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## Review on Colon Targeted Drug Delivery System

	
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### ABSTRACT

In the present research work sustained release matrix formulation of Meloxicam targeted to colon by using various polymers .Meloxicam (MLX) is a non-steroidal anti-inflammatory drug (NSAIDs) from the Oxicam family. MLX has been described as a COX-2 selective inhibitor. Its use has some advantages regarding its selectivity, namely, less adverse effects as gastrointestinal aggression and anticlotting activity. As MLX is better absorbed in colon and its properties against colon cancer and colonic inflammatory diseases are being studied, it is interesting to investigate a new MLX formulation for colonic delivery. Recently, their activity in chemoprevention, chemo-suppression, UV-sensitization and UV protection was also identified. Meloxicam is a selective cyclooxygenase-2 inhibitor with pH-dependent solubility. To achieve pH-independent drug release of meloxicam, pH modifying agents (buffering agents) were used.

## INTRODUCTION

The oral route is considered to be most convenient for administration of drugs to patients. Oral administration of conventional dosage forms normally dissolves in the stomach fluid or intestinal fluid and gets absorbed from these regions of the gastrointestinal tract (GIT) depending upon the physicochemical properties of the drug.

The rectal route has traditionally been used to administer medicaments in the form of suppositories and enemas to the distal gut, although such formulations rarely succeed in spreading beyond the descending colon. Also, the rectal route is not convenient or acceptable for most patients and hence the oral route is the preferred route of drug administration. However, colonic drug delivery via the oral route is not without its challenges. The colon<sup>1</sup> constitutes the most distal segment of the gastrointestinal tract and so an orally administered formulation must retard drug release in the upper gastrointestinal regions but release the drug promptly on entry into the colon.

Numerous drug entities based on oral delivery have been successfully commercialized, but many others are not readily available for oral administration, which are incompatible with the physical and/or chemical environments of the upper gastrointestinal tract (GIT) and/or demonstrate poor uptake in the upper GIT. Due to the lack of digestive enzymes, colon is considered as suitable site for the absorption of various +-drugs. Over the past two decades the major challenge for scientist is to target the drugs specifically to the colonic region of GIT. Previously colon was considered as an innocuous organ solely responsible for absorption of water, electrolytes and temporary storage of stools. But now it is accepted as important site for drug delivery.

### **Colon targeting is used to treat:**

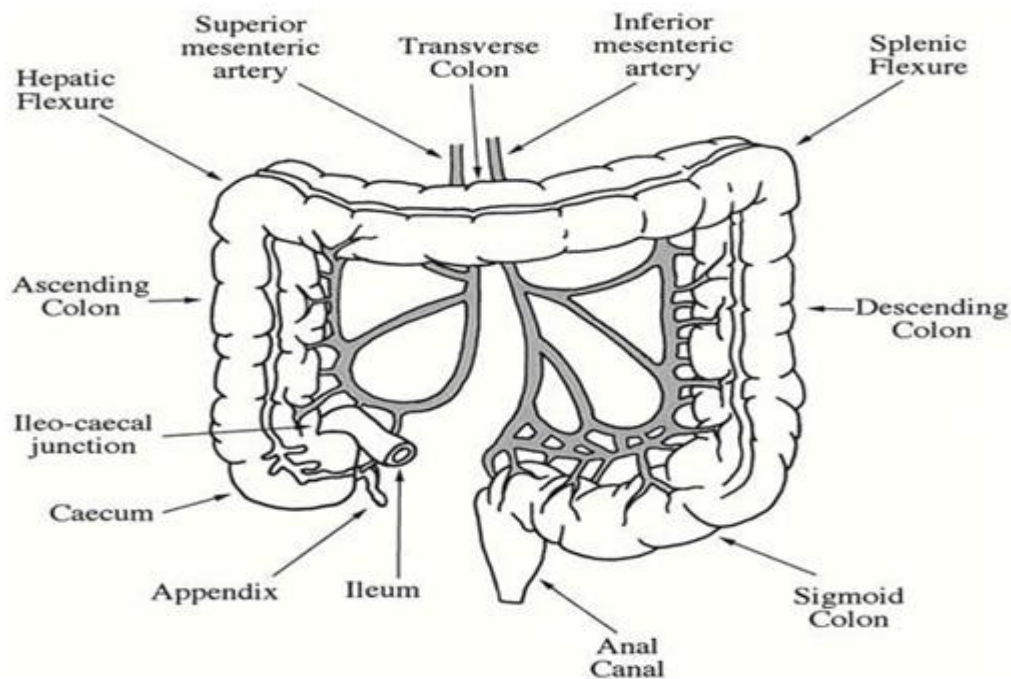
Seriousness from constipation and diarrhoea to the debilitating inflammatory bowel diseases<sup>2</sup> (ulcerative colitis and Crohn's disease) through to colon carcinoma which is two third cause of cancer in both man and women. Colon can be utilized as portal for the entry of drugs into the blood stream for the systemic therapy. Colon having the lower level of luminal and mucosal digestive enzymes as compared with the small intestine reduces the chances of drug degradation.e.g.to facilitate absorption of acid and enzymatically labile material especially

proteins and peptides. Colon delivery also a mean of achieving chronotherapy of disease that is sensitive to circadian rhythm such as asthma and arthritis. Targeted delivery ensures the direct treatment at the disease site, lower dosing, and reduction in side effects. Colonic drug delivery is also found useful for improving systemic absorption of drugs like nitrendipine (calcium channel blocker), metoprolol (anti-hypertensive), isosorbide mononitrate (anti-anginal). The rectal route has traditionally been used to administer medicaments in the form of suppositories and enemas to the distal gut, although such formulations rarely succeed in spreading beyond the descending colon. Also, the rectal route is not convenient or acceptable for most patients and hence the oral route is the preferred route of drug administration. However, colonic drug delivery via the oral route is not without its challenges. The colon constitutes the most distal segment of the gastrointestinal tract and so an orally administered formulation must retard drug release in the upper gastrointestinal regions but release the drug promptly on entry into the colon. Retardation of drug release in the diverse and hostile conditions of the stomach and small intestine is not easily achieved since the dosage form will be subjected to a physical and chemical assault that is designed to break down ingested materials. While in the colon, the low fluid environment and viscous nature of luminal contents may hinder the dissolution and release of the drug from the formulation. Moreover, the resident colonic microflora may impact on the stability of the released drug via metabolic degradation. In spite of these potential difficulties, a variety of approaches have been used and systems have been developed for the purpose of achieving colonic targeting. Targeted drug delivery is reliant on the identification and exploitation of a characteristic that is specific to the target organ. In the context of colonic targeting, the exploitable gastrointestinal features include pH, transit time, pressure, bacteria and prodrug approach.

### **Anatomy and Physiology of Colon<sup>3-5</sup>**

The GIT is divided into stomach, small intestine and large intestine. The large intestine extending from the ileocecal junction to the anus is divided into three main parts. These are the colon, the rectum and the anal canal. The location of the parts of the colon is either in the abdominal cavity or behind it in the retroperitoneum. The colon itself 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 (Figure 1). It is about 1.5 m long, the transverse colon being the longest and most mobile part and has an average diameter of about 6.5 cm. The colon from the cecum to the splenic

flexure (the junction between the transverse and descending colon) is also known as the right colon. The remainder is known as the left colon. Arterial supply to the colon of humans comes from branches of the superior and inferior mesenteric arteries. Venous drainage usually mirrors colonic arterial supply, with the inferior mesenteric vein draining into the splenic vein, and the superior mesenteric vein joining the splenic vein to form the portal vein, which then enters the liver. Lymphatic drainage from the entire colon and proximal two-thirds of the rectum is to the paraaortic nodes, which then drain into the cisterna chyli. The lymph from the remaining rectum and anus can either follow the same route or drain to the internal iliac and superficial inguinal nodes.



**Fig 1: Main Features of the Colon**

### **Functions of Colon:**

The colon serves four major functions<sup>6</sup>. They are

1. Creation of suitable environment for the growth of colonic microorganisms.
2. Storage reservoir of faecal contents.
3. Expulsion of the contents of the colon at an appropriate time and
4. Absorption of potassium and bicarbonate.

### **Factors to be considered in the design of colon specific drug delivery system**

To reach the colon and to be able to specifically deliver and absorb the drug there, the dosage forms must be formulated taking into account the obstacles of the gastrointestinal tract. The various strategies developed to achieve this goal have used the specific characteristics of this organ, i.e. transit time, pH, microflora, enzymes disease and the colonic environment. Nevertheless, these parameters can vary from one individual to the next and also according to the pathological condition and diet documented that gastric emptying varies with different types of dosage forms.

#### **Physiological Factors<sup>7-9</sup>:**

##### **a) Gastrointestinal transit:**

Gastrointestinal transit time is important for nearly all orally targeting delivery systems. The drug delivery systems first enter into stomach and small intestine via mouth and then reach colon. In fasted state, the motility proceeds through four phases occurring in stomach and small intestine that span over a period of 2-3 hours. Phase I is a quiescent period of 40-60 min, Phase II consists of intermittent contractions for a period of 40-60 min. Phase III is a period of intense contractions sweeping material out of the stomach and down the small intestine followed by Phase IV with contractions dissipating. The feeding state affects the normal pattern by irregular contractile activity. It has been well documented that gastric emptying varies with different types of dosage forms small intestinal transit. Normally, transit times through the small intestine generally found to be 3-4 hrs. Liquids, small solids (beads, small tablets) and larger capsule-sized units moved essentially at the same rates and the transit is unaffected by food status. In a more recent study concerning dosing in relation to the timing of food intake found that although SIT is relatively independent of food and dosage form, it was actually shortened significantly if the dose is given 30 min before food intake. This can have adverse impact on the *in-vivo* performance of the dosage forms.

##### **b) Colonic Transit:**

In the stomach and small intestine, food residue and endogenous secretions are exposed to an essentially sterile environment through which their transit can be measured by hours. On entering

the large intestine, dosage forms encounter a rich bacterial flora and transit through the large intestine can be as long as many several days. It was reported that overall mean transit time is 36 hrs with a range of 1 to 72 hrs and that the transit of liquids and small solids is equal. Thus, absorption from colon may be incomplete and erratic depending on the dose and physicochemical properties of a particular drug. In general absorption of an insoluble drug with high dose or a drug with limited permeability is unfavourable in this region because of the limited volume of fluid available for dissolution and the significantly reduced surface area.

### c) pH in the Colon:

The pH gradient in the GIT is not in an increased order and is subjected to both inter-subject and intra-subject variations. In stomach the pH is 1.5-2.0 and 2-6 in fasted and fed conditions, respectively. The acidic pH is responsible for the degradation of various pH sensitive drugs and enteric coating may prevent it. In small intestine, the pH increases slightly from 6.6 – 7.5. On entry into the colon, the pH dropped to 6.4 in right colon. The pH of mid colon was found to be 6.6 and in the left colon Colonic pH has been shown reduced in disease state. The mean pH in a group of 7 patients with untreated ulcerative colitis was 4.7 whereas in 5 patients receiving treatment it was 5.5.

### d) Colonic microflora:

The human colon is a dynamic and ecologically diverse environment containing over 400 distinct species of bacteria with a population of  $10^{10}$  to  $10^{11}$  colonic bacteria/mL (*Bacteroides*, *Bifidobacterium*, *Eubacterium*, *Lactobacillus*), etc greatly outnumbering other species. For example, it was reported that *Bacteroides*, *Bifidobacterium* and *Eubacterium* could constitute as much as over 60% of the total cultivable flora. These bacteria produce a wide spectrum of enzymes that, being reductive and hydrolytic in nature, are actively involved in many processes in the colon, such as carbohydrate and protein fermentation, bile acid and steroid transformation, metabolism of xenobiotic substances, as well as the activation and destruction of potential mutagenic metabolites. *Nitroreductase*, *azoreductase*, N-oxide and *sulfoxide reductase* are the most extensively investigate reductive enzymes, while *glucosidase* and *glucuronidase* are the most extensively studied hydrolytic enzymes. The primary source of nutrition for these anaerobic bacteria is carbohydrates such as non-starch polysaccharides (i.e., dietary fibers) from the

intestinal chime. It is well established that non-starch polysaccharides are fermented during transit through the colon and the breakdown in the stomach and small intestine is negligible. Enzymes responsible for the degradation of polysaccharides include *α-L-arabinofuranosidase*, *β-D-fucosidase*, *β-D-galactosidase*, *β-D-glucosidase*, *β-xylosidase*, with the last three enzymes being the most active. Additionally, the composition of colonic bacteria and corresponding enzymes can be influenced by many factors, including age, diet, diseases, medication such as antibiotics and geographic regions. A unique feature of colon microflora is that the growth and activity of certain specific species, most notably bifidobacteria and lactobacilli, can be selectively stimulated by non-digestible oligosaccharides which are known as prebiotics.

**e) Volume of the ascending colon:**

Up to 1,500 g of liquids and undigested materials (dietary fibers, resistant starch, partially degraded polysaccharides proteins, mucins, exfoliated epithelial cells, etc.) enters colon per day, which act as the substrates for microflora fermentation. Water together with the products of the fermentation and other nutrients was efficiently absorbed in the colon, condensing the contents into feces through the transit in the colon for eventual defecation. Therefore, it is very likely that the ascending colon contains the largest quantity of liquid. It would be expected that the low water–high gas environment of the transverse colon limits dissolution of materials. About 86% of the moisture is present in the caecal contents. The volume of the ascending colon was measured in healthy subjects using a single photon emission computed tomography by acquiring the imaging of the ascending colon filled with Tc -labelled amberlite pellets and was found to be  $170\pm 40$  ml. If the moisture content in the ascending colon is approximately comparable to that of caecal contents, the quantity of fluid in the ascending colon should be  $146\pm 34$  ml.

**f) Disease and the Colonic Environment:**

General intestinal diseases such as inflammatory bowel disease, Crohn's disease, constipation and diarrhoea may affect the release and absorption of colon specific drug delivery systems. All the specific approaches so far mentioned rely on the concept that enzymes produced by colonic microflora provide the trigger for specific delivery of fermentable coatings, anti-inflammatory azo bond drugs and other prodrugs to the cecum. *Azoreductase* activity in feces of 14 patients with active Crohn's disease was 20% of that of healthy subjects and similarly, beta-D-glucosidase and

beta-D-glucuronidase activities in fecal homogenates incubated under anaerobic conditions were also decreased in patients. These data probably reflect large-bowel hypermotility and the associated diarrhoea, leading to lower bacterial mass in the colon and might contribute to the therapeutic failure of targeting mechanisms in active ileocolic and colic Crohn's disease.

### **Drugs Suitable For Colonic Drug Delivery**

Drug delivery selectively to the colon through the oral route is becoming increasingly popular for the treatment of large intestinal diseases and for systemic absorption of protein and peptide drugs. There has been an increasing interest in utilizing the colon as a site for systemic absorption of these drugs in view of the less hostile environment prevailing in the colon. A variety of protein and peptide drugs like calcitonin, interferon, interleukins, erythropoietin and even insulin are being investigated for their absorption using colon specific drug delivery. Inflammatory bowel disease (IBD) such as ulcerative colitis and Crohn's disease require selective local delivery of drugs to the colon. Sulfasalazine<sup>10</sup> is the most commonly prescribed drug for such diseases. Selective delivery of the drug to the colon is required for therapeutic efficacy with less or no side effects. The other drugs used in IBD are steroids, such as dexamethasone, prednisolone, and hydrocortisone. In colonic cancer, anticancer drugs like 5-fluorouracil, doxorubicin, and nimustine are to be delivered specifically to the colon. The site specific delivery of drugs like, metronidazole, mebendazole, albendazole is used in the treatment of infectious diseases, such as amoebiasis and helminthiasis. Besides peptide and protein drugs, the colon is also a good site for the absorption of drugs that are not stable in the acidic environment of the stomach, cause gastric irritation (e.g. aspirin, iron supplements) or those degraded by small intestinal enzymes. A number of drugs available as sustained release or delayed release or timed release tablets or capsules for oral administration are anti-inflammatory drugs, anti-hypertensive drugs, etc. Unless these drugs have good absorption characteristics in the colon, their intended use in the management of respective disorders through sustained release or timed release formulations will be in question. The drugs that are having good absorption properties from the colon include theophylline, glibenclamide and oxprenolol. Diclofenac, ibuprofen, nitrendipine, isosorbide, metoprolol (anti-hypertensive), nifedipine etc. and hence can be investigated for better bioavailability through colon specific drug delivery.



## Approaches to colon-specific drug delivery<sup>11-14</sup>

In recent years, a large number of solid formulations targeting the lower parts of the Gastro-Intestinal Tract, especially the colon, have been reported. These formulations may be broadly divided into four types, which are:

1. pH- dependent system designed to release a drug in response to change in pH
2. Time controlled (or Time-dependent) system designed to release a drug after a predetermined time.
3. Microbially-controlled system making use of the abundant entero-bacteria in the colon.
4. Enzyme- based system. Prodrug.
5. Pressure-dependent system making use of luminal pressure of the colon.

Among these, first three are most widespread formulation technologies being developed for pharmaceutical market.

### **pH-dependent Systems:**

Solid formulations for colonic delivery that are based on pH-dependent drug release mechanism are similar to conventional enteric-coated formulations but they differ in target site for delivery and therefore type of enteric polymers. In contrast to conventional enteric-coated formulations, colonic formulations are designed to deliver drugs to the distal (terminal) ileum and colon and utilize enteric polymers that have relatively higher threshold pH for dissolution most commonly used polymers (Table 1) are derivatives of acrylic acid and cellulose. These polymers have ability to withstand an environment ranging from low pH (~1.2) to neutral pH (~7.5) for several hours. Apparently, it is highly desirable for pH- dependent colonic formulations to maintain their physical and chemical integrity during passage through the stomach and small intestine and reach the large intestine where the coat should disintegrate to release the drug locally. It should be however noted that gastrointestinal fluids might pass through the coat while the dosage form transits through the small intestine. This could lead to premature drug release in the upper parts of gastrointestinal tract and as a result loss of therapeutic efficacy may occur. One approach to overcome this problem is to apply higher coating levels of enteric polymers; however, this also allows influx of gastrointestinal fluids through the coat, and the thicker coats often rupture under

the influence of contractile activity in the stomach. 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.

Widely used polymers are methacrylic resins (Eudragit S), which are available in water soluble and water-insoluble forms. Eudragit L and S are copolymers of methacrylic acid and methyl methacrylate. To overcome the problem of premature drug release, a copolymer of methacrylic acid, methyl methacrylate and ethyl acrylate (Eudragit FS), which dissolves at a slower rate and at a higher threshold pH (7–7.5), has been developed recently colon targeted drug delivery systems based on methacrylic resins has described for insulin, prednisolone, quinolones, salsalazine, cyclospore beclomethasone dipropionate, and naproxane, pH-sensitive delivery systems are commercially available for mesalazine, (5-aminosalicylic acid) and budesonide for the treatment of ulcerative colitis and Crohn's disease respectively.

**Table 1: Threshold pH of commonly used polymers**

Polymer	Threshold pH
Eudragit L100	6.0
Eudragit S100	7.0
Eudragit K100	8.0
Eudragit FS 30D	6.8
PVAP	5.0
HPMCP	4.5-4.8
HPMCP 50	5.2
CAP	5.0

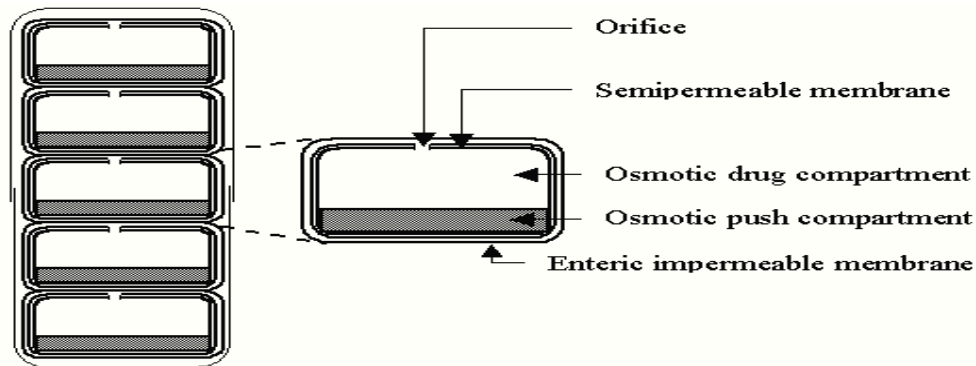
**Time-controlled (or time-dependent) systems:**

Time-controlled systems are useful for synchronous delivery of a drug either at pre-selected times such that patient receives the drug when needed or at a pre-selected site of the GIT. These systems are therefore particularly useful in the therapy of diseases, which depend on circadian rhythms. Time-controlled formulations for colonic delivery are also delayed-release formulations in which

the delay in delivery of the drug is time- based. In these systems, it has been suggested that colonic targeting can be achieved by incorporating a lag time into the formulation equivalent to the mouth to colon transit time. Ideally, formulations are designed such that the site of delivery (i.e. colon) is not affected by the individual differences in the gastric emptying time, pH of the stomach and small intestine or presence of anaerobic bacteria in the colon. A nominal lag time of 5 hrs is usually considered sufficient since small intestinal transit has been considered relatively constant at 3 to 4 hrs . In principle, time-controlled systems rely on this consistent small intestinal transit time. The drug release from these systems, therefore, occurs after a predetermined lag phase, which is precisely programmed by selecting a suitable combination of controlled-release mechanisms.

**Available technologies based on the time-controlled systems are:**

1. **Codes system:** comprises a series of polymers that are combined to protect the drug core until the formulation arrives in the colon.
2. **Colon-Targeted Delivery System** - uses lag time to achieve colon delivery. The system is comprised of three parts: an outer enteric coat, an inner semipermeable polymer membrane, and a central core comprising swelling excipients and an active component.
3. **Oros-CT:** is a technology developed by alza corporation and consists of an enteric coating, a semipermeable membrane, a layer to delay drug release, and a core consisting of two compartments.
4. **Time Clock - delivery device:** developed by pozzi and colleagues is pulsed delivery system based on a coated solid dosage form.



**Figure 2: Cross section of the OROS-CT colon targeted drug delivery System.**

### **Microbially-Controlled Systems:**

These systems are based on the exploitation of the specific enzymatic activity of the microflora (enterobacteria) present in the colon. The colonic bacteria are predominately anaerobic in nature and secrete enzymes (*azoreductases*,  *$\beta$ -glucuronidase*,  *$\beta$ -xylosidase*, *dextranases*, *esterases*, *nitroreductase*, etc.) that are capable of metabolizing substrates such as carbohydrates and proteins that escape the digestion in the upper GIT. Polysaccharides offer an alternative substrate for the bacterial enzymes present in the colon. A number of naturally occurring polysaccharides are stable in the upper intestine yet susceptible to hydrolytic degradation in the lower intestine. Most polysaccharides can be chemically modified to optimize specific properties, such as the ability to form impermeable films pectin is a non-starch linear polysaccharide composed mainly of  $\alpha$ -(1,4)-linked D-galacturonic acid groups with some 1,2 linked L-rhamnose groups pectin, like many other polysaccharides, is stable in the stomach and small intestine but susceptible to enzymatic degradation in the large intestine. Calcium and zinc salts of pectin are preferred for lower intestinal delivery since they have lower water solubility and hence better dissolution delaying properties than sodium pectinate or pectic acid. Improved targeted delivery to the lower intestine using pectin and other naturally occurring polysaccharides is accomplished by coating tablet or multiparticulate formulations with traditional enteric polymers. This formulation approach was tested in a human study with normal volunteers using gamma scintigraphy. The formulations were composed of enteric-coated calcium pectinate matrix tablets prepared with and without guar gum as a binder. The tablets were found to reach the colon in most cases intact and there they disintegrated. Another approach used to limit drug dissolution in the upper intestine involves mixed films. Mixed films are composed of polysaccharides co-formulated with water-insoluble polymers such as ethyl cellulose or chitosan (partially deacetylated chitin) and gel forming polymers such as hydroxyl propyl methylcellulose (HPMC). These mixed films were used to prepare coatings for tablets to deliver drugs into the colon. In vitro dissolution testing of the coated tablets using a pectinolytic enzyme preparation showed that drug release was accelerated by action of this enzyme preparation compared with dissolution medium free of the enzyme. Another polysaccharide examined for its ability to delay release of drugs in the gastrointestinal tract is guar gum (GG). GG is a galactomannan material composed of linear chains of (1,4)- $\beta$ -D-mannopyranosyl units with  $\alpha$ -D-galactopyranosyl units linked by (1,6). The

colon contains enzymes (galactomannanases) capable of degrading GC to short chain fatty acids. Both matrix tablets and compression coated tablets have been administered in humans. Tablets composed primarily of GG and the drug dexamethasone were dosed orally in humans and their transit and disintegration followed using gamma scintigraphy. Some drug was released from the tablets prior to colonic arrival but the majority of drug was released in the large intestine and release was generally correlated with tablet disintegration.

#### **Enzyme- based systems – prodrug:**

A successful prodrug-based delivery system is one in which the pro moiety i.e, inactive portion of the prodrug) minimizes absorption until the active is released (usually by enzymatic action) near the target site. Thus, the pro moiety is used to increase the hydrophilicity of the parent drug, increase molecular size, or both, thus minimizing absorption of the drug prior to reaching the target site.

This principle has been exploited commercially to deliver 5-aminosalicylic acid to the colon by way of a prodrug carrier. The prodrug sulphasalazine consists of two separate moieties, sulphapyridine and 5-aminosalicylic acid, linked by an azo -bond. The prodrug passes through the upper gut intact, but, once in the colon the azo- bond is cleaved by the host bacteria, liberating the carrier molecule sulphapyridine and the pharmacologically active agent 5-aminosalicylic acid this concept has led to the development of novel azo-bond-based polymers (azo-polymers) for the purpose of obtaining universal carrier systems. However, issues with regard to the safety and toxicity of these synthetic polymers have yet to be addressed.

#### **Pressure-dependent system:**

Another approach to controlling the site (and potentially the rate) of drug release in the GIT is using the pressure. Due to the reabsorption of water from the large intestine, the viscosity of the luminal contents increases. As a result, intestinal pressures increase due to peristalsis in the distal intestine providing a potential means to trigger release of a drug from a formulation susceptible to pressure changes. Formulations susceptible to changes in pressure are prepared from capsule-shaped suppositories coated with ethyl cellulose. Intestinal pressures increase due to peristalsis in the distal intestine providing a potential means to trigger release of a drug from a formulation

susceptible to pressure changes. Formulations susceptible to changes in pressure are prepared from capsule-shaped suppositories coated with ethyl cellulose.

### **Evaluation of colon-targeted drug delivery systems<sup>15-17</sup>:**

Various *in-vitro and in vivo* evaluation techniques have been developed and proposed to test the performance and stability of colon- specific drug delivery systems.

#### ***In-vitro* dissolution testing:**

Dissolution testing has been an integral component in pharmaceutical research and development of solid dosage forms. It provides decisive information on formulation selection, the critical processing variables *in vitro/ in vivo* correlation and quality assurance during clinical manufacturing. In order to provide this information, dissolution testing should be conducted in physiochemically and hydrodynamically defined conditions to simulate the environment that the dosage form encounters in the gastrointestinal tract . Currently, four dissolution apparatus are recommended in the USP to accommodate different actives and dosage forms, basket method, paddle method, Bio-Dis method and flow-through cell method. For *in- vitro* evaluation of colon-specific drug delivery systems, the ideal dissolution testing should closely mimic the *in vivo* conditions with regard to pH, bacteria and types of enzymes, enzymatic activity, fluid volume and mixing intensity.

#### ***In-vivo* evaluation of colon-specific drug delivery systems:**

As in other controlled release delivery systems, the successful development of a colon-specific drug delivery system is ultimately determined by its ability to achieve colon-specific drug release and thus exert the intended therapeutic effect. When the system design is conceived and prototype formulation with acceptable *in vitro* characteristics is obtained *in-vivo* studies are usually conducted to evaluate the site specificity of drug release and to obtain relevant pharmacokinetics information of the delivery system. Although animal models have obvious advantages in assessing colon-specific drug delivery, human subjects are increasingly utilized for evaluation of this type of delivery systems with visualization techniques such as scintigraphy imaging.

### **A. Animal studies:**

Different animals have been used to evaluate the performance of colon-specific drug delivery systems, such as rats, pigs and dogs. To closely simulate the human physiological environment of the colon, the selection of an appropriate animal model for evaluating a colon-specific delivery system depends on its triggering mechanism and system design. For instance, guinea pigs have comparable glycosidase and *glucuronidase* activities in, the colon and similar digestive anatomy and physiology to that of human, so they are more suitable in evaluating glucoside and glucuronate conjugated prodrugs intended for colon delivery.

### **B. Gamma-Scintigraphy:**

In most cases, conventional pharmacokinetic evaluation may not generate sufficient information to elucidate the intended rationale of system design. Scintigraphy is an imaging modality, which enables the in vivo performance of drug delivery systems to be visualized under normal physiological conditions in a non-invasive manner.

Through scintigraphy imaging, the following information regarding the performance of a colon-specific delivery system within human GI tract can be obtained: the location as a function of time, the time and location of initial and complete system disintegration, the extent of dispersion, the colon arrival time, stomach residence and small intestine transit times.

### **C. Roentgenography:**

The inclusion of a radio-opaque material into a solid dosage form enables it to be visualized by the use of X-rays. By incorporating barium sulphate into a pharmaceutical dosage form, it is possible to follow the movement, location and the integrity of the dosage form after oral administration by placing the subject under fluoroscope and taking series of X-rays at various time points.

### **Disease Status:**

Colon targeted matrix tablet is one controlled release dosage form, which release the drug in continuous manner at colon. The release of drug by both dissolution controlled as well as diffusion controlled maintaining therapeutic blood or tissue levels at of the drug for extended

period of time with minimized local or systemic adverse effects. Colon is concerned with number of diseases like IBD, colon cancer etc. The term inflammatory bowel disease (IBD) covers a group of disorders in which the intestines become inflamed (red and swollen). Two major types of IBD are described: ulcerative colitis and Crohn's disease. As the name suggests, ulcerative colitis is limited to the colon (large intestine). Although Crohn's disease can involve any part of the gastrointestinal tract from the mouth to the anus, it most commonly affects the small intestine and/or the colon. Both ulcerative colitis and Crohn's disease usually run a waxing and waning course in the intensity and severity illness. When there is severe inflammation, the disease is considered to be in an active stage, and the person experiences a flare-up of the condition. It is very challenging task to prepare such dosage form which could be target the colon hence, one of active drug Meloxicam (MLX) is an oxicam derivative nonsteroidal anti-inflammatory drug (NSAID) with analgesic and fever reducer effects. Recently has been reported that MLX play important role in colorectal carcinogenesis therapy

## CONCLUSION

Hence, it appears that the effective way of treating ulcers is to employ the concept of receptor-mediated drug delivery approach which involves use of specific receptors present on the surface of intestine. Once reached the target site, the drug (loaded into carrier-like nanoparticles) will be taken up by receptor-mediated endocytosis. For achieving this goal successfully, development of a drug carrier that can remain stable in upper part of GIT and that can deliver the active ingredient in the close proximity of target cell is the need of an hour. Thus, it is high time to develop targeted and site-specific delivery system for the colons that are effective, safe and commercially viable so as to render a sigh of relief to the patients suffering from this condition of ulcers.

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