Review Article

Colonic Drug Delivery System: A Review

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ABSTRACT

Targeted drug delivery into the colon is highly desirable for local treatment of a variety of bowel diseases such as ulcerative colitis, crohn's disease, amoebiosis, colonic cancer, local treatment of colonic pathologies, and systemic delivery of protein and peptide drugs. To achieve successful colon targeted drug delivery, a drug need to be protect from degradation, release and absorption in upper portion of the GI tract and then to be ensured abrupt or controlled release in proximal colon. This review is focused on the merits and demerits, novel approaches in the colon targeted drug delivery, clinical evaluation techniques and some information on the marketed dosage forms.

Keywords: G.I.T, Colon Drug Delivery System, Colonic.

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INTRODUCTION

Day by day there are new developments in field of colon specific drug delivery system. 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, etc. but also for the systemic delivery of anti-asthmatic drugs, antihypertensive drugs and anti-diabetic agents. New systems and technologies have been developed for colon targeting and to overcome previous method's limitations. Colon targeting holds a great potential and still need more innovative work.

Traditionally solid oral dosage forms have been designed to release their drug load in upper region of G.I.T. where conditions are generally more suited to drug dissolution and absorption[1]. Recently greater emphasis has been placed on controlling the rate and site of drug release from oral formulations for the purpose of patient compliance and treatment efficiency.

The colonic region of G.I.T. is one of that would benefit from the development and such modified release technologies. Although considered by many to be an innocence organ that may simple functions in the form of water and electro light absorption and the formation storage and explosion of fecal material, the colon is valuable to a no of disorders including alternative qualities corn's disease irritable bower syndrome and carcinomas[1,2]. Targeted drug delivery to the colon would therefore ensure direct treatment at the disease site lower closing and favour systemic side effects.

In addition to local therapy, the color can also be utilized as a portal for entry of drug into the systemic circulation. E.g.:- molecules that are degraded parry absorbed in upper get, such as peptides and proteins, may be better absorbed from more being environment of colon. In addition, systemic absorption from colon can also be used as a means of achieving chemotherapy for diseases that are sensitive to circadian rhythms such as asthma, angina, orthotics[1,2].

TARGETING MECHANISM OF DRUG ACTING ON COLON

1. Pre-dependent delivery
2. Time-dependent delivery
3. Pressure-dependent delivery
4. Bacteria dependent delivery

Successful colonic drug delivery requires careful considerations of a number of factors, including the properties of drug, the type of delivery system and its interaction with the healthy or diseased gut[1].

1. Pre-dependent Delivery

Pre-sensitive enteric coatings have been used routing to deliver drugs to small intensive. These polymer coatings are insensitive to the acidic conditions of stomach yet dissolve at the higher PH environment of small intestine. This PH differential principle has also been attempted for colonic delivery purposes although polymers used for solenoid targeting and to have a threshold PH for dissolution that is higher than those used in conventional enteric coating application[1,7]. Most commonly co-

polymers of methacrylic acid and methyl methacrylate that dissolve at PH 5 PH 7 have been investigated./ this approach is based on assumptions that G.I. PH increases progressively from the small intestine to colon. In fact, the small intestine is usually around 7.5, while the PH in proximal colon is closer to 6 these delivery systems therefore have a tendency to release their drug load prior to reaching colon[1].

To overcome the problem of premature drug release a copolymer of methacrylic acid, methyl methacrylate and ethyl threshold PH, has been developed recently.

The inter subject variability in G.I.T. and possibly certain other intersect various such as electrolyte concentration and transit time will therefore impact on in vivo behaviour of PH responsive systems, ranging from early drug release is small intensive to are release at all with the formulation passing throughout gut intact the latter situation will also arise when PH of colon, and possibly the small intensive is considerably lower than normal as the case in patients with creative qualities in spite of their limitations, PH sensitive delivery systems are commercially available for mesalazine in and budesonide for treatment of ulcerative colitis and crohn's disease, respectively.

2. Time Dependent Delivery

It has also been proposed as a means of targeting the colon. Time dependence systems release their drug load after a preprogrammed time delay. To attain colonic release, the log, time should equate to time taken for system to react the colon. This time is difficult to predict in advance, although a log time of five hours is usually considerate sufficient, given that small intestinal transit time is reported to be relatively consistent at three to four hours[1]. One of the earliest systems to utilize this principle was the pulsincap device. System consist of an importable capsule fined with drug and stoppered at one end with a hydroges plug, on contact with gastrointestinal fluids, the plug hydrates and swells and after a set log time, ejects from the capsules body, thereby allowing drug release to occur the log time is controlled by the size and composition of play.

3. Pressure Dependent Delivery

G.I pressure has also been utilized drug release in distal gut. This pressure which is generated via muscular contraction of gut wall for grinding and proposition of intestinal contents, varies in intensity and duration through the gastro intestinal tract, with the colon considered to have a higher internal pressure due to process that occur during stool formation. The system have therefore been developed to resist the pressure of upper G.I tract but in rupture response to the raised pressure of colon[7]. Capsule shells fabricated from water insoluble polymer entry cellulose have been used for this purpose. The system can be modified to withstand and rupture at different pressures by changing the size of capsule and thickness of capsule shell wall.

Enzymes that are capable of metabolizing endogeneous and exogeneous substrates such as carbohydrates, proteins that are escapee digestion in upper G.I tract, therefore materials that are recalcitrant to the conditions of stomach and small intestine, yet suspicious to degradation by bacterial enzymes within colon, can be utilized as carriers for drug delivery to colon.

Eg.: This principle has been exploited commercially to deliver 5 anniosalicylic acid to the colon by way of a drug carrier. The prodrug sulphasalazinc consist of two separate moieties, suiphaphyridine and 5-amonosalcylic acid, linked by as azo-bond. The prodrug possess through three upper gut intract, but once in colon the azo-bond is cleave by the host bacteria, liberating the carrier molecule sulphaphyridin and pharmacologically active agent 5-aminosalicylic acid[1,7].

4. Bacteria Dependent Delivery[14]

The resident G.I bacteria provide a further means of effecting drug release in colon, these bacteria predominantly colonise the distas region of G.I.tract where bacterial count in the colon is 10'per gram as compared with 10'per gram in upper small intestine moreover, 400 different species are present colonic bacteria are pre-dominantly in nature and produce once of gastric copying on performance of pulsincap was reduced by a application of an outer enteric coat[1]. The outer enteric coat dissolves on entering the small intestine to reveal by either swelling, eroding or dissolving over a period of time equivalent to small intestinal transit.

Although the use of an over enteric coat overcomes to a certain attempt the availability in G.I. emptying, the intrinsic problems with such systems is over all inter and intra subject variability in transit[1,7]. Transit is slower in evening as compared with morning.

Table 1: Colon targeting diseases, drugs and sites

Target Sites	Disease Condition	Drug active agents
Topical action	IBD Irritable bowel disease Crohns disease Cronic pancreatitis	Hydrocortisone, Budenoside Prednisolone Sulfaselazine Olasazine, measalazine
Local action	Pancreatactomy cystifibrosis Colorectal cancer	Digestive Enzyme supplements 5- Flourouracil
Systemic action	To prevent gastric irritation and first pass metabolism of orally ingested drugs like peptides and vaccines	NSAIDS, Steroid, Insulin Typhoid

Advantages of CDDS Over Convectional Drug Delivery

Chronic colitis, namely ulcerative colitis and crohn's disease are currently treated with glucocorticoids and other anti-inflammatory agents Administration of glucocorticoid namely dexamethasone and methyl prednisolone by oral and intracenous routs produce systemic side effects including adenosuppression, immunosuppressant, cushiniod symptoms, and bone resorption[1].Thus selective delivery of drugs to the colon could not only lower the required but also reduce the systemic side effects caused by high dose.

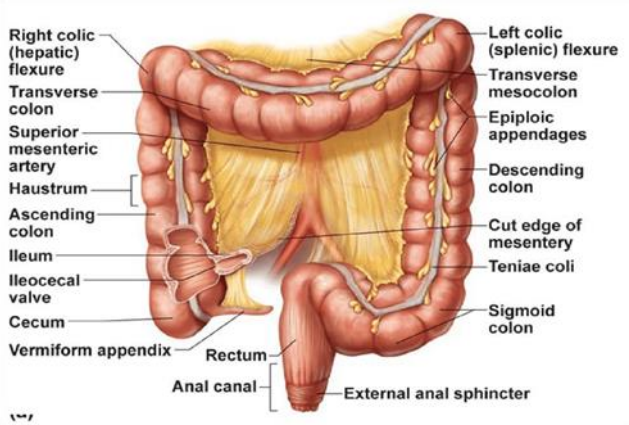

Figure 1: Anatomy of the colon

Factors Affected in the Design of Colon Specific Drug Delivery System

The anatomy of the colon is shown in **figure 1.** The GIT 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 of the cecum ascending colon, hepatic flexure and the right half of the transverse colon and the values were shown in table 2[1,13]. 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.

Table 2: Measures of different parts of colon.

Large intestine	Length (cm)
Ascending colon	20-25
Descending colon	10-15
Transverse colon	40-45
Sigmoid colon	35-40
Rectum	12

Colon pH

The ph of the GIT is subject to both inter and intra subject variation. Diet, diseased state and food intake influences the pH of the gastrointestinal fluid[13]. 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 GIT. Intestinal enzymes are used to trigger drug release in various parts of the GIT. Usually, these enzymes are derived from gut microflora 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[14]. The most important anaerobic bacteria are bacteroides, bifidobacterium, eubacterium, peptococcus, peptostreptococcus, ruminococcus, and clostridium.

Transit of material in the colon

Compared to other regions of the gastrointestinal tract, movement of materials through the colon is slow. 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[22]. Colonic transit times ranged from 50 to 70 hours. Stool weights increased significantly with the presence of active disease presumably due to excudates 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. Trancellular 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[1]. 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[22]. This causes a reduced dissolution rate, slow diffusion of dissolved drug through the mucosa.

CRITERIA FOR SELECTION OF DRUG FOR CDDS

The best candidates for CDDS are drugs which is show poor absorption from the stomach or intestine including peptides. The drugs used in the treatment of inflammatory bowel disease (IBD), ulcerative colitis, diarrhea, and colon cancer is ideally candidates for local colon delivery. The

criteria for selection of drugs CDDS are summarized in table 3 drug carrier is another factor which influences CDDS the selection of carrier for particular drugs depends on the physiological nature of the drug as well as the disease for which the system is to be used. Factors such as chemical nature, stability and partition coefficient of the drug and type of absorption enhancer chosen influence the carrier selection. Moreover, the choice of drug carrier depends on the functional groups of the drug molecule. For example, aniline or nitro groups on a drug may be used to link it to another benzene group through an azo bond. The carriers, which contain additives like polymers (may be used as matrices and hydro gels or coating agents) may influence the release properties and efficacy of the systems[1].

Table 3: Criteria for selection of drugs for CDDS

Criteria	Pharmacological class	Non-peptide drugs	Peptide drugs
Drugs used for local effects in colon against GIT diseases	Anti-inflammatory drugs	Oxyprenolol, metoprolol, nifedine.	Amylin, antisense oligonucleotide.
Drugs poorly absorbed from upper GIT	Antihypertensive, antianginal drugs.	Ibuprofen, isosorbides, theophylline.	Cyclosporine, desmopressin.
Drugs for colon cancer	Antineoplastic drugs.	Psuedoephidrene	Epoetin, glucagoan.
Drugs that degrade in stomach and small intestine	Peptides and proteins.	Bromophenaramine, 5-flourouracil, doxorubicin.	Gonadoreline, insulin, interferons.
Drugs undergo extensive first pass metabolism	Nitroglycerin, corticosteroids.	Bleomycin, nicotine.	Protirelin, sermorelin, saloatonin.
Drugs for targeting	Antiarthritic, antiasthamatic drugs.	Prednisolone, hydrocortisone, 5-amino-salicylic acid.	Somatropin, urotoilitin.

PHARMACEUTICAL APPROACH TO COLON TARGETED DRUG DELIVERY

Coating with biodurabable polymers

The bio environment inside the human G.I.T. is characterized by presence of complex microflora especially the colon that is rich in micro organizing that are involved in the process of reduction of dietary component or other materials. Drugs that are coated with polymers, which are showing degradability due to influence of colonic micro organisms, can be exploited in designing drugs for colon targeting[25]. These bacterial degradable polymers especially also polymers have been explored in order to release as orally administrated drug in colon.

Actually upon passage of dosage from through G.I.T. it remains intact in stomach and small intestine where very little microbially degrades activity is present that is quiet insufficient for cleavage of polymer coating, release of the drugs from azo polymer coated formulation is supposed to take place after reductionism thus degradation of azo reductase enzymes released by azo batters in colonic microflora[1].

Mesalazine is the active component of sulfasalazine exerting a predominant local topical action independent of blood levels[22]. Its effectiveness depends on the site of ulceration in relation to the drug's dissolution profile. This is very important when choosing aminosalicylate preparations.

The optimal dose of sulfasalazine to achieve and maintain remission is usually in the range of 2-4gm per day in four divided doses. Acute attacks require 4-8gm per day in divided doses until remission occurs, but at these doses associated side-effects begin to appear[1,22]. Patients taking sulfasalazine, 30% experience adverse effects that are either dose-related, dependent on acetylator, phenotype or idiosyncreatic non-dose, related reactions. The first group includes nausea, vomiting, headache, malaise, haemolytic anaemia, reticulocytosis, and methamemoglobulinaemia. The second includes skin rash, hepatic and pulmonary disfunction, aplastic anaemia and reversible azoospermia. Adverse effects usually occur during the first 2 weeks of therapy, the majority being related to serum sulfapyridine levels.

Many of the adverse effects listed above can be avoided by using one of the aminosalicylate formulations now available[1]. As mesalazine is unstable in acid medium and rapidly absorbed from the gastrointestinal tract, the new preparations have been developed using three different approaches.

- A mesalazine tablet coated with a pH-dependent acrylic resin.
- Ethylcellulose-coated mesalazine granules diazotization of mesalazine to itself or to an inert carrier.

Asacol contains 400 mg of mesalazine coated with an acrylic resin, eudragit-S, that dissolves at pH7 and releases mesalazine in the terminal ileum and the colon. salofakd tablets are similar formulation containing 250 mg mesalizine with sodium carbonate-glycine and a cellulose ether, coated with eudragit-L which dissolves at pH 6 and above, releasing mesalaxine in the jejunum and ileum.

Covalent linkage of the drug with a carrier

It involves the formation of a covalent linkage between drug and carrier in such a manner that upon oral administration the moiety remains intact in the stomach and small intestine. This approach chiefly involves the formation of prodrug, which is a pharmacologically inactive derivative of a parent drug molecule that requires spontaneous or enzymatic transformation in the biological environment to release the active drug[11]. Formation of prodrugs has improved delivery properties over the parent drug molecule. The problem of stability of certain drugs from the adverse environment of the upper GIT can be eliminated by prodrug formation, which is converted into parent drug molecule once it reaches into the colon. Site specific drug delivery through site specific prodrug activation may be accomplished by the utilization of some specific property at the target site, such as altered pH or high activity of certain enzymes relative to the non-target tissues for the prodrug-drug conversion[9].

Azo bond conjugates

The intestinal microflora is characterized by a complex and relatively stable community of microorganism, many with physiological functions, which ply vital roles in health and disease. In addition to protection of the patient against colonization of the intestinal tract by potentially pathogenic bacteria, the indigenous microflora[14] are responsible for a wide variety of metabolic processes, including the reduction of nitro and azo[16] groups in environmental and therapeutic compounds.

Sulphasalazine[17] was introduced for the treatment of rheumatoid arthritis and anti-inflammatory disease. Chemically it is salicylazosulphapyridine (SASP), where sulfapyridine is linked to a salicylate radical by an azo bond. When taken orally, only a small proportion of the ingested dose is absorbed from the small intestine and the bulk of the sulphasalazine reaches the colon intact. There it is split at the azo bond by the colonic bacteria with the liberation of sulphapyridine (SP) and 5 ASA. However sulphapyridine is seems to be responsible for the most of the side effects of sulphasalazine[18] and hence various new approaches for the treatment of IBD have emerged.

Glycoside conjugates

Steroid glycosides and the unique glycosidase activity of the colonic microflora from the basis of a new colon targeted drug delivery system. Drug glycosides are hydrophilic and thus, poorly absorbed from the small intestine[14]. 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 human feces are b-D-galactosidase, b-D-glucosidase, a-L-arabinofuranosidase, b-D-xylopyranosidase. These enzymes are located at the brush border and hence access to the substrate is relatively easy. In the plant kingdom numerous compounds are found as glycosides[15]. Certain drugs act as glycon and can be conjugated to different sugar moieties which results in the formation of glycosides. Due to the bulky and hydrophilic nature of these glycosides, they do not penetrate the biological membrane upon ingestion. Various naturally occurring glycosides, e.g., the sennosides[17], have been used for laxative action for ages. When taken orally, intact sennosides are more efficient as laxative than sugar free aglycones. These sennosides are activated are activated by colonic microflora to generate in the once, which gives the desired laxative effect. Glycosidase activity of the GIT is derived from anaerobic microflora in the large bowel or the sloghed or exfoliated cells of the small intestine.

Glucuronide conjugates

Glucuronide and sulphate conjugation are the major mechanisms for the inactivation and preparation for clearance of a variety of drugs. Bacteria of the lower GIT, however, secrete b-glucuronidase and can deglucuronidate a variety of drugs in the intestine[18]. Since the deglucuronidation process results in the release of active drug and enables its reabsorption, glucuronide prodrugs would be expected to be superior for colon targeted drug delivery.

Morphine-dependent rats were used to evaluate the effects of the narcotic antagonists, naloxone and nalmefene[20] and their glucuronide conjugates on the gastrointestinal tract and various parameter of brain-mediated withdrawal. When administered subcutaneously nalmefene hydrochloride caused a dose-dependent tail skin temperature increase, whereas nalmefene glucuronide was ineffective malmefene precipitated brain-mediated morphine withdrawal at doses as low as 10mg/kg, whereas nalmefene glucuronide was ineffective at doses as high as 1 mg/kg[17,18,19] after per oral administration of the drugs, nalozone hydrochloride and nalmefene hydrochloride caused diarrhea, withdrawal behavior and tail skin temperature responses by 15 min. in contrast, after per oral administration of the glucuronide conjugate of either narcotic antagonist, diarrhea was delayed for 75 to 203 min. this latency probably reflects the required transit time to the lower gastrointestinal tract[22]. About 0.2 to 0.5% of the dose of the narcotic antagonist administered orally as the glucuronide was absorbed systemically. These results indicate that per oral administration of the glucuronide conjugates of nalox one and nalmefene results in delivery of the narcotic antagonists to the colon. Haeberlin et al. prepared a dexamethasone b-D-glucuronide prodrug[20].

APPROACHES FOR CDDS

pH sensitive system

This approach is based on the pH-dependent release of the drug from the system. In this case the pH differential between the upper and terminal parts of GIT is exploited to effectively deliver drugs to the colon[1,8]. One should not forget that the pH in the intestine and Colon depends on many factors such as diet, food intake and intestinal motility and disease states.

This makes it more challenging for the specialists working in this field to design a delivery system that would be robust enough to withstand the variability in the gastric pH as it moves from the stomach to the small intestine. By combining knowledge of polymers and their solubility at different pH environments, delivery systems have been designed to deliver the drug at the target site[8]. Commonly used copolymers of methacrylic acid and methyl methacrylate have been extensively investigated for colonic drug delivery systems. In vitro evolution of Eudragit S and Eudragit FS was performed and it was found that the latter would be more appropriate for drug delivery to the ileocolonic region. Several factors, such as combinations of different polymers, pH of the media, coating level of the tablets and presence of plasticizers[8]. Inter and intra-subject variability, electrolyte concentration and transit time are some of the key variables impacting success through this route. In spite of these limitations, pH-based systems are commercially available for mesalazine (5 ASA) and budesonide for the treatment of ulcerative colitis and crohn's disease, respectively.

Table 4: Enteric polymers used in the development of modified release formulations for CDDS

Enteric polymers	Optimum pH for dissolution
Polyvinyl acetate phthalate (PVAP)	5.0
Methacrylic acid copolymer, Type A	_>6.0
Eudragist FS30D	>7.0
Hydroxypropylmethylcellulose phthalate (HPMCP)	_>5.5
Methacrylie acid copolymer, Type C(Eudragit L100-55)	>6.0
Methacrylic acid copolymer, dispersion (Eudragit L30D-55)	>5
Cellulose acetate trimelitate(CAT)	5.5
Hydroxypropyl methylcellulose acetate succinate (HPMCAS)	_>6.0
Shellac (MarCoat 125 & 125N)	7.0
Methacrylic acid copolymer, Type B	_>7.0

In general the amount of coating required depends upon the solubility characteristics (solubility, dose/solubility ratio) of the drug, desired release profile and surface area of the formulation, and composition of the coating solution/dispersion. Coating approach is one of the simplest formulation available for colon-specific delivery. It also offers significant advantage in terms of cost and ease of manufacture[8]. From formulation standpoint, coated dosage forms may be either single-unit system or a multi-particulate system and each of these may be a single layer product or a multi-layer product.

In case of single layered products, the coating may be composed of a single enteric polymer that has a pH-dependent solubility or a mixture of two polymers one of which is pH-dependent while other is pH independent. On the other hand, in case of multilayer products, the coating is applied in successive layers which could be either based on two enteric polymers that have different pH-dependent solubility profiles, or two polymers one of which is enteric while other has a pH independent solubility but permeable to intestinal fluids. In either case, the coating can be applied to a wide variety of solid core formulations such as tablets, capsules, minitablets, pellets or granules.

When coated pellets or granules are filled into a gelatin capsule or compressed together with conventional excipients in the form of tablets, the formulation is regarded as multi-particulate dosage form. The tablets or capsules coated pellets or granules can be further coated with a suitable enteric polymer which may be same or different than that used for coating of pellets or granules[11]. Modified-release formulations that are based on the combination of a pH-dependent and pH-independent polymer are described in a European patent assigned to aktiebolaget hassle. The approach involves coating of an active ingredient (e.g., mesalazine) with a mixture of an anionic acrylic polymer soluble just at pH 5.5 (e.g., eudragit L) and a cationic acrylic polymer insoluble in water (e.g., eudragit RS or RL)[10]. The quantities of an anionic acrylic polymer can range from 10 to85% while that of pH independent polymers may vary from 15 to 90%. The blending with one or more polymers having a pH independent solubility thus prevents the active ingredient from being released too rapidly, once the soluble polymer has reached the optimum pH of solubilisation[9].

USES

a. Local actions

1) Ulcerative colitis.
2) Chron's disease.
3) Irritable bowel syndrome.
4) Metastatic human colon cancer.

b. Systemic actions

1) Molecules degraded/poorly absorbed from upper GIT such as peptides and proteins are better absorbed from colon.
2) For achieving chemotherapy for diseases that are sensitive to cardiac rhythm such as asthma, angina, arthritis[25].

ADVANTAGES AND DISADVANTAGES

Advantages

i. Patient compliance the treatment efficacy.

ii. Useful in treatment of ulcerative colitis, chron's disease, irritable bowel syndrome and carcinomas.

iii. Low dose is required, so less side effects.

iv. Used for local and systemic action.

v. Gastric irritation can be avoided.

Disadvantage

i. There is less fluid in colon than in small intestine and hence dissolution is a major problem for water soluble drugs.

ii. Binding of drug to dietary residues, intestinal secretions etc reduce concentration of free drugs.

iii. Some microflora may degrade the drug.

iv. Small luminal surface area and relative tightness of tight junctions in colon, delay the systemic absorption[25].

v. Onset of action is slow.

CONCLUSION

The colonic region of the GIT has become an increasingly important site for drug delivery and absorption. Drug targeting to the diseased colon is advantageous in reducing the systemic side effects, lowering dose of a drug, supply of the drug only when it is required and maintenance of the drug in its intact form as close as possible to the target site. All the approaches of colon drug delivery provide means for treatment of local diseases associated with the colon or for systemic absorption of poorly absorbable drugs. 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, makes the reliability, delivery efficiency of formulation and targeting to colon complicated.

In summary two controlled release mechanism, i.e, time and pH-dependent, could achieve colonic specific drug delivery following oral administration. In addition, both CDDS were relatively in expensive and easy to be manufactured using conventional pharmaceutical coating technique, and provided the promising candidates for specifically delivering drug to targeted colon region, in particular for DS and 5-ASA in this study, respectively.

ABBREVIATIONS

Colonic drug delivery system (CDDS); example (e.g); gastrointestinal tract (GIT); that is (i.e.); kilogram (kg); milligram (mg).

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