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# A Review on Colon Targeted Drug Delivery System by Novel Approaches

***Rushukesh A. Patil[1], Bhimashankar S. Hucche[2], Shyamlila B. Bavage[3]***

[1] B. pharm Final Year Student, Latur College of Pharmacy, Hasegaon TQ- Ausa Dist.- Latur-413512
[2] Assistant Professor, Latur College of Pharmacy, Hasegaon TQ- Ausa Dist.- Latur-413512.
[3] Department of Pharmacognosy, Latur College of Pharmacy, Hasegaon TQ- Ausa Dist.- Latur-413512.

ABSTRACT

Targeted drug delivery to the colon was tested not only for local colonic diseases, but also for the systematic delivery of drugs such as proteins and peptides. Local delivery may allow for topical treatment of inflammatory bowel disease. Treatment can be made more effective if the drug is directed directly at the colon helps and the systemic side effects can be reduced. Certain Colon systems may also allow oral administration of peptide and protein drugs, which are usually reduced in the upper parts of the intestinal tract. Treatment of colonic disorders (such as colon), such as colon cancer, irritable bowel syndrome IBS), inflammatory bowel disease ( (IBD) i.e. Ulcerative colitis and Crohn's disease, Diverticulitis and other intestinal diseases, where it is necessary to obtain high concentration of an effective therapeutic agent , can best be achieved with direct colon delivery. This is also a potential source of treatment for circadian-sensory diseases such as asthma, angina, high blood pressure, and rheumatoid arthritis. The main delivery mechanisms of certain colonic drugs (CDDS), including prodrugs, pH and time-dependent systems and the viral drug delivery system have been limited and limited. Newly developed CDDS, which include pressure controlled colonic delivery capsules (PCDCS) and delivery of osmotic-controlled drugs differs in achieving the in-vivo site specification and feasibility of the production process. The focus of this review is to provide a detailed understanding of the various diseases of the colony, the methods used to identify medical personnel especially in the colon.

## INTRODUCTION

Targeted drug delivery to the colon is highly desirable for local treatment of a variety of bowel diseases such as ulcerative colitis, crohan's disease amebiosis, colonic cancer, and for local treatment of local colonic pathologies, and the systemic delivery of protein and peptide drugs [1] .

The Dosage forms that bring drugs to the colon rather than the above GIT have many advantages. Oral administration of the drug to the colon is important in the treatment of colonic diseases where it can be obtained with high local concentration while minimizing side effects. Colon attracts interest as a site where a malfunctioning drug molecule may have improved availability because the colon has a long shelf life and appears to be responsible for agents that increase the absorption of poorly absorbed drugs. An easy way to identify drugs in the colony is to obtain slow release rates or longer duration of discharge through the use of thick layers of standard enteric dressings or slow matric release [2].

There are various ways or techniques in which colon drug administration can be achieved, for example, prodrug formulation, coating with pHsensitive polymers, coating with decaying polymers, formulation using polysaccharides, time-consuming systems, drug control systems of osmotic controlled systems. Coating the drug with pH-sensitive polymers provides an easy way colony-specific drug delivery [3]

## Advantage of CTDDS over Conventional Drug

- The colon has a low peptidase activity so peptides, oral insulin injections, growth hormones can be delivered through this route [4]
- Colon is a good place to bring in agents to treat local colon disease [5]
- Reduce abdominal irritation caused by many medications such as NSAIDS.
- Bypass the first digestion process.

- Extra night time work.
- Improve patient compatibility.
- It has a long shelf life and appears to be highly responsive to agents that increase the absorption of an intolerant drug [6,7].

## Limitation of Colon targeting drug delivery system-

- Lots of production steps.
- Incomplete release rate.
- The Bioavailability of drug Bioavailability may be low due to the drug binding in an unspecified form of food residue, waste, rash and intestinal obstruction.
- The lack of a suitable melting test method to test the in vitro measurement form [8].
- The drug should be in solution before ingestion and when limited to a step in reducing insoluble drugs.
- An important limitation of the PH cover-up approach is the uncertainty of the location where the garment can begin to melt. Common in a patient with ulceration colitis [9]

**TABLE No. 01-Colonic diseases, its sites and active drug components.[10]**

| **Targeted site** | **Disease** | **Drug** |
|---|---|---|
| **Topical** | Inflammatory bowel diseases (Crohn's disease, ulcerative colitis), Irritable bowel diseases, Amoebiasis | Hydrocortisone, Prednisolone, Sulfasalazine, Mesalazine, Mercaptopurine, Metronidazole, Mebendazole, Tinidazole. |
| **Systemic** | Oral delivery of peptide, oral delivery of vaccines, to prevent gastric irritation, To prevent first pass metabolism of orally administered drug. | Typhoid, NSAIDS, Steroids, Insulin |
| **Local** | Pancreatactomy, Colorectal cancer, cystic fibrosis, Chronic pancreatitis | 5- Fluorouracil, digestive enzymes |

**Factor affecting Colon targeted drug delivery system:- [11].**

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

1) Physiological factors

2) Pharmaceutical factors

**1) Physiological factors:-**

The factor which involve physiologically in drug delivery and responsible for affecting the targeting of drug to the colon are:-

**a) Gastric emptying**

Colon delivery of drugs to oral administration is highly dependent on abortion and bowel movement, which means that when you reach the colon the time of drug delivery depends on the nature and size of the particles. Larger particles have less travel time compared to smaller particles.

**b) pH of colon**

The pH of the intestinal tract is responsible for a variety of intermediate subjects. Disease status, Diet and diet affect the pH of the GI Tract. This change in pH in various parts of the GIT is the basis for the development of drug-specific drug delivery systems in Colon. Coating with different polymers is done to identify the tree at the site. [12].

**c. Colonic micro flora and enzymes**

GIT contains a variety of viruses that produce many enzymes that require metabolism. The growth of these microflora is controlled by GIT content and peristaltic movements. Enzymes secreted by various microorganisms E. coli, Clostridia, Lactobacilli, Eubacteria, Streptococci are responsible for a variety of immune responses that occur in GIT.

**2. Pharmaceutical factors**

**a. Drug candidates**

Due to the high colonization time, the colony causes an increase in the absorption of inactive substances such as peptides, etc. Drugs used for the treatment of inflammatory bowel diseases, etc. They are ready for the colonial drug delivery system.

**b. Drug carriers**

The choice of the CDDS carrier depends on the nature of the drug, the disease used for the drug. The various physicochemical features of the drug that make the choice of carriers include chemical nature, stability, equilibrium equilibrium, active groups of drug molecules etc.

**Polymers Used in Colon Targeting**

Polymer consists of a large number of construction units that are connected by a connection of the same type, forming a chain as a structure. These are the days that are used to make various pharmaceutical products. A naturally occurring polymer, which includes gummy exudates, proteins, enzymes, muscle fiber, polysaccharides. In the old days natural polymers were widely used in pharmacies but with the use of various types of synthetic polymers nowadays for the development of medicines and cosmetics, using many of these physical therapies, namely drug delivery control systems, are available [13,14]

**Natural polymer**

Guar gum, Inulin, Pectin, Cyclodextrin, Dextran, Amylase, Chitosan, Chondrotinsulphate, Locust bean gum.

**Synthetic polymer**

Shellac, Ethyl cellulose, Cellulosw acetate phthalate, Hydroxy propyl methyl cellulose, Eudragit, Poly vinyl acetate phthalate.

**Approaches for Colon Targeting**

Approaches used for site-specific drug delivery are:

**Primary Approaches for CDDS**

**pH Sensitive Polymer Coated Drug Delivery to Colon**

In the stomach the pH is between 1 and 2, during fasting but increases after meals. The pH is about 6.5 in the adjoining small intestine and about 7.5 in the distal small intestine. From the ileum to the colon pH dropped dramatically. About 6.4 in the ceacum. However, pH values as low as 5.7 were estimated in the rising colon for healthy volunteers. The pH in the flexible colon is 6.6, in the descending colon 7.0. The use of pH-based polymers depends on these variations in pH levels. Polymers defined as the pH dependence on the delivery of certain colon drugs are not solved at low pH levels but are increasingly melting as the pH increases. Although a pH-dependent polymer can prevent the formation of stomach and intestines in the small intestine, it can begin to melt even in the lower intestine and the specificity of the formation site can be poor. Decreased pH from the end of the small intestine to the colon can also lead to complications. Prolonged delays in the ileo-cecal organization or rapid escalation of the ascending colony can also lead to incorrect site specification of the embedded single unit. [15].

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

Time management system (TCRS) as a continuous or delayed release rate form is also very promising. However, due to the large diversity of time-consuming waste of volume forms in humans, in this way the timing of the arrival of colonization of dosage forms cannot be accurately predicted, leading to inaccurate colonization. Measurement forms can also serve as colonization measurement forms by extending the remaining time to about 5.5 h (grade 5 to 6 h).

The disadvantages of this approach are:

• The duration of an abortion varies greatly between subjects or depending on the type and amount of food eaten.

• Intestinal bowel movements, especially peristalsis or abdominal cramps can lead to changes in the bowel movement of the drug.

• Emergency mobility in different parts of the colon has been observed in patients with IBD.

• Timely programs are therefore not suitable for colonization of drugs, especially in the treatment of colon-related diseases. Proper integration of sensitive pH functions and release time into a single measurement form can improve the specification of a drug delivery site in a colony. That is because the duration of the flow of dosage forms in the small intestine is not very flexible which means about 3 ± 1 h. The digestive function (or part-time function) should be more efficient in the small intestine compared to the abdomen. In a small container of intestinal drugs will be delivered to the intended side and the withdrawal of the drug will begin at the prescribed time after the abortion. On the other side of the stomach, the release of the drug should be suppressed by the pH (acid-resistant) sensory function in the dosage form, which will reduce the variability in the duration of stay in the stomach.

**Enteric-Coated Time-Release Press Coated (ETP) Tablets**

ETP tablets are made up of three components, a core-containing drug tablet (fast extraction function), a hydrophobic polymer filling machine (Hydroxy propyl cellulose layer, a temporary extraction function) and an enteric coating (resistant function). acid). The tablet does not expel the drug from the stomach due to the acid resistance of the outer outer layer. After discharge, the enteric layer dissolves rapidly and the intestinal fluid begins to slowly erode the pressurized polymer layer (HPC) and when soil erosion reaches the main tablet, rapid drug release occurs since the erosion process takes a long time without drug withdrawal (phase -lag) after abortion. The duration of the lag phase is controlled by the weight or composition of the polymer layer (HPC).

**Microbially Triggered Drug Delivery To Colon**

The colon microflora is in the range of 1011-1012 CFU / mL, which contains mainly anaerobic bacteria e.g. Bacteroides, Bifidobacteria, Eubacteria, Clostridia, Enterococci, Enterobacteria and Ruminococcus etc. This large microflora fulfills its energy needs by digesting a variety of nutrients left undigested in the small intestine, e.g. di- and tri-saccharides, polysaccharides etc. In this fermentation the microflora produces large amounts of enzymes such as glucoronidase, xylosidase, arabinosidase, galactosidase, nitroreductase, azareducatase, deaminase, and urea dehydroxylase. Due to the presence of decaying enzymes only in the colon, the use of decaying polymers for the delivery of certain drugs to the colon appears to be a more site-specific approach compared to other methods. These polymers protect the drug in the areas of the stomach and small intestines and are able to deliver the drug to the colon. When they reach the colon, they are found to be thinner or damaged by enzymes or a breakdown of the polymer back bone leading to a subsequent reduction in their cellular weight and thus loss of mechanical strength. After that they can no longer run a drug business.

***Prodrug Approach for Drug Delivery to Colon***

Prodrug is based on an inactive drug molecule of the parent drug that requires automatic or enzymatic modification in-vivo to extract the active drug. Colon delivery Theprodrug is designed for small absorption and in the above GIT it undergoes an enzymatic conversion to the colon, which by releasing an active drug from the drug administrator. Azo chemical metabolism by intestinal bacteria is one of the most studied bacterial metabolic processes. Many other compounds involved in bacterial hydrolysis especially in the colon are prepared when the drug adheres to hydrophobic moitions such as amino acids, glucoronic acid, glucose, galactose, cellulose etc. as its composition depends on the active group available to drug interactions through chemical interactions. In addition prodrugs are new chemical substances and require extensive testing before being used as carriers.

***Azo-Polymeric Prodrugs***

New approaches are aimed at using polymers as carriers of drug delivery to the colon. Both synthetic and natural synthetic polymers are used for this purpose. Subsynthetic polymers used to form polymer prodrug and Azo interactions between the polymer body and the drug. These were tested with CDDS, various Azo polymers were also tested as coatings in addition to drug cores. These have been found to be similarly affected by Azo-reducatase in the large intestine. The discovery of peptide tablets and cross polymers linked to the Azo-aromatic group has been found to protect the drug from digestion in the stomach and intestines. In the colony Azo bonds are reduced and the tree is released.

***Polysaccharide Based Delivery System***

The use of naturally occurring polysaccharides attracts a lot of attention in the targeting of drugs in the colon because these monosaccharide polymers are widely available, widely available and inexpensive and available in frames with a variety of properties. They can be easily modified chemically and chemically and are very stable, safe, non-toxic, use hydrophilic and gel and add decomposition. These include naturally occurring polysaccharides found in plants (guar gum, inulin) animal (chitosan, chondrotinsulphate) algal (alginates) or microbial origin (dextran). This is separated by colonic microflora into simple saccharides.[16,17,18,].

**Newly Developed Approaches for CDDS**

**Pressure Controlled Drug Delivery Systems**

As a result of peristalsis, higher pressures converge on the colon than in the lower abdomen. Takaya et al. produce pressure-controlled anti-depressant pills prepared using ethyl cellulose, insoluble in water. In such systems drug withdrawal occurs after the dissolution of an insoluble polymer pill as a result of pressure on the colon light. The size of the ethyl cellulose membrane is the most important factor in structural fragmentation [19]. The system has emerged based on capsule size and size. Due to the recycling of water from the colon, the viscosity of the light content is higher in the colon than in the small intestine. It has therefore been concluded that drug depletion in the colony can pose a problem with regard to certain oral delivery systems. In ethyl cellulose single-unit capsules administered intravenously the drug is a liquid. Lag intervals of three to five hours in relation to drug absorption were noted when pressure-controlled pills were given to a person [20].

**Osmotic Controlled Drug Delivery (ORDS-CT)**

OROS-CT (Alzacorporation) can be used to identify a local drug in a colon to treat disease or to achieve systemic absorption that cannot be achieved otherwise. The OROS-CT system can be a single osmotic unit or can include 5-6 push-pull units, 4-mm wide each, enclosed within a hard gelatin capsule. Each draft blister unit consists of a layer of osmotic push and a layer of drugs, both surrounded by a impermeable membrane. The orifice is pierced in the membrane next to the drug layer. Immediately after the swallowing of OROS-CT, the gelatin capsule containing push-pull units dissolves. Due to its non-drug-absorbent coating, each suction unit is restricted from absorbing water to the acidic area of the stomach and therefore no medication is delivered. As the unit penetrates the small intestine, the coating dissolves at a higher pH (pH> 7), water entering the unit, causing the osmotic pressure chamber to swell and at the same time forming a gel flowing in the drug chamber. Inflammation of the osmotic pressure chamber forces the drug gel out of the orifice at a rate that is precisely controlled by the rate of fluid flow through the immeasurable membrane. In the treatment of ulcerative colitis, each push-pull unit is designed for 3-4 h post abdominal delays to prevent the delivery of the drug into the small intestine. Drug withdrawal begins when the unit reaches the colon. OROS-CT units can maintain an average discharge rate of up to 24 h in the colon. Various in vitro / in-vivo testing methods have been developed and proposed to test the effectiveness and stability of CDDS.[21,22]

## CONCLUSIONS

The GIT colonic region has become an extremely important center for drug delivery and absorption. Drug administration in a sick colony is beneficial in reducing the side effects of the system, reducing the dose of the drug, prescribing the drug only when necessary and keeping the drug in its immediate state as much as possible in the target area. All colonial drug delivery methods provide treatment options for local colon-related diseases or

systemic absorption of intolerant drugs. The wide range of pH values and various enzymes present throughout the intestinal tract, where the dosage form has to go before reaching the intended site, makes reliability, delivery of efficient naming and colonization work difficult.

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