, which is a highly water soluble drug. It was thus concluded that the drug release from swellable floating systems was dependent upon uninhibited swelling, surface exposure, and the solubility of the drug in water.

c) Weight variation: In practice, composite samples of tablets (usually 10) are taken and weighed throughout the compression process. The composite weight divided by 10, however provides an average weight but contains a problem of averaged value. To help alleviate this problem, the United States pharmacopeia (USP) provides limits for the permissible variations in the weights of individual tablets expressed as a percentage of the average weight of the sample. The USP provides the weight variation test by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weights to the average. The tablets meet the USP test if no more than 2 tablets are outside the percentage limit, and if no tablet differs by more than 2 times the percentage limit.

d) Hardness & friability: Hardness is defined as the "force required to break a tablet in diametric compression test." Hardness is hence, also termed as the tablet crushing strength. Some devices which are used to test hardness are Monsanto tester, strong Cobb tester, Pfizer tester, etc. The laboratory friability tester is known as the Roche Friabilator. This consists of a device which subjects a number of tablets to the combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm & drop the tablet to a distance of six inches with each revolution. Normally, a pre weighed tablet sample is placed in the friabilator which is then operated for 100 revolutions. Conventional compressed tablets that lose less than 0.5 to 1.0 % of their weight are generally considered acceptable. Most of the effervescent tablets undergo high friability weight losses, which accounts for the special stack packaging,that may be required for these types of tablets.

e) Particle size analysis, surface characterization (for floating microspheres and beads): The particle size and the size distribution of beads or microspheres are determined in the dry state using the optical microscopy method. The external and cross sectional morphology (surface characterization) is done by scanning electron microscope (SEM).

f) XRay/ gamma scintigraphy: X-Ray/Gamma Scintigraphy is a very popular evaluation parameter for floating dosage form nowadays. It helps to locate dosage form in thegastrointestinal tract, by which one can predict and correlate the gastric emptying time and the passage of dosage form in the GIT. Here the inclusion of a radio opaque material into a solid dosage form enables it to be visualized by X-rays. Similarly, the inclusion of a γ-emitting radionuclide in a formulation allows indirect external observation using a γ-camera or scintiscanner. In case of γscintigraphy, the γ-rays emitted by the radionuclide are focused on a camera, which helps to monitor the location of the dosage form in the GIT.

g) Pharmacokinetic studies: Pharmacokinetic studies are an integral part of the in vivo studies and several works have been reported on these. Sawicki studied the pharmacokinetics of verapamil, from the floating pellets containing drug, filled into a capsule, and compared with the conventional verapamil tablets of similar dose (40 mg). The tmax and AUC (0- infinity) values (3.75 h and 364.65ng/ml /1h respectively) for floating pellets were comparatively higher than those obtained for the conventional verapamil tablets. (tmax value 1.21 h, and AUC value 224.22 mg/ml/1h) . Recent advances in stomach specific floating dosage forms: Sungthongjeen et al have prepared a floating multilayer coated tablets based on gas formation. The system consists of a drugcontaining core tablet coated with a protective layer (hydroxylpropyl methyl cellulose), a gas forming layer (sodium bicarbonate) and a gas-entrapped membrane, respectively. Eudragit RL 30D was chosen as a gas-entrapped membrane due to its high flexibility and high water permeability. The obtained tablets enabled to float due to the CO2 gas formation and the gas entrapment by polymeric membrane. The effect of formulation variables on floating properties and drug release was investigated. The floating tablets using directcompressed cores had shorter the time to float and faster drug release than those using wet granulated cores. The increased amount of a gas forming agent did not affect time to float but increased the drug release from the floating tablets.

Some of the marketed formulations available as GRDDS

SR.NO.	BRAND NAME	DELIVERY SYSTEM	DRUG CATEGORY	COMPANY NAME
1	TOPALKAN	FLOATING LIQUID ALGINATE PREPARATION	AL-Mg ANTACID	PIERRE FABREDRUG,FRANCE
2	CONVIRON	COLLOIDAL GEL FORMING FDDS	FERROUS SULPHATE ANTIANEMIC	RANBAXY,INDIA
3	CIFRAN OD	GAS GENERATING FLOATING FORM	CIPROFLOXACIN ANTIBIOTIC	RANBAXY,INDIA
4	VALRELEASE	FLOATING CAPSULE DIAZEPAM	CNS DEPRESSANT HOFFMANN	LaRoche,USA
5	MADOPAR	FLOATING CR CAPSULE	BENSERAZIDE AND L-DOPA ANTIPARKISONS	ROCHE PRODUCTS,USA

CONCLUSION

Development of an efficient gastroretentive dosage form for stomach specific drug delivery is an actual challenge. Thus, to produce the preferred gastro retention several methods have been used, out of which, the floating drug delivery system has emerged as the best promising method. These systems provide the benefit of better absorption of drugs that are absorbed from upper part of stomach. Local action of drug is increased as the system rests in stomach for longer time. This leads to less frequent dosing and enhanced efficiency of the treatment. Good stability and better drug release as compared to other conventional dosage forms make such system more reliable. Drug absorption in GIT is a highly variable procedure and prolonging GI retention of the dosage form prolongs the time of drug absorption. Floating drug delivery system promises to be a potential approach for gastric retention. Though there are number of complications to be worked out to achieve extended GI retention, many companies are focusing toward commercializing this method.

REFERENCES

1. Rouge N, Buri P, Doelker E.; Drug Absorption Sites in the Gastrointestinal Tract and Dosage Forms for Site Specific Delivery; Int JPharma, 1996; 136: 117-139.
2. Streubel A, Siepmann J, Bodmeier R; Gastroretentive Drug Delivery System; Expert Opin Drug Delivery; 2006; 3(2): 217-233.

3. Singh BN and Kim; Floating Drug Delivery Systems; An Approach to Controlled Drug Delivery via Gastric Retention; J. Control. Release, 2000; 63: 235-239.
4. Ali J, Arora S, Khar RK. ; Floating Drug Delivery System: A Review; AAPS Pharm Sci Tech, 2005; 06(03): E372-E390.
5. Yie W, Chein; Novel Drug Delivery System 2nd ed. Marcel dekker Inc. New York, 1992; 1-3.
6. Sanjay Garg, Shringi Sharma; Gastroretentive Drug Delivery Systems; Pharmatech, 2003; 160-166.
7. Vedha Hari; The Recent Developments on Gastric Floating Drug Delivery Systems: An Overview; Int Journal pharmtech Res., 2010; 2(1): 524-534.

a. Badoni, A. Ojha, G. Gnanarajani, P. Kothiyali; Review on Gastro Retentive Drug Delivery System; The Pharma Innovation, 2012; 1(8): 32-42.

8. Devkant Sharma, Anjali Sharma; Gastroretentive Drug Delivery System - a mini review; Asian pacific Journal of Health Sciences, 2014; 1(2): 80-89.
9. Robinson J, Lee R. Controlled Drug Delivery, 2nd edition, 1987; 418.
10. Bardonnet PL, Faivre V, Pugh WJ, Piffaretti JC, Falson F; Gastroretentive Dosage Forms; Journal of Controlled Release, 2006; 111: 1-18.
11. Arora S, Javed A, Ahuja A, Khar RK, Baboota S; Floating Drug Delivery System : AReview;AAPS Pharm Sci Tech, 2000; 6(3): 372-390.
12. Patel GM, Patel HR, Patel M.; Floating drug delivery system an innovative approaches to prolong gastric retention; Pharmainfo.net, 2007.
13. Amit Kumar Nayak, RumaMaji, Biswarup Das; Gastroretentive Drug Delivery Systems: A Review; Asian Journal of Pharmaceutical and Clinical Research, 2010; 3(1): 2-10.
14. Klusner EA, Eyal S, Lavy E, Friedman M, Hoffman A; Novel Levodopa Gasrtroretentive Dosage form: In Vivo Evaluation in Dogs; J Control Release, 2003; 88: 117- 26.
15. Hoffman A; Pharmacodynamic aspects of sustained release preparation; A Drug Delivery; Rev, 1998; 33: 185-99.
16. Stephen E. Harding; Biopolymer mucoadhesive a genetic engineering reviews; aprit, 1990; 16: 41-86.
17. Singh B and Kim KH; Floating drug delivery system: an approach to oral controlled drug delivery system via Gastric Retention; Journal of Controlled Release, 2000; 63: 235-259.
18. Waterman KC; A Critical Review of Gastric Retentive Controlled Drug Delivery; Pharmaceutical Development and Technology, 2007; 12: 1-10.

19. Arora, S; Ali, J; Ahuja, A; Khar, RK and Baboota, S. Floating Drug Delivery Systems: A Review; AAPS Pharm Sci. Tech, 2005; 47: 372-390.
20. Moes, AJ; Gastroretentive Dosage forms; Crit Rev The Drug Carrier Syst, 1993; 10(2): 193-195.
21. Singh, BN and Kim, KH; Floating Drug Delivery Systems: An Approach to Oral Controlled Drug Delivery via Gastric Retention; Journal of Controlled Release, 2000; 63: 235-259.
22. Klausner, EA; Lavy, E; Friedman, M and Hoffman, A; Expandable Gastroretentive Dosage Forms; J. Control. Rel., 2003; 90: 143-162.
23. Maryam Kouchaka, Fatemeh Atyabib; Ion-exchange, an Approach to Prepare an Oral Floating Drug Delivery System for Diclofenac; Iranian Journal of Pharmaceutical Research, 2004; 2: 93-97.
24. Mayavanshi AV and Gajjar SS; Floating Drug Delivery System to Increase Gastric Retention ofDrugs; RJPT, 2008; 1(4): 345-348.
25. Atyabi, F; Sharma, HL; Mohammad, HAH and Fell, JT; Controlled Drug Release from Coated Floating Ion Exchange Resin Beads; J. Control. Release, 1996; 42: 25- 28.
26. Vishal Bhardwaj, Nirmala, S.L. Harikumar; Floating Drug Delivery System: a review;Pharmacophore, 2013; 4(1): 26-38.
27. Jamil F, Sunil K, Sharma S, Vishvakarma P,Singh L; Review on Stomach Specific DrugDelivery Development and Evaluation;IJRPBS, 2011; 2(4): 1427- 1433.
28. Vishal Bhardwaj, Nirmala, S.L. Harikumar; Floating Drug Delivery System: A Review; Pharmacophore, 2013; 4(1): 26-38.
29. Whitehead L, Fell JT and Collett JH; Development of a Gastroretentive Dosage form; Eur J Pharm Sci., 1996; 4: 182.
30. Jain NK; Progress in Controlled and Novel Drug Delivery Systems; First Ed. CBSS. Gopalakrishnanet al; Journal of Pharmaceutical Science and Technology. Publishers and Distributors, New Delhi Bangalore 2004; 3(2): 84-85.
31. Goyal M, Prajapati R, Purohit KK, Mehta S; Floating Drug Delivery System; Journal of Current Pharmaceutical Research, 2011; 5(1): 7- 18.
32. Talukder R, Fassihi R. Gastroretentive Delivery Systems;Drug Development and Industrial Pharmacy, 2004; 30(10): 1019-1028.
33. Krogel I and Bodmeier R; Floating or PulsatileDrug Delivery System Based on Coated Effervescent Cores; International Journal of Pharmaceutics, 1999; 187: 175- 184.

34. Sunil Kumar, Farazjamil; Gastro Retentive Drug Delivery System: Features and Facts; International Journal of Research in Pharmaceutical and Biomedical Sciences, 2012; 3(1): 125 -136.
35. Moes AJ; Gastroretentive Dosage Forms; Crit. Rev, The Drug Carrier System, 1993; 10: 143- 195.
36. Chien YW; Oral Drug Delivery System; Marcel Dekker, New York, 1992; 139.
37. Shrma S and Pawar A; Low Density Multiparticulate System for Pulsatile Release of Meloxicam; Int J Pharm, 2006; 313: 150-58.
38. Groning R, Heun; Oral Dosage forms with Controlled Gastrointestinal Transit Drug Delivery, 1984; 10(4): 527- 539.
39. Agyilirah GA, Green M, Ducret R; Evaluationof Gastric Retention Properties of Cross linked Polymercoated tablet versus those of non Disintegrating Tablets; Int JPharma, 1991; 75: 241-247.
40. Despande AA, Shah NH, Rhodes CT, MalickW; Development of a Novel Controlled Release System for Gastric Retention; Pharmaceutical Research, 1997; 14(6): 815-819.
41. Nayak AK, Maji R, Das B; Gastroretentive Drug Delivery System a review; Asian Journal of Pharm Clin Res., 2010; 3(1): 2-10.
42. Satinder Kakar, Deepa Batra, Ramandeep Singh, Ujjwal Nautiyal. Magnetic Microspheres as Magical Novel Drug Delivery System: A review; Journal of acute disease, 2013; 1-12.