Review Article

REVIEW ON GASTRO RETENTIVE DRUG DELIVERY SYSTEMS

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ABSRACT

Oral controlled release and site specific drug delivery system has been of great interest in pharmaceutical field to improve therapy with several important drugs. Concept of novel drug delivery system arose systems to overcome physiological adversities such as short gastric residence times and unpredictable gastric emptying times. Gastro retentive drug delivery system is one of such novel approaches to prolonged and continuous release of the drug to the upper part of Gastro intestinal tract (GIT) and this significantly extend the duration of drug release and improve bioavailability of drugs that have narrow therapeutic window, by this way they prolong dosing interval and increase compliance of the patient. In this review we have been discussed the gastro retentive drug delivery (GRDD), factors related to GRDD, its advantages disadvantages, various approaches of gastro retentive drug delivery system, various polymers used for gastro retention.

INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve and maintain the desired drug concentration. The oral route is the most preferred route of administration of drugs because of low cost of therapy, ease of administration, patient compliance and flexibility in formulation[1].

Effective oral drug delivery may depend upon the factors such as gastric emptying process, gastrointestinal transit time of dosage form, drug release from the dosage form and site of absorption of drugs. Most of the oral dosage forms possess several physiological limitations such as variable gastrointestinal transit, because of variable gastric emptying leading to non-uniform absorption profiles, variation of pH in different segments of gastrointestinal tract (GIT), incomplete drug release and shorter residence time of the dosage form in the stomach. This leads to incomplete absorption of drugs having absorption window especially in the upper part of the small intestine, as once the drug passes down the absorption site, the remaining quantity goes unabsorbed[2].

To overcome this physiological problem, several drug delivery systems with prolonged gastric retention time have been investigated. Attempts are being made to develop a controlled drug delivery system that can provide therapeutically effective plasma drug concentration levels for longer durations, thereby reducing the dosing frequency and minimizing fluctuations in plasma drug concentration at steady state by delivering drug in a controlled and reproducible manner[3]. FDDS are widely explored for gastro retention purposes and have a bulk density lower than gastric fluids and thus remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time so that system is floating on gastric contents, the drug is released slowly at a desired rate from the system.

To achieve controlled gastric retention of dosage unit in stomach many approaches have emerged like bio adhesive systems, swelling and expanding systems, floating systems, modified shape systems, high-density systems and other delayed gastric emptying devices[2,3,4].

BASIC GIT PHYSIOLOGY

Anatomically the stomach is divided in to three regions

Fundus, Body and Antrum (pylorus). The proximal part made of fundus and body acts as a reservoir for undigested materials, whereas the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions[5] (Yie W. Chein et al, 1992, Sanjay Garg et al, 2003). Gastric emptying occurs in both the fasting and fed states. During the fasting state an inter digestive series of electrical events take place which cycle both through stomach and intestine every 2-3 hrs, which is called as inter digestive myoelectric cycle or migrating myoelectric cycle (MMC) which is further divided in to four phases After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state which is also termed as digestive motility pattern[6,7] (Fig1)

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

2. Phase 2-(Pre burst 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 cycles[7] (Fig1)

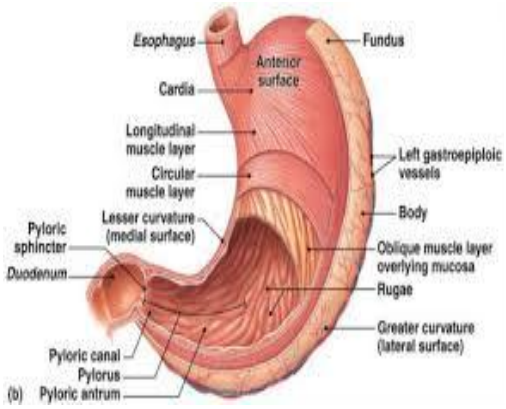


Fig. 1: GIT Physiology

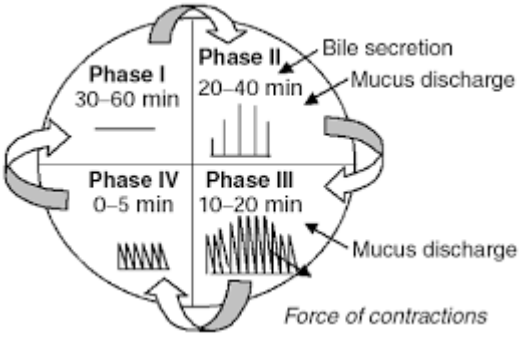


Fig. 2: schematic representation of inter digestive motility

Factors affecting gastric retention of dosage forms

A. Formulation factors

- **Shape and Size of the Dosage Form**

Shape and size of the dosage forms are important factor which affects gastric emptying process. Small tablets are emptied quickly from the stomach during the digestive phase, but larger ones will not quickly pass through the pyloric antrum into the intestine[8,9].

The diameter of the dosage unit is also equally important as a formulation parameter in which dosage forms that are having a diameter of more than 7.5mm show a better gastric residence time compared with one having 9.9 mm[9].

The shape of dosage form is one of the factors that affect its gastric residence time. Six shapes (ring tetrahedron, clover leaf, string, pellets and disk)were screened in vivo for their gastric retention potential. The tetrahedron (each leg 2cm long) rings (3.6cm in diameter) exhibit nearly 100%retention at 24hrs

- **Density of dosage forms**

The density of a dosage form also important factor which affects the gastric emptying rate and determines the location of the dosage form in the stomach.
A buoyant dosage formshavinga density of less than 1.004g/ml i.e. less than that of gastric contents floats, since it is away from the pyloric sphincter, the dosage unit is retained in the stomach for a prolonged period[9].

- **Viscosity grade of polymer**

Viscosity of polymers and their interaction greatly affects the drug release rate and floating properties of FDDS. Low viscosity polymers (e.g., HPMC K100 LV) enhance floating properties compared to high viscosity polymers (e.g., HPMC K4M). In addition, high viscosity polymers show decrease in the release rate of the drug from the system[12].

B. Idiosyncratic factors

- **Gender**

Men have faster gastric emptying time than women. Mean ambulatory GRT in males (3.4 ± 0.6 hours) is less compared with their age and race matched female counterparts (4.6 ± 1.2 hours), regardless of the weight, height and body surface[13].

- **Age**

Geriatric people have slower gastric emptying time as well as longer GRT. Intrasubject and intersubject variations also are observed in gastric and intestinal transit time[13].

- **Posture**

a. Upright position

An upright position protects floating forms against postprandial emptying because the floating form remains above the gastric contents irrespective of its size[14].

b. Supine position

This position offers no reliable protection against postprandial emptying. The floating dosage form remain buoyant experience prolonged retention anywhere between lesser and greater curvature of the stomach. On moving distally, compared to upright subjects significant reduction in GRT is seen due to the units may be swept away by the peristaltic movements that propel the gastric contents towards the pylorus[15].

C. Concomitant intake of drug

The coadministration of GI-motility decreasing drugs can increase gastric emptying time[15].
Concomitant intake of drugs affects the performance of FDDS.
For eg: Drugs such as prokinetic agents (e.g., metoclopramide and cisapride) decrease GRT, anti Cholinergics (e.g., atropine or propantheline) increase GRT.

D. Disease state:

Gastric ulcer, diabetes and hypothyroidism enhance the GRT. Hyperthyroidism and duodenal ulcers decrease the GRT.

E. Fed or unfed state:

Under fasting conditions, gastro intestinal motility is characterized by periods of strong motor activity that occurs every 1.5 to 2 hours and GRT of the unit will be very short if the timing of administration of the dosage form coincides with that of the MMC.
Under fed state, MMC is delayed and GRT is significantly longer[18].

F. Feeding regimen and Nature of meal

In the presence of food there is increase in gastric residence time, leading to increased drug dissolution of the dosage form at the most favourable site of absorption. After a meal of fats and proteins a GRT of 4-10 hr has been reported[16]. 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.

G. Caloric content:

GRT can be enhanced by 4 to 10 hours with a meal that is high in proteins and fats[18].

H. Frequency of feed:

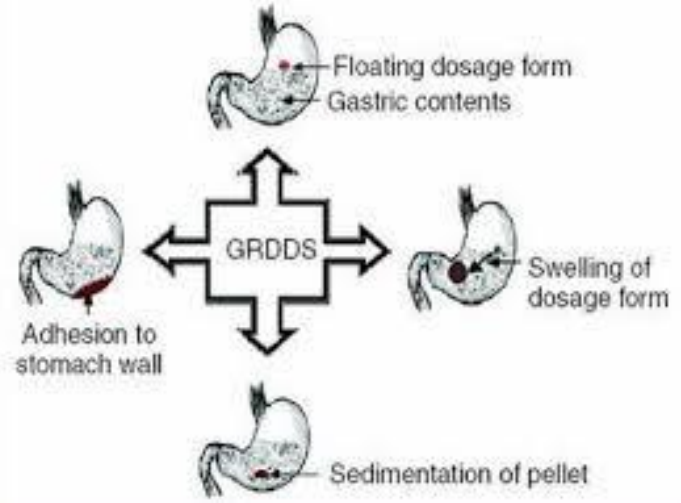
When successive meals are given there is increase in GRT by over 400 minutes due to low frequency of MMC.

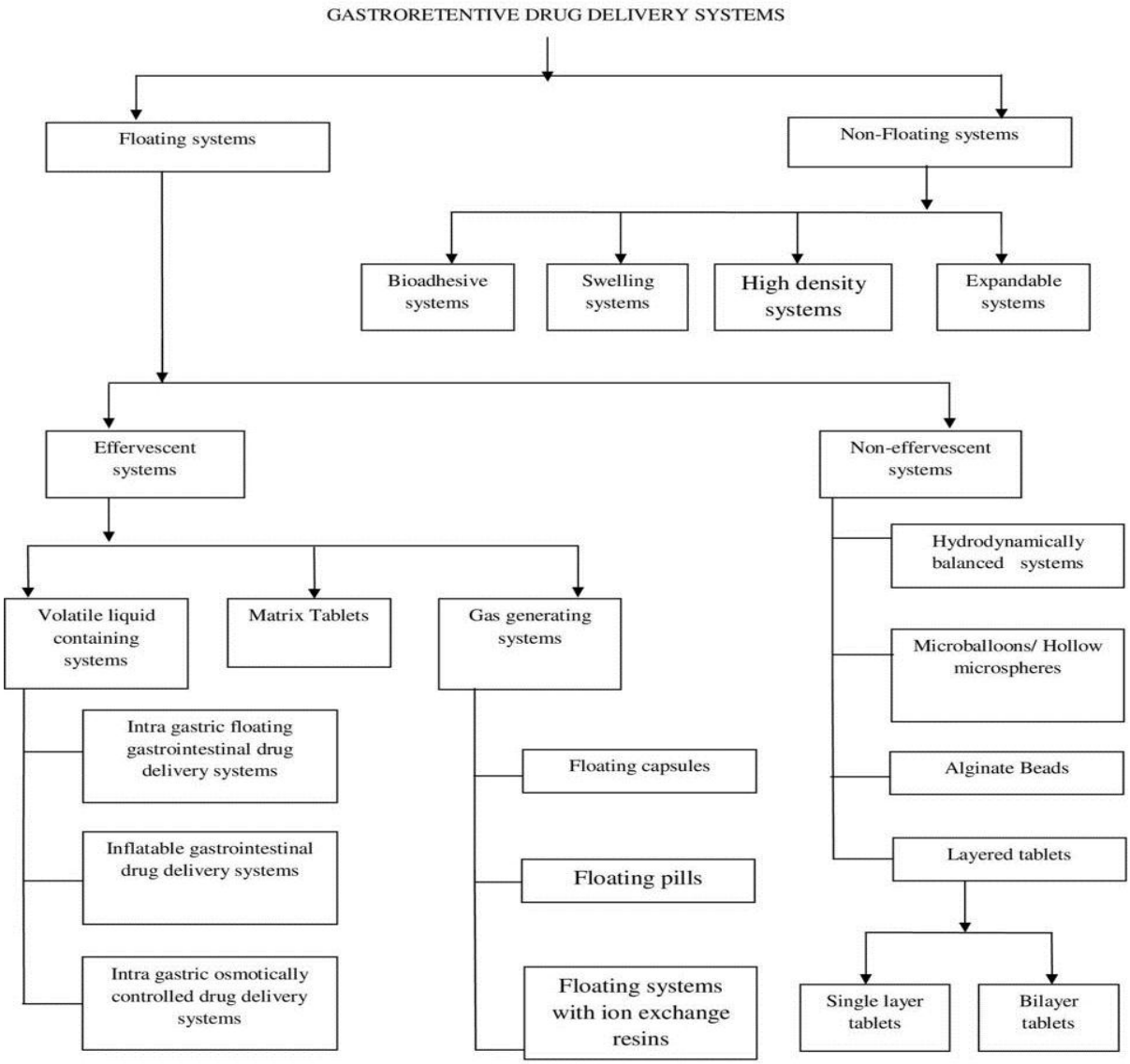
I. Food intake and its nature

Food intake, viscosity and volume of food, caloric value and frequency of feeding have an effect on the gastric retention of dosage forms. Usually the presence of food in the gastrointestinal tract (GIT) increases the gastric retention time (GRT) of the dosage form and thus, the drugs absorption increases. Again, increase in acidity and caloric value decreases gastric emptying time (GET), which can improve the gastric retention of dosage forms [18].

APPROACHES TO GASTRO RETENTION

Several techniques are reported in the literature to increase the gastric retention of drugs[16-19].





1. FLOATING SYSTEMS

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remai n buoyant in the stomach, the drug releases slowly from the system at the predetermined rate for a prolonged period of time without affecting the gastric emptying rate.

After release of drug, the residual system is emptied from the stomach results in an increased gastric retention time (GRT). This results in better control of the fluctuation in plasma drug concentration and better bioavailabilty[19]. This delivery systems is desirable for drugs with an absorption window in the stomach or in the upper small intestine[20].

The major requirements for floating drug delivery system are [18]:

• It should release contents in controlled manner to serve as a reservoir.

• the specific gravity of the system must be more than that of gastric contents (specific gravity of gastric contents: 1.004 – 1.01 gm/cm3).

• the system must form a cohesive gel barrier.

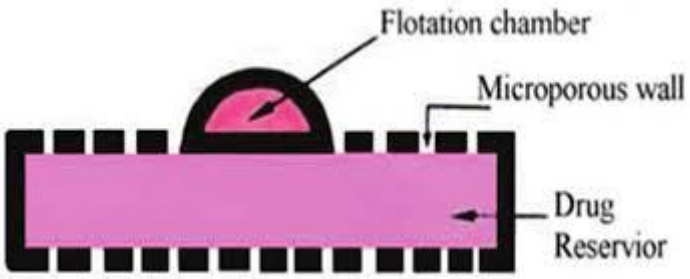
A. Effervescent system

a. Volatile liquid containing systems

The volatile liquid containing systems consists of inflatation chamber made up of bio erodible polymer (PVA, polyethylene etc,) that gasifies at body temperature to cause the inflatation of the chamber in the stomach[21].

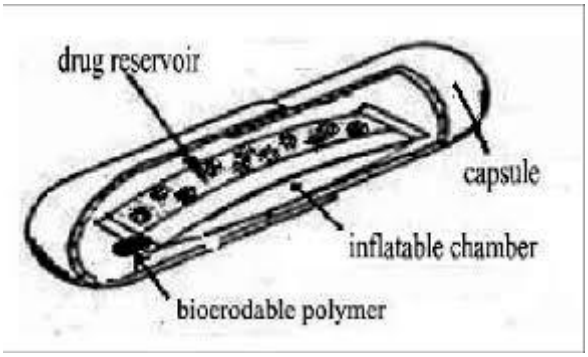
I. Intragastric floating gastrointestinal drug delivery system

In these system a floatable chamber is incorporated, which may be vacuum or filled with air or a harmless gas results in inflatation of chamber in the stomach, while drug reservoir is encapsulated inside a microporous compartment[22].



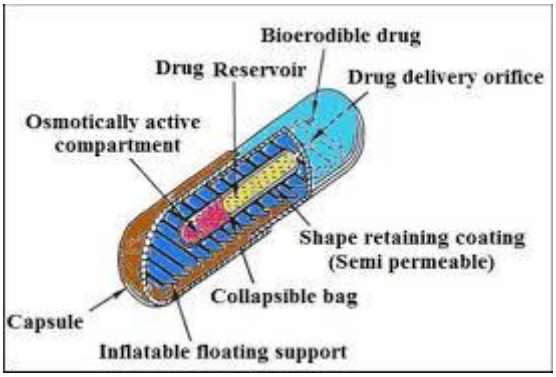
II. Inflatable gastrointestinal delivery system

These systems are fabricated by loading the inflatation chamber with drug reservoir, which can be a drug, impregnated polymeric matrix, then encapsulated in a gelatine capsule. The inflatation chamber contains a volatile liquid (e.g. ether, cyclopentane,) that gasifies at body temperature to cause the inflatation of the chamber in the stomach and the bio erodible polymer filament (copolymer of PVA, polyethylene) gradually dissolves causes the drug reservoir to retain in the gastric fluid finally results in controlled release of drug[23].



III. Intragastric osmotically controlled drug delivery system[24]

This system is composed of an osmotic pressure controlled drug delivery device and an inflatable floating support. In the stomach, the capsule quickly disintegrates to release the intragastric osmotically controlled drug delivery device. The osmotic pressure controlled drug delivery device consists of two components: drug reservoir compartment and an osmotically active compartment. The drug reservoir compartment is enclosed by a pressure responsive collapsible bag, which is impermeable to vapour and liquid and has a drug delivery orifice. The osmotically active compartment contains an osmotically active salt and is enclosed within a semi-permeable housing. In the stomach, the water in the GI fluid is continuously absorbed through the semi-permeable membrane into osmotically active compartment to dissolve the osmotically salt. An osmotic pressure is then created which acts on the collapsible bag and in turn forces the bag reservoir compartment to reduce its volume and activate the drug release of a drug solution formulation through the delivery orifice. The floating support is also made to contain a bio-erodible plug that erodes after a predetermined time to deflat the support. The deflated drug delivery system is then emptied from the stomach.

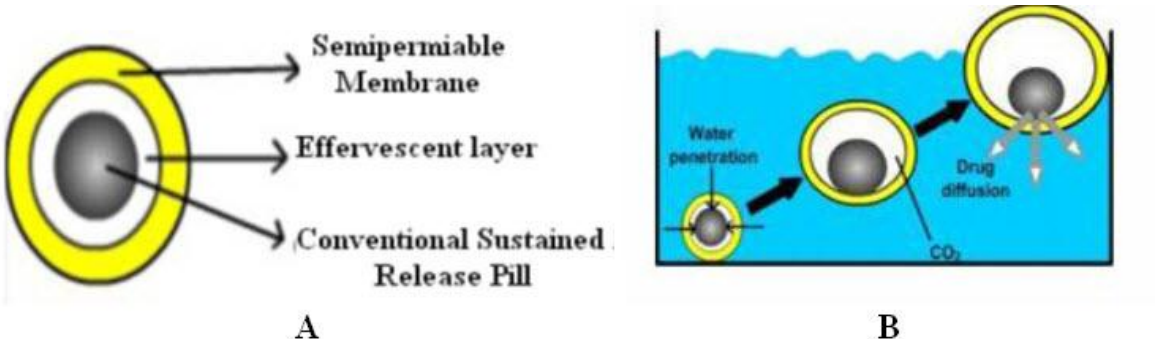


b. Matrix system:

Single matrix tablet is prepared by incorporation of bicarbonates in matrix forming hydrocolloid gelling agent and drug. Bilayer matrix tablet can also be prepared by gas generating matrix in one layer and second layer with drug for its SR effect. Floating capsule can also prepared by using such mixtures. Triple layer matrix tablet can also prepared having first swell able floating layer, second sustained release layer of 2 drug , third rapid dissolving bismuth salt.

b. Gas generating system

These buoyant systems utilize matrices prepared with the help of
swellable polymers such as methylcellulose and polysaccharides (e.g. Chitosan), effervescent components (e.g. sodium bicarbonate, citric acid or tartaric acid).
The optimal stoichiometric ratio of citric acid and sodium bicarbonate for generation of gas is reported to be 0.76:1. These systems are formulated in such a way that when dosage form come in contact with the acidic gastric contents, CO_2 is liberated and gets entrapped in swollen hydrocolloids, which causes formulation to float in the stomach[25].



I. floating capsules

These are prepared by formulating mixture of sodium bi carbonate and sodium alginate. On exposure to acidic environment, CO_2 gas is generated which is trapped in the hydrating gel network and makes the system to float.

II. Floating pills

These are multiple types of unit dosage forms which releases drug in controlled and sustained manner. These pills consists of two layers in which inner layer consist of effervescent agents which is surrounded by outer swellable membrane. The system when reaches to acidic environment of the stomach get swell due to swelleble membrane and then sink. Due to presence of effervescent agent, CO_2 is released and the system floats.

III. Floating system with ion exchange resin:

The most common approach for formulating these systems involves ion exchange resin beads loaded with bi carbonates as gastro retentive drug delivery systems. This is then coated with polymer which is usually insoluble but permeable to water. In the presence of hydrochloric acid bicarbonate was liberated, which formed carbon dioxide. The later was trapped inside the membrane resulting in flotation of the resin particle[26].

B. Non Effervescent Systems

The non-effervescent FDDS based on mechanism of swelling of polymer or bio adhesion to mucosal layer in GI tract. The most commonly used excipients in non-effervescent FDDS are gel forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming material such as polycarbonate, polyacrylate, polymethacrylate, polystyrene as well as bio-adhesive polymer such as chitosan and carbopol.

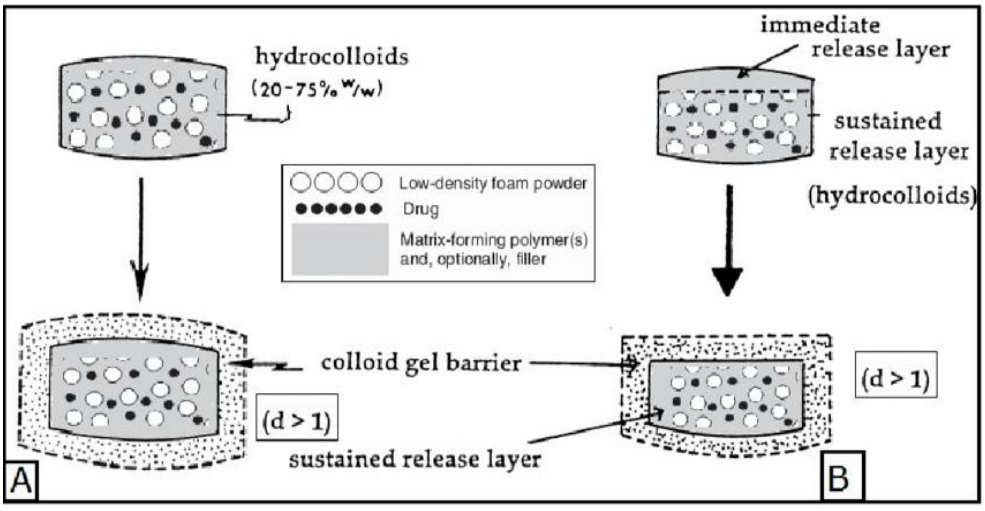
The various type of this systems are as follows:

a. Single layer floating tablets

This single layer tablets mainly consists of gel forming hydrocolloid and drug, which swells in contact with gastric fluid and maintain bulk density of less than unity as **figure A**. The air trapped by the swollen polymer confers buoyancy to these dosage forms.

b. Bilayer floating tablets

A bilayer tablet contains two layer such as immediate release layer and sustain release layer as **figure B**. Immediate release layer releases initial dose from system while the another sustained release layer absorbs gastric fluid, forming an impermeable colloidal gel barrier on its surface, and maintain a bulk density of less than unity and thereby it remains buoyant in the stomach. [40]

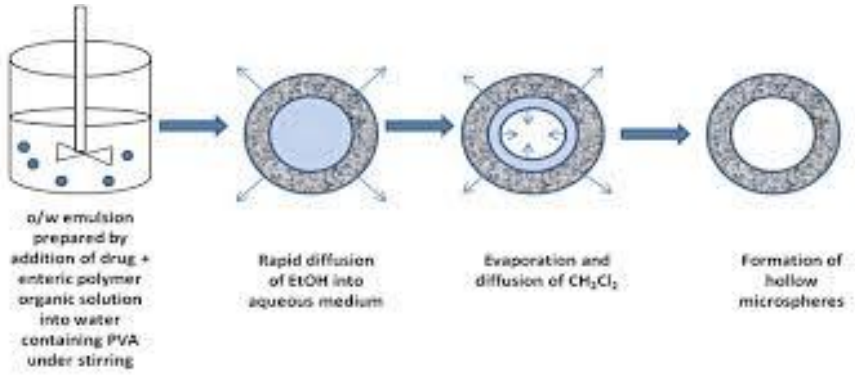


c. Alginate beads

Multi unit floating dosage forms are developed from freeze dried calcium alginate. Spherical beads of approximately 2.5 mm diameter can be prepared by dropping a sodium alginate solution into aqueous solution of calcium chloride, causing precipitation of calcium alginate leading to formation of porous system, which can maintain a floating force for over 12 hours. When compared with solid beads, which gave a short residence, time of 1 hour, and these floating beads gave a prolonged residence time of more than 5.5 hours.

d. Hollow microspheres

Hollow microspheres (microballons) loaded with drug in their outer polymer shells were prepared by simple solvent evopration or solvent diffusion or evaporation methods . The ethanol: dichloromethane solution of drug and enteric acrylic polymer was poured into an agitated aqueous solution of PVA that was thermally controlled at 40^0C. The gas phase generated in dispersed polymer droplet by evaporation of dichloromethane formed an internal cavity in microsphere of polymer with drug. The microballons floated continuously over the surface of acidic dissolution media containing surfactant for more than 12 hours in vitro.



2. NON-FLOATING SYSTEM:

These gastro retentive drug delivery systems do not float in the stomach however they remain retained there by different mechanism

A. High density systems

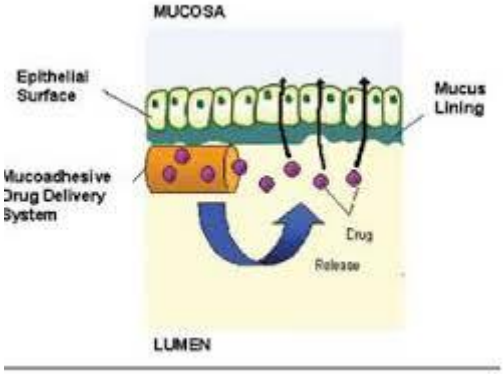
These systems possess density greater than the gastric fluids results in dosage form gets retained in the rugae of the stomach and capable of withstanding its peristaltic movement. Such high density formulations can be formulated by coating drug on heavy inert materials like zinc oxide, titanium dioxide, iron powder, etc.

B. Swelling system

These systems are also called as plug-type system. These non floating gastroretentive drug delivery system which when enter to stomach, dosage form on contact with gastric fluid the polymer imbibes water and swells to an extent that their exit from the pylorus is prevented, as a result the dosage form is retained in the stomach for a prolonged period of time. Controlled and sustained release may be achieved by selection of swellable polymers. The physical-chemical cross links in the hydrophilic polymer network results in extensive swelling of these polymers retards the dissolution of the polymer and thus maintain the physical integrity of the dosage form[28].

C. Mucoadhesive & bioadhesive systems

Bio adhesive and mucoadhesive drug delivery systems contain a polymer that adheres to gastric mucosal layer results in localization of delivery device within the lumen to enhance the drug absorption in a site specific manner. This approach involves the use of bio adhesive polymers, which can adhere to the epithelial surface in the stomach. These polymers can be natural such as sodium alginate, gelatine, guar gum etc. semisynthetic polymers such as HPMC, carbopol, sodium carboxy methyl cellulose.



The adhesion of polymers with mucous membrane may be mediated by hydration, bonding, or receptor mediated [27].

a. Hydration – mediated adhesion

Certain hydrophilic polymers have the tendency to imbibe large amount of water and become mucoadhesive and sticky, results in prolonged gastro retention of the mucoadhesive drug delivery system is further controlled by the dissolution rate of the polymer.

b. Bonding –mediated adhesion

Adhesion of polymers to mucus/epithelial cell surface involves varying bonding mechanism. Physical or mechanical bonds can result from deposition and inclusion of the polymeric material in the crevices of the mucosa. Secondary chemical bonds, may involve ionic or covalent bonds or Vander Waal forces between the polymer molecule and the mucous membrane.

c. Receptor -mediated adhesion

Receptor mediated adhesion takes place between certain polymers and specific receptors expressed on gastric cells hence enhancing gastric retention of the dosage form[28].

D. Expendable system:

These systems are formulated as a capsule containing folded and compact dosage form which is capable of expanding and retain in the stomach for longer periods. these capsules after being exposed to stomach environment, capsule shell disintegrates and dosage form expands preventing its exit through the stomach. By using a suitable polymer, sustained and controlled drug delivery can be achieved[29].

Polymers

Polymer are used in floating system so as to target the drug delivery at specific region in the GI tract i.e. stomach. Both synthetic and natural polymers are used in the floating drug delivery. Natural polymer used in floating system are Guar gum, Chitosan, xanthum gum, Gellan gum, Sodium alginate, etc. Synthetic polymer used for the floating drug delivery are HPMC, Eudragit, ethyl cellulose, etc.[30,34]

Natural polymers

Natural gums (obtained from plants) are hydrophilic carbohydrate polymer of high molecular weight. They are generally insoluble in organic solvents like hydrocarbon, ether. Gums either water soluble or absorb water and swell up or disperse in cold water to give a viscous solution or jelly[30]. List of natural gum given below:

List of Natural Polymer Used In Floating Drug Delivery System[30]

S. No.	Polymer	Source
1	guar gum	Endosperm of seed of cynopsis tetragonolobus
2	Chitosan	Shell of marine invertibrates
3	xanthum gum	Fermentation of glucose Xanthomonas compestris
4	gellan gum	Pseudomonas elodea
5	sodium alginate	Laminaria hyperboria

Natural polymer has advantages over synthetic polymer.

They are as follows:

1. Biodegradable.
2. Biocompatible and non-toxic.
3. Low cost.
4. Environment friendly processing.
5. Local availability(especially in developing countries).
6. They have better patient tolerance as well aspublic acceptance.

Natural polymer has some disadvantages.

They are as follows:

1. Microbial contamination.
2. Batch to batch variation.
3. Uncontrolled rate of hydration.
4. Reduced viscosity on storage.

1. Guar gum

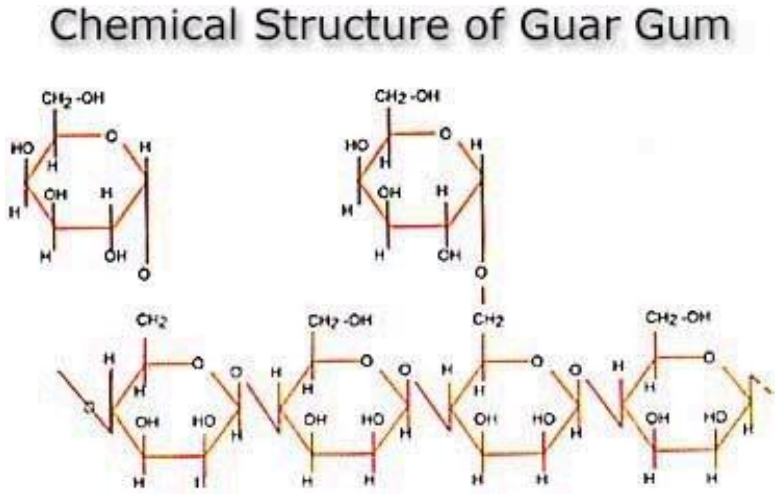
Guar gum is naturally occurring galactomannan polysaccharide. Guar gum has ability to hydrates rapidly and swells in cold water to attain uniform and high viscous colloidal dispersions at relatively low concentrations. This gelling property retard the drug release and make it a flexible carrier for extended release Dosage forms[31]. In pharmaceutical guar gum is used as disintegrants and as a polymer in floating drug delivery system.

Properties of guar gum

1. It is soluble in hot and cold water but insoluble in most organic solvents.
2. Strong hydrogen bond property.
3. Excellent thickening, emulsion, stabilizing and film forming property.
4. Ability to control rheology.

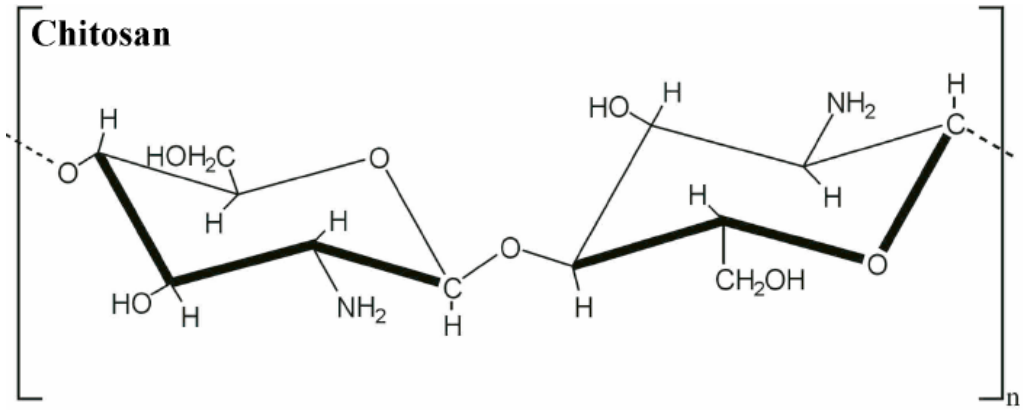
Advantages of guar gum in floating drug delivery system

It has been reported that polymer swelling play an important role to prolong gastric residence time and increase drug bioavailability. It was found that guar gum formulation were relatively insensitive to changes in stirring speed during in vitro drug dissolution testing and dissolution profile were not affected significantly[31].



2. Chitosan

Chitosan is natural and versatile polymer obtained by deacetylation of chitin. It has favourable biological properties such as nontoxic, biodegradable to normal body constituents, safe, haemostatic, anticancerogen, anticholesteremic, biocompatible. It is a bio adhesive polymer and have anti-bacterial properties thus make it suitable for site specific delivery[32]. Chitosan is high molecular weight polycationic weak base with pKa value of the D-glucosamine residue of about 6.2-7.0 and therefore, is insoluble a neutral and alkaine pH values. On addition to acidic pH of 1.2 it become buoyant in nature and provide control release. By increasing thickness of chitosan film release rate can be decreased.

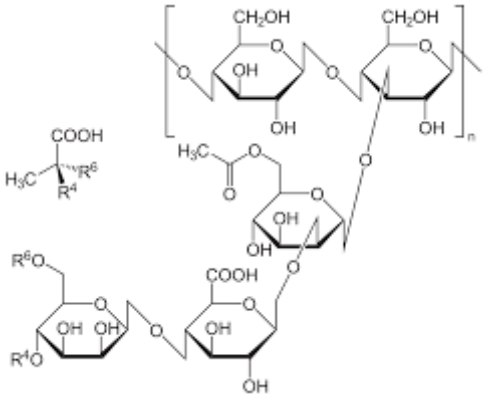


Advantages of chitosan

1. Chitosan granules and chitosan laminated preparations could be helpful in developing DDS that will reduce the effect of gastrointestinal transit time.
2. Most of the Hallow microcapsule tended to float on gastric fluid for more than 12hrs.
3. Release of drug followed zero order kinetics and controlled by both diffusion and erosion mechanism.[30]

3. Xanthum gum

Xanthan gum is a high molecular weight extracellular hetero-polysaccharide produced by pure culture aerobic fermentation of carbohydrate with bacterium *xanthomonas campestris*. Xanthan is a long chained polysaccharide with large number of trisaccharide side chains. Gum also has an excellent solubility and stability under acidic and alkaline conditions and in the presence of salts and resists common enzymes.[31]



Advantages of Xanthum gum

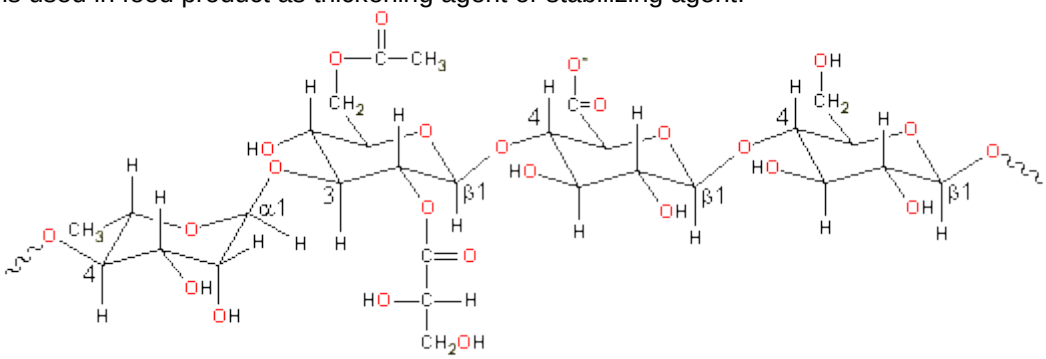
1. It is used to increase or decrease rate of release of drug from formulation.
2. Soluble in water.
3. High viscosity at low concentration.
4. It has potential advantage of drug release at zero order kinetics.
5. Some tablet containing xanthum gum and citric acid show buoyancy for more than 24hrs.

4. Gellan gum

Gellan gum is an anionic, high molecular weight, deacetylated extracellular linear polysaccharide comprising glucuronic acid, rhamnose and glucose. This gum has an outstanding flavour release, high gel strength, an excellent stability, process flexibility, high clarity, good film former and thermally reversible gel characteristics. Gellan gum is produced as a fermentation product from spingomonas elodea.[30]

Advantages of Gellan gum

1. It has excellent flavour release, high gel strength, and excellent stability.
2. It forms gel when positively charged ions are added.
3. It is used in food product as thickening agent or stabilizing agent.[34]



Structure of Gellan gum

5.Sodium alginate

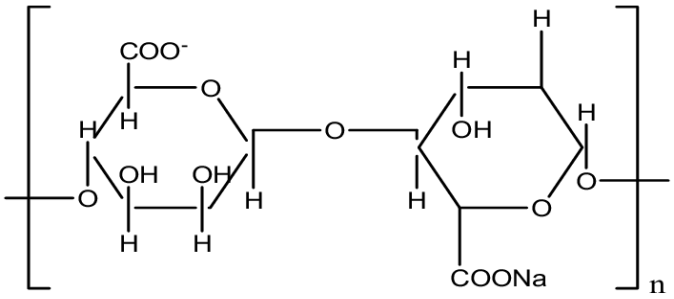
Sodium alginates have been used and investigated as stabilizers in emulsions, suspending agents, tablets binders and tablet disintegrants. Sodium alginate consists chiefly of the sodium salt of alginic acid, which is a mixture of polyuronic acids composed of residues of dmannuronic acid and L guluronic acid. The block structure and molecular weight of sodium alginate Samples have been investigated. [32]

Typical Properties

Acidity/alkalinity pH 7.2 (1% w/v aqueous solution).

Solubility: Practically insoluble in ethanol (95%), ether, chloroform, and ethanol/water mixtures in which the ethanol content is greater than 30%. Also, practically insoluble in other organic Solvents and aqueous acidic solutions in which the ph is less than 3. Slowly soluble in water, forming a viscous colloidal Solution.[34]

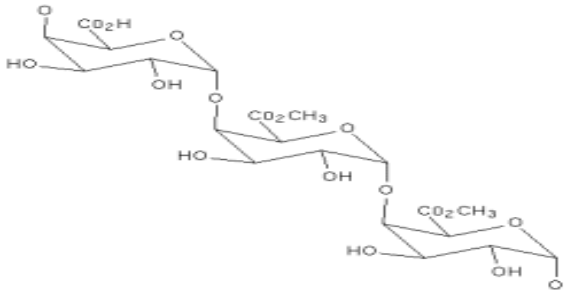
Viscosity (dynamic): Various grades of sodium alginate are commercially available that yield aqueous solutions of varying Viscosity. Typically, a 1% w/v aqueous solution, at 208C, will have a viscosity of 20–400mpa s (20–400cp). Viscosity may vary depending upon concentration, ph, temperature, or the Presence of metal ions. Above ph 10, viscosity decreases.[35]



Structure of sodium alginate [24]

Pectin

Pectin is non toxic and economic polysaccharide extracted from apple pomaces and citrus peels. Actually it is a D- galacturonic acid with 1-4linkages. [36]It is used as bulking agent,food additive and gelling agentdue the pectin ability to form gel based ondegree of esterification and molecular suze, it is alluring candidate for pharmaceutical care, for example, as a drug carrier for the controlled release application.[37]



Advantages of pectin

1. Pectin gel beads have been shown to be an effective medium for controlling the release of drug within GI tract.
2. Pectin are used as nutritional aspects as source of fibers, anticancer action, cholesterol regulation, prebiotics effect.

Synthetic polymers

Synthetic polymer are becoming increasingly important in pharmaceuticals. Use of synthetic polymer ranges from binder, film coating agent, etc. Polymer are macromolecule having very large, contain a variety of functional group. Synthetic polymers are either purely synthetic or they are modified form of natural polymer know as semi-synthetic.

List of synthetic polymer used is as follows:

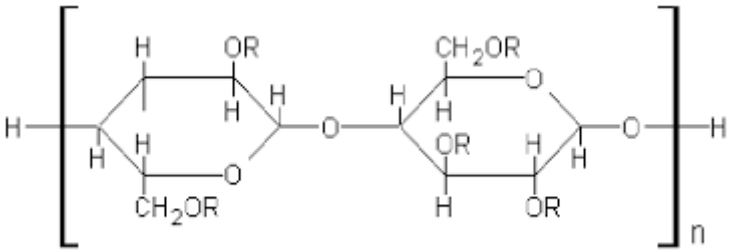
1. Hydroxy propyl methyl cellulose.
2. Eudragit.
3. Ethyl cellulose.

Disadvantages of synthetic polymer are as follows:

1. High cost toxicity environmental pollution.
2. Acute and chronic adverse effect.
3. Poor biocompatible.
4. Inflammatory response and local reaction.

1. Hydroxy propyl methyl cellulose

Hydroxy propyl methyl cellulose ethers belong to an extensive family of white to off-white, odourless, water soluble polymers that bind, retain water, thicken, form films, lubricate. It is a semi synthetic, inert, viscoelastic polymer, used as an excipient and controlled-delivery component in oral medicaments, found in a variety of commercial products. Synonym for hydroxypropyl methylcellulose (HPMC) is Hypromellose.



Properties

General properties common to the Hypremellose are listed below. Individual type exhibits these properties to varying degrees and may have additional properties that are desirable for specific applications.

1) Apparent density: 0.25~0.70g/cm 3.
2) The refractive index=1.336.
3) Surface tension: 42 to 56mn/m.
4) Solubility: dissolve in water and some solvent.

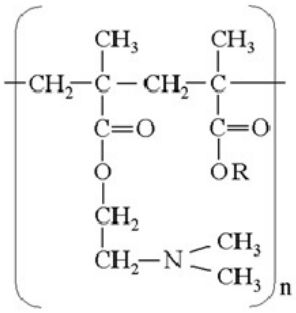
Advantages

1. Water soluble and most abundant polymer in nature.
2. Used as a thickener, film former and water retention agent.
3. Hydrophilic matrix is the simplest sustained release technology for oral dosage form.

2. Eudragit[38]

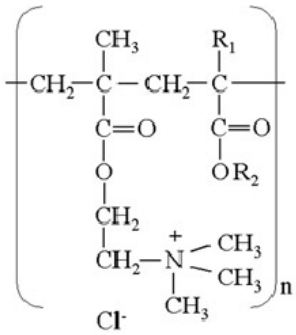
Polymethacrylates (Eudragit) are primarily used in oral capsule and tablet formulations as film-coating agents. Depending on the type of polymer used, films of different solubility characteristics can be produced. Soluble in gastric fluid below pH 5. Eudragit RL, RS, NE 30D, NE 40D, andNM30D are used to form water-insoluble film coats for sustainedrelease products. Eudragit RL films are more permeable than those of Eudragit RS, and films of varying permeability can be obtained by mixing the two types together. In contrast, Eudragit L, S and FS types are used as enteric coating agents because they are resistant to gastric fluid. Different types of enteric coatings are soluble at different pH values: e.g. Eudragit L is soluble at pH >6 whereas Eudragit S and FS are soluble at pH >7.Polymethacrylates are also used as binders in both aqueous and organic wet-granulation processes. Larger quantities (5–20%) of dry polymer are used to control the release of an active substance from a tablet matrix. Solid polymers may be used in direct compression processes in quantities of 10–50%. Polymethacrylates polymers may additionally be used to form the matrix layers of transdermal delivery systems and have also been used to prepare novel gel formulations for rectal administration.

EUDRAGIT E



$R = CH_3, C_4H_9$

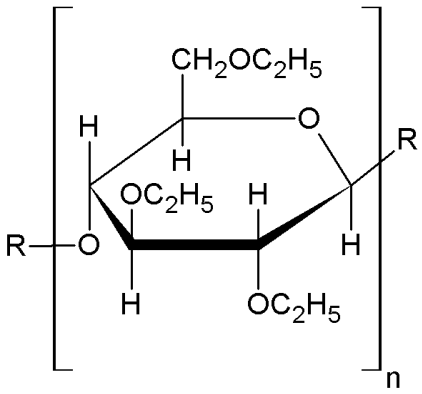
EUDRAGIT RL/RS



$R_1 = H, CH_3$
$R_2 = CH_3, C_2H_5$

3. Ethyl cellulose [33,39]

Ethocel (Ethyl cellulose polymers) has been widely used in the pharmaceutical industry for over 50 years. Ethyl cellulose has been used for choice in pharmaceutical formulations for various purposes, such as taste-masking of bitter actives, moisture protection, stabilizer, extended release multi particulate coating, micro-encapsulation of actives, extended release binder in inert matrix systems, solvent and extrusion granulation. Ethyl cellulose is an ideal polymer for the formation of products allowing modified drug release. It is insoluble at any pH that occurs in organism, but in the presence of the gastric Juice it undergoes swelling. This makes it suitable for improved patient compliance.
Several types of such Ethyl cellulose exist, e.g. Ethocel 4, Ethocel 10 and Ethocel 45, which differ in the length of the polymer chains.



CONCLUSION

Based on the literature, it may be concluded that drug absorption in the gastrointestinal tract is a highly variable process and prolonging gastric retention of the dosage form extends the time for drug absorption. Gastro retentive drug delivery systems have emerged as current approaches to prolong the continuous delivery of drug and improve the bioavailability of many drugs and enhancing bioavailability. Gastroretentive drug delivery approaches comprised mainly of floating, non floating, bioadhesive, swelling, high density systems etc. These systems not only provide controlled release of the drug but also present the drug in an absorbable form at the regions of optimal absorption. All these drug delivery systems have their own advantages and drawbacks. To design a successful GRDDS, it is necessary to take into consideration. GRDDS have multiple advantages that include greater flexibility and adaptability of dosage forms which give clinicians and pharmacists powerful tools to optimize pharmacotherapy. The increasing growth of delivery technology will ensure the development of increasing number of GRDDSs in order to optimize the delivery of drugs that exhibit narrow absorption window, low bioavailability and extensive first pass metabolism. The control of gastro intestinal transit could be the focus of the future studies and may result in new therapeutic capacities with considerable benefits for patient and hence it is very probable that these systems can gain popularity. To design a successful GRDDS, it is necessary to take into consideration.

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