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DESCRIPTIVE REVIEW ON COLON TARGETED DRUG DELIVERY SYSTEM

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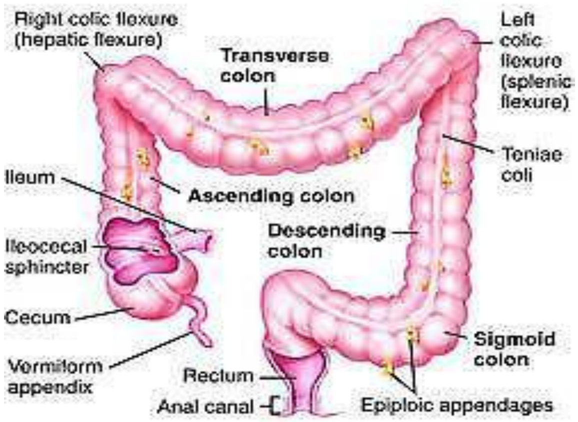
ABSTRACT
Colon specific drug delivery system has attracted considerable attention for the past few years in order to develop drug delivery systems that are able to release drugs specifically in the colon in a predictable and reproducible manner. The colon is a site where both local and systemic delivery of drugs can take place. Colon targeted drug delivery system involves the targeting of drug to colon and is used for the treatment of various diseases related to colon like inflammatory bowel disease, colon cancer, crohn's diseases etc. Beside these different new approaches were also used for colon targeting like pressure controlled, osmotic controlled drug delivery systems are highly effective. This review is aimed at understanding recent approaches for dosage forms which is targeting to colon through pH sensitive system, microbial triggered system.

KEYWORDS:- Crohn's diseases, pH sensitive, colon cancer, osmotically controlled system.

INTRODUCTION

Anatomy and Physiology of Colon

The GI tract is divided into stomach, small intestine and large intestine. The large intestine extending from the ileocecal junction to the anus is divided in to three main parts. These are the colon, the rectum and anal canal. The entire colon is about 5 feet (150 cm) long, and is divided in to five major segments. Peritoneal folds called as mesentery which is supported by ascending and descending colon. The right colon consists of the cecum, ascending colon, hepatic flexure and the right half of the transverse colon. 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. The human colon were shown in Figure1.The major function of the colon is the creation of suitable environment for the growth of colonic microorganisms, storage reservoir of faecal contents, expulsion of the contents of the colon at an appropriate time and absorption of potassium and water from the lumen. The absorptive capacity is very high, each about 2000ml of fluid enters the colon through the ileocecal valve from which more than 90% of the fluid is absorbed.[1]



Dig 1: Anatomy and Physiology of Colon

During the past decades research is going on in developing the methods to target the drug to the specific region. The goal of targeted drug delivery is to deliver the drug to the specific organ.[2] Drug delivery to the colon is beneficial not only for the oral delivery of proteins and peptide drugs (degraded by digestive enzymes of stomach and small intestine) but also for the delivery of low molecular weight compounds used to treat diseases associated with the colon or large intestine such as ulcerative colitis, diarrhoea, and colon cancer.[3] The colon is believed to be a suitable absorption site for peptides and protein drugs for the following reasons; (i) less diversity, and intensity of digestive enzymes, (ii) comparative proteolytic activity of colon mucosa is much less than that observed in the small intestine, thus CDDS protects peptide drugs from hydrolysis, and enzymatic degradation in duodenum and jejunum, and eventually releases the drug into ileum or colon which leads to greater systemic bioavailability.[4] The human colon has over 400 distinct species of bacteria as resident flora, a possible population of up to 1010 bacteria per gram of colonic contents. Among the reactions carried out by these gut flora are azoreduction and enzymatic cleavage i.e. glycosides.[5]

Factors Affecting Colon Targeted Drug Delivery.[5]

1. Physiological factors
2. Pharmaceutical factors

1. Physiological factors

a. Gastric emptying

Drug delivery to the colon upon oral administration depends mainly on gastric emptying and bowel transit time. Upon reaching the colon the transit time of dosage form depends on the size of the particles. Smaller particles have more transit time compared to larger particles. Diarrhoea patients have shorter transit time whereas constipation patients have longer transit times.

b. pH of colon

The pH of GIT varies between different individuals. The food intakes, diseased state, etc. Influences the pH of the GIT. This change in the pH in different parts of GIT is the basis for the development of colon targeted drug delivery systems. Coating with different polymers is done to target the drug to the site.

c. Colonic micro flora and enzymes

The GIT contains a variety of microorganisms that produces many enzymes need for metabolism. Growth of this micro flora is controlled by the GIT contents and peristaltic movements. The enzymes released by different microorganisms E. coli, Clostridia, Lactobacilli, Eubacteria, Streptococci are responsible for the various metabolic reactions that take place in the GIT.

2. Pharmaceutical factors

a. Drug candidates

Due to high retention time of colon, colon causes an increase in the absorption of poorly absorbed agents like peptides, etc. drugs used for treatment of inflammatory bowel diseases, etc. are suitable for colon targeted drug delivery system.

b. Drug carriers

The selection of carrier for CDDS depends on the nature of the drug, disease for which the drug is used. The various physicochemical factors of drug that effect the carrier selection includes chemical nature, stability, partition coefficient, functional groups of drug molecule etc.

COLON TARGETED DRUG DELIVERY SYSTEMS (CTDDS)

Drug delivery to the colon should be capable of protecting the drug en route to the colon i.e. drug release and absorption should not occur in the stomach as well as the small intestine and neither the bioactive agent should be degraded in either of the dissolution sites but only released and absorbed once the system reaches the colon. The colon specific drug delivery System (CDDS) is beneficial not only for the oral delivery of proteins and peptide drugs (degraded by digestive enzymes of stomach and small intestine) but also for the delivery of low molecular weight compounds used to treat diseases associated with the colon or large intestine such as ulcerative colitis, diarrhoea and colon cancer. Clinically relevant bioavailability may be achieved if the peptide can be protected from acid and enzymes in the stomach and upper intestine (Anil and Betty, 2010). The colon is having high water absorption capacity, the colonic contents are considerably viscous and their mixing is not efficient, thus availability of most drugs to the absorptive membrane is low. The human colon has over 400 distinct species of bacteria as resident flora, a possible population of up to 1010 bacteria per gram of colonic contents. Among the reactions carried out by these gut flora are azo reduction and enzymatic cleavage i.e. glycosides. These metabolic processes may be responsible for the metabolism of many drugs and may also be applied to colon-targeted delivery of peptide based macromolecules such as insulin by oral administration (Chien, 1992). Colon is rich in lymphoid tissue, eg., uptake of antigen into mast cells of colonic mucosa produces rapid local production of antibodies and this helps in efficient vaccine delivery. Region of colon is recognised as having a somewhat less hostile environment with less diversity and intensity of activity than stomach and small intestine (Chourasia et al., 2003) Target sites, colonic disease conditions, and drugs used for treatment are shown in Table 1 (Reddy et al., 1999).[6]

Table1: Colon targeting diseases, drugs and sites.[7]

Target sites	Disease conditions	Drug and active agents
Topical Action	IBD, Irritable bowel disease Crohn's disease Chronic pancreatitis	Hydrocortisone, Budenoside, Prednisolone, Sulfaselazine, Olsalazine, Mesalazine.
Local action	Pancreatactomy cysti fibrosis	Digestive enzyme supplements

	Colorectal cancer	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 Colon targeted drug delivery system.[8,9,10]

i. Minimization of Adverse effect by targeted delivery in case of ulcerative colitis & crohn's disease
ii. Gastric upset by NSAIDS can be overcome.
iii. Steroidal drugs extensive first pass metabolism can be avoided by designing colon targeted drug delivery system and this prevents the various adverse effect caused by steroidal drug on oral and I.V administration such as methylprednisolone and dexamethasone produces adeno suppression, Immunosuppression, cushing syndrome, bone resorption.
iv. Minimisation of dose of particular drug because of targeted delivery.
v. Novel site for targeting of anticancerous drug particularly in colorectal cancer.
vi. High retention time leads to increased bioavailability of poorly absorbale drugs
vii. Improved patient compliance

CURRENT STATUS

Targeting of drugs to the colon is of increasing importance for local treatment of inflammatory bowel diseases (IBD) of the colon such as ulcerative colitis and crohn's disease (CD).[11, 12] The prevalence of ulcerative colitis and CD ranges from 10 to 70 per 100,000 people, but recent studies in Manitoba, Canada, and Rochester, MN, have shown prevalence as high as 200 per 100,000 people.[13, 14] Such inflammatory conditions are usually treated with conventional oral dosage forms.[15, 16]

POLYMERS USED IN COLON TARGETING.[17]

Polymer contains a large number of structural unit joined by same type linkage, form into a chain like structure. These are nowadays used in formulating various pharmaceutical products. Naturally found polymer, which include gummy exudates, proteins, enzymes, muscle fibre, polysaccharides. In olden days natural polymers are widely used in pharmacy but a variety of synthetic polymer are used nowadays for pharmaceutical and cosmetic development, using these Polymer many therapeutic system of body namely controlled drug delivery systems, are achieved.

Natural polymer

Guar gum, Pectin, Cyclodextrin, Dextran, Amylase, Chitosan, Chondrotin sulphate, Locust bean gum.

Synthetic polymer

Shellac, Ethyl cellulose, Cellulose acetate phthalate, Hydroxy propyl methyl cellulose, Eudragit, Poly vinyl acetate phthalate.

CRITERIA FOR SELECTION OF SUITABLE CANDIDATE FOR CDDS

Most suitable candidates for CDDS are those which have poor absorption in stomach and intestine including peptides. Protein and peptide drugs e.g. growth hormones, calcitonin, insulin, interleukin, interferon and erythropoietin. Azo-bonds containing drug such as mesalazine sulfasalazine and olsalazine, Steroids like budesonide, fludrocortisone, prednisolone and dexamethasone requires local drug delivery used to treat irritable bowel disease (IBD) Colonic cancer drugs require local delivery e.g. 5-fluorouracil, doxorubicin, and methotrexate. Small extent of par cellular transport facilate selective absorption of drugs than small intestine e.g. Diclofencac, theophylline, glibenclamide, ibuprofen and metoprolol. To treat infectious diseases such as amoebiasis & helminthiasis requires site specific delivery e.g. metronidazole, mebendazole and albendazole.[18, 19, 20]

Table 2: Criteria for selection of drugs for CDDS

Criteria	Pharmacological class	Non peptide drugs	Peptide drugs
Drugs used for local action in colon against GIT diseases	Anti- inflammatory drugs	Metoprolol, Nifedipine	Amylin, Oligonucleotide
Drugs used for colon cancer	Antineoplastic drugs	Pseudoephedrine	Glucagon, Epoetin
Drugs poorly absorbed	Antihypertensive & Antianginal drugs	Ibuprofen, Theophylline	Cyclosporine, Desmopressin
Drugs that undergo extensive first pass metabolism	Nitroglycerin & Corticosteroids	Bleomycin, Nicotine	Sermorelin, Saloatonin
Drugs for targeting	Antiarthritic and antiasthamatic drugs	5-Amino-salicylic acid, hydrocortisone Prednisolone,	Somatropin, Urotoilitin

APPROACHES USED FOR SITE SPECIFIC DRUG DELIVERY TO COLON

Several approaches are used for site-specific drug delivery. Among the primary approaches for CDDS, These include:

Primary approaches of colon specific drug delivery system

A. PH- dependent delivery

In the stomach, pH ranges between 1 and 2 during fasting but increases after eating. The pH is about 6.5 in the proximal small intestine and about 7.5 in the distal small intestine. From the ileum to the colon, pH declines significantly. It is about 6.4 in the cecum. However, 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 and 7.0 in the descending colon. Use of pH dependent polymers is based on these differences in pH levels [21]. The polymers described as pH dependent in colon specific drug delivery are insoluble at low pH levels but become increasingly soluble as pH rises. Although a pH dependent polymer can protect a formulation in the stomach and proximal small intestine, it may start to dissolve in the lower small intestine and the site-specificity of formulations can be poor. The decline in pH from the end of the small intestine to the colon can also result in problems, lengthy lag times at the ileocecal junction or rapid transit through the ascending colon which can also result in poor site-specificity of enteric-coated single-unit formulations.[22]

Most commonly used pH dependent coating polymers are methacrylic acid copolymers, commonly known as Eudragit S, more specifically Eudragit L and S. Colon targeted drug delivery systems based on methacrylic resins has describedfor insulin, prednisolone, quinolones, salsalazine, cyclosporine, beclomethasone dipropionate and naproxen. Dissolution studies performed on the mesalazine tablets further confirmed that the release profiles of the drug could be manipulated by changing the Eudragit L100-55 and Eudragit S100 ratios within the pH range of 5.5 to 7.0 in which the individual polymers are soluble respectively, and a coating formulation consisting of a combination of the two copolymers can overcome the issue of high GI pH variability among individuals.[23]

Delayed (Time controlled release system) release drug delivery to colon

Time controlled release system (TCRS) such as sustained or delayed release dosage forms are also very promising. However due to potentially large variation of gastric emptying time of dosage forms in humans, in this approach colon arrival time of dosage forms can not accurately predicted, resulting in poor colonical availability. The dosage forms may also applicable as colon targeting dosage forms by prolonging the lag time of about 5.5 hours (range 5 to 6 hours). Disadvantages of this system are- (i) Gastric emptying time varies markedly between subjects or in a manner dependent on type and amount of food intake.(ii) Gastrointestinal movement, especially peristalsis or contraction in the stomach would result in change in gastrointestinal transit of the drug. (iii) Accelerated transit through different regions of the colon has been observed in patients with the IBD, the carcinoid syndrome and diarrhea and the ulcerative colitis.

Microbially triggered system

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 that are capable of metabolizing substrates such as carbohydrates and proteins that escape the digestion in the upper GI tract6-8. Bacterial count in colon is much higher around 1011-1012 CFU/ml with some 400 different species which are: Fundamentally aerobic, predominant species such as Bacteroides, Bifid bacterium and Eubacterum etc., whose major metabolic process occurring in colon are hydrolysis and reduction. The enzymes present in the colon are: 1. Reducing enzymes: Nitroreductase, Azoreductase, N-oxide reductase, sulfoxide reductase, Hydrogenase etc. 2. Hydrolytic enzymes: Esterases, Amidases, Glycosidases, Glucuronidase, sulfatase etc.

(i) Prodrug approach for drug delivery to colon

Prodrug is the main approach of microbial triggered drug delivery system in which the drug release from the formulation is triggered by the microflora present in the gut. Prodrug is the inactive form of an active parent drug that undergoes enzymatic transformation to release the active drug. The produrgs are prepared by linking the active drug with hydrophobic moieties like amino acids, glucoronic acids, glucose, galactose, cellulose, etc.

(ii) Polysaccharide based delivery systems

Polysaccharide based delivery system is the other form of microbial triggered drug delivery system. Naturally occurring polysaccharides like guar gum, xanthan gum, chitosan, alginates, etc. are used in targeting the drug delivery. These are broken down by the colonic micro flora to simple saccharides.[17]

B. Newly developed approaches for CDDS

a) Pressure-controlled drug-delivery systems

As a result of peristalsis, higher pressures are encountered in the colon than in the small intestine, have developed pressure controlled colon-delivery capsules prepared using ethyl cellulose, which is insoluble in water. 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 the10. The system also appeared to depend on capsule size and density. Because of reabsorption of water from the colon, the viscosity of luminal content is higher in the colon than in the small intestine. It has therefore been concluded that drug dissolution in the colon could present a problem in relation to colon-specific oral drug delivery systems. In pressure-controlled ethyl cellulose single-unit capsules the drug is in a liquid. Lag times of three to five hours in relation to drug absorption were noted when pressure-controlled capsules were administered to human.[24]

b) Pulsatile colon targeted drug delivery
i) Pulsincap system
In this system (Figure No.3) the formulation is developed in a capsule form. The plug placed in the capsule controls the release of the drug. Swellable hydrogels are used to seal the drug contents. The capsule gets swelled when it comes in contact with the dissolution fluid and after a lag time the plug gets pushed off from the capsule and the drug will be released. Polymers such as different grades of hydroxyl propyl methyl cellulose (HPMC), poly methyl methacrylate and polyvinyl acetate are used as hydrogel plugs. The lag time is controlled by the length and point of intersection of the plug in the capsule body.[25]

ii) Port system
In this system (Figure No.4) the capsule body is enclosed in a semi permeable membrane. The capsule body consists of an insoluble plug consisting of osmotically active agent and drug formulation. When the capsule comes in contact with the dissolution fluid the semi permeable membrane permits the fluid flow into the capsule resulting in the development of pressure in the capsule body which leads to release of drug due to expelling of the plug. The drug is released at regular intervals with time gap between the successive intervals.[26]

C) Osmotically controlled system (ORDS- CT)
The OROS-CT (Alza Corporation) can be used to target the drug locally to the colon for the treatment of disease or to achieve systemic absorption that is otherwise unattainable.[27] 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. 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).[27]

D) CODES technology (combination of pH dependent and microbially triggered CDDS)
This method is developed to minimize the problems\associated with the pH and time dependent drug delivery systems. In this system the pH sensitive polymers are used along with the polysaccharides that are degraded only by specific bacteria present in the intestine. This system consists of a core tablet coated with three layers of polymer coatings. The outer coating is composed of the polymer Eudragit L. This coating gets dissolved once the tablet passes though the pyloric and duodenum and exposes the next coating. The next coating is composed of Eudragit E. This layer allows the release of lactulose present in the inner core. This released lactulose gets metabolized into short chain fatty acids that lower the surrounding pH where the Eudragit E layer dissolves. The dissolving of Eudragit E results in the exposure of the drug. The other polysaccharides that are used along with the drug in the core tablet are mannitol, maltose, etc. The bacteria present in the colon are responsible for the degradation of polysaccharides that are released from the core tablet.[28]

Marketed drugs for colon specific drug delivery systems:
There are some marketed drug discovered for colon targeting listed in table.

Table 3 : Marketed colon specific drug delivery systems[29]

Drug	Trade Name	Coating Polymers
Mesalazine	Mesazal Asacol	Eudragit® L100 Eudragit® S
Budesonide	Entrocort® Budenofalk®	Eudragit® L100-55 Eudragit® S
Sulfasalazine	Azulfidine Colo-Pleon	Cellulose acetate phthalate Eudragit® L100-55

INTRODUCTION TO POLYMERS
Eudragit® S100.[30, 31]
The aim of the present investigation was to design and develop CTDDS. Eudargit S100 dissolves above pH 7.0 and thus helps protect the system against harsh acidic condition of stomach and thus it may act as one of the guiding tool to target drug to colon.

Description
White powder with a faint characteristic odour.

Chemical name
Poly (methacrylic acid, methyl methacrylate) 1:2

Solubility
1 g Eudragit S 100 dissolves in 7 g methanol, ethanol, in aqueous isopropyl alcohol and acetone (containing approx. 3 % water), as well as in 1 N sodium hydroxide to give clear to slightly cloudy solutions. Eudragit S 100 is practically insoluble in ethyl acetate, methylene chloride, petroleum ether and water.

Safety
A daily intake of 2mg/kg body weight of Eudragit (equivalent to approximately 150 mg for an average adult) may be regarded as essentially safe in humans.

Regulatory Status
Included in the FDA Inactive Ingredients Guide (oral capsules and tablets). Included in nonparenteral medicines licensed in the UK. Included in Canadian list of Applicable Non-medicinal Ingredients.

Pectin [30]
Nonproprietary names:

USPNF: Pectin

Description:
Pectin occurs as a coarse or fine, yellowish-white, odorless powder that has a mucilaginous taste.

Chemical name
Pectin

Solubility
Soluble in water, insoluble in ethanol (95%) and other organic solvents.

Safety
Pectin is generally regarded as an essentially nontoxic and nonirritant material.

Regulatory Status
GRAS listed. Accepted for use as food additive in Europe. Included in the FDA Inactive Ingredients Guide (dental paste; oral powders; topical pastes). Included in nonparenteral medicines licensed in the UK. Included in Canadian list of Applicable Non-medicinal Ingredients.

CURRENT STATUS OF PHARMACOLOGICAL TREATMENT OF COLORECTAL CANCER

Colon and rectal cancer are cancers that involve the lowest part of the digestive system: the large intestine and the rectum. Despite early diagnosis and treatment, cancers involving the colon or rectum (colorectal cancer) can reappear at a later time, even if the cancer was entirely removed during the initial treatment. Reappearance of the colorectal cancer after initial curative therapy is referred to as a recurrence or a relapse. A colorectal cancer recurrence can be either local (confined to the area where the cancer was initially diagnosed or nearby tissues) or at a distant site. When the recurrence develops at a site away from the colon or rectum, it is called a metastasis. In other cases, a colorectal cancer has already spread to distant sites by the time it is diagnosed. This is referred to as metastatic (stage IV) colorectal cancer.

Cure is not possible for most patients with metastatic colorectal cancer, although some patients who have limited involvement of distant organs (particularly restricted to the liver and/or lung) can be cured with surgery. For others, chemotherapy is the most appropriate option. Chemotherapy does not cure metastatic colorectal cancer, but it can improve symptoms and prolong life. Sometimes both chemotherapy and surgery are recommended.

Colorectal cancer (CRC) is a malignant neoplasm arising from the lining of the large intestine (colon and rectum). It is the third most common cancer in males and the second in females. Countries such as Australia, New Zealand, Canada, the United States and parts of Europe have the highest incidence rates, whereas China, India, parts of Africa and South America have the lowest risk of colorectal cancer in the world.[32] This geographical variation in incidence across the world can be attributed to differences in the consumption of red and processed meat, fiber and alcohol as well as body weight and physical activity. However, the incidence of colorectal cancer is increasing in Japan and other Asian countries as there has been a shift towards westernized diets and lifestyles.[33] The survival rate for colorectal cancer varies with stage of disease at diagnosis and typically varies from 90% for cancers detected at the localized stage to 10% for distant metastatic cancer. The incidence of colorectal cancer has been known to increase with age. The likelihood of colorectal cancer diagnosis increases progressively from a younger age (< 40 years) and rises sharply after the age of 50 years [34, 35]. Several factors such as poor quality diets [36], lack of physical activity, obesity [37], cigarette smoking [38] and heavy alcohol consumption [39] are associated with an increased risk of colorectal cancer. An individual with a history of adenomatous polyps or inflammatory bowel disease has an increased risk of developing colorectal cancer compared to an individual with no history of either.[38, 39, 40]

Colorectal cancer includes malignant growths from the mucosa of the colon and rectum. Cancer cells may eventually spread to nearby lymph nodes and subsequently to more remote lymph nodes and other organs in the body like the liver and lungs, among others. The treatment, prognosis and survival rate largely depends on the stage of disease at diagnosis. Screening for colorectal cancer is particularly effective. Screening can prevent cancer from occurring as it can detect adenomatous polyps that can be successfully removed.[15] Treatment for colorectal cancer varies by tumor location and stage at diagnosis. Surgical removal of tumor and nearby lymph nodes is the most common treatment for early stage (stage I or II) colorectal cancer. For patients with late-stage disease, chemotherapy alone or in combination with radiation therapy is often given before or after surgery.[41]

HYPOTHESIS

Turkoglu Murat; Ugurlu Timucin et al., (2002) studied, pectin-HPMC compression coated core tablets of 5- aminosalicylic acid (5-ASA) for colonic delivery. It was found that pectin alone was not sufficient to protect the core tablets and HPMC addition was required to control the solubility of pectin. The optimum HPMC concentration was 20% and such system would protect the cores up to 6 h that corresponded to 25-35% erosion and after that under the influence of pectinase the system would degrade faster and delivering 5-ASA to the colon. The pectin-HPMC envelope was found to be a promising drug delivery system for those drugs to be delivered to the colon.[42]

Jurairat Nunthanid *et al.*, (2007) developed a colonic drug delivery with a new concept based on a combination of time, pH and enzyme controlled system. They prepared spray-dried chitosan acetate (CSA) from low molecular weight chitosan and characterized. A combination of CSA and hydroxy propyl methyl cellulose (HPMC) was used as new compression-coatsfor 5- amino salicylic acid. They evaluated the factors affecting *in vitro* drug release i.e % weight ratio of coating polymers, etc. they proved that the delayed release was time and pH controlled owing to the swelling of the CSA and HPMC and degradation of CSA by β- glucoridase in the colonic fluid.[43]

Mura P *et al*., (2003) developed a new colonic drug delivery system which takes advantage of the combined approaches of a specifically enteric coated colonbiodegradable pectin matrix of theophylline with pH sensitive Eudragit S 100 polymeric coating. They found that the developed system was able to suitably retard the onset of drug release and provided a colon targeting which overcome the problems of pectin solubility in the upper GI tract and low site-specificity of simple pH-dependent systems.[44]

Avachat A *et al*., (2007) have developed and characterized an oral controlled release drug delivery system for concomitant administration of diclofenac sodium (DS) and chondroitin sulfate (CS). They prepared hydrophilic matrix tablets using different concentrations of hydroxy propyl methyl cellulose (HPMC) using wet granulation technique. They induced CS as an active ingredient for its chondroprotective action and cartilage rebuilding. Since, chondroitin sulfate is water soluble polymer they added HPMC in an increasing ratio to give a controlled release of DS and CS within a matrix system.[45]

Aiedeh. K and Taha. M et al., (1999) synthesized potential matrices of chitosan succinate and chitosan phthalate in oral drug delivery systems in colon-specific drug delivery and their evaluation. Sodium diclofenac was used as the dispersed model drug. The prepared matrices were incorporated into tablets and tested *in -vitro*. They suggested the suitability of the prepared matrices in colon specific, orally administrated drug delivery.[46]

CONCLUSION

Colon targeted drug delivery system offers benefits of local and systemic effects. The main advantage of CDDS is that the colon offers near neutral pH, a long transit time, reduced enzymatic activity and increased responsiveness to absorption enhancers. The biodegradable polymers are used for the colon specific delivery of the drug. For the invitro evaluation of the system the current dissolution techniques are not suitable. Research is going on to develop suitable dissolution methods to evaluate the colon targeted drug delivery systems.

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