Floating Drug Delivery Systems
Conventional drug delivery system achieves as well as maintains the drug concentration within the therapeutically effective range needed for treatment only when taken several times a day. This results in a significant fluctuation in drug levels.
The most important objectives of new drug delivery systems are:

• Increase the duration of treatment: single dose to release the active ingredient over an extended period of time.

• Deliver the active entity directly to the site of action, thus minimizing or eliminating side effects.
Variables facing oral controlled release dosage forms

• Gastric emptying
• Motility patterns
• Physiological variables
• Formulation variables
Gastric emptying process
Interdigestive myloelectric cycle

Migrating myloelectric cycle (MMC), during fasting

1. Phase I (basal phase) lasts from 40 to 60 minutes with rare contractions.
2. Phase II (preburst phase) lasts for 40 to 60 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.
3. Phase III (burst phase) lasts for 4 to 6 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.
4. Phase IV lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.
Digestive motility pattern (Fed state)

It comprises continuous contractions. 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.
Factors affecting gastric emptying rate
Approaches to gastric retention

- **Incorporation of passage delaying food excipients**, principally fatty acids, to decrease the gastric emptying rate.
- **Bioadhesive dosage forms** using special polymers that adhere to glycoprotein (Mucin) at the surface epithelium of the stomach and intestine.
- **Plug type system**: swell to an extent that prevents their exit from the stomach through the pylorus.
- **Modified shape systems**: are nondisintegrating geometric shapes which extend the gastric retention time depending on size, shape and flexural modulus of the drug delivery system.
- **Altered density approach**:  
  - **high-density dosage forms**: drug can be coated on a heavy core or mixed with heavy inert materials such as barium sulfate, titanium dioxide, iron powder and oxide.  
  - **low-density dosage forms**: floating drug delivery systems (FDDS)
Applications of gastroretentive Drug Delivery Systems

- Site-Specific Drug Delivery
- Sustained Drug Delivery
- Absorption Enhancement
Applications of gastroretentive Drug Delivery Systems

• Effective therapy of local diseases: as H. pylori infection with drugs such as antibiotics or acidity treatment with antacids.
• Suitable for improving absorption and controlling release of drugs having absorption window in stomach or upper part of small intestine, e.g. metformin, levodopa, riboflavin.
• Suitable for administering drugs unstable in intestine or colon e.g. captopril.
• Effective delivery of sparingly soluble and insoluble drugs or drugs having low solubility at intestinal pH e.g. diazepam.
• Reduction in variability in drug absorption which is commonly due to differences in gastric transit time.
Limitations

• There are certain situations where gastric retention is not desirable. Aspirin and non-steroidal anti-inflammatory drugs are known to cause gastric lesions, and slow release of such drugs in the stomach is unwanted.
• Thus, drugs that may irritate the stomach lining or are unstable in its acidic environment should not be formulated in gastroretentive systems.
• Furthermore, other drugs, such as isosorbide dinitrate, that are absorbed equally well throughout the GI tract will not benefit from incorporation into a gastric retention system.
Floating delivery systems
Types of floating delivery systems

Based on the design approach

Single unit
(all-or-nothing) unreliable

Multiple unit
lower the probability of dose-dumping.
reduce the inter-subject variability in absorption
Types of floating delivery systems

Based on the mechanism of buoyancy

Non effervescent     Effervescent
Types of floating delivery systems

Based on dosage form

Tablet → Capsules → Film → Solution → Microspheres → Granules
Non-Effervescent Floating Dosage Forms

Swellable polymers (gel forming)

These dosage forms swell in contact with gastric fluids and attain a bulk density of < 1. The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so formed swollen gel-like structure acts as a reservoir and allows sustained release of drug through the gelatinous mass.
Buoyancy is governed by both the swelling of the hydrocolloid particles on the tablet surface when it contacts the gastric fluids and the presence of internal voids in the center of the tablet (porosity).
Non-Effervescent Floating Dosage Forms

Diagram:

A. Hydrocolloids (20-75% w/w) → Gastric Fluid d > 1 → Colloid, Gel Barrier

B. Immediate Release Layer → Sustained Release Layer (Hydrocolloids) → Gastric Fluid d > 1 → Colloid, Gel Barrier

Sustained Release Layer
Non-Effervescent Floating Dosage Forms
Non-Effervescent Floating Dosage Forms

Matrix forming polymers

Matrix forming polymers + highly porous polypropylene foam powder in matrix tablets → density much lower than that of the release medium.
Non-Effervescent Floating Dosage Forms

Fluid-filled system

Gas-filled floatation chamber

Drug reservoir

Microporous compartment

The device is of swallowable size
Non-Effervescent Floating Dosage Forms

Coated globular shells

Sugar polymeric materials

Shell (popcorn, poprice)

Drug-polymer mixture
Non-Effervescent Floating Dosage Forms

Hollow microspheres

have a characteristic internal hollow structure
floating alginate beads were produced by dropwise addition of alginate into calcium chloride solution, followed by removal of gel beads and freeze-drying.
Effervescent Floating Dosage Forms

Swellable polymers + effervescent component

- methylcellulose
- chitosan
- sodium bicarbonate
- tartaric acid
- citric acid

in contact with the acidic gastric contents, CO$_2$ is liberated and gets entrapped in swollen hydrocolloids, which provides buoyancy to the dosage forms.
Effervescent Floating Dosage Forms

**Triple-layer system.**

(A) Initial configuration of triple-layer tablet.  
(B) On contact with the dissolution medium the bismuth layer rapidly dissolves and matrix starts swelling.  
(C) Tablet swells and erodes.  
(D) and (E) Tablet erodes completely.
Effervescent Floating Dosage Forms
ion exchange resin. On contact with gastric contents, an exchange of ions took place that resulted in CO$_2$ generation.

ion exchange resin that was loaded with bicarbonate (mixing the beads with 1 M sodium bicarbonate solution. and surrounded by a semipermeable membrane to avoid sudden loss of CO$_2$. 

Effervescent Floating Dosage Forms
Evaluation of floating drug delivery systems

In-vitro

In-vivo
Evaluation of floating drug delivery systems

- The time for the dosage form to be floating
- Floating duration
Evaluation of floating drug delivery systems

- The time for the dosage form to be floating
- Floating duration
Evaluation of floating drug delivery systems

• The time for the dosage form to be floating
• Floating duration
• Dissolution profiles
(Both are done in simulated gastric fluids at 37°C).
• Specific gravity
• Other tests according to the dosage form, eg.:
  • For solid dosage forms: content uniformity, hardness, and friability.
  • For multiparticulate drug delivery systems: DSC, particle size analysis, flow properties, surface morphology, and mechanical properties.
Evaluation of floating drug delivery systems

Experimental animals?

Gastric motility and stomach emptying are similar to humans.
Evaluation of floating drug delivery systems

Bioavailability studies

Radiographic studies
## Marketed Products

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Delivery system</th>
<th>Drug (dose)</th>
<th>Company name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valrelease®</td>
<td>Floating capsule</td>
<td>Diazepam (15mg)</td>
<td>Hoffmann-LaRoche, USA</td>
</tr>
<tr>
<td>Madopar® HBS (Prolopa® HBS)</td>
<td>Floating, CR capsule</td>
<td>Benserazide (25mg) and L-Dopa (100mg)</td>
<td>Roche Products, USA</td>
</tr>
<tr>
<td>Liquid Gaviscon®</td>
<td>Effervescent Floating liquid alginate preparations</td>
<td>Al hydroxide (95 mg), Mg Carbonate (358 mg)</td>
<td>GlaxoSmithkline, India</td>
</tr>
<tr>
<td>Topalkan®</td>
<td>Floating liquid alginate preparation</td>
<td>Al – Mg antacid</td>
<td>Pierre Fabre Drug, France</td>
</tr>
<tr>
<td>Almagate Flotcoat®</td>
<td>Floating dosage form</td>
<td>Al – Mg antacid</td>
<td>--------</td>
</tr>
<tr>
<td>Conviron®</td>
<td>Colloidal gel forming FDDS</td>
<td>Ferrous sulphate</td>
<td>Ranbaxy, India</td>
</tr>
<tr>
<td>Cytotech®</td>
<td>Bilayer floating capsule</td>
<td>Misoprostol (100µg/200µg)</td>
<td>Pharmacia, USA</td>
</tr>
<tr>
<td>Cifran OD®</td>
<td>Gas-generating floating form</td>
<td>Ciprofloxacin (1gm)</td>
<td>Ranbaxy, India</td>
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