

# OVERVIEW ON COLON TARGETING DRUG DELIVERY SYSTEM

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## Abstract

In field of medicine oral route is mostly used path for the administration of drug. so, the oral route is not preferred for lower GIT disorder. So, to overcome this problem drug directly targeting to the specific site. In this review article overview on the colon targeting drug delivery system. Colon is the site where drug is targeted on the local site and used for the local colon disease. Colon targeting drug delivery system not just for the local disease but also used for the systemic delivery of the drug such as proteins, therapeutic peptides, anti-asthmatic, anti-hypertensive drug, antidiabetic drug. Now a day number of method are used to formulate CTDDS such as formation of pro drug, coating of polymers etc. colon targeting drug delivery system is a new system for targeting a drug in specific site for enhance the therapeutic effect of poorly absorbed drug. And now a day drug targeted on colon through rectal route. But this route is very painful. In this article discuss about the anatomy of the colon, factor affecting the colon targeting drug delivery system, advantages of colon targeting drug delivery system, limitation of colon targeting drug delivery system and evaluation of the colon targeting drug delivery system. But in this review mainly discuss about the new method used for colon targeting drug delivery system such as Microspheres, carbon nanotube, metal nanoparticles etc.

## Keywords:

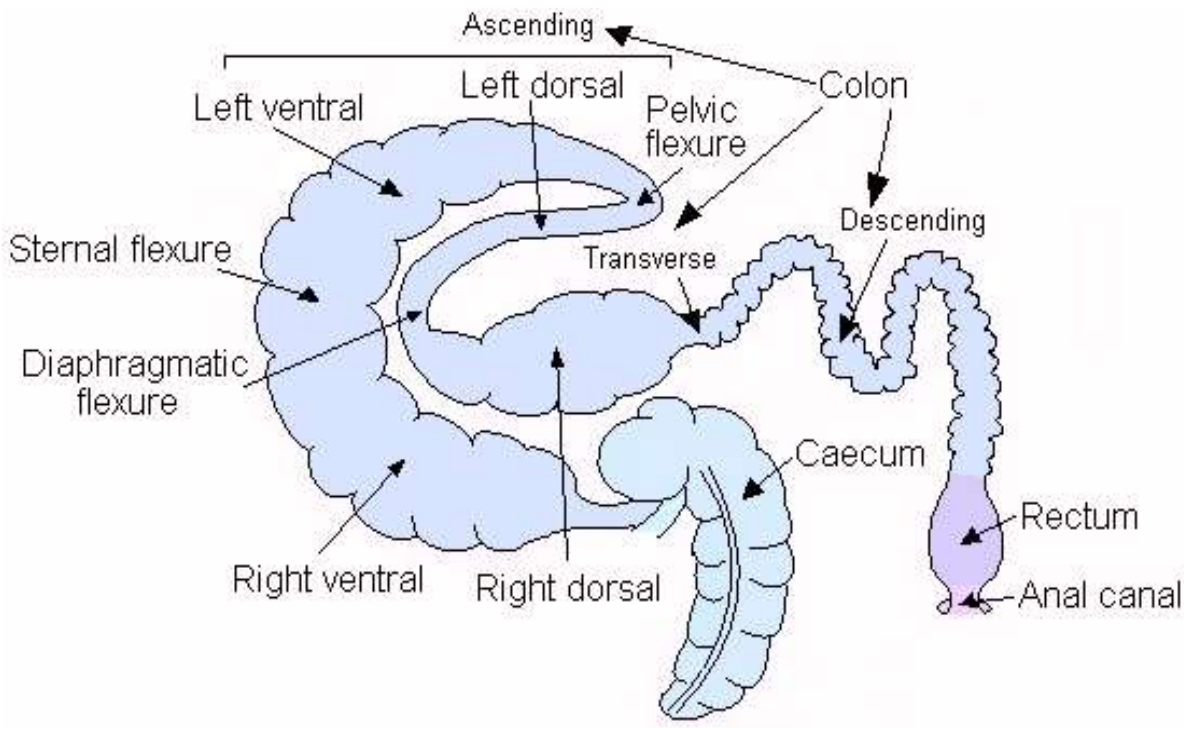
Colon targeting drug delivery system, Drug targeted through rectal route, new strategy used for colon targeting drug delivery system.

## Introduction

Oral route is a very simple and effective route for drug administration and more patient compliance by this route. But various factor that affect the absorption of the drug which are administered by oral route such as pH, presence of various enzyme etc. For overcome this problem drug directly targeting to the specific site for example drug targeted to colon. Before going to study about colon targeting drug delivery system firstly understand the anatomy of colon and different parts of colon.

## Anatomy of colon

Colon is a part of large intestine and large intestine part of GIT. The colon is a U-shaped tube formed by muscle and lies below the stomach. The rectum is a small tube attached to the colon. The length of colon and rectum both are about 2 meters (6.5 feet) long. They are present nearby other organs such as the spleen, liver, pancreas, bladder and reproductive organs.



“Diagrammatical representation of colon”

CTDDS is very important system for reach the drug to the specific site. In this system drug targeted to the local site and used for the local colonic disease and number of GIT disease. (Anil and Betty,2011). Number of polymers are used to prevent degradation of drug in stomach because some drugs are degraded in acidic pH so drug coated by polymers then the drug degrade only colon not in acidic pH. (Neha H. Rajpurohit et al., 2010) Drug are administered through rectum because this is shortest route for CTDDS by proximal part. But rectal route is a very difficult and painful then patient compliance decrease. (Massimo Campieri et al., 1992). 50% drugs are administered through oral route because this route has more advantages and high patient compliance. (Akhil et al., 2011) But when drug is administered through oral route then drug pass through the GIT, due to presence of enzymes and acidic pH are reduce the absorption or the drugs then absorption of drug decreases so bioavailability of drug also decreased. To overcome this problem by new system are developed this system is called “colon targeting drug delivery system”. They are new targeting system. Colon targeting drug delivery system comes in the category of control release and sustain release of drug. (Gupta Vinay et al., 2012) Example of drugs for the treatment of the colon disease are sulfasalazine, dexamethasone, hydrocortisone, metronidazole, prednisolone etc. (Leuva VR, Patel BG, et.al.2012).

### Application of “CTDDS”

- CTDDS useful for local colonic diseases because drug directly bind to the colon (site specific) such as ulcerative colitis, Chron’s diseases, amoebiasis.
- Colon targeting drug delivery system useful for poorly absorbed molecules such as protein, peptides and amino acid.
- This system is very useful for those drugs which are degrade in the presence of the enzyme in GIT.
- Reduced dosage of the drug.
- CTDDS mainly Used for the treatment of the local disease.
- In this system the frequency of the dosage is less.
- Due to longer residence time of the drug in the colon, this system is very useful for poorly absorbed drug because in this system increase bioavailability (up to 5 days).

- Drugs which are used by CTDDS they are prevent the degradation of the drugs in acidic pH of stomach.
- It is useful for nicotine addiction.
- This system helpful for those drugs that caused gastric irritation decrease the irritation of those drugs (NSAIDS). (Singh N and Khanna RC et.al)

## Limitation of “CTDDS”

1. GIT physiology is very complicated due the pH, presence of enzyme, are decrease the absorption of the drug.
2. Presence of food and metabolic enzyme are also produced the complication.
3. Drug Solubility is also important factor due to various factors the solubility of the drug is affected such as low volume of luminal fluid, high viscosity, neutral pH
4. Stability is also a main factor so it is very important for CTDDS the drugs is stable in the colon but due to drug interaction with colonic content such as microflora, secretions of digestive and hormones, mucus, and feces are reducing the stability of the drug.
5. Presence of bacterial enzyme are responsible for degradation of the drugs. (Amidon et al., 2015)

## Polymers

Various type polymers are used in CTDDS

- Natural polymer
- Synthetic polymer.

Example of natural polymers: Pectin, Chitosan, chondroitin sulfate, guar gum, dextrin, Cyclodextrins, inulin, Laminates, Amylose, Xanthan gum etc.

Example of synthetic polymer: Eudragit, Shellac, etc. (Neha Sharma and harikumar, 2013)

## Factors affecting “CTDDS”

Various factors that affect the CTDDS and decrease the bioavailability of the formulation. but we discussed some factors:

### 1. Anatomical and physiological factor

### 2. Pharmaceutical factor

#### 1. Anatomical and physiological factor

- a. The physiology and the physical properties of the colon are different.
- b. The presence of food and change the movement of food in colon which are the work as a barrier for CTDDS.
- c. The pH of the colon is changed in various conditions such as disease state, fasted state, sexes, and age are also the factors that influence the CTDDS.
- d. Other physiological factor is viscosity, colonic fluid and microbial enzymes present in the colon are also influence CTDDS.

## 1.1 Intestinal transit time

Colonic transit time change in disease state. So, they influence the CTDDS. The intestinal-colonic transit time play a very important role for CTDDS and for the colonic bioavailability of drugs. Colonic disease also affects the intestine transit times. (Hebden JM, Blackshaw PE, et.al.2000). The time of drug administration, presence/absence of food, and the type of dosage form are also very important for the transit of dosage. The results showed that colonic transit was prolonged when patient in sleep and use larger dosage form. (Stubbs JB, Valenzuela GA, et.al.1991)

## 1.2 Volume of fluid in colon

Colon has high water absorbing capacity as compare to other part of GIT. Around 1.5kg/day food eat by human and this food contain undigested proteins, carbohydrates and fats. (Christl SU, Scheppach W. et.al.1997) They absorb 90% water then the colonic fluid volume decreases and decreasing volume of fluid challenge the dissolution parameters. (Sandle GI. et.al.1998) Dissolution of drug not done then they reduce the bioavailability of drug.

And other factors which influence the CDDS are:

- Colonic pH
- Viscosity of colonial content
- Colonic enzymes and metabolism. (Seth Amidon, Jack E. et.al.2015)

## 2. Pharmaceutical factor

### 2.1 Drug candidate

Drug candidate and carrier molecule are show more interaction with each other and drug stable in the alkaline pH of GIT. when drug candidate not compatible with drug carriers then they are produced various unwanted effects so both drug candidate and drug carriers are compatible with each other. And also stable in basic pH drug candidate not degraded in basic pH. Drug candidate used for "CTDDS" for local disease and poorly absorbed drugs are also administered by this route for example peptide, protein, antihypertensive drugs etc.

### 2.2 Drug carrier

Drug carrier is very important factor to design CTDDS. For Selection of drug carrier firstly know about the type of drug and type of disease. According to drug and disease select the carrier. Carrier selection are affected by numerous factors such as

- Chemical nature of drug
- Stability of drug
- Partition coefficient of drug
- Type of absorption enhancers.

Functional group of drug carrier are very important for the selection of drug carrier. (Singh, C.K, Saxena et.al 2018)

## Colonic diseases

1. Angiodysplasia
2. Inflammatory Bowel Disease
  - a. Ulcerative colitis
  - b. Crohn's disease
  - c. Colorectal cancer
  - d. Constipation
  - e. Diarrhea
3. Diverticulitis and Diverticulosis
4. Hirschsprung's disease (A ganglionitis)
5. Intussusception
6. Irritable bowel syndrome
7. Pseudomembranous colitis
8. Ileus (intestinal obstructions)
9. Haemorrhoids (piles) (Akhil Gupta, Anuj Mittal et al 2011)

## Different approaches for "CTDDS"

1. Formation of prodrugs:
  - 1.1 Azo bond conjugate
  - 1.2 Glucuronide conjugate
  - 1.3 Cyclodextrin conjugates
  - 1.4 Dextran conjugates
  - 1.5 Amino-acid conjugates
2. Hydrogels
3. Coating with pH dependent polymers
4. Timed released systems (Bhushan Prabhakar Kolte et al 2012)

## New Technology for "CTDDS"

1. Minitablets approach
2. Microspheres
3. Mucoadhesive approach

4. Multimatrix system
5. Nanoparticles
6. Metal nanoparticles
7. liposomes
8. Magnetic nanoparticles
9. Carbon nanotube (Nagina Belali, Nasrul Wathoni et al. 2019)
10. CODESTM
11. Pressure Controlled system
12. Osmotically controlled system (Prasanth V.V, Jayaprakash et al. 2012)

## 1. Formation of prodrug

Prodrug play a very important role for release of drug to specific site because prodrug is a “pharmacologically and therapeutically inactive part of a parent molecule”. In this method the drug is unchanged and do not degrade in GIT because covalent linkage occurs between carrier and drug. (Vinay K Gupta, G. Gnanarajan et al. 2012). Prodrug is a nonspecific chemical approach and used to increase the bioavailability, site specificity, and chemical stability. Specific enzyme targeted to specific site for treatment for colon cancer chemotherapy by prodrug formation. Example-For treatment of local colonic disease sulfasalazine used.

### 1.1 Azo bond conjugate

The azo compound is mostly metabolized in presence of intestinal bacteria, both by intracellular enzymatic components and extracellular reduction. Hydrogels used as a coating material for azo compounds. This azo type compounds used for the treatment of inflammatory bowel diseases. But 85% dose of the sulfasalazine are not absorbed in the colon. Increase the absorption of the drug by anaerobic environment sulfasalazine is converted into the 5-Amino salicylic acid and sulfa-pyridine. (Klotz U et al. 1985) Number of studies are managed on sulfa-pyridine for the development for new prodrug for example Olsalazine, Balsalazine, 4-amino benzoyl -beta-alanine. (Chan R. P., et al. 1983)

### 1.2 Glucuronide conjugate

Glucuronide and sulphate conjugation are very useful for the clearance of number of drugs. which are useful for inactivation and preparation or drug clearance. Various bacteria are present in the lower GIT. These bacteria are responsible for the secretion of the glucuronidase. The result of the glucuronidation process to release of active drug and not able its reabsorption, glucuronide prodrugs are used for the CTDDS.

### 1.3 Cyclodextrine conjugate

Hydrophilic and ionizable Cyclodextrins can be used for such type of formulation which are used for fast and delayed release of the drug. Hydrophobic Cyclodextrins can stop the rate of water release. But the drug carrier can be capable for the drug targeted to the desired site of action. Conjugates of a drug with Cyclodextrins can be a changeable for formulate a new class of colon targeting prodrugs for soluble drugs.  $\alpha$ -,  $\beta$ - and  $\gamma$ -Cyclodextrins are developed a prodrug of Ibuprofen. (Bhushan Prabhakar Kolte, Kalyani V. Tele et al. 2012)

### 1.4 Dextran conjugate

Number of drugs are prepared by Dextran conjugate such as prodrugs of metronidazole have been formulated. Dexamethasone and methyl prednisolone are prepared by help of dextran ester prodrugs to increase the efficacy of the prodrugs for delivering drugs to the colon. Succinate linker covalently bound the Methyl prednisolone and dexamethasone to the dextran. (Bhushan Prabhakar Kolte, Kalyani V. Tele et.al.2012)

### 1.5 Amino acid conjugate

Amino acid contains polar group and this polar groups are hydrophilic in nature. Protein are containing polar group because they are come in the class of amino acid. they are decrease the amino acids and proteins membrane permeability. Number of prodrugs are formulated by the conjugation of drug molecules to the polar amino acids such as Tyrosine, glycine, methionine and glutamic acid were conjugated to Salicylic acid are the example of the non-essential amino acid. (Ratnaparkhi Mukesh P., Somvanshi Fattesingh U. et.al.2013)

## 2. Hydrogels

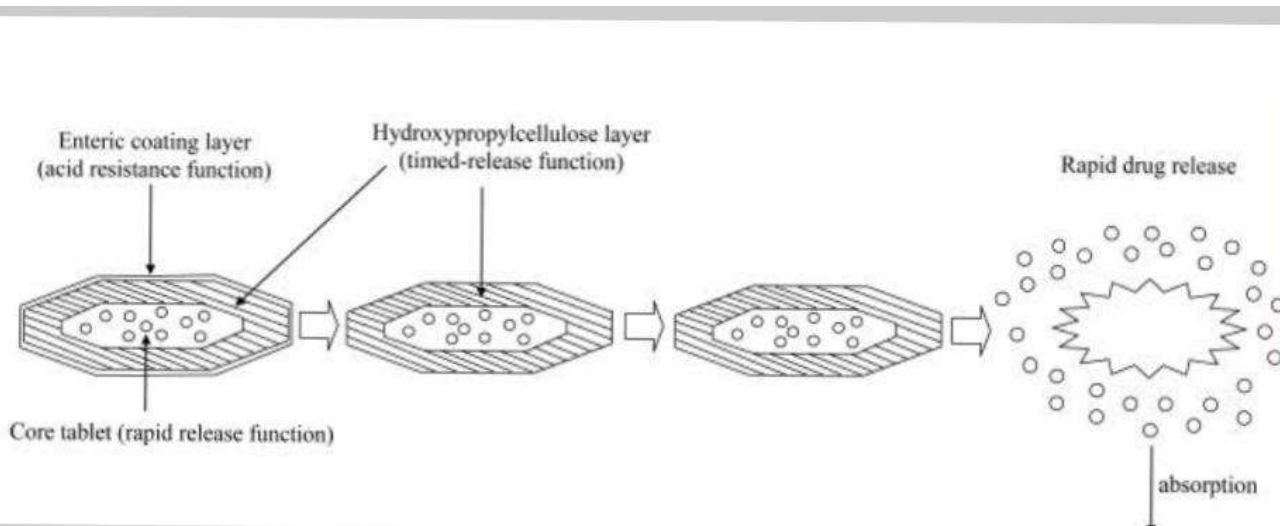
Peptide and protein are administered by CTDDS. they are administered in the hydrogels form. The Hydrogels are formed by acidic compounds and enzymatically degradable azo aromatic crosslinks. Because these are helpful for inhibit the drugs swelling and drug degradation in acidic pH because when pH of environment increases then drugs start swelling of the drug and drug release in basic pH (Bhushan Prabhakar Kolte, Kalyani V. Tele et.al.2012)

### 3. Use pH dependent polymers (pH dependent biodegradable polymers):

The pH of the colon is greater than the upper GIT. Then use pH dependent polymer for the colon targeting drug delivery system. The time of formulation to reach in the colon cannot be exactly estimated. So, with the help of the pH dependent polymer increase the gastric resistance time and drug not release for 3-4hr. The drug core coated by three polymeric layers. first layer dissolves at acid pH then the second layer are Swellable layer, and last layer release the drug at the desire site. This system is very useful for the delayed release of the drug. Numerous other drug delivery systems have developed. Polymers are used to develop novel drug delivery system for drug release to the colon. (Vinay K Gupta, et al volume 7 2012)

### 4. Time released system

Time released systems is very important to avoid in small intestine for 3-5 hrs. In this system increase the drug release time.



(Time released enteric coated tablet)

The drug released in the colon after specify time is come in the timed-released system. When the stomach is empty then changed the gastric emptying time and also change after food intake. Food intake is very important for gastric emptying time because gastric emptying time depend on the food intake. pH-sensitive polymers and a timed-release approach are used for the CTDDS. A formulation containing a drug core of a drug covered with three polymeric layers (one layer is hydrophilic and other two pH-sensitive layers) was developed. (Akhil Gupta, Anuj Mittal et al 2011)

## New approaches for “CTDDS”

### 1. Minitablets approach

In this approach unchanged release of drug and a very good patient compliance. (Mohd AH, Guggilla N, et.al.2014). In this mini-tablets approaches different techniques are used for the formulation such as core mini tablet filled with pulsincap in this technique polymers are used that release the drug in time depended manner and other techniques are capsule filled with matrix mini tablet in this technique use pH dependent and microsomal enzyme-dependent polymers. Hadi MA, R. Rao NG, et.al.2018)

### 2. Microspheres

Practical size of microsphere is 5200 nm. Microspheres having free flowing properties and various advantages compare to oral drug delivery system. Microsphere are used for to increase the stability of sensitive drug, local diseases and also used for sustained release of the drug. (Hua S, Marks E, et.al 2015) Matrix system is useful for microspheres preparation preparation for example polysaccharide-based microspheres. A combination of prodrug approach along with multi-particulate system used for amebiasis treatment by production of pectin metronidazole microsphere. (Vaidya A, Jain S, et.al 2015) A microemulsion fil with 5-ASA silicon dioxide nanoparticles for ulcerative colitis. Because they have less cytotoxicity and very good efficacy. (Tang H, Xiang D, et.al.2017)



### 3. Mucoadhesive approach

For CTDDS nanocarriers and microspheres are developed. Nanocarriers and microcarriers are formed for anti-inflammatory drugs for example prepare the Valdecoxib mucoadhesive matrix with the help of the sodium alginate and used the polymer for coating Eudragit S 100. (Zhang L, Sang Y, et al. 2016). Prepare the Naproxen sodium mucoadhesive with the help of sodium alginate and Eudragit S100 polymer for the treatment of colitis. (Chawla A, Sharma P, et al. 2012) NPs with better mucoadhesive properties are developed for increase the resistance time of drug and bioavailability of the drug. (Chuah LH, Billa Net. al. 2013) Preparation of the gelatin-based oxaliplatin hydrogel suspension for colon cancer. (Ullah K, Ali Khan S, et al. 2019)

### 4. Multi-matrix system

This system has been useful for the one dose therapy for improve patient compliance and efficacy of therapy. For example, prepare the multi-matrix system of mesalamine as a single dose for the treatment of the local diseases such as ulcerative colitis and inflammatory bowel disease. (Fiorino G, Fries W, et al. 2010) Time-dependent delivery system was useful for the delivery of the insulin to the colon. For the long-term stability chrono topic system. (Maroni A, Del Curto MD, et al. 2009)

### 5. Nanoparticles (Nanoparticles)

NPs are the type of novel drug delivery system. This method is used to target the drug to the colon. Different types of NPs they are metallic NPs and CNTs (carbon nanotubes). NPs are consisting a unique property due to this unique property this method are used in medicine industry. For example, preparation of the doxorubicin nanoparticles with the help of acid pH sensitive polymer polyacrylic acid to increase efficacy and safety of drug with more bioavailability. (Tian Liu S.K, et al. 2017) To prepare the mesosphere silica nanoparticles of 5-fluorouracil, drug encapsulated in the layer of the guar gum for increase the release of the drug in the presence of the enzymes. (Kumar B, Kulanthaivel S, et al. 2017)

### 6. Metal nanoparticles

Reductive technology is used to produce Metal nano particles they are mostly colloidal system. Seed -based technology are used for synthesized Some metal nano particles such as NPs of porous silica. When liquid carrier is magnetized the colloidal suspensions and this colloidal suspension are more ability to contact with external magnetic fields and fluidity this is medically useful. In current study nickel oxide nanoparticle with size range 20-25nm are formulated and study their cytotoxicity and show decrease cytotoxicity. But most metallic NPs are accumulating in the body and reported as a toxic. (Khan S, Ansari AA, et al. 2019)

### 7. Magnetic nanoparticles

Magnetic fluctuation (alternating magnetic field) in magnetic nanoparticles is produced the heating power this power used for the cancer and tumor treatment. (Tietze R, Zalora J, et al. 2015) A recent study magnetic nanoparticles show natural fabrication produced by magneto tactic bacteria is generated from MSR-1 strain of *Magneto spirillum gryphiswaldense*. It is useful for the antineoplastic activity for colon carcinoma. (Mannucci S, Ghin L, et al. 2014) On the other hand, thermotherapy is used for number of tumor but unluckily it has poor specificity. In this technique increase the intra tumoral delivery of magnetic nanoparticles by this process the magnetic fluid hyperthermia undergoes alternating magnetic field in which it is helpful to increase tissue temperature, then it is maximizing the efficacy of the method by increasing the intra-tumoral delivery of magnetic nanoparticles. (Creixell M, Herrera AP, et al. 2010)

## 9. Carbon nanotube

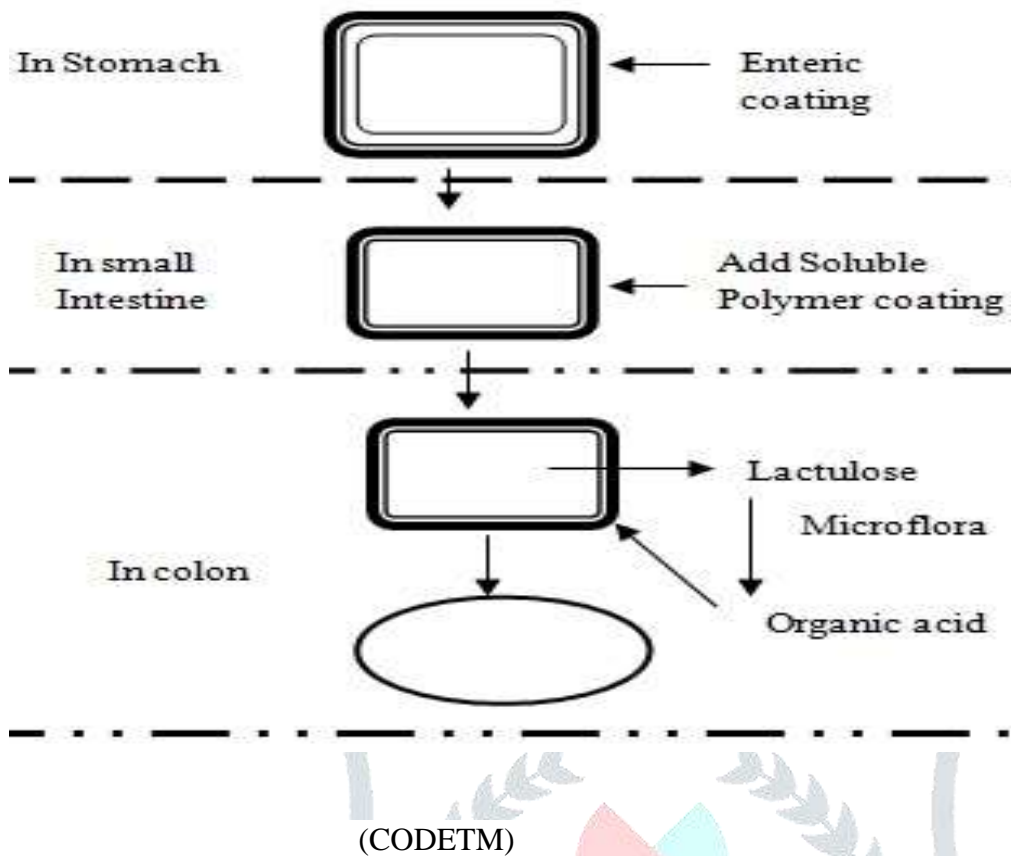
In carbon nanotube the formation of the single-walled carbon nanotubes (SWNTs) of paclitaxel. This is consisting a high suppressive activity on tumors in which the paclitaxel is insoluble in water, is linked to poly ethylated single-walled nanotubes. Therefore, it is reducing the toxicity in normal cells and increase the water solubility. (Liu Z, Chen K, et.al.2008 the production of C225 antibody (cetuximab) inside SWNTs used for targeted therapy of EGFR (epidermal growth factor receptor) that are mostly overexpressed in colon cancer. SWNT are assuring used for chemotherapeutic drugs. (Lee PC, Chiou YC, et.al.2013) Gemcitabine multi-walled carbon nanotubes are used for the colon cancer. It is loaded by conjugated hyaluronic acid with polyethylene glycol are formulated for to target colon cancer, and evaluation done by in vitro and in vivo studies, this study show an effective application of carbon nanotubes in colon cancer. (Kumar S, Jain A, et.al.2019. It is a new approach used for colon cancer it is very effective and useful based on the study of the discussion in the different international journal.

## 10. Pressure controlled system

Due to the result of the peristalsis, colon consist the higher pressures than in the small intestine. Pressure controlled colon targeting drug delivery capsules are insoluble polymer such as ethyl cellulose. (Takaya T, Niwa prepared by the help of water K, et.al.1998.) Peristaltic motion is the reason of the luminal pressure of the large intestine, due to peristaltic motion increase the large intestine pressure more than that of the small intestine because its contents are more viscous due to the reabsorption of water. Various studies have been devolved for CTDDS by using colonic luminal pressure. (S. Amidon et al., 2015). The pressure-controlled drug delivery system is developed by the help of capsule in which drug is present. Water insoluble polymer (ethyl cellulose) are used for coating this gelatin capsule. drug is introduced in the inner side into the capsule, the base of the suppository dissolves at body temperature. Intestinal increase the viscosity by water absorbed by the intestine. Due to increase the viscosity which increase the pressure in the capsule release the drug into the colon (T. Nalanda and Prashant, 2015).

## 11. CODESTM

CODESTM is a new CTDDS technology, this technology is used for overcome the problem related with pH dependent systems (Watanabe S, Kawai H, et.al 1997) (Takemura S, Watanabe S, et.al.2000) CODESTM is mixed method of pH dependent and microbially triggered CTDDS.

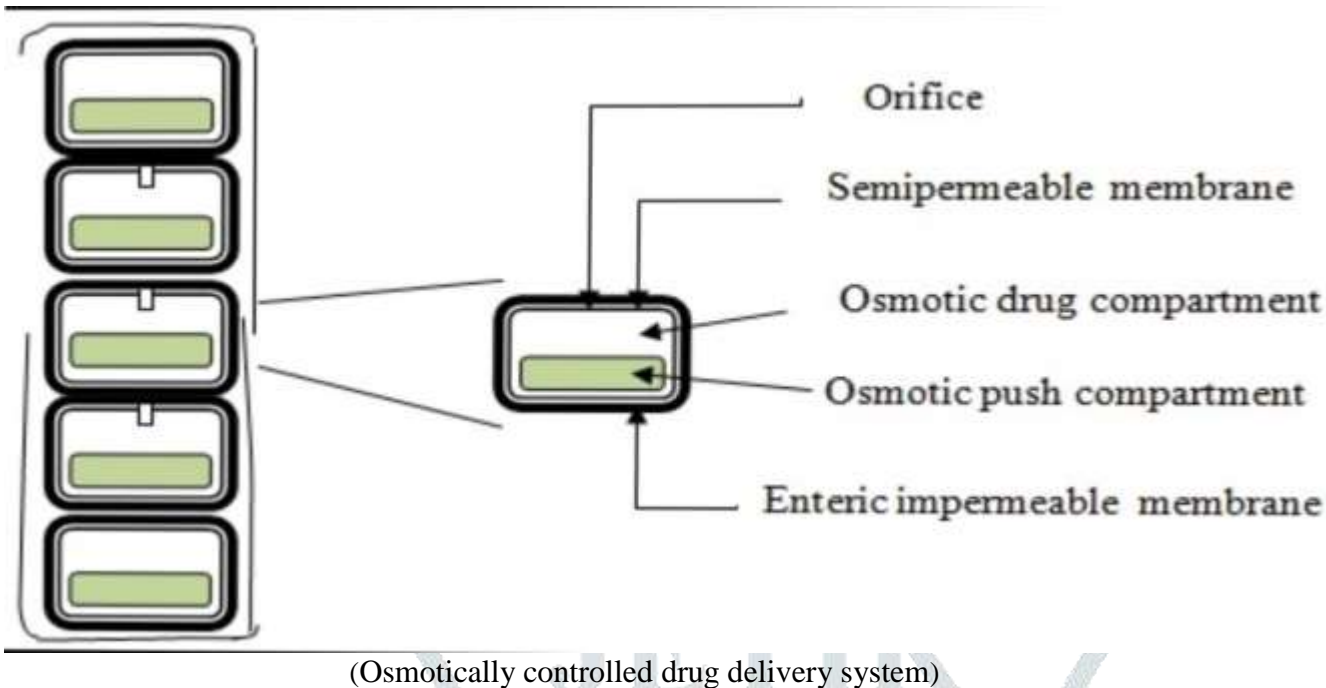


This method is formulated by unique mechanism by using lactulose, which acts as a trigger for site specific drug release in the colon. This system consists of a traditional tablet core containing lactulose, core of lactulose is coated with acid soluble material, by using other enteric material for overcoated the drug core such as Eudragit E and Eudragit L are used as an enteric material. The main target of this method is to protect the release of the drug in the stomach by enteric coating material and increase gastric emptying time. And the acid soluble material is used for protect the preparation in the alkaline pH and passage the small intestine (Masataka K, Watanabe S. et.al.2004). when the tablet reach in the colon then the bacteria present in the colon are helpful for the enzymatically degradation of the polysaccharide (lactulose) into organic acid. And after the degradation pH of surrounding the system is decreases and affect the dissolution of the acid soluble coating and subsequent drug release (Masataka K, Watanabe S. et.al.2002)

## 12. Osmotically controlled drug delivery system:

Osmotically controlled drug delivery system consists of osmotic units. Osmotic unit is an important part of this system. The osmotic units are used as a single or 5-6 push pull unit. (S

Pradeep Kumar, D. Pratibha, R. et.al.2012.



The OROS-CT is an example of system regulated by osmotic pressure. This system is used for drug locally targeted drug to the colon and for systemic absorption of the drug. (Theeuwes F, Guitta Vaidya, et.al) It is a single osmotic unit or include as a 5-6 push-pull units and the diameter of the osmotic unit is 4 mm and encapsulated within a hard gelatin capsule, (Swanson D, Barclay B, et.al) Osmotic push layer and drug layer are present in the bilayer push pull unit, both units enclosed in a semipermeable membrane. membrane drilled the orifice to the drug layer. Immediately after the When the OROS-CT is swallowed then the push-pull units of the gelatin capsule dissolves. Because the drug is enteric coated and push-pull unit of the drug are not absorbed the water in acidic pH it means the drug is not delivered in the stomach. When the drug push-pull unit reach in the small intestine the coating start disintegrate at higher pH. When water is enters the push-pull unit and osmotic pressure is developed this osmotic pressure push the drug and swell the drug and convert in the flowable gel in the drug compartment. The osmotic push-pull compartment are swelled and force the drug gel flow through the orifice and the semipermeable membrane helpful for control the water rate. Ulcerative colitis is a local disease for treating this disease designed each push pull unit with a 3-4 h post gastric delay which is helpful to prevent the release of the drug in the small intestine then the drug release in the colon. OROS-CT system helpful for the constant release of the drug in a constant time. Now a day, new phase transited systems have developed for targeting a drug to the colon (Philip AK, Pathak k, et.al.2006) (Philip AK, Pathak Googlal.2008)

### 13. Pulsatile colon targeting drug delivery system

#### 13.1 Pulsi cap system

Capsule form is used in the pulsi cap system. The plug is used and located in the capsule for control release of the drug. Drug content are covered by the Swellable hydrogels. Because when the capsule is interacted with the dissolution fluid then they swelled. And after a lag time the drug released because plug gets pushed off from capsule and release the drug. Various polymers are used as hydrogel plugs such as different grades of hydroxyl propyl methyl cellulose (HPMC), poly methyl methacrylate. (Vishal V. Rajguru, Preeti D. et.al.2011)

## 13.2 Port system

In port system semi permeable membrane enclosed the capsule body. Insoluble plug present in the capsule body this insoluble plug contain osmotically active agent consists of an insoluble and drug formulation. When capsule interact with the dissolution fluid then the fluid flow into the capsule and the pressure developed in the capsule body and ejecting of plug after expelling a plug the drug is released. The release of drug in usual gap time intervals for the successive release of the drug in time intervals (Sachin D. Bhalersao, et.al)

## Evaluation parameter

### 1. In-vitro dissolution test

Conventional basket method is used for the dissolution study. The Different buffer are used for the dissolution study such as pH6.8 and 7.4 phosphate buffer. Study the release of the drug at different pH levels. Various media that are used for the dissolution testing of CTDDS. This method useful for study the release of the drug in the GIT. (R.B. Desi Reddy, et.al.2013)

### 2. In-vitro enzymatic test

In-vitro enzymatic test provide two tests. Firstly, to prepare a desirable medium for bacteria and then the carrier drug system is incubated in fermenter. The release of amount drug different time intervals is calculated. Buffer medium is important for the study of release of drug these medium consisting enzyme pectinases, dextranase of rat, guinea pig. The release amount of drug in a particular time is related to degradation of polymer carrier. (Asija Rajesh, et.al.2012)

### 3. In-vivo evaluation test

In- vivo study for CTDDS various animals is used such as dogs, guinea pigs, rats etc. Because, anatomy and microflora of human GIT look like the dog, guinea pigs, and rats. The environment of the GIT of the rat, dog, and guinea pig is same as human GIT. (Gaurav Tiwari et.al.2012)(Singh Amritpal, Sharma Ankush et.al.2017)

### 4. Gamma scintigraphy

This method is used for study the passage time of drug through the GIT. The passage time is measured by this method. The sites of drug absorption are identified in pharmacokinetic studies because pharmacokinetic studies adopting the scintigraphy. The gamma radiations detect by crystal which developing from the subject. They give the digital result when the energy is transformed to light scintillation and amplified. In this technique low radiation are used in patients and is noninvasive. Gamma scintigraphy is also useful for study the clearance of the drug and food to the GIT. This technique also helpful for understanding the drug delivery process.

### 5. High frequency capsules

This method is important for study absorption properties of drug in colon. This method is used for to check the bioavailability of the drug in the colonic site. High frequency capsule is used for evaluating the relative bioavailability of the CTDDS. Drug release at various sites of GIT and advantages of relative bioavailability are evaluated and compare the absorption parameters. (Vyas, Khar Journal.2005) (Sangalli ME et al.2001) (Sinha VR, Kumria R. et.al.2003)

**Marketed product for colon disease: - (Singh N and Khanna RC et.al.2012)**

“MARKETED NAME”	“COMPANY NAME”	“DISEASE”	“DRUG”
“Mesacol tablet“	“Sunpharma”	“Ulcerative colitis”	“Mesalamine”
“Asacol”	“Win Medicare pharma”	“Ulcerative colitis, Crohn’s disease”	“Mesalamine”
“SAZO”	“Wallac India”	“Ulcerative colitis”, “Crohn’s disease”	“Sulphasalazine”
“Intazide”	“Intas,India”	“Ulcerative colitis”	“Balsalazide”
“COLOSPA”	“Solvay, India”	“Irritable colon syndrome”	“Mabeverine”
“CYCLOMINOL”	“Neol India”	“Irritable colon syndrome”	“Dicyclomine”

**Conclusion**

Colon is the part of the large intestine. The colonic region of the GIT has important site for drug delivery and this route increase the absorption of drug. This system is very useful for the local diseases because when drug administered through oral route then drug is not reach in colon because drug degrade in the GIT. CTDDS used for number of advantages to patients for both local and systemic treatment. It’s a very difficult task for the industry to manufacture colon targeting drugs because various factors that are produced difficulty to form CTDDS. It is very challenging to develop good formulation for the colon targeting because the drug only releases in the colon. Number of methods are used to formulate CTDDS. Nowadays other strategy, and other methods are used for CTDDS. CTDDS obtain importance in novel drug delivery.

we will study the new technology for colon targeting drug delivery system.

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