COLON DRUG DELIVERY SYSTEM: A NOVEL PERSPECTIVE

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ABSTRACT

In the recent year colonic drug delivery has gained importance for delivery of drug for the treatment of local diseases associated with colon and systemic delivery of therapeutic peptides and proteins. Colonic drug delivery has gained increased importance not just for the delivery of the drugs for the treatment of local diseases associated with the colon like Crohn’s disease, ulcerative colitis, etc. but also for the systemic delivery of proteins, therapeutic peptides, anti-asthmatic drugs, antihypertensive drugs and anti-diabetic agents. Primary approaches for CTDDS (Colon targeted Drug Delivery System), which includes prodrugs, pH and time dependent systems, Bacterial enzyme dependent colonic DDS and pH and bacterial enzyme dependent colonic DDS. The novel approach of CTDDS, which includes pressure controlled colonic delivery capsules (PCDCS), CODES and osmotic controlled drug delivery are specific technique. This review article discusses introduction of colon, need and approaches of colonic drug delivery, factor effecting colonic transition, colonic diseases and the novel and emerging technologies for colon targeting.

Key Words: Colon specific drug delivery system, Advantages, Approaches.

INTRODUCTION

Targeted drug delivery to the colon is more desirable for local treatment of a variety of bowel diseases such as ulcerative colitis, Crohn’s disease, amebiosis, colonic cancer, and systemic delivery of protein and peptide drug. The delivery of drugs to the colon via gastrointestinal (GI) tract requires the protection of a drug from being released in stomach and small....

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intestine. It can be achieved by the use of drug delivery system (DDS) that can protect the drug during its passage to colon. And the drug must be released in the colon from the drug delivery system. Targeting depends on exploiting a unique feature of specific site and protecting the drug until it reaches to the site. Delivery of drugs via colon offers many therapeutic advantages. Drugs, which are destroyed by the stomach acid and metabolized by pancreatic enzymes, are protected. Sustained release of drugs into colon can be useful in the treatment of certain diseases. The colonic delivery is also useful for the systemic absorption of drugs like nifedipine, isosorbide, and theophylline.

The colon is the most suitable site for absorption of peptides and protein drugs for the following reasons:

- less degradation by digestive enzymes,
- proteolytic activity of colon mucosa is less than that observed in small intestine, thus CDDS protect peptide and protein drugs from hydrolysis, and enzymatic degradation in the duodenum and jejunum, and releases the drug into the ileum or colon which produces greater systemic bioavailability.

The colon has a long residence time which is up to 5 days and hence it is highly responsible for enhancement of absorption. The human colon has about 400 different species of bacteria as resident flora, The reactions carried out by this gut flora are azo-reduction and enzymatic cleavage i.e. glycosides\(^{[1,2]}\).

**Anatomy and Physiology of Colon\(^{[3,4]}\):** The large intestine extends from the distal end of the ileum to the anus. Human large intestine is about 1.5 m long. The colon is upper five feet of the large intestine and mainly situated in the abdomen. The colon is a cylindrical tube that is lined by moist, soft pink lining called mucosa; the pathway is called the lumen and is approximately 2-3 inches in diameter. The cecum forms the first part of the colon and leads to the right colon or the ascending colon (just under the liver) followed by the transverse colon, the descending colon, sigmoid colon, rectum and the anal canal (Figure 1). The physiology of the proximal and distal colon differs in several respects that have an effect on drug absorption at each site. The physical properties of the luminal content of the colon also change, from liquid in the cecum to semisolid in the distal colon.
Table 1: Length of different parts in colon \cite{4}

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Large Intestine</th>
<th>Length (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cecum</td>
<td>6-10</td>
</tr>
<tr>
<td>2</td>
<td>Ascending colon</td>
<td>20-25</td>
</tr>
<tr>
<td>3</td>
<td>Descending colon</td>
<td>10-15</td>
</tr>
<tr>
<td>4</td>
<td>Transverse colon</td>
<td>40-45</td>
</tr>
<tr>
<td>5</td>
<td>Sigmoid colon</td>
<td>35-40</td>
</tr>
<tr>
<td>6</td>
<td>Rectum</td>
<td>12</td>
</tr>
<tr>
<td>7</td>
<td>Anal canal</td>
<td>3</td>
</tr>
</tbody>
</table>

**pH in the Colon**: The pH of the gastrointestinal tract is subject to both inter and intra subject variations. Diet, diseased state and food intake influence the pH of the gastrointestinal fluid. The change in pH along the gastrointestinal tract has been used as a means for targeted colon drug delivery.

Table 2: pH of various parts in gastrointestinal tract \cite{4}

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Location</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><strong>Stomach</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fasted condition</td>
<td>1.5 - 2.0</td>
</tr>
<tr>
<td></td>
<td>Fed condition</td>
<td>3.0 - 5.0</td>
</tr>
<tr>
<td>2</td>
<td><strong>Small intestine</strong></td>
<td>5.0 - 6.4</td>
</tr>
<tr>
<td></td>
<td>Jejunum</td>
<td>6.0 - 7.5</td>
</tr>
</tbody>
</table>
Colon targeted Drug Delivery system (CTDDS)

Colon targeted Drug Delivery system (CTDDS) may be follow the concept of sustained or controlled drug delivery system, for CTDDS oral route of administration has received most attention. This is because of the flexibility in dosage form designed for oral than parenteral route because

I. Patient acceptance for the oral administration of the drug is quite high.

II. It is relatively safe route of drug administration compared with parenteral route and potential damage at site of administration is minimal.

Most of the conventional drug delivery systems for treating the colonic disorder such as Inflammatory bowel diseases i.e. Ulcerative colitis, Cohn’s diseases, Colon cancer and Amoebiasis are failing as drug do not reach the site of action in appropriate concentration. For effective and safe therapy of these colonic disorders, colon specific drug delivery is necessary. Today, colon specific drug delivery is challenging task to pharmaceutical technologists. Therapeutic advantages of targeting drug to the diseased organ include.

Therapeutic advantages of targeting drug to the diseased organ includes [5,6]

a) The ability to cut down the conventional dose
b) Reduced the incidence of adverse site effects
c) Delivery of drug in its intact form as close as possible to the target sites.

Colon specific drug delivery systems are also gaining importance for the delivery of protein and peptides due to several reasons as follow

a) Rapid development of biotechnology and genetic engineering resulting into the availability of protein and peptide drugs at reasonable cost.
b) Proteins and peptide drugs are destroyed and inactivated in acidic environment of the stomach or by pancreatic enzymes in small intestine.

<table>
<thead>
<tr>
<th></th>
<th>Ileum</th>
<th>6.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td><strong>Large intestine</strong></td>
<td>6.7 – 7.2</td>
</tr>
<tr>
<td></td>
<td>Right colon</td>
<td>6.4</td>
</tr>
<tr>
<td></td>
<td>Mid colon &amp; Left colon</td>
<td>6.0 – 7.0</td>
</tr>
</tbody>
</table>
c) Parental route is expensive and inconvenient.

d) Longer residence time, less peptidase activity and natural absorptive characteristics make the colon as promising site for the delivery of protein and peptide drug for systemic absorption.

e) Less diversity and intensity of digestive enzymes.

f) Comparative proteolytic activity of colon mucosa is much less than that observed in the small intestine, thus CDDS protects peptide drugs from hydrolysis, and enzymatic degradation in duodenum and jejunum, and eventually releases the drug into ileum or colon which leads to greater systemic bioavailability.

**Advantages of CTDDS over Conventional Drug Delivery:** Chronic colitis, namely ulcerative colitis, and Crohn’s disease are currently treated with glucocorticoids, and other anti-inflammatory agents. Administration of glucocorticoids namely dexamethasone and methyl prednisolone by oral and intravenous routes produce systemic side effects including adeno suppression, immune suppression, cushinoid symptoms, and bone resorption. Thus selective delivery of drugs to the colon could not only lower the required dose but also reduce the systemic side effects caused by high doses \[6\].

**Need of colon targeted drug delivery** \[^{7,8}\]
Targeted drug delivery to the colon would ensure direct treatment at the disease site, lower dosing and fewer systemic side effects.

Site-specific or targeted drug delivery system would allow oral administration of peptide and protein drugs, colon-specific formulation could also be used to prolong the drug delivery.

Colon-specific drug delivery system is considered to be beneficial in the treatment of colon diseases.

The colon is a site where both local or systemic drug delivery could be achieved, topical treatment of inflammatory bowel disease, e.g. ulcerative colitis or Crohn’s disease. Such inflammatory conditions are usually treated with glucocorticoids and sulphasalazine (targeted).

A number of others serious diseases of the colon, e.g. colorectal cancer, might also be capable of being treated more effectively if drugs were targeted to the colon.
Formulations for colonic delivery are also suitable for delivery of drugs which are polar and/or susceptible to chemical and enzymatic degradation in the upper GI tract, highly affected by hepatic metabolism, in particular, therapeutic proteins and peptides.

Limitations [8,9]
- As a site for drug delivery, the colon offers a near neutral pH, reduced digestive enzymatic activity, a long transit time and increased responsiveness to absorption enhancers. However, the targeting of drugs to the colon is very complicated.
- Due to its location at the distal portion of the alimentary canal, the colon is particularly difficult to access.
- In addition, the wide range of pH values and different enzymes present throughout the GI tract, through which the dosage form has to travel before reaching the target site, further complicate the reliability and delivery efficiency.
- Successful delivery through this site also requires the drug to be in solution form before it arrives in the colon or, alternatively, it should dissolve in the luminal fluids of the colon, but this can be a limiting factor for poorly soluble drugs as the fluid content in the colon is much lower and it is more viscous than in the upper part of the GI tract.
- The drug could potentially bind in a nonspecific manner to dietary residues, intestinal secretions, mucus or faecal matter. The resident microflora could also affect colonic performance via metabolic degradation of the drug.
- Lower surface area and relative ‘tightness’ of the tight junctions in the colon can also restrict drug transport across the mucosa and into the systemic circulation.

Criteria for Selection of Drug for CDDS [10]
CTDDS are drugs which show poor absorption from the stomach or intestine including peptides.
The drugs used in the treatment of IBD, ulcerative colitis, diarrhea, and colon cancer are prominent for local colon delivery.
- Drugs used for local effects in colon against GIT diseases
- Drugs poorly absorbed from upper GIT
- Drugs for colon cancer Drugs that degrade in stomach and small intestine
Drugs that undergo extensive first pass metabolism
Drugs poorly absorbed from upper GIT
Drugs for targeting

Factors affecting colon targeted drug delivery \cite{10}

1) Physiological factors
   a. Gastric emptying
   b. pH of colon
   c. Colonic microflora and enzymes

2. Pharmaceutical factors
   a. Drug candidates
   b. Drug carriers

Table 3: Drug metabolizing enzymes in the colon that catalyze reactions \cite{11}

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

Approaches for colon targeted drug Delivery \cite{12}

1. Primary approaches for colon targeted drug delivery
   a. pH sensitive polymer coated drug delivery system
   b. Delayed release drug delivery system
   c. Microbially triggered drug delivery
      i. Prodrug approach
      ii. Polysaccharide based system.

2. New approaches for colon targeted drug delivery
   a. Pressure controlled drug delivery system (PCDDDS)
   b. CODE
c. Osmotic controlled drug delivery system (OROS-CT)
d. Pulsatile
   i. Pulsincap system
   ii. Port system
e. Azo hydrogels
f. Multiparticulate system based drug delivery

a) pH sensitive polymer coated drug delivery system
The pH varies in different parts of the gastrointestinal tract. The pH in stomach ranges between 1 and 2 during fasting. The pH in the proximal part of small intestine is 6.5 and in distal part of small intestine it is 7.5. The pH is 6.4 in caecum, 5.7 in ascending colon, 6.6 in transverse colon and 7.0 in descending colon. The pH dependent drug delivery system is based on the solubility of different polymers at different pH ranges. The polymers are insoluble at lower pH values and get solubilized as the pH increases. As the polymers are insoluble at lower pH values the polymer can protect a formulation in stomach and to some extent in small intestine. In this way by altering the polymers used the release of drug from the formulation can be controlled\(^{[13]}\).

b) Delayed or time controlled release drug delivery system: Time controlled drug delivery system\(^{[2]}\) includes sustained or delayed release systems. In this system the delayed release or colon targeted drug delivery is attained by prolonging the lag time. The transit time varies in different parts of gastrointestinal tract. This transit time is responsible for the delayed release of drug. The main drawbacks of this delivery system are that the transit time varies from one person to other and amount of food intake. It also varies with the peristalsis or contraction in the gastrointestinal tract.

c) Microbial triggered drug delivery system: The various microflora of the colon are Bacteroides, Bifidobacteria, Eubacteria, Clostridia, Enterococci, Enterobacteria and Ruminococcus, etc. This microflora of gut depends on fermentation of undigested materials in the small intestine for their energy requirements. The microflora performs fermentation by producing a large number of enzymes like glucoronidase, xylosidase, arabinosidase, galactosidase, nitroreductase, and deaminase and urea dehydroxylase. These biodegradable enzymes are capable of degrading the polymers used for targeting the drug delivery to colon. Different polymers are used for preventing the release of drug in the stomach and small intestine. When the coated formulations reach the intestine the biodegradable polymers get...
degraded by the enzymes produced by the microbial flora and the drug gets released in the targeted region.

Prodrug \cite{14} is the main approach of microbial triggered drug delivery system in which the drug release from the formulation is triggered by the microflora present in the gut. Prodrug is the inactive form of an active parent drug that undergoes enzymatic transformation to release the active drug. The produrgs are prepared by linking the active drug with hydrophobic moieties like amino acids, glucoronic acids, glucose, galactose, cellulose, etc. These produrg molecules get hydrolysed in the presence of the enzymes released by the microflora.

The main drawback of this approach is that the formulation depends on the functional groups available on drug moiety for chemical linkage. The produrgs formed upon linkage results in the formation of new chemical entities that need a lot of evaluation before using them as carriers.

The most widely used prodrug approach is the metabolism of azo compounds by intestinal bacteria. Polysaccharide based delivery system is the other form of microbial triggered drug delivery system. Naturally occurring polysaccharides like guar gum, xanthan gum, chitosan, alginates, etc. are used in targeting the drug delivery. These are broken down by the colonic microflora to simple saccharides.

Table 4: Different polymers used for CDDS based on Microbial drug delivery system \cite{14}

<table>
<thead>
<tr>
<th>Class</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disaccharides</td>
<td>Lactose, Maltose</td>
</tr>
<tr>
<td>Oligosaccharides</td>
<td>Cyclodextrins, Lactulose, Raffinose, Stachyose</td>
</tr>
<tr>
<td>Polysaccharides</td>
<td>Alginates, Amylose, Cellulose, Chitosan, Starch, Chondroitin sulphate, pectin, xanthan gum, etc.</td>
</tr>
</tbody>
</table>

d) Pulsatile colon targeted drug delivery

i) Pulsincap system: In this system the formulation is developed in a capsule form. The plug placed in the capsule controls the release of the drug. Swellable hydrogels are used to seal the drug contents.

The capsule, \cite{15} gets swelled when it comes in contact with the dissolution fluid and after a lag time the plug gets pushed off from the capsule and the drug will be released. Polymers such as different grades of hydroxy propyl methyl cellulose (HPMC), poly methyl
methacrylate and polyvinyl acetate are used as hydrogel plugs. The lag time is controlled by the length and point of intersection of the plug in the capsule body.

![Fig 2: Pulsincap system](image)

**ii) Port system**

In this system the capsule body is enclosed in a semipermeable membrane. The capsule body consists of an insoluble plug consisting of osmotically active agent and drug formulation. When the capsule comes in contact with the dissolution fluid the semi permeable membrane permits the fluid flow into the capsule resulting in the development of pressure in the capsule body which leads to release of drug due to expelling of the plug. The drug is released at regular intervals with time gap between the successive intervals [16].

![Fig 3: Port system](image)

**e) Pressure controlled drug delivery system:** Digestion mainly occurs due to the contractility of the stomach and peristaltic movement of the intestine. The contractility
movement of stomach leads to the digestion or breakdown of larger particles to smaller ones which are then transferred to intestine. The peristaltic movement of intestine is responsible for the passage of bolus from one part of GIT to the next part. The peristaltic movement of ascending colon transfers the bolus to transverse colon called as mass peristalsis. These peristaltic movements occur in limited number i.e. three to four times a day.

These peristaltic movements of intestine results in an increase in the luminal pressure. This increase in luminal pressure is the key point in the development of pressure controlled drug delivery system.

The pressure controlled drug delivery system \[17\] consists of a capsule in which the drug is present. These gelatin capsules are coated with water insoluble polymer like ethyl cellulose on their inner side. The drug is introduced into the capsule along with suppository base. The thickness of ethyl cellulose coating determines the disintegration capacity of the capsule. After administration the suppository base dissolves at body temperature. The water from intestinal contents is absorbed resulting in increased viscosity which leads to an increase in the pressure in the capsule. The pressure in the capsule expels the drug into the colon. The intestinal pressure developed varies with the circadian rhythms, state of body, food administration, etc.

f) CODES technology

This method is developed to minimize the problems associated with the pH and time dependent drug delivery systems. In this system the pH sensitive polymers are used along with the polysaccharides that are degraded only by specific bacteria present in the intestine. This system consists of a core tablet coated with three layers of polymer coatings \[15\].

The outer coating is composed of the polymer Eudragit L. This coating gets dissolved once the tablet passes through the pyloric and duodenum and exposes the next coating. The next coating is composed of Eudragit E. This layer allows the release of lactulose present in the inner core. This released lactulose gets metabolized into short chain fatty acids that lower the surrounding pH where the Eudragit E layer dissolves. The dissolving of Eudragit E results in the exposure of the drug. The other polysaccharides that are used along with the drug in the core tablet are mannitol, maltose, etc. The bacteria present in the colon are responsible for the degradation of polysaccharides that are released from the core tablet. The degradation of
polysaccharides results in organic acids formation that lowers the pH of the contents surrounding the tablet.

g) Osmotically controlled colon targeted drug delivery system
This system [18] consists of osmotic units. The osmotic units are used either singly or as many as 5-6 push pull units that are encapsulated in a hard gelatin capsule. The push pull units are bilayered with outer enteric impermeable membrane and inner semi permeable membrane. The internal or central part of the push pull consists of the drug layer and push payer. The semi permeable membrane which is present next to the drug layer consists of an orifice through which the drug contents are expelled during the course of time.

The capsule body enclosing the push pull units gets dissolved immediately after administration. During the passage of the push pull units through the GIT the enteric impermeable membrane prevents the water absorption into the unit. The coating gets dissolved once it reaches the small intestine due to higher pH (>7). Water enters the unit through the semi permeable membrane causing the push layer to swell. The swelling of the push compartment forces the drug into the surrounding environment through the orifice. These osmotic controlled drug delivery systems deliver the drug at a constant rate for up to 24hr.

h) Multi particulate system based drug delivery
The various advantages of multi-particulate systems are increased bioavailability, reduced risk of local irritation, reduced risk of systemic toxicity. The various multi-particulate approaches include pellets, micro particles, granules and nano particles. Multi-particulates systems are preferred over single unit dosage forms as the multi-particulate systems enables the drug to reach the colon quickly and retained in colon for long period of time. These systems pass through the GIT easily due to their smaller size. Multi-particulate systems are dispersed more uniformly in the GIT resulting in more uniform drug absorption.

Nano particles
The preparation of nano particles [19] is simple and these are capable of protecting the protein and peptide drugs from the chemical and enzymatic degradation in GIT resulting in an increase in their stability and absorption of through the intestinal epithelium. The polymeric nano particles are prepared by various techniques like polymerization, nano precipitation, inverse microemulsion. The methods involve the use of organic solvents, heat and agitation.
The drawback of these methods is that the heat, agitation is harmful to proteins and peptide drugs. Ionic gelation technique is the most widely used method for proteins and peptide drugs.

i) Azo hydrogels
The pH sensitive monomers and azo cross linking agents in the hydrogel produce the colon specificity. During their passage through the GIT these hydrogels swell as the pH increases. This swelling of hydrogels cleaves the cross links in the hydrogel network causing the release of drug entrapped in the hydrogel. These hydrogels are prepared by cross linking polymerization of N- substituted (meth) acrylamides, N- tert- butyl acrylamide and acrylic acid with 4, 4-di (methacryloylamino) azobenzene as cross linking agents. The hydrogels are also prepared by crosslinking polymeric precursors, polymer- polymer reaction using same polymeric precursor with the corresponding copolymer containing side chains terminating in NH2 groups. The degradation rate of hydrogel is associated with the degree of swelling and inversely proportional to the cross linking density.[19].

EVALUATION
In Vitro Evaluation
No standardized evaluation technique is available for evaluation of CDDS because an ideal in vitro model should posses the in vivo conditions of GIT such as pH, volume, stirring, bacteria, enzymes, enzyme activity and other components of food. Generally these conditions are influenced by the diet and physical stress and these factors make it difficult to design a slandered in vitro model. In vitro model used for CDDS are:

In vitro dissolution test: Dissolution of controlled-release formulations used for colon-specific drug delivery are usually complex, and the dissolution methods described in the USP cannot wholly mimic in vivo conditions such as those relating to pH, bacterial environment and mixing forces. Dissolution tests relating to CDDS may be carried out using the conventional basket method. Parallel dissolution studies in different buffers may be undertaken to characterize the behavior of formulations at different pH levels. Dissolution tests of a colon- specific formulation in various media simulating pH conditions and times likely to be encountered at various locations in the gastrointestinal tract. The media chosen were, for example, pH 1.2 to simulate gastric fluid, pH 6.8 to simulate the jejunal region of the small intestine, and pH 7.2 to simulate the ileal segment. Enteric-coated capsules for CDDS have been investigated in a gradient dissolution study in three buffers. In vitro test for
intactness of coatings and carriers in simulated conditions of stomach and intestine. Drug release study in 0.1 N HCl for 2 hours (mean gastric emptying time) Drug release study in phosphate buffer for 3 hours (mean small intestine transit time)

**In vitro enzymatic test:** For this there are 2 tests:

1. Incubate carrier drug system in fermenter containing suitable medium for bacteria (Streptococcus faecium or B.ovatus) amount of drug released at different time intervals determined.

2. Drug release study is done in buffer medium containing enzymes (enzyme pectinase, dextranase), or rat or guinea pig or rabbit cecal contents. The amount of drug released in particular time is determined, which is directly proportional to the rate of degradation of polymer carrier.

**In Vivo Evaluation:** A number of animals such as dogs, guinea pigs, rats and pigs are used to evaluate the delivery of drug to colon because they resemble the anatomic and physiological conditions as well as the microflora of human GIT. While choosing a model for testing a CDDS, relative model for the colonic diseases should also be considered. Eg. Guinea pigs are commonly used for experimental IBD model. The distribution of azoreductase and glucouronidase activity in the GIT of rat and rabbit is fairly comparable to that in the human. For rapid evaluation of CDDS a novel model has been proposed. In this model the human fetal bowel is transplanted into a subcutaneous tullel on the back of thymic nude mice, which vascularizes within 4 weeks, matures and becomes capable of developing of mucosal immune system from the host. **Clinical Evaluation** Absorption of drugs from the colon is monitored by colonoscopy and intubation. Currently gamma scintigraphy and high frequency capsules are the most preferred techniques employed to evaluate colon drug delivery systems.

- **High frequency capsule:** Smooth plastic capsule containing small latex balloon, drug and radiotracer taken orally. Triggering system is high frequency generator. Release of drug & radiotracer triggered by an impulse, the release is monitored in different parts of GIT by radiological localization. It checks the absorption properties of drug in colon.

- **Gammascintigraphy:** By means of gammascintigraphic imaging, information can be obtained regarding time of arrival of a colon-specific drug delivery system in the colon, times of transit through the stomach and small intestine, and disintegration. Information about the
spreading or dispersion of a formulation and the site at which release from it takes place can also be obtained. Gammascintigraphic studies can also provide information about regional permeability in the colon. Information about gastrointestinal transit and the release behaviour of dosage forms can be obtained by combining pharmacokinetic studies and gammascintigraphic studies (pharmacoscintigraphy).

CONCLUSION
Colon targeted drug delivery system offers benefits of local and systemic effects. The main advantage of CDDS is that the colon offers near neutral pH, a long transit time, reduced enzymatic activity and increased responsiveness to absorption enhancers. Biodegradable polymers are used for the colon specific delivery of the drug. The novel approaches from past two year were really more specific compared to the primary approaches especially in overcoming the side effect. Considering the sophistication of colon-specific drug delivery systems, and the uncertainty of current dissolution methods in establishing possible in-vitro/in-vivo correlation, challenges remain for pharmaceutical scientists to develop and validate a dissolution method that incorporates the physiological features of the colon, and yet can be used routinely in an industry setting for the evaluation of CDDS.

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