1. Introduction

Oral delivery of drugs is the most preferable route among all the drug delivery due to the ease of administration, patient compliance and flexibility in formulation. From immediate release to site specific delivery, oral dosage forms have really progressed. The goal of any drug delivery system is to provide a therapeutic amount of the drug to the proper site in the body to achieve promptly, and then maintain, the desired drug concentration (Garg et. al., 2008).

Technological attempts have been made in the pharmaceutical research and development of rate-controlled oral drug delivery systems to overcome physiological adversities, such as short gastric residence times (GRT) and unpredictable gastric emptying times (GET). Dosage forms that can be retained in the stomach are called Gastro retentive drug delivery systems (GRDDS). GRDDS can improve the controlled delivery of drugs that have an absorption window by continuously releasing the drug for a prolonged period of time before it reaches its absorption site, thus ensuring its optimal Bioavailability (Chien, 1992).

Invariably, conventional dosage forms do not maintain the drug blood levels within the therapeutic range for an extended period of time. To achieve the same, a drug may be administered repeatedly using a fixed dosing interval. This causes several potential problems like saw tooth kinetics characterized by large peaks and troughs in the drug concentration-time curve (Fig.1).

![Fig. 1: Plasma level profiles following conventional and controlled release dosing.](image-url)
Conventional oral dosage forms provide a specific drug concentration in systemic circulation without offering any control over drug delivery. Controlled-release drug delivery systems (CRDDS) provide drug release at a predetermined, predictable, and controlled rate. An important requisite for the successful performance of oral CRDDS is that the drug should have good absorption throughout the gastrointestinal tract (GIT), preferably by passive diffusion, to ensure continuous absorption of the released drug. The average time required for a dosage unit to traverse the GIT is 3-4 hrs, although slight variations exist among various dosage forms (Arora, et. al., 2005).

Orally administered drugs are absorbed by passive diffusion processes and by nonpassive means. Drugs absorbed by active and facilitated transport mechanisms show higher regional specificity because of the prevalence of these mechanisms in only certain regions of the GIT (fig.2). Many drugs show poor BA because of the presence of enzymes and efflux pumps. Intestinal metabolic enzymes primarily, Phase I metabolizers such as cytochrome P450 (CYP3A) are abundantly present in the intestinal epithelium. Their activity decreases longitudinally along the small intestine, with levels rising slightly from the duodenum to the jejunum and declining in the ileum and colon.

In addition, carriers like secretary transporter is P-glycoprotein (P-gp) may affect drug absorption. An example of such a, which is present in the villus tip of enterocytes and has the capacity to interact with a vast variety of drugs. P-gp sends the absorbed drug from the cytoplasm of the enterocytes back to the intestinal lumen, thus reducing the drug’s bioavailability.

**Fig. 2:** Depicts the mechanism involved in the interaction between drug efflux and metabolism.
The enzyme metabolizes the drug molecule absorbed into the enterocytes. Then that portion of the drug is transported from the enterocytes back into the intestinal lumen by the action of P-gp, following which it is reabsorbed and again subjected to metabolism and efflux. Therefore, the drug is continually cycled between the enterocytes and the gut lumen, which allows the enzyme to have repeated access to the drug molecule, thus reducing absorption.

**Fig. 3:** Drug absorption in the case of (a) Conventional dosage forms and (b) Gastroretentive drug delivery systems.

A major constraint in oral controlled drug delivery is that not all drug candidates are absorbed uniformly throughout the GIT. Some drugs are absorbed in a particular portion of the GIT only or are absorbed to a different extent in various segments of the GIT. Such drugs are said to have an absorption window, which identifies the drug’s primary region of absorption in the GIT (Singh et al., 2000). An absorption window exists because of physiological, physicochemical, or biochemical factors. The pH-dependent solubility and stability level of a drug plays an important role in its absorption. A drug must be in a solubilized and stable form to successfully cross the biological membrane, and it will experience a pH range from 1 to 8 as it travels through the GIT.

Because most drugs are absorbed by passive diffusion of the un-ionized form, the extent of ionization at various pH levels can lead to non uniform absorption or an absorption window. After crossing the absorption window, the released drug goes to waste with negligible or no absorption (Fig. 3a and 3b). This phenomenon drastically
decreases the time available for drug absorption after its release and jeopardizes the success of the delivery system.

**Gastric Retention Platform**

![Gastroretentive drug delivery systems.](image)

**Fig. 4:** Gastroretentive drug delivery systems.

There are a large number of drugs that are not absorbed to the same extent once they pass the upper small intestine and thus, once-daily formulations are exclusive for these drugs (Fig.4). One method to overcome the fast GI transit is to maintain the dosage form in the stomach for extended periods of time, and therefore, research efforts have been focused on development of gastric retention platforms. Several drugs are absorbed to the most extent in the upper part of the small intestine (Rouge et al., 1996).

One of the major scientific challenges in the development of gastric retention devices is overcoming the housekeeping waves that consist of strong gastric contractions that occur every few hours, particularly in the fasted state.

**Physiology of Stomach**
The stomach is divided into three anatomical regions: fundus, body, and pylorus. The proximal stomach consisted of fundus and body which serve as a reservoir for ingested materials, whereas the distal region (pylorus) is the major site of mixing motions, acting as a pump to propel gastric contents for gastric emptying occurs both in fasting as well as fed stages. Anatomical and physiological features of the gastrointestinal tract are shown in Table 1.

**Histology of the Stomach**

The stomach wall is composed of four basic layers. The surface of mucosa is a layer of simple columnar epithelium cells called mucous surface cells. Epithelia cells also extend down into the lamina propria, forming many narrow channels called gastric pits and columns of secretory cells called gastric glands. Secretions from the gastric glands flow into the gastric pits and then into the lumen of the stomach. The glands contain three types of exocrine gland cells that secrete their products into the stomach lumen: mucous neck cells, chief cells, and parietal cells.

**Gastric Emptying**

The GIT is always in a state of continuous motility. There are two modes of motility pattern: the digestive mode and interdigestive (or fasted) mode involved in the digestion of food. In the fasted state, it is characterized by an interdigestive series of electrical events which cycle both through the stomach and small intestine every 2-3 hrs.

![Stomach Diagram](image)

**Fig. 5:** Physiology of stomach.
### Table 1: Anatomical and physiological features of the GIT

<table>
<thead>
<tr>
<th>Section</th>
<th>Average length (cm)</th>
<th>pH</th>
<th>Major constituents</th>
<th>Transit time of food (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity</td>
<td>15 – 20</td>
<td>5.2 – 6.8</td>
<td>Amylase, maltase, ptyalin, mucin</td>
<td>Short</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>25</td>
<td>5 – 6</td>
<td>-</td>
<td>Very Short</td>
</tr>
<tr>
<td>Stomach</td>
<td>20</td>
<td>1.2 -3.5</td>
<td>HCL, pepsin, rennin, lipase, inosine, sodium, citrate</td>
<td>0.25-3.0</td>
</tr>
<tr>
<td>Duodenum</td>
<td>25</td>
<td>4.6 – 6.0</td>
<td>Bile, trypsin, chymotrypsin, amylase, maltase, sucrase,CYP3A4</td>
<td>1 – 2</td>
</tr>
<tr>
<td>Jejunum</td>
<td>300</td>
<td>6.3 – 7.3</td>
<td>Amylase, maltase, lactase, sucrase, CYP3A5</td>
<td>-</td>
</tr>
<tr>
<td>Ileum</td>
<td>300</td>
<td>7.6</td>
<td>Lipase, nucleasenucleotidase, enterokinase.</td>
<td>1 – 10</td>
</tr>
<tr>
<td>Cecum</td>
<td>10 – 30</td>
<td>7.5 – 8.0</td>
<td>-</td>
<td>Short</td>
</tr>
<tr>
<td>Colon</td>
<td>150</td>
<td>7.9 – 8.0</td>
<td>-</td>
<td>4 - 20</td>
</tr>
<tr>
<td>Rectum</td>
<td>15 - 19</td>
<td>7.5 – 8.0</td>
<td>-</td>
<td>Variable</td>
</tr>
</tbody>
</table>

**Gastrointestinal Motility Patterns Affecting Dosage Form Retention**

The complex anatomy and physiology of the GIT, including variations in acidity, bile salts, enzyme content, and the mucosal absorptive surface, significantly influence the release, dissolution, and absorption of orally administered dosage. Two distinct patterns of gastrointestinal (GI) motility and secretion exist, corresponding to the fasted and fed states. The fasted state is associated with various cyclic events, commonly referred to as the Migrating Myoelectric Complex (MMC), which regulates GI motility patterns. The MMC is organized into alternating cycles of activity and quiescence and can be subdivided into basal (Phase I), preburst (Phase II), and burst (Phase III) intervals (Fig.6).

**Phase I** the quiescent period, lasts from 30 to 60 min and is characterized by a lack of secretary, electrical, and contractile activity.
Phase II exhibits intermittent action for 20–40 min, during which contractile motions increase in frequency and size. Bile enters the duodenum during this phase, whereas gastric mucus discharge occurs during the latter part of Phase II and throughout Phase III.

Phase III is characterized by intense, large, and regular contractions, termed *housekeeper waves* that sweep off undigested food and last 10–20 min.

Phase IV is the transition period of 0–5 min between Phases III and I.

![Motility patterns of the GIT in the fasted state.](image)

This series of electrical events originates in the foregut and continues to the terminal ileum in the fasted state, repeating every 2–3 h. Feeding sets off a continuous pattern of spike potentials and contractions called *postprandial motility*. When CRDDS are administered in the fasted state, the MMC may be in any of its phases, which can significantly influence the total gastric residence time (GRT) and transit time in the GIT. This assumes significance for drugs that have an absorption window, as it will affect the amount of time the dosage form spends in the region preceding and around the window. The less time spent, the lower the degree of absorption. Therefore, the design of GRDDS depends on the resistance of the dosage form to gastric emptying during Phase III of the MMC in the fasted state and also to continuous gastric emptying through the pyloric sphincter in the fed state.

**Approaches to increased gastric retention**

Several techniques, including swelling, floating and mucoadhesion, have been explored to increase the gastro retention of dosage forms (Fig. 7). (Chawla et al., 2003, A .A .Deshpande et al., 1996, Chen, 2000)
Fig. 7: Classification of gastro retentive drug delivery systems.

Swelling systems
After being swallowed, these dosage forms swell to a size that prevents their passage through the pylorus. As a result, the dosage form is retained in the stomach for a long period of time. These systems are sometimes referred to as plug type systems because they tend to remain lodged at the pyloric sphincter. These polymeric matrices remain in the gastric cavity for several hours even in the fed state. Upon coming in contact with gastric fluid, the polymer imbibes water and swells (Fig.8). The extensive swelling of these polymers is a result of the presence of physical–chemical cross-links in the hydrophilic polymer network. (Chawla et al., 2003)

Fig. 8: Relationship between the degree of cross-linking of the polymeric chains and the swelling behavior of swelling systems.
On the other hand, a low degree of cross-linking results in extensive swelling followed by the rapid dissolution of the polymer. An optimum amount of cross-linking is required to maintain a balance between swelling and dissolution.

**Expandable systems** (Klausner, 2003)

A dosage form in the stomach will withstand gastric transit if it is bigger than the 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, three configurations are required: a small configuration for oral intake, an expanded gastroretentive form and a final Small form enabling evacuation following drug release.

Unfoldable and swellable systems have been investigated. Unfoldable systems are made of biodegradable polymers. The concept is to make a carrier, such as a capsule, incorporating a compressed system which extends in the stomach.

**Caldwell et al.** proposed different geometric forms tetrahedron, ring or planar membrane lobed, disc or 4-limbed cross form of bioerodible polymer compressed within a capsule.

**High-density systems**

Sedimentation has been employed as a retention mechanism for pellets that are small enough to be retained in the rugae or folds of the stomach body near the pyloric region, which is the part of the organ with the lowest position in an upright posture. Dense pellets (approximately 3 gm/cm$^3$) trapped in rugae also tend to withstand the peristaltic movements of the stomach wall. With pellets, the GI transit time can be extended from an average of 5.8–25 hours, depending more on density than on diameter of the pellets, although many conflicting reports stating otherwise also abound in literature. Commonly used excipients are barium sulphate, zinc oxide, titanium dioxide and iron powder, etc.

**Floating systems**

Floating systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach for a prolonged period without affecting the gastric emptying rate. While the system floats over the gastric contents in the fundus where it does not experience much friction, the drug is released slowly only by diffusion at the desired rate, which results in increased GRT and reduces fluctuation 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 fig. 9 A.

**Fig. 9 A:** Hydrodynamically balanced system.

The gelatinous polymer barrier formation results from hydrophilic polymer swelling. Drug is released by diffusion and erosion of the gel barrier.

Floating systems can be classified as Effervescent and Non Effervescent Systems.

(a) Effervescent Systems

The floating system is intended to float in and over the gastric contents resulting in prolonged GRT. Floatability can be achieved by generation of gas bubbles. CO₂ can be generated in situ by incorporation of carbonates or bicarbonates, which react with acid either the natural gastric acid entrapped of liquid, which forms a gas at body temperature. The approach has been used for single and multiple unit systems.

Also, volatile organic solvents have been introduced into the floating chamber to generate gas at physiological temperature. The trapped nascent gas inside the system keeps it floated. Since one of the main limitations of a Hydro dynamically Balanced System (HBS) appeared to be lack of a good floating mechanism, systems with an improved buoyant property have been designed. The buoyant delivery systems utilize effervescent reaction between carbonate/bicarbonate salts and citric/tartaric acid to liberate CO₂, which gets entrapped in the jellified hydrocolloid layer of the system,
thus decreasing its specific gravity and making it float over chime. These tablets may be either single layered wherein the CO\textsubscript{2}, generating components are intimately mixed within the tablet matrix, or they may be bilayered in which the gas generating components are compressed in one hydrocolloid containing layer, and the drug in other layer formulated for a SR effect (Fig. 9 B).

![Diagram of gas-generating systems](image)

**Fig. 9 B**: Gas-generating systems a) Monolayer drug delivery system.

b) Bilayer gas generating systems without semi permeable membrane.

c) Bilayer gas generating systems with semi permeable membrane.

**Improvements to be made**

The main problem here is that the persistence of the buoyant property has not been carefully examined in most of the devices. For this reason, it was suggested that the initial bulk density of the dosage unit and changes of the floating and non-floating units. Human studies using scintigraphy showed that floating capsules or floating tablets, generally have short (<2h) gastric retention times under fasted conditions but may have prolonged (≥4h) gastric retention times under fed conditions. Thus, it appears that, as with other devices, the presence of food prolongs the gastric retention time of the floating devices.

**(b) Non-effervescent Systems**

Hydro dynamically Balanced System (HBS) was first designed by Sheth and Tossounian in 1984. Such systems contain drugs with gel-forming hydrocolloids meant to remain buoyant on the stomach contents. These systems incorporate a high level (20-75% w/w) of one or more gel-forming, highly swellable, cellulose-type hydrocolloids [e.g. Hydroxyethyl cellulose (HEC), Hydroxypropyl cellulose (HPC),
Hydroxypropyl methyl cellulose (HPMC), sodium Carboxymethylcellulose (NaCMC), polysaccharides and matrix forming polymers such as Polycarbophil, Polyacrylates and polystyrene, incorporated either in tablets or in capsules. On coming in contact with gastric fluid, the hydrocolloid in the system hydrates and forms a colloidal gel barrier around its surface. This gel barrier controls the rate of fluid penetration into the device and consequent release of the drug (Sheth and Tossounian, 1984). As the exterior surface of the dosage form goes into the solution, the gel layer is maintained by the adjacent hydrocolloid layer becoming hydrated. The air trapped in by the swollen polymer maintains a density less than unity and confers buoyancy to these dosage forms.

**Improvements to be made**

The potential limitation of this approach is that the floating concept in an HBS is rather passive, i.e. it mainly depends on the air captured in the dry mass inside the hydrating gelatinous surface layer. The presence of a small amount of fatty materials added to impede wetting, also aids buoyancy. Because of this passivity, the buoyancy of an HBS largely depends on the characteristics and amount of hydrophilic polymer used in an HBS largely depends on the characteristics and amount of hydrophilic polymer used. To make a better floating HBS, many investigators tried other combinations of hydrophilic polymers agar, carrageenans, alginic acid and hydrophobic materials (e.g. Oil and porous calcium silicate).

Some of the marketed formulations are listed as follows:
- Valrelease® - Floating capsule of Diazepam;
- Madopar® - Benserazide and L-Dopa combination formulation;
- Topalkan® - Aluminium-Magnesium antacid preparation.

**Factors affecting gastric retention time of the dosage form** (Arora et al., 2005)

Gastric residence time of an oral dosage forms is affected by several factors. The pH of stomach in fasting state is ~1.5 to 2.0 and in fed state is 2.0 to 6.0. The rate of gastric emptying depends mainly on viscosity, volume, and caloric content of meal. Biological factors such as age, body mass index, gender, posture, and diseased state. In case of elderly persons, gastric emptying is slowed down. Generally females have slower gastric emptying rate than males. Stress increases gastric emptying rates while depression slows down.

**Volume of Stomach**
The resulting volume of stomach is 25 to 30 ml. When volume is large, the emptying is faster. Fluids taken at body temperature leave the stomach faster than colder or warmer fluids.

**Density:** GRT is a function of dosage form buoyancy that is dependent on the density. The density of dosage forms affects the gastric emptying rate. Floating dosage form having density less than that of gastric fluids therefore it will float on gastric contents. Since it is away from the pyloric sphincter, the dosage units are retained in the stomach for a prolonged period.

**Size:** Dosage form units with a diameter of more than 7.5 mm are reported to have an increased GRT compared with those with a diameter of 9.9 mm;

**Shape of dosage form:** Tetrahedron and ring shaped devices with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to have better GRT ≥90 % to 100 % retention at 24 hours compared with other shapes (Garg et. al., 2003);

Single or multiple unit formulation-Multiple unit formulations show a more predictable release profile and insignificant impairing of performance due to failure of units, allow co administration of units with different release profiles or containing incompatible substances and permit a larger margin of safety against dosage form failure compared with single unit dosage forms;

**Fed or unfed state:** Under fasting conditions, the GI motility is characterized by periods of strong motor activity or the migrating myoelectric complex (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and, if the timing of administration of the formulation coincides with that of the MMC, the GRT of the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer;

Nature of meal- Feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging drug release (Garg et. al., 2003);

**Caloric content:** GRT can be increased by four to 10 hours with a meal that is high in proteins and fats;

**Frequency of feed:** The GRT can increase by over 400 minutes when successive meals are given compared with a single meal due to the low frequency of MMC;

Gender- Mean ambulatory GRT in males (3.4±0.6 hours) is less compared with their age and racematched female counterparts (4.6±1.2 hours), regardless of the weight, height and body surface;
Age- Elderly people, especially those over 70, have a significantly longer GRT;
Posture: Stomach contents are emptied faster when standing up than lying down. This posture effect may explain why bed-striken patient tend to have poor appetites.
Concomitant drug administration – Anticholinergics like atropine and propantheline, opiates like codeine and prokinetic agents like metoclopramide and cisapride;

**Biological factors** – Diabetes, Crohn’s disease.

**Limitations of floating GRDDS**
One of the major disadvantages of floating systems is the requirement of high levels of fluids in the stomach for the delivery system to float and work efficiently. These systems also require the presence of food to delay their gastric emptying. In addition, there are limitations to the applicability of floating systems for drugs that have solubility or stability problems in the highly acidic gastric environment or that are irritants to the gastric mucosa.

Furthermore, the relatively brief gastric emptying time in humans, which normally averages 2-3 hrs through the major absorption zone (stomach or upper part of the intestine), can result in incomplete drug release from the DDS leading to diminished efficacy of the administered dose. Thus placement of the DDS in a specific region of the GIT offers numerous advantages, especially to the drugs having narrow absorption window in GIT, primarily absorption in the stomach, stability problems in intestine, poor solubility at alkaline pH, local activity in stomach, and property to degrade in colon. It has been suggested that compounding the drugs with narrow absorption window in a dosage form, which prolongs the gastric residence time would an extended absorption phase of these drugs.

**Sustained Drug Delivery**
Floating systems can remain in the stomach for longer period and hence can release the drug over a prolonged period of time. The problem of short gastric residence time encountered with an oral CR formulation hence can be overcome with these systems. These systems have a bulk density of GI as a result of which they can float on the gastric contents.

**Absorption Enhancement**
Drugs that have poor bioavailability because of site specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating
drug delivery systems, thereby maximizing their absorption. In developed a multiparticulate system that consisted of floating pills of a drug (p- amino benzoic acid) having a limited absorption site in the gastrointestinal tract. It was found to have 1.61 times greater AUC than the control pills (Ichikawa et al).

FDDS also serves as an excellent drug delivery system for the eradication of Helicobacter pylori, which causes chronic gastritis and peptic ulcers. The treatment requires high drug concentrations to be maintained at the site of infection that is within the gastric mucosa. By virtue of its floating ability these dosage forms can be retained in the gastric region for a prolonged period so that the drug can be targeted.

(Blaser MJ)

Limitations

1) The requirement of high level of fluid in the stomach for the delivery system to float and work efficiently.
2) These systems also require the presence of food to delay their gastric emptying.
3) In addition, there are limitations to the applicability of floating system for drugs that have solubility or stability problem in the highly acidic gastric environment or that are irritants to the gastric mucosa.
4) Drugs such as Nifedipine as well as Isosorbide dinitrate, which are well absorbed along the entire GI tract and those undergoes significant first pass metabolism may not be desirable candidate for GRDFs, because the slow gastric emptying may lead to reduced systemic bioavailability.
5) These systems do not offer significant advantages over the conventional dosage forms for drugs, which are absorbed throughout the gastrointestinal tract.

Mucoadhesive systems

The concept of Mucoadhesive (or bioadhesive) systems is that an oral dosage form in the stomach can stick to the mucosal surface of gastric tissue. Once the dosage form firmly sticks to the mucosal surface, its gastric residence time is expected to be prolonged until it is removed by turnover of mucin it is a simple and yet highly innovative concept.

Mechanism of permeation via gastrointestinal mucosa: There are two routes potentially involved in drug permeation across epithelial membranes. The Trans
cellular route: Also known as lipoidal pathway where the permeation is mainly by partitioning and depends on the lipophilicity of the drugs.

The Para cellular route: Also known as aqueous pore pathway. In this the drug is transported through the aqueous pores of mucus layer. Low molecular weight compounds are transported through this route, like sugar, salts and vitamins etc. Transmucosal permeation of polar molecules, such as peptide-based pharmaceuticals, may be by way of para cellular route; however several barriers like basal lamina, keratin layer, exist during the course of para cellular permeation (Chein et al. 2005).

**Advantages of mucoadhesive system**

Permits localization of the drug at the absorption site for a prolonged period of time.

1. A significant reduction in dose can be achieved, increasing patient compliance.
2. Drugs, which show poor bioavailability, can be administered conveniently.
3. It reduces dose dependent side effects due to lowering of frequency of drug dosing.

**Limitations of mucoadhesive system**

1. Drugs which irritate the mucosa cannot be administered by this route.
2. Drugs which are unstable at gastrointestinal pH cannot be administered by this route.
3. Only low dose drugs can be administered.
4. Over hydration may lead to formation of slippery surface disrupting the structural integrity of the formulation by swelling and hydration of the bioadhesive polymers.

Gastroretentive drug delivery system is an approach to prolong gastric residence time, thereby targeting site specific drug release in upper gastrointestinal (GI) tract. Floating drug delivery system (FDDS) and bioadhesive drug delivery are widely used techniques for gastro retention (Singh and Kim, 2000).

We will elaborate the most important features of the core research pursued on the above mentioned subject. The following chapter gives the review of literature in the light of subject discussed here.
Criteria for Selection of Drug Candidate for GRDDS

Drugs required to exert local therapeutic action in the stomach
e.g. Misoprostol, 5-Flourouracil, antacids and antireflux preparations, anti
*Helicobacter pylori* agents and certain enzymes.

1. Drugs exhibiting site-specific absorption in the stomach or upper part of the small
intestine:
e.g. Atenolol, Furosemide, Levodopa, p-Aminobenzoic acid, Piretanide, Salbutamol.

2. Drugs unstable in lower part of GI tract:
e.g. Captopril.

3. Drugs insoluble in intestinal fluids (acid soluble basic drugs):
e.g. Chlordiazepoxide, Chlorpheniramine, Cinnarizine, Dizapam, Diltiazem,
Metoprolol, Propranolol, Verapamil.

4. Drugs with variable bioavailability:
e.g. Sotalol hydrochloride and Levodopa.

Pharmacokinetic Advantages

Any solute released in the stomach will empty together with fluids and have the
whole surface of small intestine available for absorption. This should particularly
be useful when an absorption window exists in proximal small intestine. In
addition, with the total GI transit duration is increased, a greater amount of drug
may be delivered and thus the relative bioavailability will consequently be
increased. For instance, a significant increase in bioavailability of furosemide has
been obtained (42.90%) when administered as a floating dosage form, compared to
the commercially available tablet (Lasix®, 33.40%). Other drugs with poor
bioavailability like verapamil hydrochloride were also formulated into FDDS
apparently due to the analogous reasons.