Decent Approaches for Colon Targeted Drug Delivery System

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ABSTRACT

Targeted drug delivery leads to optimum therapy that meets the patient need by improving the safety and efficiency of the administered drug. Colon target drug delivery system has been gained great importance not only for the treatment of local diseases but also for the systemic delivery of proteins, therapeutic peptides, anti-asthmatic drugs, antihypertensive drugs and anti-diabetic agents. In order to overcome the upper GIT warriors different approaches have been given forward. By the implementation of these approaches the formulation acts a survivor in the upper GIT so as to get colon targeted drug delivery system. This review article discusses, in brief, introduction to targeted drug delivery system, anatomy and physiology of the colon and approaches utilized in the colon targeted drug delivery system.

Keywords: Colon specific drug delivery, Advantages, Approaches

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INTRODUCTION

The oral route of drug administration has been considered as the most convenient and preferred route (Anil K. Philip et al 2010), 50% of the drug delivery system available in the market are oral formulations (Akhil Gupta et al 2010). The oral route starts from the oral cavity to the rectum and anus (Nishant Singh et al 2012). Thus the administered drug passes through various regions (organ) that alter in the environment. Thus the administered drug faces a lot of warriors that leads to the undesirable effects. In order to overcome these problems the targeted drug delivery approach has been adopted.

Targeted drug delivery approach is a technique in which the physicochemical properties have been altered or appended with suitable site directing molecule by the virtue of which the drug recognizes the targeted receptor (S.P.Vyas et al 2002).
During the last decade there has been a great increase of interest in site specific formulations for targeting colon (Akhil Gupta et al 2010).Because colon is an perfect location for the delivery of drugs to cure local as well as systemic diseases (Nishant Singh et al 2012).

Table 1 : Targeting disease and site for colon

S.NO	Target Site	Disease Conditions
1	Topical action	Inflammatory Bowel Disease, Irritable bowel disease and Crohn's disease.
2	Systemic action	Nocturnal asthma, Angina, Arthiritis.

Advantages of colon drug delivery system (Nishant Singh et al 2012):

1> Reduces dosage frequency. Thus, lower cost of expensive drugs.
2> Possibility leading to a reduced incidence of side effects and drug interactions.
3> Extended daytime or nighttime activity.
4> It has a longer retention time thus enhances the absorption of poorly absorbed drugs.
5> Improve patient compliance.
6> Bypass initial first pass metabolism.
7> Reduces gastric irritation.
8> It has low hostile environment, less peptidase activity thus peptides, oral vaccines, insulin, growth hormones, can be given through this route.

Limitations of colon targeting drug delivery system (Nishant Singh et al 2012):

1> Multiple manufacturing steps.
2> Incomplete release rate.
3> The resident microflora could also affect colonic performance via metabolic degradation of the drug.
4> Non availability of an appropriate dissolution testing method to evaluate the dosage form in-vitro.
5> Bioavailability of drug may be low due to potentially binding of drug in a nonspecific way to dietary residues, mucus or fecal matter.

FACTORS TO CONSIDERSD DURING DESIGN OF COLON – SPECIFIC DRUG DELIVERY SYSTEM

In order to get a colon targeted drug delivery system it is essential to familiarize with the various factors that influences the targeted drug delivery. These factors are:-

(a) Anatomy and physiology of the colon.
(b) Parameters influencing bioavailability of drug in colon.

(a) Anatomy and physiology of the colon:

Colon has been considered as the BLACK BOX as most of the drugs are absorbed from the upper part of gastro intestinal tract. Gastrointestinal tract has been divided in to three major parts (Nishant Singh et al 2012):

(1) Stomach
(2) Small Intestine
(3) Large Intestine

Table 2 : Summary of anatomical and physiological features of small intestine and colon(Asha Patel et al 2011)

Region of Gastrointestinal Tract	Length (cm)	pH	Internal diameter (cm)
Stomach	-------	1.5(fastened) 2-5(fed)	-------
Small intestine Duodenum	20-30	6.1(fasted) 5.4(fed)	3.4
Jejunum	150-200	5.4	
Ileum	200-350	7.8	
Large intestine Cecum	6-7	5.5-7	6
Ascending colon	20		
Transverse colon	45		
Descending colon	30		
Sigmoid colon	40	7-8	
Rectum	12		
Anal canal	3		

The large intestine starts from the ileacecal junction to the anus, it includes three parts (Nishant Singh et al 2012): Colon, Rectum and Anus.

The colon is a cylindrical tube about 5 feet long and 2-3 inches in diameter (Asha Patel et al 2011) , it lacks villi but due to the presence of pilcae semilunares (cresetntic folds) it is about 1300 cm(2) in area. Colon has been divided in to five major segments(Sateesh Kumar Vermula et al 2009):-

(1) Caecum
(2) Ascending colon
(3) Transverse colon
(4) Descending colon
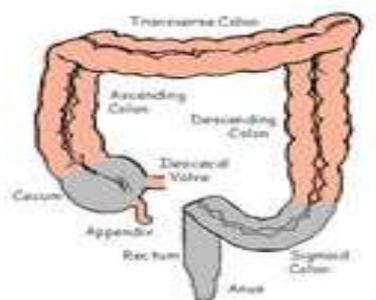(5) Sigmoid colon

Fig 1 : Segments of colon

Each segment is made up of four layers (Sateesh Kumar Vermula et al 2009):Serosa, Muscularis externa, Sub Mucosa and Mucosa.

Activity of colon can be divided in two types (Akhil Gupta et al 2010):-
        (1) Segmenting movement
        (2) Propulsive movement

(1)   Segmenting movement has been caused by circular muscle and causing the appearance of the sac like haustra, predominate and result in mixing of the luminal content.

(2)   Propulsive movement associated with deflection and affected by longitudinal muscle is less common and occurs at an average of three or four times daily.

(b) Factors influencing bioavailability of drug in colon: There are basically three factors influencing bioavailability of drug in colon. These are

Physiological parameters	Pharmaceutical parameters	Patient related parametrs
• Clonic microflora & enzymes • Drug stability • pKa value of drug, lipophilicity	• Drug candidate • Drug carrier	• Age • Gastric pH • Gastric emptying

1 Physicochemical parameters:

(a) pKa of the drug, lipophilicity and gastrointestinal pH: The pH partition explains the process of drug absorption from the GIT and its distribution across all biological membranes. The theory states that for drug molecules of molecular weight greater than 100, which are primarily transported across the biomembrane by passive diffusion, the process of absorption is governed by (D. M. Brahmankar et al 2009) :

(1) The dissociation constant (pKa) of the drug.
(2) The lipid solubility of unionized drug.
(3) The pH at the absorption site.

Since most of the drugs are weak electrolytes (weak acids or weak bases), their degree of ionization depends upon the pH of the biological fluid. If the pH on the either side of the membrane is different, then the compartment whose pH favors greater ionization of the drug will contain greater amount of drug, and only the unionized form of drug, if sufficiently lipid soluble, can permeate the membrane passively until the concentration of unionized drug on either side of the membrane becomes equal i.e. until equilibrium is attained.

The above statement of the hypothesis was based on the assumptions that:

(1) The GIT is a simple lipoidal barrier to the transport of drug.
(2) Larger the fraction of unionized drug, faster the absorption.

(b) Drug stability: A drug for oral use may destabilize either during its shelf life or in the GIT. Two major stability problems resulting in poor bioavailability of an orally administered drug are: Degradation of the drug into inactive form and Interaction with one or more different components either of the dosage form or those present in the GIT that form a complex which is poorly soluble or is unabsorbable.

(c) Colonic microflora and enzymes: The GIT contains a variety of microorganisms that participate in the metabolism of ingested material. The growth of the bacteria is regulated by gastric acids, peristaltic activity and microbial interaction including bacterial metabolic byproducts.

Table 3 Drug metabolizing enzymes in the human colon that catalyze reductive reaction:

Enzyme	Microorganism	Metabolic reaction catalysed
Nitroreductase	E.coli, Bacteroids	Reduced aromatic and heterocyclic nitro compounds
Azoreductase	Clostridia, Lactobacilli, E.coli	Reduced cleavage of azo compounds
N-oxide reductase, Sulfoxide reductase	E.coli	Reduced N-oxides and sulfoxides
Hydrogenase	Clostridia, Lactobacilli	Reduced carbonyl groups and aliphatic double bonds

Table 4 Drug metabolizing enzyme in the colon that catalyze hydrolytic reaction:-

Enzyme	Microorganism	Metabolic reaction catalyzed
Esterases and amidases	E.coli, P.vulgaris, B.subtilis, B.mycoides	Cleavage of esters or amidases of carboxylic acids
Glucosidase	Clostridia, Eubacteria	Cleavage of b-glycosidases of alcohols and phenols
Glucuronidase	E.coli, A.aerogenes	Cleavage of b-glycosidases of alcohols and phenols
Sulfatase	Eubacteria, Streptococci	Cleavage of O-sulfates and sulfamates

2   Pharmaceutical parameters:

(a) Drug candidate: Drugs which show poor absorption in the stomach and intestine are most suitable for colon delivery. Drugs such as theophylline, nifedipine, ibuprofen, diclofenac, metoprolol, dinitrate, isoosorbide, oxyprenolol and low molecular weight peptides and peptide like drugs have been shown to be effectively absorbed from the colon.

(b) Drug carrier:The selection of carrier for a particular drug candidate depends on the physicochemical nature of the drug as well as the disease for which the system is to be used. The factors such as chemical nature, stability and partition coefficient of drug and the type of absorption enhancers influences the carrier selection.

The carrier which contain additives like polymers my influence the release properties and efficacy of the system.

3:        Patient related parameters

(a) Gastric emptying : Apart from dissolution of a drug and its permeation through the biomembrane, the passage from the stomach to the intestine, called as gastric emptying. It can also be a rate-limiting step in drug absorption because the major site for drug absorption is intestine (colon).

A large number of factors influence gastric emptying are:-

   (1) Volume of meal
   (2) Composition of meal
   (3) Emotional state
   (4) Body posture

(b) Age:- In infants the gastric pH is high and intestinal surface and blood flow to the GIT is low resulting in altered absorption pattern in comparison to adults. In elderly persons, causes of impaired drug absorption include altered gastric emptying, decreased intestinal surface area and GI blood flow.

(c) Gastrointestinal pH: A tremendous 10^7 fold difference in the hydrogen ion concentration is observed between the gastric and colon fluids. The GI pH generally increases gradually as one move down the stomach to the colon and rectum This alteration in the pH leads to:-

   (1) Earlier disintegration

(2) Earlier dissolution

(3) Destalisation

Approaches for colon targeted drug delivery:- In order to overcome the warriors certain approaches have been adopted for colon targeted drug delivery system.

Table 5 : Various pharmaceutical approaches to colon targeted drug delivery systems.

S.NO	Approach	Basic features
1	**Covalent linkage of drug with carrier**	
1(a)	*Prodrug approach*	
1(a1)	Azo bond conjugate	The drug is conjugated with azo bond
1(a2)	Glycosiide conjugation	The drug is conjugated with glycoside
1(a3)	Cyclodetrin conjugation	The drug is conjugated with cyclodextrin
1(a4)	Dextran conjugation	The drug is conjugated with dextran
1(a5)	Amino acid conjugation	The drug is conjugated with amino acids
1(a6)	Polymeric prodrug	The drug is conjugated with polymer
1(a7)	Glucoronide conjugates	The drug is conjugated with glucurunates
2	**Approach to deliver the intact molecule to Colon**	
2(a)	*pH dependent approach*	
2(a1)	Coating of drug core with pH sensitive polymers	Formulation coated with enteric matrices releases drug when pH moves towards alkaline
2(a2)	Embedding in pH sensitive matrices	Degradation of the pH sensitive polymer in the GIT release the embedded drug
2(b)	*Time dependent delivery*	Drug after a lag time of 3-5 hours that is equivalent to small intestine transit Time
2(b1)	Pulsatile system	The barrier swells, erodes, or dissolves after a specific lag period that leads to subsequent release of drug
2(b2)	Pulniscap	Drug has been encapsulated in a capsular pulsatile system with polymeric plugs
2(b3)	Colon-targeted delivery capsule based on pH sensitive and time release principles	Drug core has been coated with outer pH dependent and inner pH independent coat

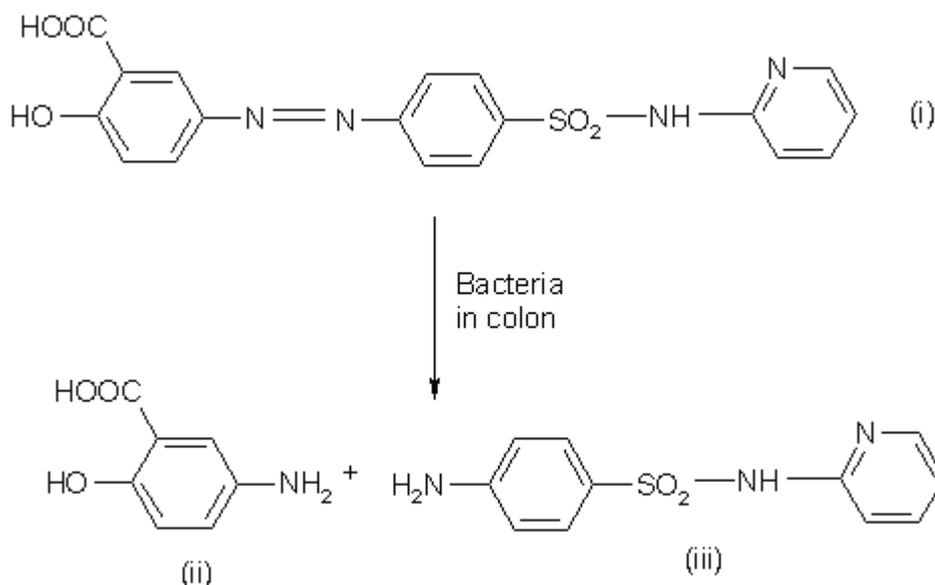| 2(c) | Microbially triggered drug delivery | Drugs are released following degradation of the polymer due to the action of colonic bacteria |
2(d)	Bioadhesive system	Drug coated with Bioadhesive polymer that selectively provides adhesion to the colonic mucosa and releases drug in the colon
2(e)	Pressure controlled system	Based on the strong peristaltic waves that lead to a temporary increase in luminal pressure in colon.
2(f)	Hydrogel approach	
2(g)	Osmotic controlled	Drug release through Semipermeable membrane due to osmotic pressure
2(g1)	Osmet pump	
2(g2)	OROS CT	
2(h)	Multiparticulate approach	Base on microparticles which are absorbed through macrophages present in colon and increase resident time of drug

1:- Covalent linkage of drug with carrier: It involves the formation of covalent linkage between drug and the carrier in such a manner that upon oral administration the moiety remains intact in the stomach and small intestine.

1(a) Prodrug approach :. A prodrug is a pharmacologically inactive derivative of the drug molecule that becomes active only after it is metabolized by the body (Nishant Singh et al 2012). Prodrug approach is an outcome of the covalent linkage of drug with carrier, thus upon oral administration the moiety remains intact in the stomach and small intestine but in the colon drug release is triggered by high activity of certain enzymes in comparison to stomach and small intestine (Nishant Singh et al 2012).

On the basis of functional group the prodrug approach can be attained by:- .

1(a1) Azo bond conjugate: In this approach drug has been conjugated by azo bond. These azo compounds are extensively metabolized by the intestinal bacteria, by intracellular enzymatic components and extracellular reduction. The azo bond is stable in the upper GIT and is cleaved in the colon by azo reductases produced by the microflora.

Sulphasalazine, used for the treatment of IBD has an azo bond between 5-ASA and sulphapyridine. In the colon, the azoreductases cleave the azo bond releasing the drug, 5-ASA and the carrier sulphapyridine(Asha Patel et al 2011) .

Hydrolysis of Sulphasalazine (i) into 5-aminosalicylic acid (ii) & sulfapyridine (iii)

1(a2) Glycosiide conjugation: This approach has been based upon the unique glycosidease activity of the colonic microflora. Certain drugs can be conjugated to different sugar moieties to form glycosides. The drug part forms aglycone and the sugar part forms glycone of the glycoside. These glycoside molecules are hydrophilic in nature thus these are impermeable to the biological membrane upon ingestion. They breakdown in to monomeric unit by the action of glycosidase enzyme, releasing the drug part from the sugar. However the presence of glycosidase activity in the small intestine could pose a problem in delivery of these conjugates to the large bowel but the transit time of the drug in small intestine, when compared to the large intestinal transit time, is short, and moreover, considering the time required for the hydrolysis of glycosidic bond, these conjugates can be expected to be good colon specific drug carriers(Asha Patel et al 2011).

The major glycosidase enzymes produced by the intestinal microflora are β - D-galactosidase, α -L-arabinofuranosidase, β -D-xylopyranosidase, and β –D glucosidase. These glycosidase enzymes are located at the brush border and hence are accessible to substrate easily (Asha Patel et al 2011).

Drugs that can be targeted by this approach are: lucosides, galactosides, and cellobiosides of dexamethasone, prednisolone, hydrocortisone, and fludrocortisone. Daxamethasone-21-β-glucoside (Asha Patel et al 2011).

1(a3) Cyclodetrin conjugation: This approach has been based upon the capability of Cyclodextrins to form inclusion complex with the drug, that improves certain properties of drugs such as solubility, stability and bioavailability. . Basically cyclodextrins are cyclic oligosaccharides consisted of six to eight glucose units through alpha -1,4 glucosidic bonds. The interior of these molecules is relatively lipophilic and the exterior relatively hydrophilic. By the virtue of which they are barely capable of being hydrolyzed and only slightly absorbed in passage through the stomach and small intestine however, Colonic bacteria are capable of degrading cyclodextrins for carbon source by stimulating cyclodextranase activity. They are fermented by the colonic microflora to form small saccharides that are then absorbed. The α and β-cyclodextrins are practically resistant to gastric acid, salivary, and pancreatic amylases. A clinical study has shown clear evidence that β-cyclodextrin is

poorly digested in the small intestine but is almost completely degraded by the colonic microflora(M.K.Chourasia et al 2002).

It leads to the synthesis of numerous formulations e.g. Ibuprofen prodrugs of α- , β-and γ-Cyclodextrins were investigated. Methotrexate prodrugs of α- and γ-Cyclodextrins were also synthesized and result established the primary aim of masking the ulcerogenic potential of free drug, by using 12-fold dose of the normal dose of methotrexate and equivalent doses of the esters(Asha Patel et al 2011).

1(a4) Dextran conjugation: This approach has been based upon polysaccharide nature of dextran that masks the drug in the upper GIT tract, the presence of dextranase in the colon leads to the delivery of drug to the colon. The dextranase activity is shown by anaerobic gram-negative bacteria, especially the Bacteroides, which are present in a concentration as high as 10^{11} per gram in colon. Dextran prodrug approach can be used for colon-specific delivery of drugs containing a carboxylic acid function (−COOH).NASIDS ware directly coupled to dextran by using carboxylic groups of drugs(Asha Patel et al 2011).

1(a5) Amino acid conjugation : This approach has been based upon the principle that the basic units of the amino acids i.e. -NH2 and –COOH are hydrophilic in nature, it reduces the membrane permeability of amino acids and proteins. Thus by increasing the hydrophilicity and chain length of the carrier amino acid and decreasing the membrane permeability of conjugate (M.K.Chourasia et al 2002).

1(a6) Polymeric prodrug : This approaches has been based upon the principle that polymers have been used as drug carriers for drug delivery to the colon. Both synthetic as well as naturally occurring polymers are used for this purpose. (Asha Patel et al 2011).

1(a7) Glucoronide conjugates: This approach has been based upon the conjugation of drug with glucuronats. The lower GIT secrete β-glucuronidase that deglucuronidate a variety of drugs in the intestine. This deglucuronidation process results in the release of the active drug again and enables its reabsorption (M.K.Chourasia et al 2002). 2 Approach to deliver the intact molecule to colon : In this case the drug molecule has been delivered in the active. The basic strategy used in this case is the usage of the targeting carrier in the delivery system. These basic techniques under this approach are:-

2(a) *pH dependent approach* : This approach has been based upon the fact that there is variation of pH gradient in the entire GIT that increases progressively from the stomach (pH 1.5-3.5) and small intestine (5.5-6.8) to the colon (6.4-7.0) (Asha Patel et al 2011). pH sensitive polymers, especially with carboxyl group have been employed in colon targeting because they are insoluble at low pH but soluble at high pH value.

Table 6 Various pH dependent coating polymers (Kothawade P.D et al 2011)

Polymer	Threshold pH
Eudragit L 100	6.0
Eudragit S 100	7.0
Eudragit L-30D	5.6
Eudragit FS 30D	6.8
Eudragit L 100-55	5.5
Hydroxy propyl methylcellulose Phthalate	4.5-4.8
Hydroxy propyl methylcellulose Phthalate 50	5.2
Hydroxy propyl methylcellulose Phthalate 55	5.4
Cellulose acetate trimellate	5.0
Cellulose acetate Phthalate	4.8

2(b) *Time dependent delivery* : This approach has been based on the transit time of the drug in the different regions of GIT. It involves delaying the release of the drug until it enters into the colon. The lag time in this case is the time requires to transit from the mouth to colon. A lag-time of 5 hours is usually considered sufficient since small intestine transit is about 3-4 hours, which is relatively constant and hardly affected by the nature of formulation administered. However this system has some disadvantages as follows :

1- Gastric emptying time varies markedly between subjects or in a manner dependent on type and amount of food intake.

2- Gastrointestinal movement, especially peristalsis or contraction in the stomach would result in change in gastrointestinal transit of the drug.

3- Accelerated transit through different regions of the colon has been observed in patients with the IBD, the carcinoid syndrome and diarrhea and the ulcerative colitis (Asha Patel et al 2011). Thus to overcome this problem certain integration of pH sensitive and time release functions into a single dosage have been carried out for colon targeting.

(a) Press-coated or multilayered approach: In this case there is either expansion of core, swelling, disruption or erosion of coat that leads to the colon delivery of the drug .
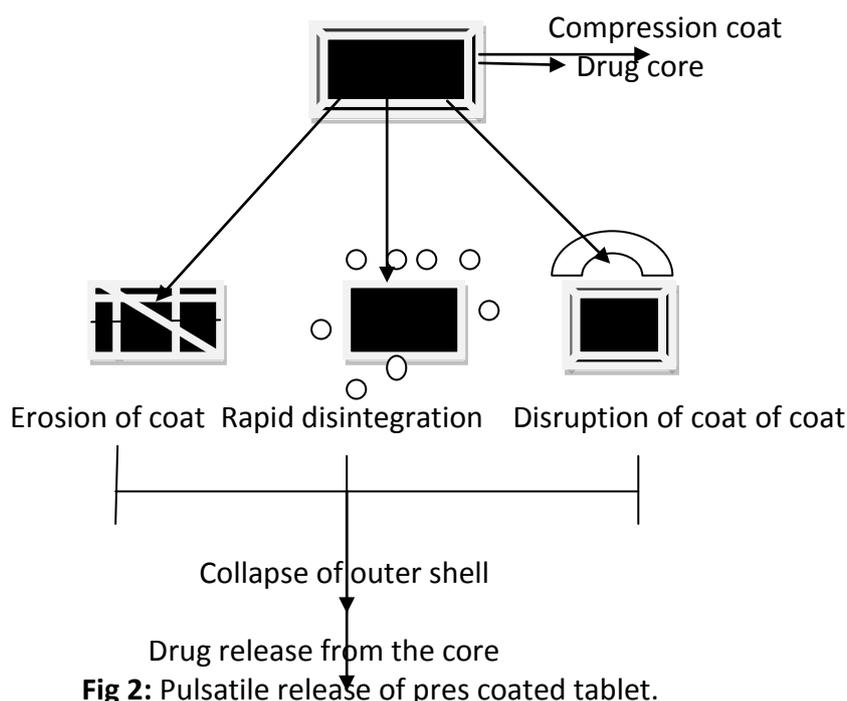
Fig 2: Pulsatile release of pres coated tablet.

Hydrophilic sandwich capsule: In this case the inter-capsule space has been filled with a layer of hydrophilic polymer (HPMC). This effectively creates a hydrophilic sandwich that forms a gel barrier layer which lead to time delay before fluid could enter the inner capsule and cause drug release.

Chonotropic system: It consist of a drug- containing core coated with high viscosity HPMC, it leads to lag phase in the onset of release.

2(c)Microbially triggered drug delivery : This approach has been based upon the fact that there is the presence of biodegradable enzyme in the colon that have been produced by colonic microflora. The microflora in the colon lies in the range of 10(11)-10(12) CFU/ml that consist of mainly anaerobic bacteria e.g. bacteroides, bifidobacteria, eubacteria, etc. Thus by using the biodegradable polymers the colon targeting can be carried out(Gurmeet Singh et al 2012).

Table 7: Various biodegradable polymers used for colon targeting are

S.NO	Class	Examples
1	Disaccharides	Lactose
		Maltose
2	Oligosaccharides	Cellulose
		Cyclodextrins
		Raffinose
		Lactulose
3	Polysaccharides	Alginates
		Amylose
		Chitosan
		Cellulose
		Dextran

2(d) Bioadhesive system: This approach has been based upon principle of adhesion between drug and the biological membrane by the virtue of which the drug molecule remains in contact with particular organ for an augmented period of time. It leads to longer residence time of the drug molecule it tends to high local concentration. This strategy can be applied to colon target delivery system. Various polymers employed for bioadhesive system are polycarbophils, polyurethanes, polyethylene oxide and polypropylene oxide(Akhil Gupta et al 2010).

1-   *2(e) Pressure controlled system:* This approach relies on the strong peristaltic waves in the colon that lead to a temporarily increased luminal pressure. Takaya et al.(1995) have developed pressure controlled colon delivery capsules by using water insoluble polymer ethyl cellulose. The release of drug occurs following disintegration of water soluble polymer capsule as a result of pressure in the lumen of colon(Asha Patel et al 2011).
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2(f) Hydrogel approach:- Hydrogel specially based upon polysaccharides, have attracted a considerable attention as an excellent candidate for controlled release as well as targetable devices. The release of the drugs from hydrogels was determined by swelling extent, the swelling extent has been based upon the composition and pH of the surrounding medium (Tarak Jayraj Mehta et al 2011).
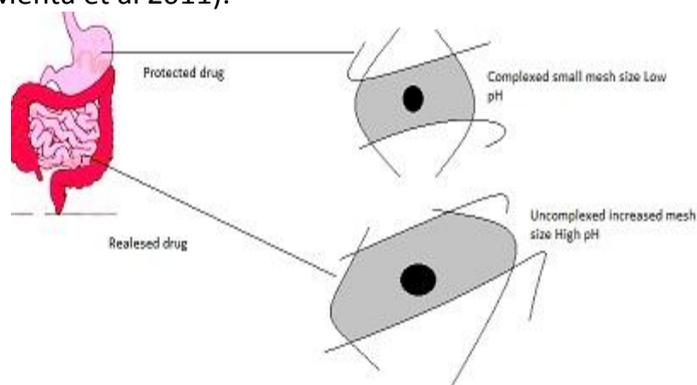

Fig 3: Drug complexed with hydrogel

The swelling of hydrogels increases at higher pH it leads to increase in amount of drug release. At lower pH –CONH2 group remains ionized it keeps the polymeric network at its collapsed state but at higher pH has been partially ionized that leads to formation of repulsive COO groups these repels each other by the virtue of this there is increase in swelling extent it results in more drug release. It leads to colon targeted drug delivery(Tarak Jayraj Mehta et al 2011).

 2(g) Osmotic controlled:- As the name indicates this approach has been based upon variation in the osmotic pressure by the virtue of this the release of drug from the formulation takes place. The osmotically controlled drug delivery system can be used to target the drug locally or systemically. There are basically two types of formulation that operate under osmotic pressure principle(D. M. Brahmankar et al 2009):-

2(g1) Osmet pump:- It is basically composed of enteric coated semipermeable, rigid shell, possessing an osmotic layer along with central impermeable and collapsible reservoir filled with drug. The water penetrate through the semipermeable membrane it leads to increase in pressure inside the device. As a result, the inner reservoir shrinks and the formulation is pumped at a constant rate via shell opening(D. M. Brahmankar et al 2009).

2(g2) OROS CT:- This system basically consist of a tablet with enteric coating by the virtue of it there is a delayed drug release. The OROS-CT system either comprises a single osmotic unit or may incorporate as many as 5-6 push-pull units, each 4mm in diameter, encapsulated within a hard gelatin capsule. Upon ingestion the hard gelatin shell dissolves the enteric coating delay the drug release from the device during its transit through the stomach. Upon arrival on the small intestine the coating dissolves at pH>7(K.V. Vinay Kumar). As a result water enters the unit causing the osmotic push compartment to swell forcing the drug out of the orifice into colon**(**Kothawade P.D et al 2011)
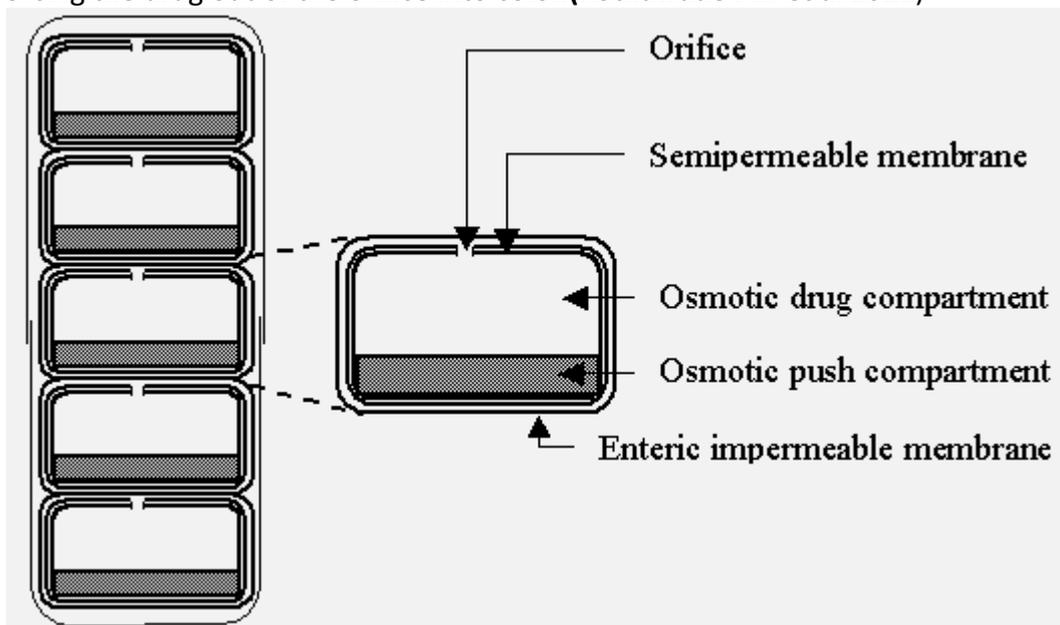

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Fig 4 Cross section of the OROS-CT colon targeted drug delivery system (Anil K. Philip et al 2010) .

2(h) Multiparticulate approach:- This approach has been adopted to devoid the danger of alteration in the drug release profile and formulation behavior due to unit to unit variation, change in the gastro luminal pH and enzyme population. Multiparticulate approach leads to better pharmacological effect in the colon thus much emphasis has been laid on the development of multiparticulate dosage forms in comparison to single unit systems. Multi-particulate drug delivery systems is basically an oral dosage forms consisting of a multiple small discrete units, each posses the desired characteristics, i.e. the dosage of the drug substances has been divided in a plurality of subunit, typically consisting of thousands of spherical particles with diameter of 0.05-2.00mm. Thus multiparticulate dosage forms are pharmaceutical formulations in which the active substance is present as a number of small independent subunits (Vibhav Patel et al 2012) .

Table 8: Different multiparticulate approaches(Vibhav Patel et al 2012)

S.NO	Approach
1	Intestinal Protective Drug Absorption System
2	Programmable Oral Drug Absorption System
3	Stabilized Pellet Delivery System
4	Minitabs
5	Multiparticle Drug Dispersing Shuttle
6	Delayed release oral polypeptides
7	Multiparticulate crystalline drug

	Compositions
8	Spheroidal oral drug absorption Systems
9	Diffucaps
10	Pelletized Delivery System
11	Pelletized tablet
12	Layering process for multiparticulate dosage form
13	Multiparticulate mucoadhesive Formulations
14	Multiparticulate as NDDS

CONCLUSION

The discovery of novel drug delivery system brings the green revolution in colon targeting. It lights up the black box by curing diseases either by virtue of local absorption or systemic absorption. Successful colonic delivery could be achieved by protecting the drug from the upper GIT warriors. Various approaches have been designed for colonic drug delivery among these microbial triggered drug delivery appears more promising since there is an increased amount of bacterial population and associated enzyme activity in the colon represent a non-continuous event, independent of GI transit time.

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