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Review Article

# COLON TARGETED DRUG DELIVERY SYSTEMS APPLICATION AND FORMULATION CONSIDERATION: A REVIEW

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## ABSTRACT

Colon targeted drug delivery systems (CTDDS) have emerged as an effective approach for the site-specific delivery of therapeutic agents to the colon, thereby improving treatment efficacy and minimizing systemic side effects. The oral route remains the most preferred method for colon targeting due to its convenience, patient compliance, and formulation flexibility. Conventional drug delivery systems often fail to deliver adequate drug concentrations to the colon for the treatment of disorders such as ulcerative colitis, Crohn's disease, colon cancer, and amoebiasis. Therefore, specialized colon-specific delivery systems are required to achieve localized and controlled drug release. Various physiological factors, including colonic pH, transit time, microflora, and enzymatic activity, play a crucial role in the design and performance of CTDDS. Different approaches such as pH-dependent, time-dependent, bacterial enzyme-triggered, pressure-controlled, osmotic-controlled, and combined systems have been extensively investigated for effective colon targeting. Natural polysaccharides such as chitosan, pectin, guar gum, alginate, and dextran have shown promising potential due to their biodegradability and susceptibility to colonic bacterial degradation. In vitro and in vivo evaluation techniques are essential for assessing the performance and site specificity of CTDDS. Colon-targeted systems offer several advantages including reduced dosing frequency, improved bioavailability, minimized gastric irritation, and enhanced local therapeutic action. However, challenges such as variable gastrointestinal conditions, limited drug absorption, and lack of ideal in vitro models still remain. Recent advances in nanotechnology and polymer science may further enhance the development of efficient and reliable colon-targeted drug delivery systems in the future.

**Keywords:** Colon targeted drug delivery system, Colon specific delivery, Polysaccharides, pH-dependent system, Bacterial enzyme-triggered delivery, Chitosan, Controlled drug delivery, Inflammatory bowel disease, Oral drug delivery, Nanotechnology.

## INTRODUCTION

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

- Patient acceptance for the oral administration of the drug is quite high (Flory, 1953).
- 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 (Mcginity *et al*., 1999).

**Therapeutic advantages of targeting drug to the diseased organ includes**

- The ability to cut down the conventional dose
- Reduced the incidence of adverse site effects
- Delivery of drug in its intact form as close as possible to the target sites (Brahamankar and Jaiswal, 1995; Chourasia and Jain, 2003).

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

- Rapid development of biotechnology and genetic engineering resulting into the availability of protein and peptide drugs at reasonable cost.
- Proteins and peptide drugs are destroyed and inactivated in acidic environment of the stomach or by pancreatic enzymes in small intestine.
- Parental route is expensive and inconvenient.
- 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 (Threveen *et al*., 2011).
- Less diversity, and intensity of digestive enzymes.
- 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 (Karanjit and Kim, 2009).

**Factors to be affected in the design of colon - targeted drug delivery system**

**Anatomy and Physiology of Colon**

The GI tract is divided into stomach, small intestine and large intestine. The large intestine extending from the ileocecal junction to the anus is divided in to three main parts. These are the colon, the rectum and anal canal. The entire colon is about 5 feet (150 cm) long, and is divided in to five major segments. The right colon consists of the cecum, ascending colon, hepatic flexure and the right half of the transverse colon and the values were shown in table. The left colon contain the left half of the transverse colon, descending colon, splenic flexure and sigmoid. The rectum is the last anatomic segment before the anus (Chourasia and Jain, 2003).

**pH in the colon**

The pH of the GI tract is subject to both inter and intra subject variations. Diet, diseased

state, and food intake influences the pH of the gastrointestinal fluid. The changes in the pH along the gastrointestinal tract have been used as a means for targeted colon drug delivery. Radio telemetry shows the highest pH (7.5±0.5) in the terminal ileum. On entry into the colon, the pH drops to 6.4±0.6. The pH in the mid colon is 6.6±0.8 and in the left colon 7.0±0.7. There is a fall in pH on entry into the colon due to the presence of short chain fatty acids arising from bacterial fermentation of polysaccharides. For example lactose is fermented by the colonic bacteria to produce large amounts of lactic acid resulting in pH drop to about 5.0.

**Colonic Microflora and Enzymes**

A large number of anaerobic and aerobic bacteria are present in the entire length of the human GI tract. Intestinal enzymes are used to trigger drug release in various parts of the GI tract. Usually, these enzymes are derived from gut micro flora residing in high numbers in the colon. These enzymes are used to degrade coatings or matrices as well as to break bonds between an inert carrier and an active agent (i.e. ., release of a drug from a prodrug).over 400 distinct bacterial species have been found 20-30% of which are of the genus bacteroids. The concentration of bacteria in the human colon is around 1000 CFU/ml. The most important anaerobic bacteria are Bacteroides, Bifidobacterium, Eubacterium, Peptococcus, and Peptostreptococcus, Ruminococcus, Clostridium (Threveen *et al*., 2011).

**Transit of Material in the Colon**

The presence of food material generally increases gastric residence and in some cases with regular feeding, dosage forms have been shown to reside in the stomach for periods in excess of 12 hours. Small intestinal transit is surprisingly constant at 3-4hours and appears to be independent of the type of dosage form and whether the subject is in the fasted or fed state. Compared to other regions of the gastrointestinal tract, movement of materials through the colon is slow. The total time for transit tends to be highly variable and influenced by a number of factors such as diet, in particular dietary fiber content, mobility, stress, disease and drugs. Colonic transit times ranged from 50 to 70 hours. Stool weights increased significantly with the presence of active disease presumably due to exudates form inflamed epithelium, increased mucus secretion, and reduction in reabsorption of fluid and electrolytes.

**Drug absorption in the colon**

Drugs are absorbed passively by either paracellular or transcellular route. Transcellular absorption involves the passage of drugs through cells and this is the route most lipophilic drugs takes, where paracellular absorption involves the transport of drug through the tight junction between cells and is the route most hydrophilic drug takes. The poor paracellular absorption of many drugs in the colon is due to the fact that epithelial cell junctions are very tight. The slow rate if transit in colon lets the drug stay in contact with the mucosa for a longer period than in small intestine which compensates the much lower surface area. The colonic contents become more viscous with progressive absorption of water as one travels further through the colon (Kaur and Kim, 2009).

The oral absorption of the majority of peptide and protein drugs is limited because of following reasons:

- Degradation in the acidic environment of the stomach

- Enzymatic degradation in the small and large intestine
- Rapid small intestine transit
- Low mucosal permeability
- Extensive first pass metabolism by the absorbing membrane and the liver

**Approaches of colonic drug delivery system**

In general, seven primary approaches have been proposed for targeted colon delivery, namely,

- Transit time dependent colonic DDS
- pH Dependent colonic DDS
- pH- and time-dependent colonic DDS
- Bacterial enzyme dependent colonic DDS
- pH and bacterial enzyme dependent colonic DDS
- Colonic pressure controlled DDS
- Osmotic pressure controlled colonic DDS (Brahamankar and Jaiswal, 1995)

**1] Transit time dependent colonic DDS**

Transit time dependent colonic DDS such as sustained or delayed release dosage forms are one of important drug release systems. However, due to potentially large variations of gastric emptying time of dosage forms in humans, in these approaches, colon arrival time of dosage forms cannot be accurately predicted, resulting in poor colonical availability. The dosage forms may also be applicable as colon targeting dosage forms by prolonging the lag time of about 5 to 6 h. However, the disadvantages of this system area. Gastric emptying time varies markedly between subjects or in a manner dependent on type and amount of food intake. Gastrointestinal movement, especially peristalsis or contraction in the stomach would result in change in gastrointestinal transit of the drug (Brahamankar and Jaiswal, 1995).

**2] pH Dependent colonic DDS**

The pH-dependent CTDDS exploit the generally accepted view that pH of the human GIT increases progressively from the stomach (pH 1-2 which increases to 4 during digestion), small intestine (pH 6-7) at the site of digestion and it increases to 7-8 in the distal ileum. The coating of pH-sensitive polymers to the tablets, capsules or pellets provide delayed release and protect the active drug from gastric fluid. The polymers used for colon targeting, how- ever, should be able to withstand the lower pH values of the stomach and of the proximal part of the small intestine and also be able to disintegrate at the neutral of slightly alkaline pH of the terminal ileum and preferably at the ile-ocecal junction. These processes distribute the drug throughout the large intestine and improve the potential of colon targeted delivery systems. While this release pattern can be studied in-vitro, there is no real substitute for confirming reliable performance in vivo in man (Chourasia and Jain, 2003).

**3] pH- and time-dependent colonic DDS**

The transit time through the small intestine is independent of the formulation. But, the time taken by the formulation to leave the stomach varies greatly. Hence, the time of arrival of a formulation in the colon cannot be accurately predicted. However, the effects of variation in gastric residence time can be minimized by using systems that prevent drug release until 3-4 hr after leaving the stomach. A multiple coated oral dosage form consisting of core coated with three polymeric layers has developed. A novel oral time based drug release system for colon specific delivery.

Drug targeting to colon would be prove useful where intentional delayed drug absorption is desired from therapeutic point of view in treatment of circadian diseases that have peak symptoms in the early morning such as nocturnal asthma, angina pectoris and rheumatoid arthritis. Colon specific drug delivery systems are gaining the importance for systemic as well as local effect. Colon specific drug delivery system is popular for treatment of inflammatory bowel diseases (IBD), delivery of protein and peptide drugs, for circadian diseases and also for improving the systemic absorption of the some drugs, additionally following chart help in selection of drug candidate for colon specific drug delivery (Threveen *et al*., 2011).

**4] Bacterial enzyme dependent colonic DDS**

The micro flora of the colon is in the range of 1011-1012 Cfu/ml consisting mainly of anaerobic bacteria, e.g. Bacteroides Bifid bacterium, Eubacteria, Clostridia, Enterococci, Enterobacteria and Ruminococcus etc.

These microflora fulfills its energy needs by fermenting various types of substrates that have been left undigested in the small intestine, like di- and trisaccharides, polysaccharides etc. For this fermentation, the micro flora produces a vast number of enzymes like glucoronidase, xylosidase, arabinosidase, galactosidase, nitroreductase, azareducatase, deaminase, and urea dehydroxylase. Because of the presence of the biodegradable enzymes only in the colon, the use of biodegradable polymers for colon-specific drug delivery seems to be a more site-specific approach as compared to other approaches.

These polymers shield the drug from the environments of stomach and small intestine, and are able to deliver the drug to the colon. On reaching the colon, they undergo assimilation by micro-organism, or degradation by enzyme or break down of the polymer back bone leading to a subsequent reduction in their molecular weight and thereby loss of mechanical strength. They are then unable to hold the drug entity any longer.

The majority of bacteria are present in the colon they are distributed throughout the GI tract. Endogenous and exogenous substrates, such as carbohydrates and proteins, escape digestion in the upper GI tract but are metabolized by the enzymes secreted by colonic bacteria.

Sulphasalazine, a Prodrug consisting of the active ingredient mesalazine, was the first bacteriasensitive delivery system designed to deliver the drug to the colon. Use of polysaccharides offers an alternative substrate for the bacterial enzymes present in the colon. Most of the polymers are used in pharmaceutical compositions and are considered generally regarded as safe (GRAS) recipients (Reddy *et al*., 1999).

**a) Azo Prodrugs**

The azo linkage exhibits a wide range of thermal, chemical, photochemical and pharmaceutical properties. The azo compounds are extensively metabolized by the intestinal bacteria, both by intracellular enzymatic components and extracellular reduction. The use of these azo compounds for colon targeting has been in the form of hydrogels as a coating material for coating the drug cores, and as prodrugs. Sulphasalazine, which was used for the treatment of rheumatoid arthritis, was later known to have

potential in the treatment of inflammatory bowel disease (IBD). This compound has an azo bond between 5-ASA and sulpha pyridine (Mcginity *et al*., 1999).

**b) Polymeric /Saccharide Prodrug**

The use of naturally occurring polysaccharides is attracting a lot of attention for drug targeting the colon since these polymers of mono saccharides are found in abundance, have wide availability are inexpensive and are available in a verity of a structures with varied properties. They can be easily modified chemically, biochemically, and are highly stable, safe, nontoxic, hydrophilic and gel forming and in addition, are biodegradable. These include naturally occurring polysaccharides obtained from plant (guar gum, inulin), animal (chitosan, chondrotin sulphate), algal (alginates) or microbial (dextran) origin. The polysaccrides can be broken down by the colonic microflora to simple saccharides. Therefore, they fall into the category of "generally regarded as safe" (GRAS).

Chitosan is a high molecular weight cationic polysacacharide, poly (Nglucosamine), derived from chitin in crab and shrimp shells by deacetylation. It is degraded by the rich colonic microflora. Chitosan has been evaluated for colon specific drug delivery mainly in the form of a capsule forming material. Pectin is another non-starch linear polysaccharides with mainly a-(1-4)- linked Dgalacturonic acid residues interrupted by 1, 2- linked Lrhamnose (Flory, 1953).

**Table 1: Polysaccharides investigated for colon-specific drug delivery**

| Drug Moiety Used | Polysaccharide Conjugation | Dosage Form Prepared |
|---|---|---|
| Diclofenac Sodium | Chitosan | Enteric-coated chitosan microspheres |
| Insulin | Chitosan | Enteric-coated chitosan capsules |
| Indomethacin | Pectin (as calcium salt) | Matrices |
| Paracetamol | Amidated pectin | Matrix tablets |
| Indomethacin | Amidated pectin | Chitosan-coated amidated pectin beads |
| Ropivacaine | Amidated pectin | Matrix tablets |
| Dexamethasone | Guar gum | Matrix tablets |
| Bovine Serum Albumin | pH-sensitive dextran | Hydrogels |
| Indomethacin | Chondroitin sulphate | Matrix tablets |
| Radioactive Tracer | Starch | Enteric-coated capsules |
| 5-ASA | Alginate (as calcium salt) | Double-coated swellable beads |
| Theophylline | Locust bean gum | Films |
| Theophylline | Dextran fatty acid esters | Films |

**c) Amino acid Prodrug**

Hydrophilic nature of polar groups like -NH2 and -COOH, that is present in the proteins and their basic units (i.e. the amino acids), they reduce the membrane permeability of amino acids and proteins.

Various prodrugs have been prepared by the conjugation of drug molecules to these polar amino acids. Non-essential amino acids such as tyrosine, glycine, methionine and glutamic acid were conjugated to SA.

The prodrug was absorbed into the systemic circulation from the upper GIT and hence it was proved unsuitable for delivery of drugs to the colon. By increasing the hydrophilicity and chain length of the carrier amino acid and decreasing the membrane permeability of conjugate Nakamura *et al*. prepared salicylic glutamic acid conjugates.

This conjugate showed splendid results with minimal absorption and degradation in the upper GIT and proved suitable for colon targeted delivery of SA.

Glycine and glutamic acid conjugates of salicylic acid: (a) Salicyluric acid. (b) Salicyl Glutamic acid conjugate (OKOR, 1982).

**5] pH and bacterial enzyme dependent colonic DDS (CODES SYSTEM)**

CODES system is a unique CTDDS technology that was designed to avoid the inherent problems associated with pH or time dependent systems. CODES system is a combined approach of pH dependent and microbially triggered CDDS. It has been developed by utilizing a unique mechanism involving lactulose, which acts as a trigger for site specific drug release in the colon. The system consists of a traditional tablet core containing lactulose, which is over coated with and acid soluble material, Eudragit E, and then subsequently overcoated with an enteric material, Eudragit L (Armand *et al*., 1987).

The premise of the technology is that the enteric coating protects the tablet while it is located in the stomach and then dissolves quickly following gastric emptying. The acid soluble material coating then protects the preparation as it passes through the alkaline pH of the small intestine. Once the tablet arrives in the colon, the bacteria enzymetically degrade the polysaccharide (lactulose) into organic acid. This lowers the pH surrounding the system sufficient to affect the dissolution of the acid soluble coating and subsequent drug release (Ashford, *et al*., 1993).

**6] Colonic pressure controlled DDS (PCDC SYSTEM)**

As a result of peristalsis, higher pressures are encountered in the colon than in the small intestine. developed pressure controlled colon- delivery capsules prepared using ethylcellulose, which is insoluble in water. In such systems, drug release occurs following the disintegration of a water-insoluble polymer capsule because of pressure in the lumen of the colon. The thickness of the ethylcellulose membrane is the most important factor for the disintegration of the formulation (Martin, 1993).

The system also appeared to depend on capsule size and density. Because of reabsorption of water from the colon, the viscosity of luminal content is higher in the colon than in the small intestine. It has therefore been concluded that drug dissolution in the colon could present a problem in relation to colon- specific oral drug delivery systems. In pressure controlled ethylcellulose

single unit capsules the drug is in a liquid. Lag times of three to five hours in relation to drug absorption were noted when pressurecontrolled capsules were administered to humans (Yasuda *et al*., 1971).

**7] Osmotic pressure controlled colonic DDS**

**a) Osmet Pump (ALZET) ALZET®**

Osmotic Pumps are miniature, infusion pumps for the continuous dosing of unrestrained laboratory animals as small as mice and young rats. These minipumps provide researchers with a convenient, reliable, and cost-effective method for controlled delivery of agents. ALZET miniosmotic pumps require no external connections or researcher intervention during the entire delivery period. Their unique design helps researchers save critical time by eliminating the need for frequent animal handling and repetitive injection schedules. These dependable drug delivery systems ensure that constant levels of compounds be maintained at therapeutic levels, thus avoiding potentially toxic or misleading side effects. An assortment of sizes, flow rates and durations is available to meet a variety of research needs. A single ALZET pump provides up to 6 weeks of continuous infusion (Dew *et al*., 1982).

**b) OROS CT**

The OROS-CT can be used to target the drug locally to the colon for the treatment of disease or to achieve systemic absorption that is otherwise unattainable. The OROS-CT system can be single osmotic unit or may incorporate as many as 5-6 push-pull units, each 4mm in diameter, encapsulated within a hard gelatin capsule. Each bilayer push pull unit contains an osmotic push layer and a drug layer, both sur- rounded by a semipermeable membrane. An orifice is drilled through the membrane next to the drug layer (Fara, 1989). Immediately after the OROS-CT is swallowed, the gelatin capsule containing the push-pull units dissolves. Because of its drug-impermeable enteric coating, each push-pull unit is prevented from absorbing water in the acidic aqueous environment of the stomach and hence no drug is delivered.

For treating ulcerative colitis, each push pull unit is designed with a 3-4 hour post gastric delay to prevent drug delivery in the small intestine. Drug release begins when the unit reaches the colon. OROS-CT units can maintain a constant release rate for up to 24 h in the colon or can deliver drug over an internal as short as 4 hour.

**Evaluations of CTDDS**

Various in vitro and in vivo techniques used to evaluate CTDDS. The in vitro studies are more difficult to buy as the conditions and physiology of the stomach not easily recreated in vitro due to the influence of factors on the GIT. Hence in vitro models should inhabit the same conditions and factors as present in vivo such as pH, volume, stirring, bacteria, enzymes, enzyme activity, and other components of food (Chaubey *et al*., 2019; Opera and Voicus, 2020). These factors also influenced by diet and physical stress. The evaluation parameters of CTDDS are of two types.

**1] *In vitro* evaluations**

Generally, depending on type of formulation, the evaluation varies like whether the formulation is pH dependent system or system degraded by bacterial microflora.

**Dissolution test:** The release of drug form controlled-release formulations is a complex mechanism. The description of the method as per USP is difficult to mimic the *in vivo* conditions using the basket-type dissolution apparatus. The drug release can study at various buffer solutions at different ph. For example, a solution of pH 1.2 used to simulate gastric fluid, pH 6.8 to simulate the jejunal segment of the small intestine, and pH 7.2 to simulate the ileum part of the small intestine. Meanwhile, enteric-coated formulations can evaluate using three different buffers, each for a specific time. For example: these formulations evaluated for two hours at pH 1.2, followed by one hour at pH 6.8, and then at pH 7.4 for 2 h in 0.1N HCl of pH 1.2 as well as Sorensen's or Phosphate buffer of pH 7.4. The formulation should release its content when the pH is 6.8 which is the colonic pH (Shete *et al*., 2020).

Enzymatic tests involve the incubation of the carrier drug delivery system in a suitable bacterial culture medium containing microorganisms such as *Streptococcus faecium* and *Streptococcus ovis* under controlled fermentation conditions.

Drug release is measured at different predetermined time intervals in alkaline buffer solutions containing enzymes such as pectinase and dextranase, or in media containing guinea pig or rabbit rectal contents. Additionally, rat fecal matter is also used because it contains colonic bacteria capable of producing enzymatic activity even after 7 days. The rate of polymer degradation is directly proportional to the amount of drug released at the specified time interval (Oprea and Voicus, 2020).

**2] *In vivo* evaluations**

Animals like dogs, guinea pigs, rats, and pigs that have similar anatomic, physiological and microflora of the human gut used to evaluate CTDDS. Guinea pigs are the most widely used animal model for IBD. Rats and rabbits have azo-reductase and glucuronidase activity in the GIT that resemble with humans.

**String technique:** A tablet attached to a string and allowed to swallow but leaving the string outside of the mouth. The string removed to examine the disintegration of tablet at different time intervals. Another method used to follow this technique is swallowing the tablet with induction of vomit in the subject (Mehta *et al*., 2011).

**Endoscope technique:** The model injected with the drug and a gastroscope used to view the disintegration of tablet at once. A sedative administered to allow for the endoscope to swallowed.

**Roentgenography:** A radio-opaque material like barium sulphate incorporated in the solid dosage form and viewed by x-ray to detect the movement of formulation as well as the disintegration of the drug after oral administration (Shete *et al*., 2020).

**Radio telemetry:** The effect of changes in the pH on disintegration of formulation captured by the insertion of a pH probe having capsule into the body.

**Drug Delivery Index (DDI) and Clinical Evaluation of Colon-Specific Drug Delivery:** This is a

pharmacokinetic (PK) parameter used to measure the DDI of colon prodrugs. It considered as the ratio of relative colonic tissue introduction to the medication to the relative measure of medication in blood for example that is relative fundamental exposal to the medication. A higher DDI indicated better medication transportation.

**γ–Scintigraphy:** It is an imaging model to visualize the activity of drug delivery without being an invasive method using a 99m-Tc DTPA tracer the process performed on guar gum matrix tablets. It followed by scintigraphy taken at various time intervals of the tablet for qualitative evaluations, however, it has disadvantages like the need of professional, qualified personnel and being an overall expensive procedure (Oprea and Voicu, 2020).

**Advantages**

- Ideal site for the delivery of active agents to cure the colon diseases (ulcerative colitis, Chron's diseases, amoebiasis, etc.).
- Smaller drug quantities should be required for local treatment.
- Less side effects and drug interactions occurs.
- Dosage frequency is less so, cost effective.
- The long retention time of colon, improved bioavailability of poorly absorbed drug molecules (up to 5 days).
- Reduce gastric irritation caused by many drugs by preventing their absorption in upper GIT (e.g., NSAIDS).
- Bypass initial first pass metabolism
- Extended daytime or night time activity (Mehta *et al*., 2011).

**Limitation and challenges**

- Hard accessibility of the colon because of its location at the distal part of the alimentary canal.
- The drug may bind non-specifically to intestinal contents (dietary residues, intestinal secretions, fecal matter) cause reduce drugs bioavailability.
- Metabolic degradation of the drug by resident microflora could also affect colonic performance.
- Restrict drug transport across the mucosa and into the systemic circulation due to lower surface area and relative tight junctions in the colon.
- Lack of an appropriate dissolution testing method to evaluate the dosage form in-vitro.
- The drug in solution form required for successful colon delivery or alternatively, it should dissolve in the luminal fluids of the colon, but this can be a limiting factor for poorly soluble drugs (Balvir *et al*., 2013).

**Conclusion**

Colon targeting drug delivery systems allows both systematic and local action of the drug molecule, supplyingtherapeutic benefits for patient's safety, efficacy, and decreasing systemic side effects. Choice of suitable technique for colon targeting depends on varied factors such as type of formulation, physiological properties of the gastrointestinal tract, and physicochemical factors and these factors may be challenging to controlled for colon

targeting drug delivery systems. A successful colon targeting delivery can obtained by preventing drug release and absorption in upper gastrointestinal tract by various technique that explained above and releasing the drug to colon, and the different colonic enzymes that formed by microorganisms help in releasing thedrug particle and metabolizing the drug carrier linkage. It is better to combine both conventional systems and newer approaches to develop a good colon drug delivery system, but for future research for colon targeting drug delivery, the exploration of nanotechnology studies seems a field for the new technique developments.

## DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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