This review explains the recent advances in gastroretentive drug delivery systems with special focus on floating drug delivery systems. Oral route is the most convenient and painless technique of drug delivery. Gastroretentive drug delivery systems have been developed which overcome physiological conditions in gastrointestinal tract such as short gastric resident time (GRT) and unpredictable gastric emptying times (GET). Various approaches used for prolonging GRT are mucoadhesive systems (Bioadhesive Systems), High Density Systems, Expandable Systems (Swelling Systems), Floating Drug Delivery systems (FDDS). In this review, authors discuss the current and recent research on gastroretentive drug delivery systems, including patented delivery systems and marketed products.

KEYWORDS: Gastroretentive drug delivery systems, floating drug delivery systems, recent advances, gastric resident time.

INTRODUCTION
Due to ease of administration, patient compliance and flexibility in formulation etc, oral delivery of drugs is the most preferable route of drug delivery. From immediate release to site-specific delivery, oral dosage forms have really progressed. One of the most feasible approaches for achieving a prolonged and predictable drug delivery profile in the GIT tract is to control the gastric resident time (GRT) for example, drugs that are absorbed in the proximal part of the gastrointestinal tract and drugs that are less soluble in or are degraded by the alkaline pH may benefit from prolonged gastric retention. In addition, for local and sustained drug delivery to the stomach and proximal small intestine to treat certain condition, prolonged gastric retention of the therapeutic moiety may offer numerous advantages including improved bioavailability and therapeutic efficacy, possible reduction of the dose size and reductions in plasma level fluctuations.

Gastroretentive drug delivery systems
After oral administration, such a dosage form would be retained in the stomach and release the drug there in a controlled and prolonged manner, so that the drug could be supplied continuously to its absorption sites in the upper gastrointestinal tract. Gastroretentive dosage forms can remain in the gastric region for several hours and hence significantly prolong the gastric resident time of drugs. Gastric Residence Time: It is a time period during which the drug floats on the gastric fluid.

Anatomical and physiological considerations of Gastrointestinal tract
The GI tract is essentially a tube about nine meters long that runs through the middle of the body from the mouth to the anus and includes throat (pharynx), oesophagus, stomach, small intestine (consisting of the duodenum, jejunum and ileum) and large intestine (consisting of the caecum, appendix, colon and rectum). The wall of the GI tract has the same general structure throughout most of its length from the oesophagus to anus, with some local variations for each region.

The stomach is an organ with a capacity of storage and mixing. The stomach is situated in the left upper part of abdominal cavity immediately under the diaphragm. Its size varies according to the amount of distention: upto 1500 ml following a meal; after food has emptied, a ‘collapsed’ state is obtained with a resting volume of only 25-50 ml. Anatomically the stomach is divided into 3 regions: Fundus, Body, Antrum (pylorus). The proximal part made of fundus and body acts as a reservoir for undigested material, while as the antrum is
the main site for mixing motions and act as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the interdigestive myoelectric cycle or migrating myoelectric cycle (MMC), which is further divided into following 4 phases.

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

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

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

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

After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state. This is also known as digestive motility pattern and comprises continuous contractions as in phase II of fasted state. These contractions result in reducing the size of food particles (to less than 1 mm), which are propelled toward the pylorus in a suspension form. During the fed state onset of MMC is delayed resulting in slowdown of gastric emptying rate.

**Suitable drug applicants for gastroretention**

In general, appropriate applicants for GRDDS are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of GIT having narrow absorption window in GIT, primarily absorbed from stomach and upper part of GIT, drugs that act locally in stomach, poorly soluble at an alkaline pH and drugs degrade in colon.

**Advantages of Gastroretentive drug delivery systems**

Several advantages of gastroretentive drug delivery systems are enhanced bioavailability, sustained drug delivery/reduced frequency of dosing, targeted therapy for local ailments in the upper GIT, reduced fluctuations of drug concentration, improved selectivity in receptor activation, reduced counter-activity of the body, extended time over critical (effective) concentration, minimized adverse activity at the colon, site specific drug delivery.

**Different approaches to prolong the gastric residence time**

Various approaches have been developed to increase GRT of a dosage form.

A. **Mucoadhesive / Bioadhesive Systems**

B. **High Density Systems**

C. **Expandable / Swelling System**

I) **Swelling GRDDS**

II) **Unfolding GRDDS**

D. **Floating Drug Delivery Systems**

**Mucoadhesive / bioadhesive systems**

The mucoadhesive systems are intended to extend the GRT by adhering them to the gastric mucous membrane. Bioadhesion on soft tissues of certain natural or synthetic polymers has been exploited to control as well as to prolong the gastric retention of delivery system.

The adhesion of polymers may be mediated by hydration, bonding, receptor mediated. Polymers used for bioadhesion are: Polycarbophil, Carbophil, Lectins, Chitosan, Gliadan.

**High density systems**

High-density systems are intended to lodge in the rugae or folds of the stomach withstanding the peristaltic movements. System with a density of 1.3g/ml or higher are expected to be retained in the lower part of the stomach.

With pellets, the GI transit time can be extended from an average of 5.8-25 hour, depending more on density than on diameter of the pellets, although many conflicting reports stating otherwise also abound in literature.

Density increasing agents or Excipients: Barium Sulphate, Iron Powder, Zinc Oxide, Titanium Dioxide. These materials increase density by upto 1.5-2.4g/cm³.

**Expandable/swelling systems**

These are easily swallowed and reach a significant larger size in the stomach due to swelling or unfolding processes that prolong their gastrointestinal tract. After drug release, their dimensions are minimized with subsequent evacuation from the stomach. Gastroretentivity is enhanced by the combination of substantial dimensions with high rigidity of the dosage form to withstand the peristalsis and mechanical contractility of the stomach. These systems are sometimes referred to as plugtype systems because they tend to remain lodged at the pyloric sphincter.

I) **Swelling GRDFs**

The significant swelling is generally due to the presence of specific hydrogel formers, which drastically increases in size following contact with aqueous media. A GRDDS comprised of an envelope from an elastic or nonelastic and nonhydratable polymeric membrane, which is drug and body fluid permeable. The envelope contains a drug...
reservoir and an expanding agent i.e. a swellable resin or hydrocolloid which causes expansion by osmotic pressure are designed by Mamajek and Moyer.20 Such devices size larger than 1.531 cm were retained in the stomach for prolonged periods of time, typically more than 12 h.

II) Unfolding GRDDS
Several geometric shapes, such as tetrahedron, ring, clover leaf, disk, string and pellet/sphere, which can be packed tightly into a gelatin capsule and unfold after dissolution of capsules shell, have been patented by Caldwell et al. These systems consist of at least one erodible polymer(e.g. polyurethanes, polyamides) and a drug that is disperse within the polymer matrix. Sonobe et al.21 developed unfolding dosage form which have the dimentions, shape and durability necessary for prolonged gastroretentivity.

Floating drug delivery systems
Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting 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 gastric resident time and a better control of the fluctuations in plasma drug concentration.

Requirements for floating drug delivery system are: It should release contents slowly to serve as a reservoir, it must maintain specific gravity lower than gastric contents (1.004 – 1.01 gm/cm³) and it must form a cohesive gel barrier.

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM
A. Effervescent Systems
I) Gas Generating Systems
II) Volatile Liquid Containing System

B. Non Effervescent Systems
I) Colloidal Gel Barrier Systems
II) Microporous Compartment System
III) Floating Microspheres / Microballoons
IV) Alginate Floating Beads

Effervescent System
Buoyancy can also be achieved by generation of gas bubbles. Carbondioxide (CO₂) can be 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 acid and matrices containing chambers of liquid that gasify at body temperature. Excipients used are:

a) Swellable polymers: Methocel, Polysachharides (Chitosan)
b) Gas Generating Agents: Sodium Bicarbonate, Citric or Tartaric Acid

I) Gas-generating systems
These are low density FDDS is based on the formation of carbon dioxide with in the device following contact with body fluids. The matrices are fabricated so that upon arrival in the stomach, carbon dioxide is liberated by the acidity of the gastric contents and is entrapped in the gellified hydrocolloid. This produces an upward motion of the dosage form and maintains its buoyancy. A decrease in specific gravity causes the dosage form to float on the chyme. The carbon dioxide generating components may be intimately mixed within the tablet matrix, in which case a single layered tablet is produced or a bilayered tablet may be compressed which contains the gas generating mechanism in one hydrocolloid containing layer and the drug in the other layer formulated for a sustained release effect.

II) Volatile liquid containing systems (osmotically controlled DDS)
As an osmotically controlled floating system, the device comprised of a hollow deformable unit that was convertible from a collapsed to an expanded position and returnable to a collapsed position after an extended period of time. A housing was attached to the deformable unit and it was internally divided into a first and second chamber with the chambers separated by an impermeable, pressure responsive movable bladder. The first chamber contained an active drug, while the second contained a volatile liquid, such as cyclopentane or ether that vaporises at physiological temperature to produce a gas, enabling the drug reservoir to float. To enable the unit to exit from the stomach, the device contained a bioerodible plug that allowed the vapour to escape.

Non-Effervescent FDDS
This type of system, after swallowing, swells unrestrained via imbibition of gastric fluid to an extent that it prevents their exit from the stomach. One of the formulation methods of such dosage forms involves the mixing of the drug with a gel-forming hydrocolloid, which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of less than one within the outer gelatinous barrier. The air trapped by the swollen polymer confers buoyancy to these dosage forms. Excipients used are: Hydroxypropyl methyl cellulose (HPMC), Polyacrylate polymers, Polyvinyl acetate, Carbopol, Sodium alginate, Calcium chloride, Polyethylene oxide, Polycarbonates.
I) Colloidal Gel Barrier Systems (Hydrodynamically Balanced Systems)

Sheth and Tossounian first designated this ‘Hydrodynamically Balanced System’ (HBS)\(^1\). Such a system contains drug with gel-forming hydrocolloids meant to remain buoyant on the stomach content. This prolongs GRT and maximizes the amount of drug that reaches its absorption sites in the solution form for ready absorption. This system incorporates a high level of one or more gel-forming highly soluble cellulose type hydrocolloid e.g. Hydroxypropyl cellulose, Hydroxyethyl cellulose, Hydroxypropyl methyl cellulose (HPMC), Polysaccharides and matrix-forming polymer such as Polycarbophil, Polyacrylate and Polystyrene. On coming in contact with gastric fluid, the hydrocolloid in the system hydrates and forms a colloid gel barrier around its surface\(^3\).

II) Microporous Compartment System

This technology is based on the encapsulation of a drug reservoir inside a microporous compartment with pores along its top and bottom walls\(^2\). The peripheral walls of the drug reservoir compartment are completely sealed to prevent any direct contact of gastric surface with the undissolved drug. In the stomach, the floatation chamber containing entrapped air causes the delivery system to float over the gastric content. Gastric fluid enters through the aperture, dissolves the gastric fluid to an extent that it prevents their exit from the drug and carries the dissolved drug for continuous transport across the intestine for absorption.

III) Hollow Microspheres / Microballoons

Hollow microspheres loaded with drug in their outer polymer shelf were prepared by a novel emulsion solvent diffusion method\(^3\). The ethanol/dichloromethane solution of the drug and an enteric acrylic polymer was poured into an agitated solution of Poly Vinyl Alcohol (PVA) that was thermally controlled at 40°C. The gas phase is generated in the dispersed polymer droplet by the evaporation of dichloromethane formed and internal cavity in the microsphere of the polymer with drug. The microballoon floated continuously over the surface of an acidic dissolution media containing surfactant for more than 12 h.

IV) Alginate Beads / Floating Beads

Multi-unit floating dosage forms have been developed from freeze-dried calcium alginate\(^4\). Spherical beads of approximately 2.5 mm in diameter can be prepared by dropping sodium alginate solution into aqueous solution of calcium chloride, causing the precipitation of calcium alginate. The beads are then separated, snap-frozen in liquid nitrogen and freeze-dried at 40°C for 24 h, leading to the formation of a porous system, which can maintain a floating force for over 12 h. These floating beads gave a prolonged residence time of more than 5.5 h.

Various techniques used for the preparation of Gastroretentive tablets

Wet Granulation: In this method the powdered medicament along with other excipients such as polymers, binding agent, diluent and a part of disintegrating agent are moistened with a sufficient quantity of granulating agent in order to make a coherent mass. The coherent mass is then passed through sieve no 10. The wet granules are dried at 60°C in hot air oven. The dried granules are passed through sieve no 20 to collect the granules of uniform size. The granules are ready to be compressed\(^35,36\).

Direct Compression: It is the easiest way to manufacture tablets. Conventional equipment, directly compressible excipients and a number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed than that of other production methods.

Hot-melt Extruded Method: A powder mixture (200g) of given drug (CPM), Eudragit RS PO or Eudragit E PO as retardants, GMS as a thermal lubricant, sodium bicarbonate was first blended. The blended powder was then placed in the hopper of a single-screw Randcastle Extruder and extruded. The extrusion temperatures for zone 1, zone 2, zone 3 and zone 4 (die) were 90, 95, 100 and 100 respectively. The screw rotation speed was 10 rpm and the die diameter was 6 mm. After melt processing, manually cut into tablets.

Marketed preparations and patents of Gastroretentive drug delivery systems

Marketed preparations of Gastroretentive Drug Delivery Systems are listed in Table 1 and patents for some Gastroretentive Drug Delivery Systems are listed in Table 2.

Evaluation of floating drug delivery systems

Evaluation of tablets

I) Buoyancy Lag Time and Duration of Buoyancy II) In vitro dissolution behaviour III) Determination of Density IV) Swelling Index V) Hardness and Friability VI) Weight Variation

Evaluation for microspheres and beads

Particle size analysis, surface characterization (SEM) In-vivo evaluation (Gamma Scintigraphy)

Evaluation of Tablets

I) Buoyancy Lag Time and Duration of Buoyancy

The buoyancy lag time and the duration of buoyancy were determined in the USP dissolution apparatus II in an acid environment. The time interval between the
introduction of the tablet into the dissolution medium and its buoyancy to the top of the dissolution medium was taken as buoyancy lag time or floating lag time (FLT) and the duration of buoyancy was observed visually\textsuperscript{37}.

II) In Vitro dissolution behaviour

The release of the medicament was studied by USP-II type dissolution apparatus (Paddle type). Dissolution study was performed at predetermined speed and temperature of about 37\pm 0.5\degree C in an appropriate dissolution medium. 5ml of sample was withdrawn at a predetermined interval and the volume of dissolution medium was maintained by adding same volume of dissolution medium. The absorption of withdrawn sample was measured spectrophotometrically with suitable dilution and the corresponding concentration was determined from the calibration curve.

III) Determination of Density

The tablet density of the floating system was determined by displacement method, using benzene as a displacing medium. A plethysmometer was employed to measure tablet density. Firstly, the instrument was calibrated using benzene (density 0.8723g/cc) for its volumetric capacity. Benzene was filled till a mark in capillary of the instrument. Subsequently, five tablets of known weight were dropped in wider mouth of plethysmometer. The system was kept undisturbed for 1 min, to let benzene displace the air in the pores of the tablets. After that, displacement in the volume of the benzene in the side capillary was noted. Knowing the weight and volume occupied by the tablets, density of five tablets was determined\textsuperscript{38}.

IV) Swelling Index

Tablets were weighed individually (W\textsubscript{0}) and placed in dissolution medium. The temperature was maintained at 37 \degree C. At regular intervals, the samples were removed using a basket and swollen weight (W\textsubscript{t}) of each tablet was determined at predefined time intervals\textsuperscript{39}. The swelling index was calculated by the following equation:

Percentage Swelling Index = \left( \frac{W_t - W_0}{W_0} \right) \times 100

Where W\textsubscript{0} is the initial weight of tablet and W\textsubscript{t} is the weight of tablet at time t.

V) Hardness and Friability

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet, the resistance of the tablet to chipping, abrasion or breakage under condition of storage, transformation and handling before usage depends on its hardness. Hardness of tablet was measured by using Monsanto Hardness Tester.

Friability of the tablets was determined using Roche friabilator. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inch in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were de dusted using a soft muslin cloth and reweighed\textsuperscript{40}.

The friability (F\%) is given by the formula:

F\% = \left( 1 - \frac{W_0}{W} \right) \times 100

Where, W\textsubscript{0} is the tablets before the test and W is the weight of the tablets after test.

VI) Weight Variation

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\textsuperscript{40}.

Evaluation for microspheres and beads

Particle size analysis, surface characterization (SEM): The particle size and the size distribution of beads or microspheres are determined in the dry state using optical microscopy method. The surface characterization is done by Scanning Electron Microscope (SEM)\textsuperscript{41}.

In-vivo evaluation (Gamma Scintigraphy)

This method helps to locate dosage form in the gastrointestinal tract by which we can predict and correlate the gastric emptying time and the passage of dosage form in the GIT. The inclusion of radio-opaque material into a solid dosage form enables it to be visualized by \textit{x}-rays. Similarly, the inclusion of a \textit{\gamma}-emitting radionucleotide in a formulation allows indirect external observation using a \textit{\gamma}-camera or scintiscanner. In case of \textit{\gamma}-scintigraphy, the \textit{\gamma}-rays emitted by the nucleotide are focused on a camera, which helps to monitor the location of the dosage form in the gastrointestinal tract\textsuperscript{41}.

Recent trends in Gastroretentive systems

Recent trends in gastroretentive systems are listed in Table 3

CONCLUSION

The real challenge in the development of gastroretentive drug delivery systems is to overcome normal physiology of stomach either by continuous propulsive forces in fed state or by housekeeper waves occurring every 1-2 hr in fasted state. The aim is to improve the bioavailability of the drugs with narrow absorption window in gastrointestinal tract region. By prolonging the drug resident time in gastrointestinal region improves the solubility of drug that is less soluble in high pH, reduces drug waste, reductions in plasma level fluctuations.
REFERENCES
Table 1: Marketed Preparations of Gastroretentive Drug Delivery Systems

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Product</th>
<th>Active Ingredient (mg)</th>
<th>Remarks</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Glumetza GRTM</td>
<td>Metformin HCL</td>
<td>Metformin HCl extended release Tablet</td>
<td>Biovail in north America; LG Life Sciences in Korea</td>
</tr>
<tr>
<td>2</td>
<td>Cytotec</td>
<td>Misoprostol (100mcg/200mcg)</td>
<td>Bilayer floating Capsule</td>
<td>Chawla et al, 2004</td>
</tr>
<tr>
<td>3</td>
<td>Conviron</td>
<td>Ferrous sulphate</td>
<td>Colloidal gel forming FDDS</td>
<td>Chawla et al, 2004</td>
</tr>
<tr>
<td>4</td>
<td>Cifran OD</td>
<td>Ciprofloxacin (1g)</td>
<td>Gas generating floating form</td>
<td>Chawla et al, 2004</td>
</tr>
<tr>
<td>5</td>
<td>Topalkan</td>
<td>Aluminium magnesium antacid</td>
<td>Floating liquid Alginate Preparation</td>
<td>Degtiareva et al, 1994</td>
</tr>
<tr>
<td>6</td>
<td>Almagate floatcoat</td>
<td>Antacid</td>
<td>Floating dosage Form</td>
<td>Fabregas et al, 1994</td>
</tr>
<tr>
<td>7</td>
<td>Madopar</td>
<td>Levodopa (100mg) and benserazide (25mg)</td>
<td>Floating, CR Capsule</td>
<td>Erni and Held, 1987</td>
</tr>
<tr>
<td>8</td>
<td>Liquid gavison</td>
<td>Alginic acid and sodium bicarbonate</td>
<td>Effervescent floating liquid alginate preparation</td>
<td>Washington et al, 1986</td>
</tr>
<tr>
<td>9</td>
<td>Valrelease</td>
<td>Diazepam (15mg)</td>
<td>Floating capsule</td>
<td>Sheth and Tossounian, 1984</td>
</tr>
</tbody>
</table>

Table 2: Patents for some Gastroretentive Drug Delivery Systems

<table>
<thead>
<tr>
<th>US Patent No.</th>
<th>Year</th>
<th>Patent Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>6,207,197</td>
<td>2001</td>
<td>Gastroretentive controlled release microspheres for improved drug delivery</td>
</tr>
<tr>
<td>6,290,989</td>
<td>2001</td>
<td>Expandable gastroretentive therapeutic system with controlled active substance release in the gastrointestinal tract</td>
</tr>
<tr>
<td>2006013876</td>
<td>2006</td>
<td>Novel floating dosage form</td>
</tr>
<tr>
<td>20070281007</td>
<td>2007</td>
<td>Mucosalheive oral dosage forms of High Permeability, High Solubility drugs</td>
</tr>
<tr>
<td>20070269512</td>
<td>2007</td>
<td>Gastroretentive sustained release formulation</td>
</tr>
<tr>
<td>20080220060</td>
<td>2008</td>
<td>Gastroretentive formulations and manufacturing Process</td>
</tr>
<tr>
<td>20090324694</td>
<td>2009</td>
<td>GRDDS comprising an extruded hydratable Polymer</td>
</tr>
<tr>
<td>20100233253</td>
<td>2010</td>
<td>Extended release GRDDS for Valsartan</td>
</tr>
<tr>
<td>20100286660</td>
<td>2010</td>
<td>Gastroretentive duodenal pill</td>
</tr>
<tr>
<td>20100015224</td>
<td>2010</td>
<td>Programmable buoyant delivery technology</td>
</tr>
</tbody>
</table>
**Table 3: RECENT TRENDS IN GASTRORETENTIVE SYSTEMS**

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Drug</th>
<th>Requirement for Development</th>
<th>Dosage form</th>
<th>References</th>
</tr>
</thead>
</table>
| 1     | Losartan | a) Short half life  
b) Low bioavailability (33%) due to first pass metabolism | Tablet | Chen et al, 2010 |
| 2     | Pantoprazole | a) Short half life  
b) Low bioavailability  
c) Acidic in nature | Beads | Singh et al, 2010 |
| 3     | Rantidine Hcl | a) Short half life  
b) Absorption window in a part of GIT  
c) Poor bioavailability | Floating-pulsatile delivery system | Shahiwala et al, 2009 |
| 4     | Famotidine | a) Low solubility  
b) Short half life (about 3 hr)  
c) Low bioavailability (45-50%) | Osmotic pump Tablet | Pan et al, 2010 |
| 5     | Ciprofloxacin Hcl | a) Short elimination half life (about 4hr)  
b) Narrow absorption window and absorbed in proximal S.I  
c) Freely soluble in water | Floating matrix tablet | Tadros et al, 2010 |
| 6     | Acyclovir | a) Short half life (2-5hr)  
b) Oral bioavailability is poor (15-30%) due to poor water solubility | Microspheres | Pan et al, 2009 |
| 7     | Verapamil Hcl | a) Low bioavailability (15-30%)  
b) Short elimination half life (4-6 hr)  
c) Degrade at high pH | Tablet | Patel et al, 2009 |
| 8     | Ziduvudine | a) Dose dependant solubility  
b) Short biological half life  
c) Poor bioavailability | Tablet | Patil et al, 2010 |
| 9     | Cephalexin | a) Acidic drug so remain unionized in stomach for better absorption  
b) Short half life (1 hr) | Tablet | Shinde et al, 2010 |