An Updated Review On Colon Targeted Drug Delivery

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ABSTRACT

Colon targeted drug delivery systems have attracted many researchers due to distinct advantages such as near neutral pH, longer transit time and reduced enzymatic activity. Colon specific drug delivery not only increases the bioavailability of the drug at the target site, but also reduces the side effects. In the recent studies, colon targeted drug delivery systems are gaining importance to treat local pathologies of the colon (crohn’s disease, inflammatory bowel disease, colonic cancer) and also for the systemic delivery of protein and peptide drugs. This is because the peptide and protein drugs gets destroyed or inactivated in acidic environment of the stomach or by pancreatic enzymes in the small intestine. Various approaches such as pressure dependent, pH-dependent, time-dependent and microflora-activated systems have been developed for colon specific drug delivery. The use of polymers, specifically biodegraded by colonic bacterial enzymes holds great promise for colon targeted drug delivery.

Key words: Colon targeted delivery, Prodrug, pH-dependent systems, time-dependent systems, azo conjugates, dextran conjugates.

INTRODUCTION

Although oral delivery has become a widely accepted route of administration of therapeutic drugs, the gastrointestinal tract presents several formidable barriers to drug delivery. Various peptide and protein drugs get destroyed or inactivated in acidic environment of the stomach or by pancreatic enzymes in the small intestine. Hence 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 but also for its potential for the delivery of proteins and therapeutic peptides.¹ To achieve successful colonic delivery, a drug needs to be protected from absorption in the environment of the upper gastrointestinal tract (GIT) and then be abruptly released into the proximal colon, which is considered as the optimum site for colon-targeted delivery of drugs. Colon targeting is naturally of value for the topical treatment of diseases of colon such as Crohn’s diseases, ulcerative colitis, colorectal cancer and amoebiasis.³

ANATOMY OF COLON

Superficial Anatomy⁴, ⁵

Colon is a part of gastro-intestinal tract (Fig. 1). The colon is a tube-like organ in the abdominal cavity. The human gastrointestinal tract is divided mainly into stomach, small intestine and large intestine. The large intestine extending from the ileocecal junction to the anus is divided into three parts namely colon, rectum and anal canal. The colon is approximately five feet (1.5 meters) in length, begins at the ileocecal valve, and ends at the rectosigmoid junction. The colon is made up of the caecum, the ascending colon, the hepatic flexure, the transverse colon, the splenic flexure, the descending colon and the sigmoid colon.

Blood Supply⁴, ⁶

Arterial blood supply to the colon from caecum to splenic flexure is through the superior mesenteric artery which gives rise to the ileocolic, right colic, and middle colic arteries (Fig. 2). The left and sigmoid colon is supplied by the inferior mesenteric artery which gives rise to the left colic and sigmoidal arteries. The venous drainage is by the inferior mesenteric vein draining into the splenic vein, and the superior mesenteric vein joining the splenic vein to form the hepatic portal vein that then enters the liver (Fig. 3). Lymphatic drainage from the entire colon is to the paraaortic lymph nodes that then drain into the cisterna chyli.

Histology⁶, ⁷

The wall of the colon is composed of four layers namely the serosa, the muscularis externa, the submucosa and the mucosa. The serosa is the exterior coat and consists of areolar tissue that is covered by a single layer of squamous mesothelial cells. The major muscular coat of colon is muscularis externa. This is composed of an inner circular layer of fibers and an outer longitudinal layer. The submucosa is the layer of connective tissue that lies immediately beneath the mucosa. Lining the lumen of colon, the mucosa is divided into
epithelium, lamina propria and muscularis mucosae. Closely spaced crypts extend down into the surface of the mucosa. The muscularis mucosa consists of a layer of smooth muscle and separates the submucosa from lamina propria. The lamina propria supports the epithelium and occupies space between the crypts and beneath the crypts. The epithelium consists of a single layer of cells, which lines the crypts and covers the surface of the mucosa. Three major cell types found in the epithelium are the columnar absorptive cells, goblet (mucous cells), and enteroendocrine cells.

Nerve supply
The sympathetic nerve supply to colon extends downwards from the coeliac plexus and its extensions on the antero-lateral aspects of the aorta, on each side, are usually one, two, or three fine bundles of intermesenteric nerves. These nerves are joined laterally by rami from the upper lumbar ganglia, or adjoining parts of the lumbar sympathetic cord, of their own side. There are usually two or three slender strands of nerve fibers passing across the aorta to connect the intermesenteric nerves of the two sides. The inferior mesenteric plexus is formed by a number of sets of fibers arising from the medial sides of the right and left intermesenteric nerves, and these fibers form a dense network around the inferior mesenteric artery about half to three-quarters of an inch beyond its origin. From the dense plexus around the stem of the inferior mesenteric artery perivasular fibers can be traced along all the branches of this vessel. Below the origin of the inferior mesenteric plexus three descending bundles are usually found, which converge to form the hypogastric plexus.

The colon receives parasympathetic fibers from splenic nerves (sacral outflow). On examining closely the lower part of the hypogastric and pelvic plexuses, a small bundle of fibers can be seen on their ventral aspect on each side. The two bundles are easily separated from the main plexuses and can be traced upwards, where they converge to meet and fuse to the left side of the hypogastric plexus. The small trunk, formed by the fusion of the two bundles, can be followed upwards over the left common iliac artery to the inferior mesenteric plexus. On joining the inferior mesenteric plexus the fibers mix with the sympathetic fibers, but with care it can be seen that these parasympathetic fibers extend as a perivasular plexus mainly on to the left colic artery and its ascending and descending divisions.

PHYSIOLOGY OF COLON
Absorption of water & electrolytes and propulsion of unabsorbed fecal waste
The major functions of the colon are absorption of water and electrolytes and propulsion of unabsorbed fecal waste for evacuation. Approximately one liter of fluid chyme enters the caecum each day with an average of only 100 ml excreted in the feces. By the time the chyme has reached to colon, most nutrients and 90% of the water present in it is absorbed by the body. At this point some electrolytes like sodium, magnesium, and chloride as well as indigestible parts of ingested food are left. As the chyme moves through the large intestine, most of the remaining water is removed, while the chyme is mixed with mucus and bacteria, and becomes feces. The descending colon receives fecal material as a liquid. The muscles of the colon then move the watery waste material forward and slowly absorb all the excess water. The stools get to become semi solid as they move along into the descending colon.

Secretion of mucus
The colon lining contains epithelial cells that secrete mucus. This mucus moisturizes and lubricates the colon lining. This lining protects the colon wall and nerve tissues.

Bacterial growth
Bacteria live and grow along the colon lining. Using the fluid and food intake, bacteria actually manufacture the nutrients that sustain their environment and their food supply.

Manufacture of some vitamins & electrolytes
Colonic bacteria change proteins into amino acids and break these amino acids down further into indole and skatole (which gives stools their odor), hydrogen sulfide, and fatty acids. Bacterial action also synthesizes some vitamins (K and some B), electrolytes, and breaks down bilirubin into a pigment that gives stools their brown color.

Production of lubrication
Colonic bacteria ferment soluble fiber into a lubricating gel that is incorporated into the stool mass as it is formed. This gel helps to make stools soft and flexible. Some of this gel also coats the exterior of the stools and is used by the colon to moisturize the colon lining. This lubrication helps to ease stool passage through the colon.
Defense against infection
Healthy intestinal bacteria help to groom the colon and keep it clean so that infections do not develop. They also help to fight the growth of infectious bacteria.

SIGNIFICANCE OF COLON TARGETED DRUG DELIVERY

a) Targeted drug delivery to the colon would ensure direct treatment at the disease site.
b) It enables lower dosing of drug.
c) Fewer systemic side effects are observed by targeted drug delivery to the colon.
d) Helps to delay the drug absorption.
e) Drugs that cause gastric irritation or ulceration can be directed to colon using targeted delivery approaches.
f) Suitable for delivery of drugs which are polar, susceptible to chemical and enzymatic degradation in the upper gastrointestinal tract, or highly affected by hepatic metabolism.
g) Lower daily cost to patient because fewer dosage units are required by the patient.

APPROACHES TO COLONIC DRUG DELIVERY

a) Drug release based on variation of pH
In the stomach pH ranges between 1 and 2 during fasting but increases up to 4 after eating. The pH is about 6.5 in the proximal small intestine and about 7.5 in the distal small intestine. pH values as low as 5.7 have been measured in the ascending colon in healthy volunteers. The pH in the transverse colon is 6.6, in the descending colon 7.0. Use of pH dependent polymers is based on these differences in pH levels.

Various pH-dependent coating polymers include cellulose acetate phthalate (CAP), poly vinyl acetate phthalate (PVAP), hydroxypropyl methyl cellulose phthalate (HPMCP) and methacrylic acid copolymers, commonly known as Eudragit. Eudragit products are pH-dependent methacrylic acid polymers containing carboxyl groups. They are of two types Eudragit S and Eudragit L. Eudragit S is soluble above pH 7 and Eudragit L above pH 6. Eudragit S coatings protect well against drug liberation in the upper parts of the gastrointestinal tract and have been used in preparing colon-specific formulations. Eudragit S coatings have been used to target the anti-inflammatory drug 5-aminosalicylic acid (5-ASA) to colon.

b) Drug release based on gastrointestinal transit time (Pulsatile drug delivery)
Pulsatile release systems are formulated to undergo a lag-time of predetermined span of time of no release, followed by a rapid & complete release loaded drugs. The approach is based on the principle of delaying the time of drug release until the system transits from mouth to colon. A lag-time of 5 hours is usually considered sufficient since small intestine transit is about 3-4 hours, which is relatively constant and hardly affected by the nature of formulation administered. This system offers many advantages over conventional oral drug delivery systems like patient compliance, reduced dosage, reduced dosage frequency, avoidance of side effects, and provides nearly constant drug level at the target site.

Enteric coated time-release press coated tablets are developed that consist of three components, a drug layer containing core tablet, the press coated swellable hydrophilic polymer layer and an enteric coating layer. The tablet does not release the drug in the stomach due to the acid resistance of the outer enteric coating layer. After gastric emptying, the enteric coating layer rapidly dissolves and the intestinal fluid begins to slowly erode the press coated polymer layer. When the erosion front reaches the core tablet, rapid drug release occurs (Fig. 4).

Fig. 4: Time controlled (Pulsatile) drug release system

[Diagram showing enteric coating layer, enteric coating layer, and rapid drug release]

Fig. 5: Conjugates for targeted colonic delivery

1. Dexamethason-21-β-glucoside conjugate. 2. α Cyclolestin ester conjugate of ibuprofen. 3. Dexamethasone- β-D-glucuronide conjugate. 4. Salicyl-glutamic acid conjugate. 5. Sulfapyridine azo conjugate

Glycoside conjugates
Steroid glycosides and the unique glycosidase activity of the colon microflora form the basis of a new colon targeted drug delivery system. Drug glycosides are hydrophilic and thus, poorly absorbed from the small intesti-
tine. Once such a glycoside reaches the colon, it can be cleaved by bacterial glycosidases, releasing the free drug to be absorbed by the colonic mucosa. The major glycosidases identified in human faeces are β-D-galactosidase, β-D-glucosidase, α-L-arabinofuranosidase, β-D-xylopyranosidase. Friend and Chang have synthesized dexamethasone-21-β-glucoside for delivery of these steroids to the colon.19

**Cyclodextrin conjugates**

Cyclodextrins (CyDs) are cyclic oligosaccharides consisting of six to eight glucose units joined through α-1,4 glucosidic bonds and have been utilized for targeting of drugs to colon. An anti-inflammatory drug biphenyldiacetic acid (BPAA) as model drug was selectively conjugated onto one of the primary hydroxyl groups of α, β and 7-CyDs through an ester or amide linkage, and the in vivo drug release behavior of these prodrugs in rat gastrointestinal tract after oral administration was investigated. The CyD prodrugs were stable in rat stomach and small intestine and released BPAA specifically in colon.20

**Dextran conjugates**

Mcleod et al synthesized dextran ester prodrugs of dexamethasone and methyldprednisolone and proved the efficacy of the prodrugs for delivering drugs to the colon.21,22 In this study, methyl prednisolone and dexamethasone were covalently attached to dextran by the use of a succinate linker.

**Glucuronide conjugates**

Bacteria of the lower GIT secrete β-glucuronidase and can de-glucuronidate a variety of drugs in the intestine. Haeberlin et al. prepared a dexamethasone-β-D-glucuronide prodrug, which successfully delivered dexamethasone specifically to colon.23 Nolen et al. investigated the steady-state pharmacokinetics of corticosteroid delivery from glucuronoid prodrugs in normal and colitic rats.24 Two prodrugs, dexamethasone-β-D-glucuronide (DXglrd) and Budesonide-β-D-glucuronide (BUDglrd) were administered by intragastric infusion to conventional and colitic rats. In addition, dexamethasone and budesonide were administered either intragastrically or subcutaneously to healthy and colitic rats and colon-specific delivery was assessed using the drug delivery index. In conventional rats, drug delivery indices for DXglrd ranged from about five to as high as 11 in the luminal contents relative to dexamethasone administered subcutaneously or intragastrically. Drug delivery index values were also elevated in the mucosa of both healthy and colitic rats following intragastric administration of DXglrd. Budesonide was delivered somewhat less effectively from BUDglrd to the rat large intestine than was dexamethasone from DXglrd.

**Amino acid conjugates**

Due to hydrophilic nature of polar groups like -NH$_2$ and -COOH present in the proteins and their basic units amino acids, their membrane permeability is reduced. Various prodrugs have been prepared by conjugation of drug molecules to these polar amino acids through the amide linkages.25, 26

**Azo bond conjugates**

Sulfasalazine, is the prodrug in which sulfapyridine is linked to a 5-aminosalicylic acid by an azo bond. Chemically it is salicylazosulfapyridine. When taken orally, only a small proportion of the ingested dose is absorbed from the small intestine and the bulk of the sulfasalazine reaches the colon intact. There it splits at the azo bond by the colonic bacteria with the liberation of 5-aminosalicylic acid and sulfapyridine respectively.9

By replacing the sulfapyridine molecule with others, a number of prodrugs of 5-aminosalicylic acid have been prepared e.g. 4-amino benzoyl-β-alanine in balsalazide and 4-amino benzoyl glycine in isalazine.27 The most interesting prodrug is olsalazine, which is a dimer representing two molecules of 5-aminosalicylic acid that are linked via an azo bond. When olsalazine reaches the large intestine, it is cleaved releasing two molecules of 5-aminosalicylic acid.28

d) **Pressure-controlled drug-delivery systems**

As a result of peristalsis, higher pressures are encountered in the colon than in the small intestine. Pressure controlled colon delivery capsules have deoveloped using an ethyl cellulose, which is insoluble in water.16 In such systems, drug release occurs following disintegration of a water-insoluble polymer capsule as a result of pressure in the lumen of the colon. The thickness of the ethyl cellulose membrane is the most important factor for disintegration of the formulation. The system also appeared to depend on capsule size. When salivary secretion of caffeine after oral administration of pressure-controlled capsules was studied in human volunteers, a correlation was found between ethyl cellulose membrane thickness and the time of first appearance of caffeine in the saliva. Lag times of three to five hours in relation to drug absorption were noted when pressure controlled capsules were administered to human subjects. It was concluded that the capsules disintegrated in the colon because of increase in pressure.

e) **Osmotically controlled system (ORDS- 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. The OROS-CT system can be a single osmotic unit or may incorporate as many as 5-6 push-pull units, each 4 mm in diameter, encapsulated within a hard gelatin capsule. Each bilayer push pull unit contains an osmotic push layer and a drug layer, both surrounded by a semi permeable membrane. An orifice is drilled through the membrane next to the drug layer.17 (Fig. 6).

![Fig. 6: Osmotically controlled drug delivery](image)

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. As the unit enters the small intestine, the coating dissolves in this higher pH environment (pH > 7), water enters the unit, causing the osmotic push compartment to swell, and concomitantly creates a flowable gel in the drug compartment. Swelling of the osmotic push compartment forces drug gel out of the orifice at a rate precisely controlled by the rate of water transport through the semi permeable membranes.

**POLYMERS FOR COLON TARGETED DELIVERY**

Due to the presence of the biodegradable enzymes only in the colon, the use of biodegradable polymers for colon-specific drug delivery seems to be a useful approach. 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-organisms, 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. This leads to the release of drug to colon. 30, 31, 32, 33, 34

**Guar gum**

Guar gum is derived from the seeds of the *cyomopsis tetragonolobus* (Family Leguminosae). Chemically, guar gum is a polysaccharide composed of the sugars galactose and mannose. The backbone is a linear chain of β- 1, 4-linked mannose residues to which galactose residues are 1, 6-linked at every second mannose, forming short side-branches. Guar gum is used in colon targeted drug delivery systems due to its drug release retarding property and susceptibility to microbial degradation in large intestine. 35

Wong et al. studied the dissolution of dexamethasone and budesonide from guar gum-based formulations using reciprocating cylinder dissolution apparatus (USP Dissolution Apparatus III) and observed that the drug release in simulated colonic fluid was markedly increased at galactomannan concentrations >0.01 mg/ml. 36

Krishniah et al. performed the pharmacokinetic evaluation of guar gum-based colon-targeted tablets of mebendazole against an immediate release tablet in six healthy human volunteers. Colon-targeted tablets showed delayed $t_{max}$ (9.4±1.7 h) and absorption time, and decreased $C_{max}$ (25.7±2.6 μg/ml) and absorption rate constant when compared to the immediate release tablets. The results of the study indicated that the guar gum-based colon-targeted tablets of mebendazole did not release the drug in stomach and small intestine, but delivered the drug to the colon resulting in a slow absorption of the drug and making the drug available for local action in the colon. 37

Core tablets containing 5-aminosalicylic acid (5-ASA) were prepared by wet granulation with starch paste and were compression coated with coating formulations containing different quantities of guar gum. The study confirmed that selective delivery of 5-ASA to the colon can be achieved using guar gum as a carrier in the form of compression coating over the drug core. 38

**Pectin**

Pectin is a linear, heterogeneous polysaccharide which is mainly composed of galacturonic acid and its methyl ester. These are predominantly linear polymers of mainly (1’4) linked D-galacturonic acid residue interrupted by 1, 2-linked L-rhamnose residue with a few hundred to about one thousand building blocks per molecule. It is one of the major sources of dietary fiber and is extracted from fruit and vegetable cell walls. 39 Calcium pectinate, the insoluble salt of pectin was used for colon targeted drug delivery of Indomethacin by Rubeinstein et al. 40

Dupuis et al. used zinc pectinate beads for colonic delivery of ketoprofen and reported similar performance when compared to calcium pectinate in hard capsules, but significant differences when the same pellets were compared encapsulated in enteric hard capsules. 41 This study revealed that zinc pectinate beads could protect drug entrapped sufficiently from the upper gastro-intestinal conditions and drug release will be controlled by pectin degradation with colonic microflora. Zinc pectinate beads in enteric hard capsules are promising as a carrier for specific colonic delivery of drugs after oral administration.

**Chondroitin Sulfate**

Chondroitin sulphate is a mucopolysaccharide, which consists of D-glucuronic acid linked to N-acetyl-D-galactosamine. 42 It is degraded by the anaerobic bacteria of the large intestine mainly by *B. thetaiotaomicron* and *B. ovatus*. The high water solubility of chondroitin sulphate put hurdles in the formulation of colon targeted drug delivery systems and hence crosslinking has been reported to alleviate this problem. Chondroitin sulphate was cross-linked with 1, 12 diaminododecanec using dicyclohexylcarbodiimide as a catalyst and formulated in a matrix with indomethacin as a drug marker. The indomethacin release kinetics from the various formulations was analyzed in PBS with and without rat caecal content at 37°C under carbon dioxide atmosphere and it was concluded that release of indomethacin was dependent upon the biodegradation action of the caecal content. 42

**Dextran**

It is a polysaccharide consisting of linear chains of α-D glucose molecules, 95% of the chains consist of 1, 6-a-linked linear glucose units while the side chains consist of 1, 3-a-linked moieties. 43 They are obtained from microorganisms of the family *Lactobacillus* (*Leuconostoc mesenteroides*). Dextrans are colloidal, hydrophilic, and water-soluble substances which are inert for the biological system. Dextranases are the enzymes that hydrolyze glycosidic linkages of the dextrans. Anaerobic gram-negative intestinal bacteria show dextranase activity of the colon especially by the bacteroides of colon. Glucocorticoid-dextran ester prodrugs have been prepared and proved efficacious in delivering drugs to colon. 44

**Chitosan**

Chitosan is functional linear polymer obtained from the alkaline deacetylation of chitin. Chitosan consists of the repeated units of (2-amino-2-deoxy-D-glucopyranose) which are linked by (1-4)-β-bonds. Chitosan is a nontoxic, biodegradable, biocompatible and bioactive polymer. It is used for the colon targeted drug delivery because it has a tendency to dissolve in acidic pH of stomach but get swollen in the intestinal pH. 45

Tozaki et al. developed colon-specific insulin delivery with chitosan capsules. *In vitro* drug release experiments from chitosan capsules containing 5 (6)-carboxyfluorescein (CF) were carried out by rotating basket method with slight modifications. The intestinal absorption of insulin was evaluated by measuring the plasma insulin levels and its hypoglycaemic effects after oral administration of the chitosan capsules containing insulin and additives. Little release of CF from the capsules was observed in an artificial gastric juice (pH 1), or in an artificial intestinal juice (pH 7). However, the release of CF was markedly increased in the presence of rat caecal contents. 46

**Cyclodextrin**

Cyclodextrins (CyDs) are cyclic oligosaccharides that consist of six to eight glucose units through 1,4 glucosidic bonds and have been utilized to improve certain properties of drugs such as solubility, stability and bioavailability. The interior of these molecules is relatively lipophilic and the exterior relatively hydrophilic, they tend to form inclusion complexes with various drug molecules. They are known to be barely capable of being hydrolyzed and only slightly absorbed in passage through the stomach and small intestine; however they are fermented by colonic microflora into small saccharides and thus absorbed in the large intestine. 47

**Inulin**

It is a naturally occurring polysaccharide found in plants such as garlic, onion and chicory. Chemically, it belongs to the glucofructans and consists of a mixture of oligomers and polymers containing 2-60 (or more) β-2-1 linked D-fructose molecules. Most of these fructose chains have a glucose unit as the initial moiety. It is not hydrolyzed by the endogenous secretions of the human digestive tract. Inulin has been incorporated into Eudragit RS films for preparation of mixed films that resisted degradation in the upper GI tract but digested in the human fecal medium by the action of bifidobacteria and bacteroides. 48
Amlose
It is a poly (1-4-α -D-glucopyranose) that consists of D-glucopyranose residues linked by α- (1-4) bonds. It being present naturally in the diet has the advantage of being safe, nontoxic, and easily available. It is resistant to pancreatic α-amylase, but gets degraded by colonic bacterial enzyme. Mixed films of amlose and ethyl cellulose as coatings have shown a great potential as colon delivery carriers.49

LIMITATIONS AND CHALLENGES IN COLON TARGETED DRUG DELIVERY57,78

a) 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 in the distal part 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 gastrointestinal tract, through which the dosage form has to travel before reaching the target site, further complicate the reliability and delivery efficiency.

b) Successful delivery through this site also requires the drug to be in solution form before it arrives in the colon or 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

c) The stability of the drug is also a concern and must be taken into consideration while designing the delivery system. The drug may potentially bind in a nonspecific way to dietary residues, intestinal secretions, mucus or faecal matter.

d) The resident microflora can 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.

CONCLUSION

The colonic region of the GIT has become an increasingly important site for drug delivery and absorption. Colon targeted drug delivery offers considerable therapeutic benefits to patients in terms of both local and systemic treatment. Drug targeting to the diseased colon are advantageous in reducing the systemic side effects, lowering dose of the drug and supplying the drug treatment. Drug targeting to the diseased colon are advantageous in reducing systemic side effects, lowering dose of the drug and supplying the drug treatment. Colon targeted drug delivery offers considerable therapeutic benefits to patients in terms of both local and systemic treatment. Drug targeting to the diseased colon are advantageous in reducing the systemic side effects, lowering dose of the drug and supplying the drug treatment. There is a need to develop a novel approach and suitable dosage form, which can result in the delivery of drugs in a safe, effective and less expensive manner with minimum fluctuation in terms of release of drugs at target site.

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