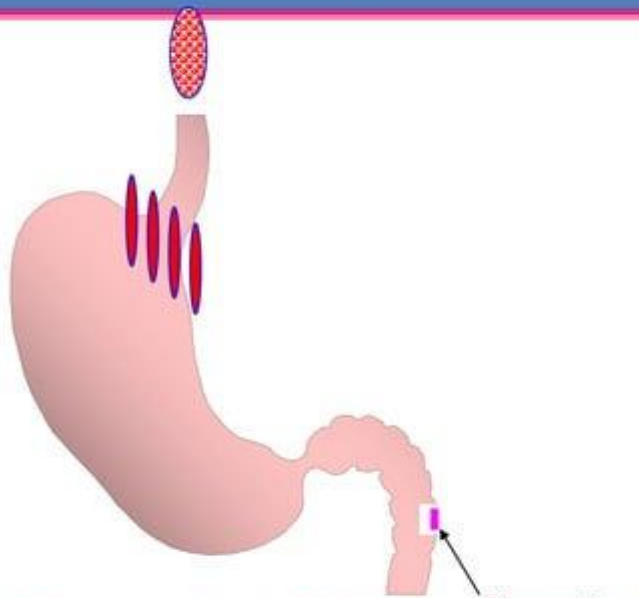
Introduction

- ✓ Conventional oral drug delivery system (DDS) is complicated by limited gastric residence time (GRT).
- ✓ Rapid GI transit can prevent complete drug release in absorption zone & reduce the efficacy of the administered dose since the majority of drugs are absorbed in stomach or the upper part of small intestine.

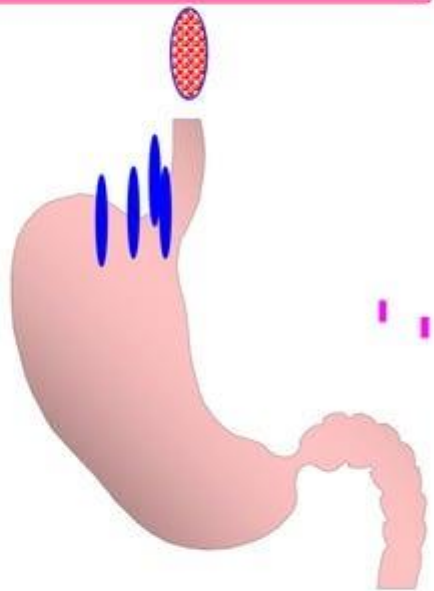
- ✓To overcome these limitations, various approaches have been proposed to increase gastric residence of drug delivery systems in the upper part of GIT includes gastro retentive drug delivery system (GRDDS).
- ✓Among the GRDDS, floating drug delivery system (FDDS) have been the most commonly used.

- ✓ Gastro-retentive delivery is one of the site specific delivery of the drugs at stomach. It is obtained by retaining dosage form into stomach and drug is being released at sustained manner to specific site either in stomach or intestine.

Differ from Conventional Release…



Conventional Release



GRDDS

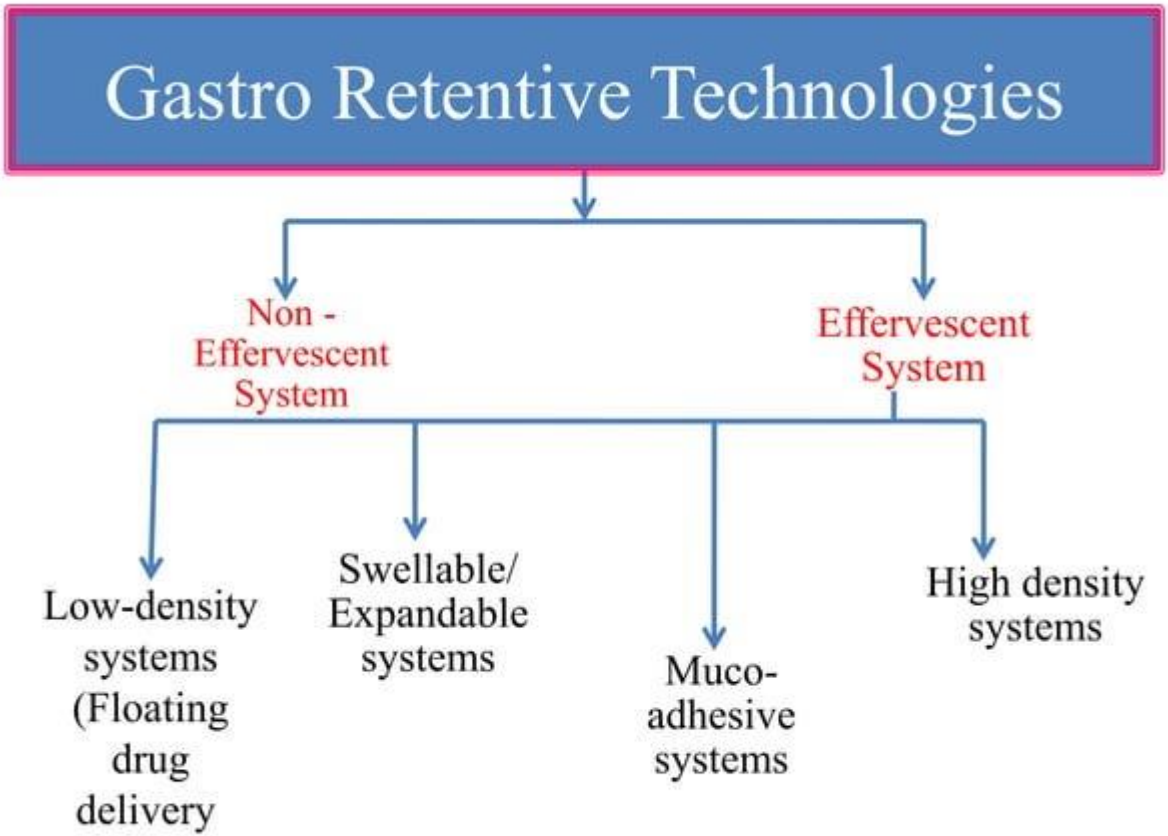
Advantages…

- ✓ Delivery of drugs with narrow **absorption window** in the small intestine region.
- ✓ Longer residence time in the stomach could be advantageous for **local action** in stomach, for example treatment of peptic ulcer disease.
- ✓ **Bio-availability** can be improved.

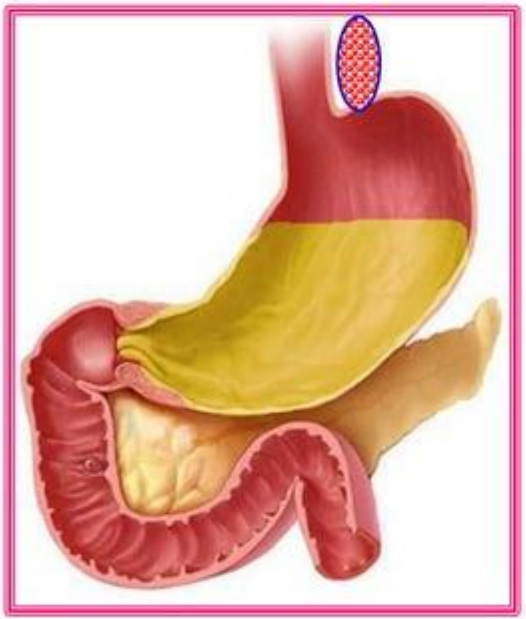
- ✓ Reduced Frequency of Dosing with improved patient compliance
- ✓ Minimize the Fluctuation of drug concentrations
- ✓ Site specific drug delivery
- ✓ Enhances the Pharmacological effects

Candidates for GRDDS

- ✓ Drugs acting locally in the stomach E.g. Antacids
- ✓ Drugs that are principally absorbed in the stomach
- ✓ Drugs that are poorly soluble at the alkaline pH
- ✓ Drugs with a narrow window of absorption E.g. Furosemide
- ✓ Drugs absorbed readily from the GI tract
- ✓ Drugs that degrade in the colon
- ✓ Drugs with variable Bioavailability
- ✓ Drugs with less half life


Gastro Retentive Technologies
Non - Effervescent System
Effervescent System
Low-density systems (Floating drug delivery
Swellable/ Expandable systems
Muco-adhesive systems
High density systems

A) Low Density Approach (Floating Drug Delivery)



- ✓ Retained in stomach
- ✓ Useful for poorly water soluble OR unstable in intestinal Fluid
- ✓ Bulk density : Less than gastric fluid, so remain buoyant in the stomach without affecting gastric emptying rate for prolonged period of time
- ✓ So drug release slowly at the desired rate from system

Advantages of Low Density Approach OR Floating Drug Delivery

Drugs those are...

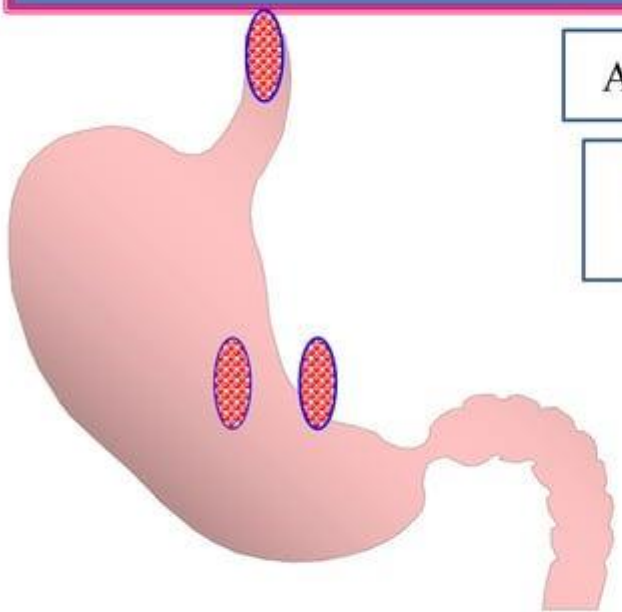
- ✓ Primarily absorbed in the stomach
- ✓ Poorly soluble at an alkaline pH
- ✓ Narrow window of absorption
- ✓ Degrade in colon

- ✓ When there is a vigorous intestinal movement and a short transit time as might occur in certain type of diarrhoea, poor absorption is expected. Under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.

Disadvantages of Low Density Approach OR Floating Drug Delivery

- ✓ Not feasible for those drugs that have solubility OR stability problem in GIT
- ✓ Require high level of fluid in stomach
- ✓ The drugs that may irritate the stomach lining OR are unstable in acidic environment
- ✓ The dosage form should be administered with a full glass of water (200-250 ml)

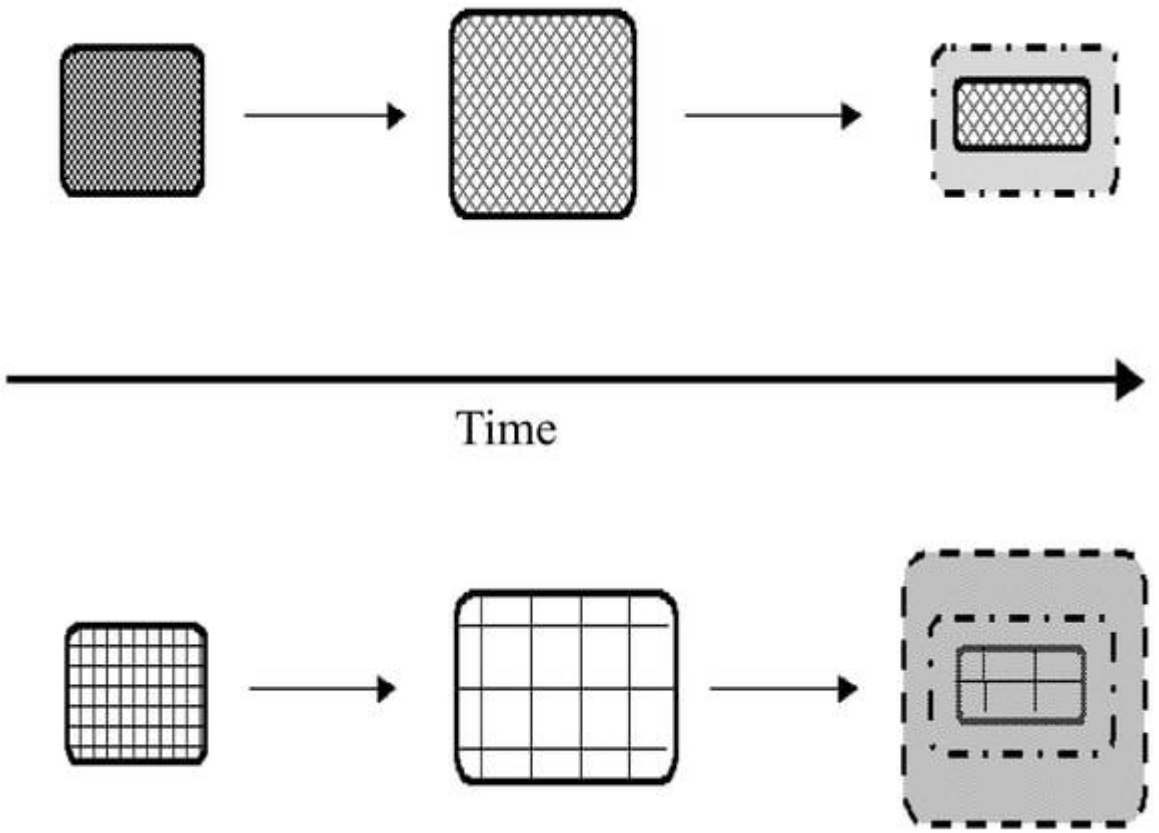
B) Swellable System



Also called ' PLUG SYSTEM'

Size of the formulation more than Pyloric sphincter

It should expand for gastric retention Should be Collapsed after lag time

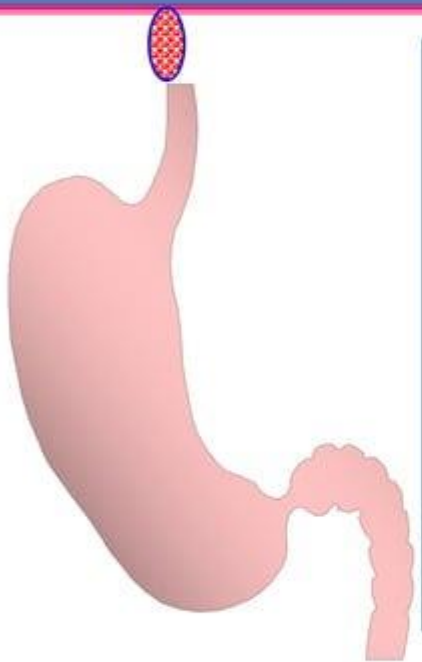

Time

Picture of tablet in Dry and Wetted state

Disadvantages of Swelling System

- ✓ The Dosage form must maintain a size larger than pyloric sphincter
- ✓ The Dosage form must resist premature gastric emptying

C) Bio/Muco Adhesive System



Here, the drug is incorporated with bio/ Muco-adhesive agents, enabling the Device to adhere to the stomach walls, Thus resisting gastric emptying.

However, the mucus on the walls of the Stomach is in a state of constant renewal, Resulting in unpredictable adherence.

Thus, this approach is not widely used.

Bio/Muco Adhesive Polymers

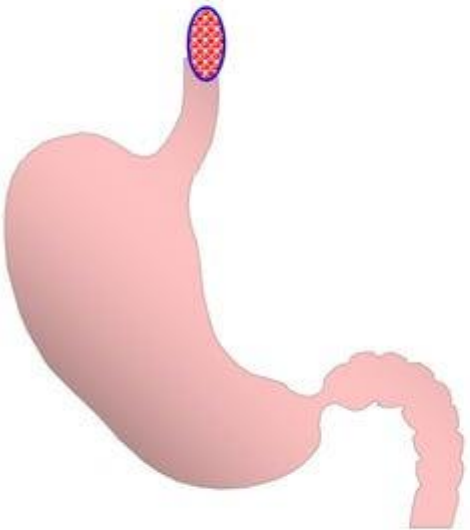
- ✓ **Chitosan**
- ✓ **Polyacrylic acid**
- ✓ **Carbopol 934P, 971P, 980**
- ✓ **Sodium alginate**

- ✓ **HPMC K4M, K15M, K100M**
- ✓ **Hydroxypropylcellulose (HPC)**
- ✓ **Cholestyramine**

Problem of Muco-adhesive System

- ✓ Rapid removal of mucus.
- ✓ We are not sure weather the DF will adhere to the mucus or epithelial cell layer
- ✓ DF may adhere to esophagus resulting in drug induced injuries

D) High Density Approch



Density should be more then stomach content i.e. 3 g/cm3

Capable to withstand with peristaltic movement of stomach

Prepared by coating or mixing drug with heavy inert material

Diluents such as…

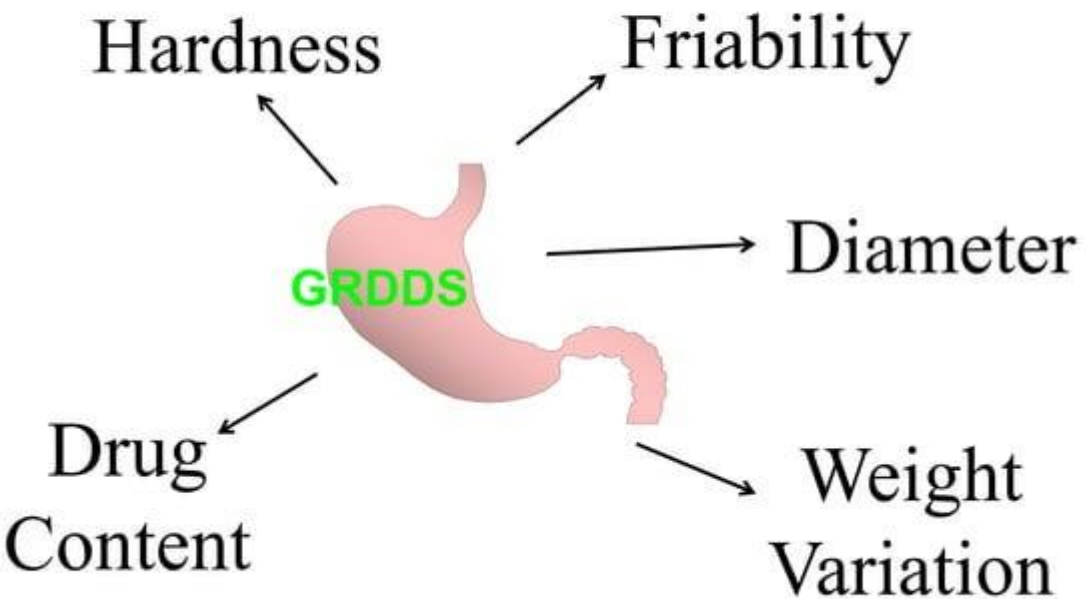
- ✓ barium sulphate (density = 4.9),
- ✓ zinc oxide,
- ✓ titanium dioxide,
- ✓ iron powder

must be used to manufacture such high-density formulations.

Problem with High Density Approch

- ✓ Higher amount of drug require
- ✓ The dosage form must stand with peristaltic movement of stomach

Evaluation of GRDDS



Evaluation of GRDDS

❖ Dissolution Study

✓ Dissolution

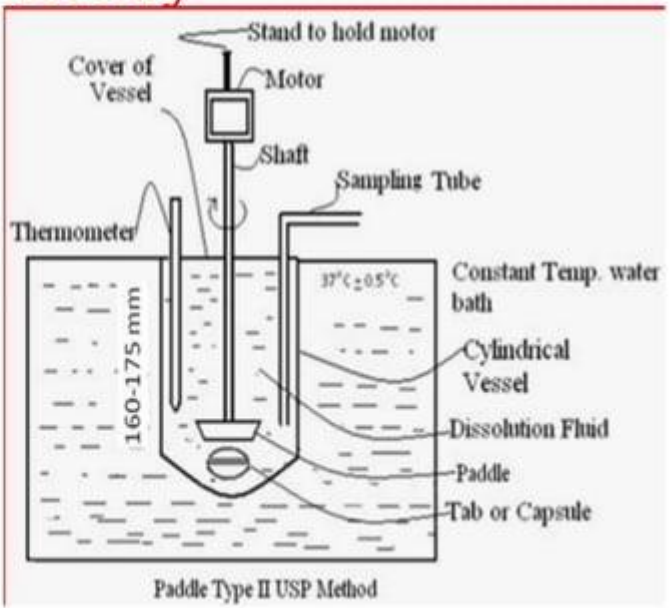
medium : 0.1 N HCl

✓ Temp. : 37 ± 0.5°C

✓ RPM : 50-100

✓ Sample analysis :

UV

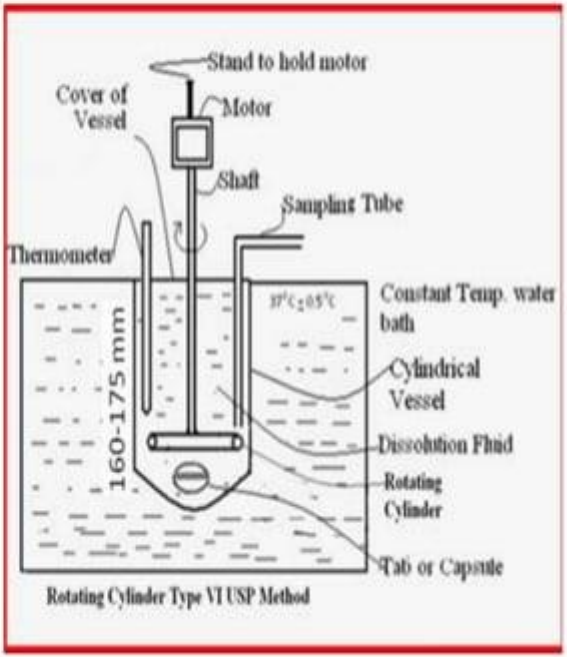


Paddle Type II USP Method

Evaluation of GRDDS

❖ **In-vitro Mucoadhesion**

- ✓ Apparatus **:** USP type VI (rotating cylinder apparatus)
- ✓ Medium : 0.1 N HCl
- ✓ Temp. : 37 ± 0.5°C
- ✓ RPM : 100



Rotating Cylinder Type VI USP Method

Evaluation of GRDDS

❖ Lag time :

- ✓ Measurement : 0.1 N HCl at pH 1.2
- ✓ Temp. : 37 ± 0.5°C
- ✓ Apparatus : USP Type II dissolution apparatus
- ✓ A tablet is placed in a beaker containing 100 – 200 ml dissolution medium & the time for a tablet to emerge on to the surface of the dissolution medium is known as lag time .

Evaluation of GRDDS

❖ Floating Time

- ✓ After achieving lag time, the time taken for a tablet to remain float on the surface of the dissolution medium is called floating time.

Evaluation of GRDDS

❖ Water uptake :

✓ Apparatus : USP type II dissolution apparatus

✓ Medium : Water

✓ Temp. : 37 ± 0.5°C

✓ RPM : 50

$$WU\ (\%) = \frac{\text{Wt. of swollen tab.} - \text{Initial wt. of tab.}}{\text{Initial wt. of tab.}} \times 100$$

Evaluation of GRDDS

- In vitro Mucoadhesive strength

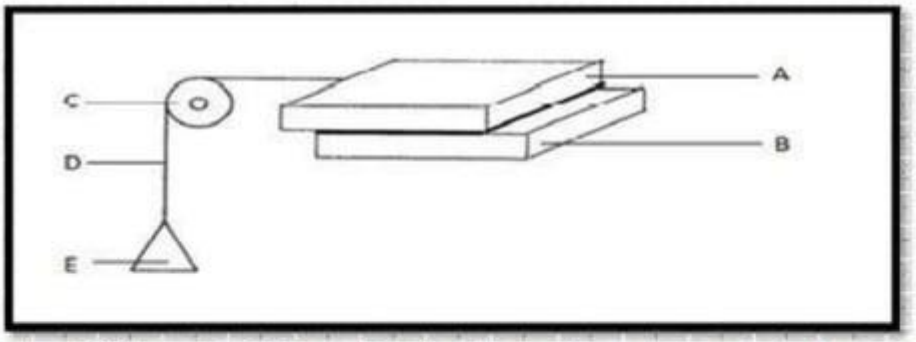


Figure 3:(The assembly used in the shear stress measurement method)
(A)Upper glass plate (B) Lower glass plate (C) Pulley (D) Thread (E) Pan

Limitation of GRDDS

- ✓ It is not recommended for drugs which are unstable at gastric/acidic pH, insoluble or very low soluble drugs and drugs which causes gastric irritation.

- ✓ For floating, high level of fluid is required in GIT. Also sleeping condition is favorable for the better results of GRDDS.

Limitation of GRDDS

- ✓ Bioadhesive systems, cannot prevail longer due to high turn-over rate of mucus layer and presence of soluble mucin
- ✓ For swelling systems, it is necessary that the formulation should not exit before the appropriate swelling
- ✓ For High density systems, High amount of drug is require

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