



REVIEW ON COLON TARGETED DRUG DELIVERY SYSTEM AND ITS APPROACHES

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ABSTRACT

Colon-targeted drug delivery systems have gained significant attention as a promising approach to enhance the therapeutic efficacy of drugs for the treatment of various gastrointestinal disorders. These systems aim to deliver drugs specifically to the colon, thereby improving drug localization, reducing systemic side effects, and increasing patient compliance. Although the oral route is thought to be the most preferred method for administering drugs with a systemic effect, it is not recommended for administering drugs for lower gastrointestinal (GI) diseases because these medications release at the upper GI tract (stomach, small intestine), which further reduces their accessibility at the lower GI tract. The review begins by discussing the physiological considerations of the colon, including its anatomy, pH, enzymes, and transit time, which influence drug delivery to this region. Various approaches for colontargeting are then presented, including pH-dependent systems, time-dependent systems, microbially triggered systems, prodrug approach to drug delivery to colon. It also consists of novel approaches of colon targeted drug delivery such as pressure Controlled drug delivery system, Osmotic controlled drug delivery (OROS-CT), CODES technology, Port System, Pulsin Cap system, Microspheres and Mucoadhesive approach. Moreover, the applications of colon-targeted drug delivery systems in the treatment of various diseases, such as inflammatory bowel disease, colorectal cancer, and irritable bowel syndrome, are explored.

Key words: Colon-targeted drug delivery systems, upper GI tract, Novel approaches, OROS-CT, CODES, inflammatory bowel disease, colorectal cancer

INTRODUCTION

Targeted drug administration into the colon is considered highly desirable for the local treatment of a number of bowel disorders, including ulcerative colitis, Crohn's disease, amebiasis, colonic cancer, the local treatment of colonic pathologies, and the systemic distribution of protein and peptide drugs. The colon-specific drug delivery system (CDDS) must be able to protect the drug while it is being delivered to the colon, which means that neither drug release nor absorption should take place in the stomach or small intestine, nor should the bioactive agent be degraded there. Instead, the drug should only be released and absorbed once the system reaches the colon.

For the following reasons, it is thought that the colon is an ideal location for the absorption of peptide and protein drugs: (i) the diversity and intensity; and (ii) the colon's mucosa has significantly lower proteolytic activity than that of the small intestine, so CDDS protects peptide drugs from hydrolysis and enzymatic degradation in the duodenum and jejunum before releasing the drug into the ileum or colon, increasing systemic bioavailability. And finally due to the colon's prolonged residence time (up to 5 days) and high responsiveness to absorption enhancers.

Oral route is the most convenient and preferred route but other routes for CDDS may be used. When administering medications directly to the colon, rectal administration is the most rapid method. Rectal administration makes it difficult to reach the proximal portion of the colon. Rectal administration may also cause patients discomfort. Solutions, foam, and suppositories are the drug administration preparations available for intrarectal delivery. Both systemic dosage and the delivery of topically active medications to the large intestine use the intrarectal route. For the treatment of ulcerative colitis, corticosteroids like hydrocortisone and prednisolone are delivered through the rectum.

In the stomach's acidic environment and in the presence of pancreatic enzyme, the proteins and peptides in drugs become inactive and are destroyed.

There are around 400 different types of bacteria that live in the human colon, with up to 10¹⁰ bacteria per gram of colonic contents. These gut bacteria also break down glycosides through enzymatic cleavage and azoreduction. These metabolic pathways may be in charge of how many drugs are metabolised. They may also be used to target the colon for oral administration of peptide-based macromolecules like insulin.

The targeted delivery of drugs into the colon is necessary because of the significant bacteria present there, including Bacteroides, Bifidobacterium, Eubacterium, Peptococcus, Lactobacillus, and Clostridium. Release a wide variety of reductive and hydrolytic enzymes, including urea hydroxylase, nitroreductase, xylosidase, galactosidase, and arabinosides. Degradation of di, tri, and polysaccharides is carried out by these enzymes.

ADVANTAGES

- The localised treatment of numerous colonic disorders (ulcerative colitis, crohn's disease, carcinomas, and infections) by site-specific administration of drugs to the lower region of the GIT.
- Used to extend medication therapy and pharmacological activity
- Used to ensure direct treatment at the site of the disease
- Prevent drug from degradation, Improved drug utilisation, Reduced dose
- Fewer systemic negative effects
- Avoidance of hepatic first pass metabolism
- Minimising mucosal irritability
- Less frequent dosing, resulting in cost-effectiveness
- Longer daytime or night time activity
- The colon is a site for both local and systemic drug delivery; local delivery enables topical treatment of inflammatory bowel disease.
- The colon's long retention time improves the bioavailability of poorly absorbed drug molecules (up to 5 days).

DISADVANTAGES

- Drugs with a longer residence time of 3-5 days have higher plasma levels and, as a result, greater bioavailability in general, but particularly for those that are substrates for this kind of enzyme.
- One drawback of single unit colon focused drug delivery systems is unintended formulation breakdown brought on by manufacturing flaws or atypical gastric physiology.
- Drug and polymer stability issues brought on by pH and enzyme activity differences.
- The amount of food consumed can affect the gastric emptying time.
- The colon's small luminal surface area and relative tightness of the tight connections cause the systemic absorption to be delayed.

ANATOMY OF COLON

The alimentary canal, its auxiliary organs, and various digestive processes are together referred to as the digestive system. Beginning at the mouth and continuing through the thorax, abdomen, and pelvis, the alimentary canal ends at the anus. The GIT is divided into stomach, small intestine and large intestine. There are three major sections of the large intestine, which runs from the ileocaecal junction to the anus. These are the rectum, the anal canal, and the colon. The colon itself is made up of the caecum, the ascending colon, the hepatic flexure, the transverse colon, the splenic flexure, the descending and the sigmoid colon.

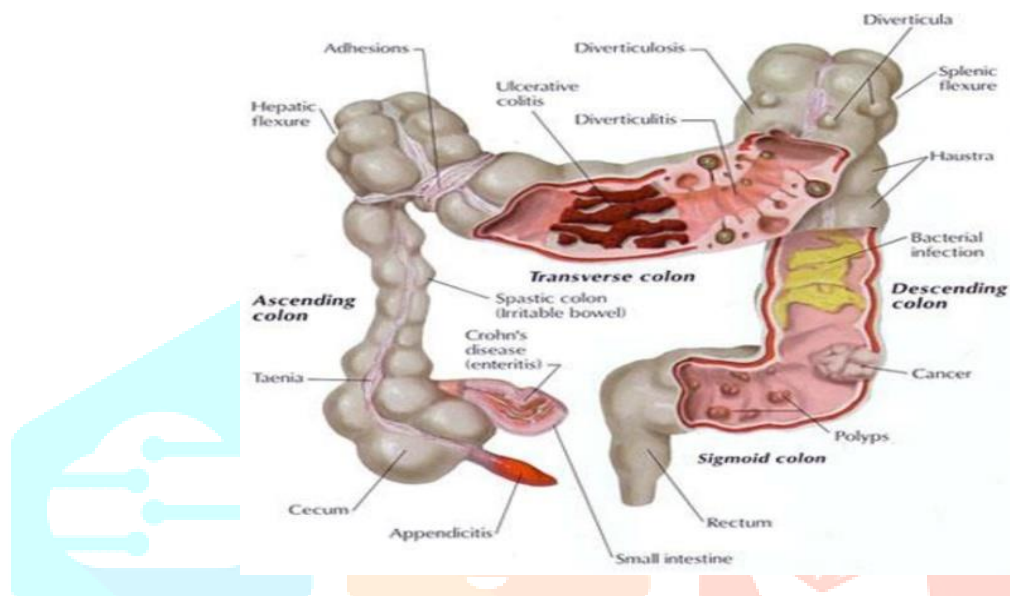


Fig: Structure of Colon

Ascending Colon-It is nearly 12.5cm, in length. It extends from the caecum to the hepatic flexure.

Transverse Colon- The ascending colon further continues as the transverse colon, from the hepatic flexure to the splenic future

Descending Colon- The transverse Colon descends down to form the descending colon. It begins at the splenic mixture and terminates at the beginning of the sigmoid colon

Sigmoid Colon- The descending colon continue as an S-Shaped Sigmoid colon, terminating at the rectum.

The serosa (external coat), muscularis externa, submucosa, and mucosa are the four layers that make up the colon wall. The mucosa, which lines the colon's lumen, is made up of three layers: epithelium, lamina propria, and muscularis mucosa. The superior mesenteric artery provides the proximal colon with arterial blood, while the distal colon receives its supply from the inferior mesenteric artery.

FUNCTIONS OF COLON

- The process of converting intestinal contents into faeces by absorbing water and electrolytes and holding on to the faeces until they are expelled from the body.
- To provide an environment that is suited for the development of colonic microbes.
- Secretion of K^+ and HCO_3^- as well as the absorption of H_2O and Na^+ from the lumen.

FACTOR AFFECTING COLON TARGETED DRUG DELIVERY SYSTEM

The factors that affect the Colon targeting are categorized in two categories:-

- Physiological factors
- Pharmaceutical factors

1. PHYSIOLOGICAL FACTORS: The following factors affect drug targeting to the colon and are physiologically involved in drug delivery:

Colonic pH: The pH of the Gastrointestinal tract is subjected to both inter and intra subject variation. This GIT pH fluctuation has been used to deliver drugs to specific areas of the colon, and it is impacted by things including nutrition, illness severity, and food consumption. Fall in pH entering the colon due to short chain fatty acid content (bacterial fermentation of poly saccharides).

Gastric emptying: After oral administration, the key factors influencing drug delivery to the colon are gastric emptying and bowel transit time, i.e., once the medication reaches the colon, the transit time of the drug is influenced by the type and size of the particles. The transit time of larger particles is shorter than that of smaller particles.

Region of Gastro intestinal Tract		Transit Time(Hrs)	Length (cm)	pH	Internal diameter (cm)
Stomach	---	<1 (Fasting) >3 (Fed)	1.5-3 (fasted) 2-5 (fed)	1-3	---
Small intestine	Duodenum	3-4	20-30	6.1(fasted) 5.4(fed)	3-4
	Jejunum		150-200	5.4	
	Ileum		200-350	7-8	
Large intestine	Cecum	20-30	6-7	5.5-7	6-7.5
	Ascending colon		20	---	
	Transverse colon		45	---	
	Descending colon		30	---	
	Sigmoid colon		40	7-8	
	Rectum		12	---	

Table: Anatomical and physiological features of small intestine and colon

Colonic Micro Flora and their Enzyme: Around 400 different bacterial species, with a concentration of 10^{11} – 10^{12} CFU/ml, have been identified in the colon, 20–30% of which are members of the genus Bacteroides. The intestinal tract has a bacterial count of 0-10³ CFU/ml, the jejunum has a count of 0-10⁵ CFU/ml, and the ileum has a count of 10³-10⁷ CFU/ml. A wide range of microorganisms in the gastrointestinal tract produce numerous enzymes required for metabolism. The GIT Contentment and peristaltic motions regulate the growth of this microflora. The many metabolic reactions that occur in the GIT are caused by the enzymes secreted by various microorganisms, including E. coli, Clostridia, Lactobacilli, Eubacteria, and Streptococci.

Enzymes	Microorganism	Metabolic reaction catalyzed
Nitroreductase	<i>E. coli</i> , Bacteroides	Reduce aromatic and heterocyclic nitro compounds
Azoreductase	Clostridia, Lactobacilli, <i>E. coli</i>	Reductive cleavage of azo compounds
Esterase and amidases	<i>E. coli</i> , <i>P. vulgaris</i> , <i>B. subtilis</i> , <i>B. mycooides</i>	Cleavage of esters or amidases of carboxylic acids
Glycosidase	Clostridia, Eubacterium	Cleavage of β -glycosidase of alcohols and phenols
Glucuronidase	<i>E. coli</i> , <i>A. aerogenes</i>	Cleavage of β -glucuronidases of alcohols and phenols

Fig: Different micro flora, enzymes released and action

Colonic Absorption: In comparison to the small intestine, the colon has a substantially smaller surface area. About 10 to 24 hours are spent in the colon. There are two different types of the colon's absorption mechanism.

- i. Transcellular transport (passing through colonocytes)
- ii. Paracellular transport (passing through adjacent colonocyte)

Transport of water, electrolytes, and ammonia across the mucosa has an impact on absorption. The use of absorption enhancers improves the drug's absorption in the colon and demonstrates efficient absorption through a variety of membranes.

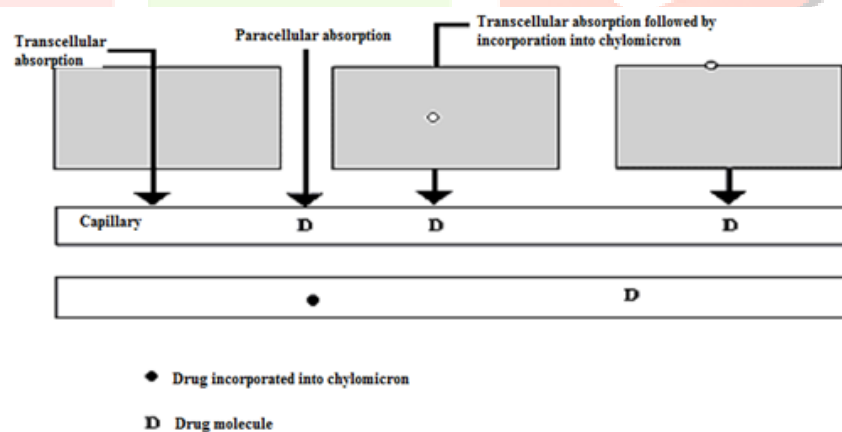


Fig: Primary routes of drugs absorption from the gastrointestinal tract

2. PHARMACEUTICAL FACTORS

Drug Candidates: The most suitable drugs for CDDS are peptide and other drugs that exhibit low absorption from the stomach or intestine. Drugs used to treat colon cancer, IBD, ulcerative colitis, and diarrhoea are ideal options for local colon administration. Colon's long retention time increases the absorption of poorly absorbed agents because it has a longer retention time.

Drug Carriers: The choice of carrier depends on the drug's physicochemical character as well as the condition that will be treated. The drug's chemical nature, stability, partition coefficient, and the kind of absorption enhancers used all have an impact on the carrier choice.

APPROACHES USED FOR COLON TARGETING

1. Primary approaches of colon specific drug delivery
 - a) PH Sensitive polymer coated drug delivery system.
 - b) Delayed (Time Controlled release System) release drug delivery system.
 - c) Microbial triggered system
2. Newly developed approaches for CDDS
 - a) Pressure Controlled drug – delivery system.
 - b) Osmotic controlled drug delivery (OROS-CT)
 - c) CODES technology
 - d) Pulsin Cap system
 - e) Port System
 - f) Microspheres
 - g) Mucoadhesive approach

1. PRIMARY APPROACHES OF COLON SPECIFIC DRUG DELIVERY

pH Sensitive Polymer Coated Drug Delivery to Colon

In the above technique, the dosage form (such as tablets or pellets) is coated with different pH sensitive polymers to provide a delayed release formulation and shield it from the upper gastrointestinal tract.

Throughout the whole GI transit, the pH ranges from 1 to 8, and it notably decreases from the ileum to the colon. The pH of the human digestive tract rises gradually starting in the stomach (pH 1-2, which rises to 4 during digestion), then moves to the small intestine (pH 6-7), where digestion takes place, and finally reaches pH 7-8 in the distal ileum. In low pH, pH sensitive polymers are insoluble, and in high pH, they become progressively soluble.

Example: Eudragit S and Eudragit L.

There are some issues with this strategy:

- Gastrointestinal pH varies across and among individuals, and it is influenced by diet and medical conditions.
- Lack of site-specificity (starts dissolving even in the lower small intestine)

The tablets, capsules, or pellets are coated with pH-sensitive polymers to delay release and shield the active ingredient from stomach acid. The most common ways involve employing either natural or synthetic polymer to cover the composition. With this technique, the medicine is placed in the formulation's central portion, which is covered in a pH-sensitive polymer. The core of the

formulation is made up of the API and excipients. The initial coating is an acid soluble polymer, while the outer coating is an enteric polymer.

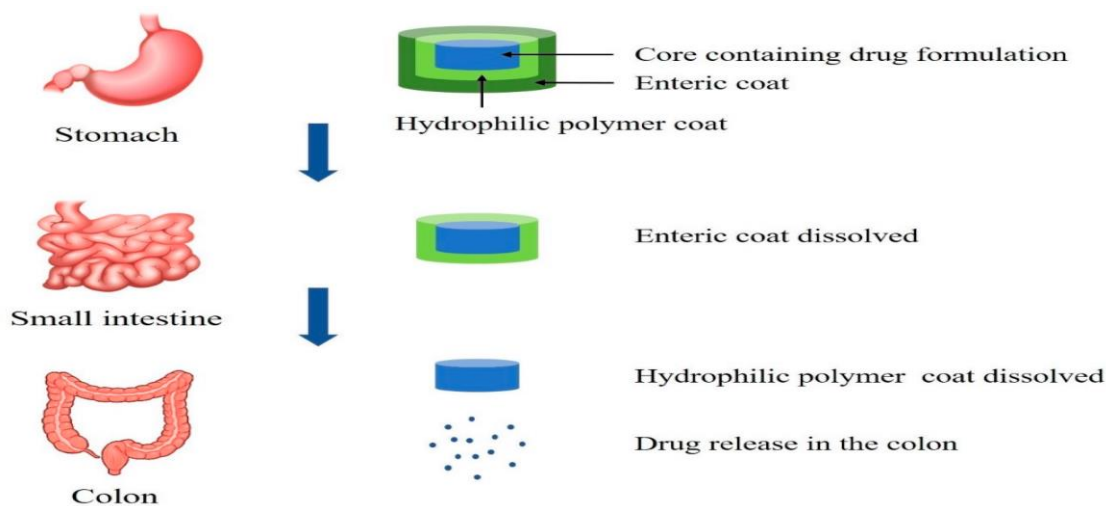


Fig: pH-sensitive polymer coated drug delivery

Delayed (Time Controlled Release System) Release Drug Delivery to Colon

The basis of time - controlled release system formulation is the medicine released in the colon after a predetermined period of time. It can take between 3 and 4 hours, depending on how long it takes to travel through the small intestine. The amount of time it takes for the stomach to empty varies from person to person and is also affected by the amount of food consumed.

A tablet-based delivery device with a time-dependent explosion mechanism that could deliver the medication reliably to the colon. Three elements make up the formulation: (i) a central core that includes the medication and excipients that cause edoema (ii) an inner semi-permeable polymer membrane with a plasticizer that permits influx of water but restricts drug diffusion outward; (iii) an exterior enteric coating that dissolves at or above pH 5.5. The outer enteric coating layer of the tablets resists acid, preventing the medicine from being released in the stomach. Intestinal fluid starts to gradually erode the press coated polymer (HPC) layer after gastric emptying causes the enteric coating layer to quickly dissolve. Since there is no drug release period (lag phase) following gastric emptying, the erosion process takes a lengthy time when it reaches the core tablet, resulting in quick drug release. Depending on the weight or composition of the polymer (HPC) layer, the length of the lag phase is determined.

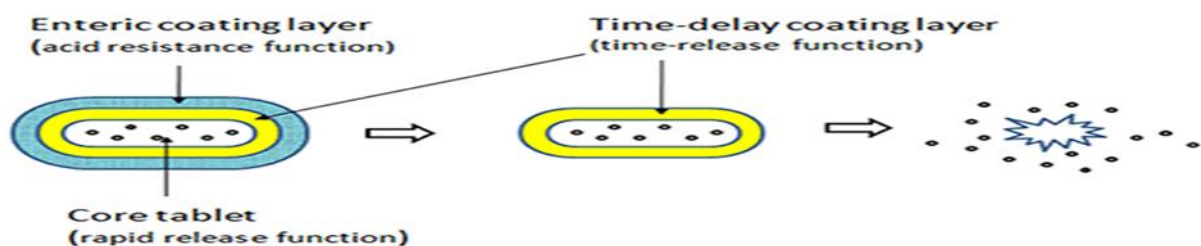


Fig: Time controlled release system

Microbially Triggered Drug Delivery to Colon

These systems work by utilising the unique enzymatic activity of the colon's microflora (enterobacteria). The colonic bacteria are primarily anaerobic in nature and release enzymes that can metabolise substrates including carbohydrates and proteins that evade digestion in the upper GIT.

This method is based on the microflora in the colon degrading the biodegradable polymer coated on the dosage forms. Microorganisms are abundant in the colon. The colon's microflora is composed primarily of anaerobic bacteria, such as Bacteroides, bi-fido bacteria, eubacteria, clostridia, enterococci, enterobacteria, and ruminococcus, and is in the range of 10^{11} - 10^{12} CFU/mL. Various substrates, such as di- and tri-saccharides, polysaccharides, etc., that have been left undigested in the small intestine are fermented by this massive microflora to meet its energy requirements. Numerous enzymes, including glucuronidase, xylosidase, arabinosidase, galactosidase, nitroreductase, azareducataase, deaminase, and urea dehydroxylase, are produced by the microflora for this fermentation. The use of biodegradable polymers for colon-specific medication administration appears to be a more site-specific method as opposed to other approaches because the biodegradable enzymes are only present in the colon. These polymers are able to transport the medicine to the colon while protecting it from the stomach and small intestine environments. When they get to the colon, they are absorbed by microorganisms, degrade by enzymes, or have the polymer backbone broken down, which causes their molecular weight to drop and their mechanical strength to decrease. The drug entity is then released from their control.

- **Prodrug Approach For Drug Delivery To Colon**

Prodrug design frequently entails a general chemical strategy to cover up undesirable drug features such limited bioavailability, reduced site specificity, and chemical instability. Prodrugs that target a particular membrane transporter, an enzyme, or both have the potential to be a drug delivery mechanism, particularly for colon cancer chemotherapy.

Sulphasalazine, for instance, is used to treat Crohn's disease and ulcerative colitis.

The prodrug is intended for enzymatic hydrolysis in the colon, which releases the active drug moiety from the drug carrier, and minimum hydrolysis in the upper tracts of the GIT for colonic delivery. One of the most thoroughly investigated bacterial metabolic processes is the digestion of azo compounds by gut bacteria. There are also additional links that can be produced where the medicine is connected to hydrophobic molecules such amino acids, glucuronic acids, glucose, galactose, cellulose, etc. and are sensitive to bacterial hydrolysis, particularly in the colon.

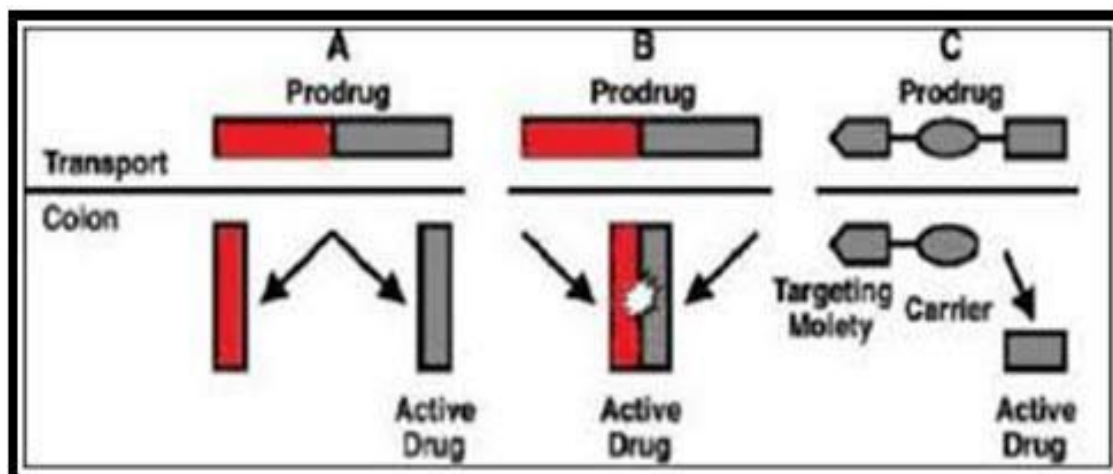


Fig: Prodrug approach

- **Azo-Polymeric Prodrug**

The use of polymers as drug carriers for drug delivery to the colon is the focus of more recent methods. For this reason, polymers that are both artificial and naturally occurring have been employed. To create polymeric prodrugs with azo linkage connecting the polymer and drug moiety, sub-synthetic polymers have been employed. For CDDS, these have been examined. As coating materials over drug cores, various azo polymers have also been investigated. These have been discovered to be equally vulnerable to cleavage by the large bowel enzyme azoreductase. It has been discovered that coating peptide capsules with polymers cross-linked with azoaromatic group prevents the medication from being digested in the stomach and small intestine. The azo bonds are broken down and the medication is released in the colon.

- **Polysaccharide Based Delivery Systems**

Since naturally occurring polymers of monosaccharides are plentiful, widely available, affordable, and come in a variety of forms with different characteristics, they are gaining a lot of attention as potential ingredients in drugs that target the colon. They are very stable, safe, nontoxic, hydrophilic, and gel-forming materials that are also easily manipulated chemically and biochemically. They are also biodegradable. These include naturally occurring polysaccharides derived from plant, animal, algal, or microbial (dextran), as well as animal (chitosan, chondroitin sulphate), and algal (alginates) sources. Colonic microflora has the ability to convert polysaccharides into simple saccharides. Therefore, they fit the definition of "generally regarded as safe" (GRAS). Chitin found in crab and prawn shells is converted by deacetylation into the high molecular weight cationic polysaccharide known as poly (N-glucosamine). Rich colonic microbiota breaks it down. Mostly in the form of a capsule-forming substance, chitosan has been tested for colon-specific medication delivery. Another non-starch linear polysaccharide, pectin has 1, 2-linked L-rhamnose residues that are mostly α -(1-4)-linked D-galacturonic acid residues.

2. NEWLY DEVELOPED APPROACHES FOR CDDS

Pressure Controlled Drug Delivery Systems (PCDDS)

On the basis of luminal pressure within the colon, the pressure-controlled systems are created. During this delivery, the medication is given in the form of a capsule that can withstand the pressure of the upper gastrointestinal tract but collapses in the large intestine as a result of increased pressure. The stomach contracts throughout the digestive process, and the peristaltic motion used to propel the contents of the intestines is part of the GI tract. Strong, brief, and only three to four times each day, the colon produces peristaltic waves.

As far as the author is aware, just one invention relates to the creation of pressure-controlled systems for colonic distribution. This specific delivery method is a capsule that can withstand the pressures of the upper GIT but collapses in the large intestine due to elevated pressure. The ethyl cellulose used to make the capsule shells allows for precise control over the thickness of the wall, which in turn affects how quickly the capsules collapse in the large intestine. About 35 to 60 μ m is the optimal range for the capsule wall thickness.

Osmotic Controlled Drug Delivery to Colon (ORDS-CT)

The medicine has been specifically targeted to the colon using the ORDS-CT (Alzacorporation) technology. It started releasing the medicine when the unit dosage reached the colon and continued to do so for up to 24 hours. One system that is controlled by osmotic pressure is the ORDS-CT.

It comprises of a hard gelatin capsule that dissolves in the pH of the small intestine and permits water into the device. It swells as a result, and the medication is subsequently driven out. There may be 5–6 units inside each capsule, and each unit is enclosed in a drug-impermeable enteric coating that keeps water out of the stomach's acidic environment. However, as soon as the capsule enters the small intestine, which has a higher pH, this coating dissolves and water enters. An osmotic push compartment and a medication compartment are both enclosed by a semipermeable membrane that is part of the enteric coating. Water makes the push compartment swell and generates a gel in the drug compartment that is pushed out of an aperture through the membrane next to the drug compartment. The rate at which the drug flows out depends on the rate at which water enters. These systems can also be created so that there is a delay between the time the enteric coating dissolves and the medicine is released in order to prevent drug release in the small intestine.

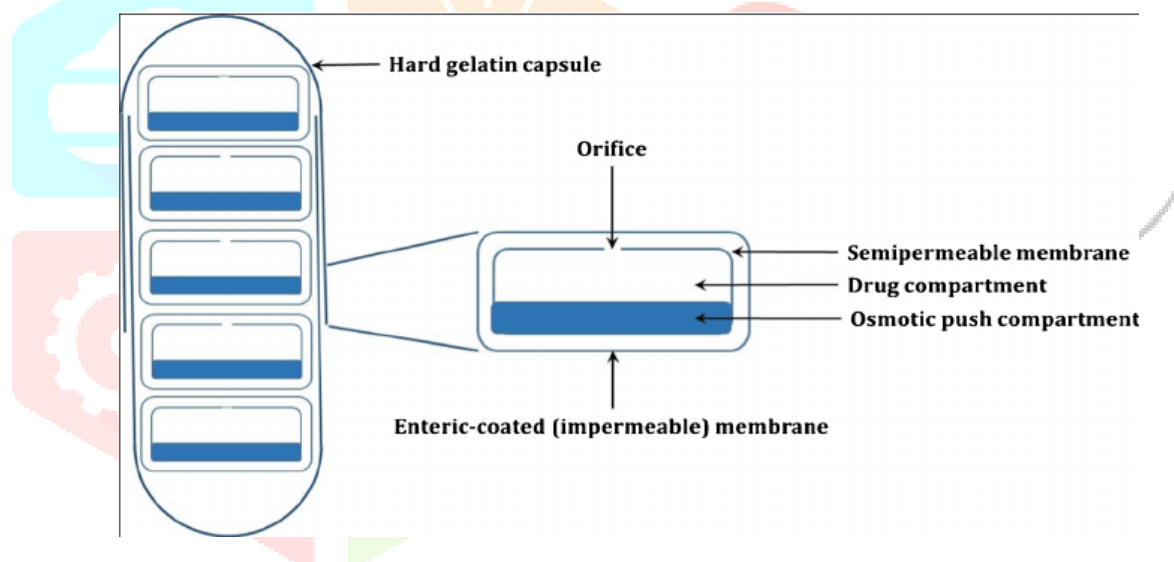


Fig: ORDS-CT

Novel Colon Targeted Delivery System (CODESTM)

CODESTM is advanced and unique CDDS technology, which overcomes the problems associated with PH or time dependent systems. It combines two methods, PH-dependent and microbially triggered CDDS. It is made up of a number of polymers that work together to shield the medication core up until the formulation reaches the colon. It was developed by utilising an innovative technique involving lactulose, which serves as a catalyst for site-specific drug release in the colon. A conventional tablet core containing lactulose is the base of the system. This core is then overcoated with an acid-soluble material, Eudragit E, and finally an enteric material, Eudragit L. The tablet is protected by this technology while it is in the stomach, and it dissolves fast after gastric emptying. The formulation is then protected by the acid-soluble coating as it passes through the small intestine's alkaline pH. The polysaccharide (lactulose) is enzyme-degraded into organic acid by the bacteria once the tablet reaches the colon. This lowers the pH around the system enough to cause the acid soluble coating to dissolve and the subsequent drug release.

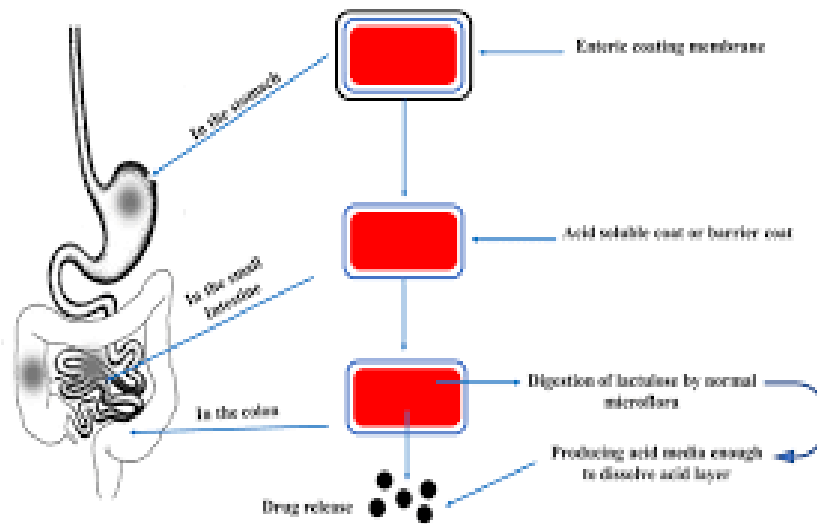


Fig: CODES System

Pulsincap System

The system consists of a drug-containing water-insoluble capsule body, a hydrogel plug that closes the capsule body's opening end, and a water-soluble cap that covers the hydrogel plug. The addition of an acid-insoluble film coating to the capsule further inhibits the drug from being released in the stomach. The enteric coating dissolves in the small intestine, causing the hydrogel plug to swell. The length of the plug and the depth at which it is inserted determine the amount of lag time, which is made possible by the plug's swelling before it releases the medicine. In order to evaluate several polymers as the plug material for their pulsincap system, Abraham et al. The formulations were evaluated at three different pH levels: pH1.2 for two hours to replicate gastric fluid, pH7.4 for three hours to simulate intestinal fluid, and pH6.8 for seven hours to simulate the colon. This modified pulsincap system may successfully target metronidazole to the colon, according to the study, which indicated that no significant drug release occurred within 5 hours of the experiment's starts.

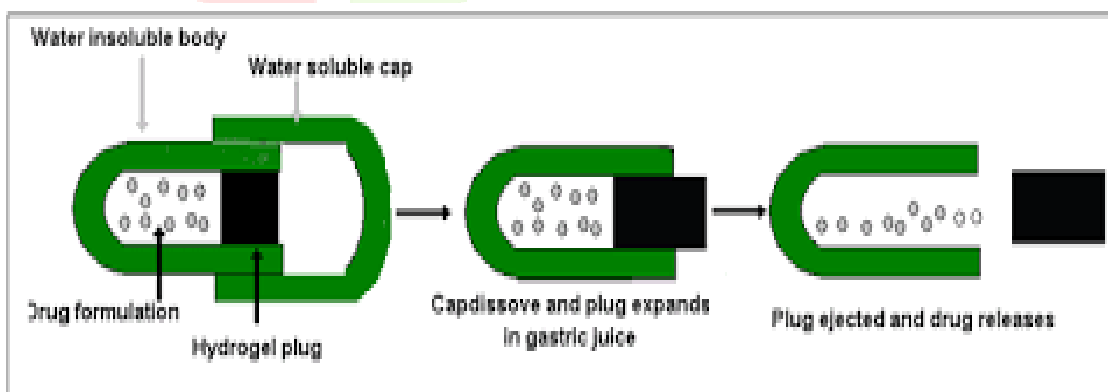


Fig: Pulsincap System

PORT System

It consists of an osmotically active agent, an insoluble plug, and a hard gelatin capsule coated with a cellulose semi-permeable membrane that also contains the drug formulation. Water diffuses through the semi-permeable membrane when it comes into contact with an aqueous medium, which causes an increase in internal pressure that eventually causes the plug to come out. Coating thickness regulates lag time.

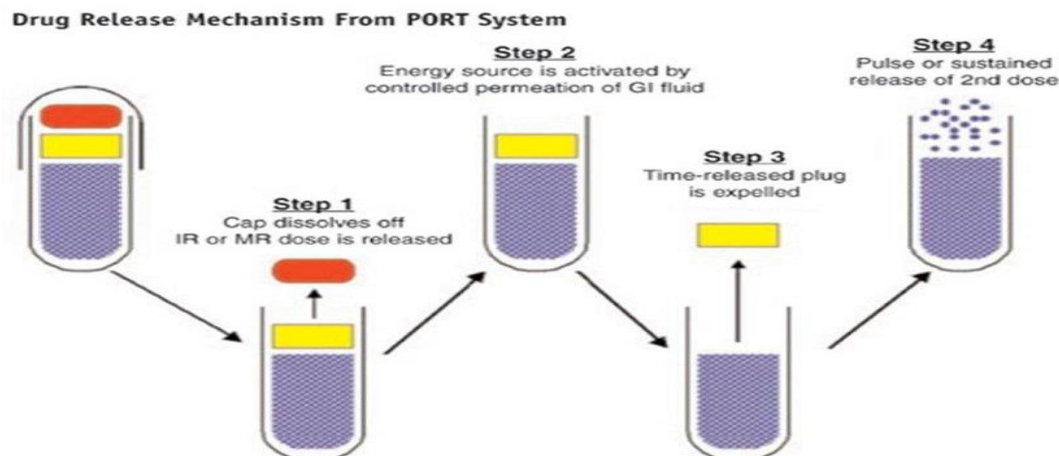


Fig: PORT System

Microspheres

A microsphere's particle size is 5200 nm. Microspheres provide a number of advantages over oral drug delivery systems, including free-flowing characteristics. Microspheres are utilised for prolonged drug release, local illnesses, and enhancing the stability of delicate medications.

For the creation of microspheres, such as polysaccharide-based microspheres, the matrix system is helpful. Production of pectin metronidazole microspheres using a prodrug method and multi-particulate system to treat amebiasis.

Mucoadhesive Approach

The mucoadhesive method is one of the advanced techniques used for CDDS. This approach increases the drug's bioavailability and residence time. The mucoadhesive polymers are used in this system's formulation. Better adhesion to the mucus layer of the colon and sustained medication release are made possible by mucoadhesive polymers.

The mucoadhesive polymer consisting of sodium alginate and eudragit 100 used to treat ulcerative colitis is an example of a mucoadhesive technique.

APPLICATIONS

- ❖ Treatment of Inflammatory Bowel Disease (IBD): Inflammatory bowel diseases such as Crohn's disease and ulcerative colitis primarily affect the colon. Colon targeted drug delivery systems can deliver anti-inflammatory drugs directly to the affected area, providing localized therapy and minimizing systemic side effects. These systems can improve the effectiveness of treatment and reduce the frequency of dosing.
- ❖ Treatment of Colorectal Cancer: Colon targeted drug delivery systems can be used to deliver anticancer drugs directly to the colon in the treatment of colorectal cancer. Targeted delivery helps to increase drug concentration at the tumor site, improving therapeutic outcomes and minimizing adverse effects on healthy tissues.
- ❖ Treatment of Colon Infections: Certain bacterial and parasitic infections, such as Clostridium difficile infection and amoebiasis, primarily affect the colon. Colon targeted drug delivery systems can deliver antimicrobial agents directly to the site of infection, improving treatment efficacy and reducing systemic exposure.
- ❖ Treatment of Colon-Specific Diseases: Several diseases are specific to the colon, such as diverticulitis and ischemic colitis. Colon targeted drug delivery systems can be used to deliver drugs for the treatment of these conditions, providing localized therapy and minimizing systemic side effects.
- ❖ Treatment of Chronobiological Disorders: The colon exhibits distinct rhythmic patterns of motility, and certain diseases, such as nocturnal asthma and morning diarrhea in patients with irritable bowel syndrome, are influenced by these rhythms. Colon targeted drug delivery systems can be designed to release drugs at specific times, aligning with the circadian rhythms of the colon and optimizing therapeutic outcomes.
- ❖ Delivery of Biologics: Biologic drugs, including peptides, proteins, and nucleic acids, are susceptible to degradation in the gastrointestinal tract. Colon targeted drug delivery systems can protect these sensitive drugs from degradation and facilitate their absorption in the colon.
- ❖ Prolonged Release Formulations: Colon targeted drug delivery systems can be designed to achieve prolonged drug release in the colon. This is particularly useful for drugs that require sustained therapeutic levels or drugs with short half-lives.
- ❖ In local colonic pathologies
- ❖ Systemic delivery of protein and peptide
- ❖ Potentials site for the treatment of diseases like asthma, arthritis and angina
- ❖ For the drugs that are absorbed through colon such as steroids

Marketed drug products for the treatment of various diseases of colon

S. No	MARKETED NAME	COMPANY NAME	DISEASE	DRUG
1	Mesacol tablet	Sun Pharma, India	Ulcerative colitis	Mesalamine
2	Mesacol enema	Sun Pharma, India	Ulcerative colitis	Mesalamine
3	Asacol	Win-medicare, India	Ulcerative colitis, crohn's disease	Mesalamine
4	SAZO	Wallace, India	Ulcerative colitis, crohn's disease	Sulphasalazine
5	BUSCOPAN	German Remedies, India	Colonic motility disorder	Hyoscine butyl bromide
6	Normaxin	Systopic labs, India	Irritable colon syndrome	Clidinium bromide
7	CYCLOMINOL	Neol, India	Irritable colon syndrome	Diclomine
8	Pro-banthine	RPG Life, India	Irritable colon syndrome	Propenthline bromide
9	Intazide	Intas, India	Ulcerative colitis	Balsalazid
10	Entofoam	Cipla, India	Ulcerative colitis	Hydrocortisone acetate

CONCLUSION

Drug delivery to the diseased colon is favourable in that it minimises systemic side effects, uses a smaller dose of the medication, is only given when necessary, and keeps the medication as close as possible to the target site in its intact form. Protecting the medication from absorption and/or the environment of the upper GIT and then quickly releasing it into the proximal colon, which is the site for colonic targeted delivery of drugs, could improve colonic delivery. All of the methods offer ways to treat colon-related local ailments or to help the body absorb poorly absorbed medications. The colon's abundant bacteria can be used to target the release of drugs there.

REFERENCES

1. Raditya Iswandana, Kurnia Sari Setio Putri, Fathia Amalia Putri, Maxius Gunawan, Sekar Arum Larasati. Challenge and Development Strategy for Colon-Targeted Drug Delivery System. *Pharmaceutical Sciences and Research* 2022; 9 (1): 17 - 27.
2. Rutuja P. Bugad, Dr. Sachinkumar V. Patil. A comprehensive review on colon targeted drug delivery system. *International Journal of Creative Research Thoughts* 2021; 9 (7): 225 - 237.
3. Sareen R, et al. pH-Sensitive Drug Delivery Systems for Targeted Treatment of Colon Diseases. *Pharmaceutics*. 2021; 13(1): 22.
4. Lokesh Choudhary, Amit Jain, Dilip Agarwal. Colon Targeted Oral Drug Delivery Systems: A Review. *Asian Journal of Pharmaceutical Research and Development* 2020; 8(4): 186 - 190

5. Manoj Kumar Sarangi, M. E. Bhanoji Rao & Versha Parcha. Smart polymers for colon targeted drug delivery systems: a review. *International Journal of Polymeric Materials and Polymeric Biomaterials* 2020; 1130 - 1166.
6. Rutuja Sawant, Shreya Parkar, Prajackta Kegade, Akshay Gade. Colon Targeted Drug Delivery: A Review on Novel Approaches. *Asian J. Res. Pharm. Sci.* 2020; 10(4): 293 - 298
7. Sang Hoon Lee, Rajiv Bajracharya, Jeong Youn Min, Ji Won Han, Byeong Ju Park and Hyo-Kyung Han. Strategic Approaches for Colon Targeted Drug Delivery: An Overview of Recent Advancements. *Pharmaceutics* 2020; 12: 1 – 20.
8. Anita, Singh.A, Dabral, A review on colon targeted drug delivery system, *International Journal of Pharmaceutical Sciences and Research.*2019;10(1):47-56
9. Vaishali Chauhan, Harshita Mishra, Kapil Kumar. A comprehensive review on colon targeted drug delivery system. *Global journal for research analysis* 2019; 8 (1): 173 – 178.
10. Nikita Sinha, Amit Kumar and Sonal Rai. A review on colon targeted drug delivery. *International Journal of Current Research* 2020; 12 (8): 13001 - 13004
11. Belali N, Wathoni N, Muchtaridi M, Advances in orally targeted drug delivery to colon, *Journal of Advanced Pharmaceutical Technology & Research.* 2019; 10(3):100-6
12. Pavan Kumar P, et al. Colon Targeted Drug Delivery Systems: A Review on Primary and Novel Approaches. *Oman Med J.* 2010; 25(2): 79-87.
13. Patel M, et al. Colon Targeted Drug Delivery Systems: A Review on Pharmaceutical Approaches with Current Trends. *AAPS Pharm SciTech.* 2019; 20(6): 228.
14. Varshosaz J, et al. Recent Advances in Colon Targeted Drug Delivery Systems: A Review. *J Control Release.* 2016; 198: 2-11.
15. Wadhwa S, et al. Colon Targeted Drug Delivery Systems: A Review on Natural and Synthetic Polymers. *J Control Release.* 2020; 321: 589-614.
16. Sharma G, et al. Novel Approaches for Colon Targeted Drug Delivery Systems. *Asian J Pharm Sci.* 2016;11(5): 575-584.
17. Sonaje K, et al. Colon-Specific Drug Delivery Systems Based on Cyclodextrin Prodrugs. *Expert Opin Drug Delivery.* 2011; 8(2): 137-160.
18. Dhamecha D, et al. Colon Targeted Drug Delivery Systems: An Overview on Primary and Novel Approaches. *Oman Med J.* 2012; 27(5): 379-390.
19. Beg S, et al. Delivery of Probiotics Using pH-Sensitive Polymeric Delivery Systems. *Expert Opin Drug Delivery.* 2016; 13(11): 1571-1585.
20. Araújo J, et al. pH-Responsive Drug Delivery Systems for Tumour Targeted Treatments. *Nanomaterials (Basel).* 2019; 9(2): 304.
21. Khattak S, et al. Recent Advances in Microbially Triggered Drug Delivery Systems. *Expert Opin Drug Deliv.*2016; 13(10): 1411-1424.