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A Novel Drug Delivery Systems Of Colon Targeted : A Review

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Abstract
In the current year colonic drug delivery has gained significance for delivery of drug for the treatment of local diseases related with colon and systemic delivery of therapeutic peptides and proteins. Management could be more effective if it is possible for drug to be directly delivered to colon. This article gives an overview on different approaches utilized for colon specific drug delivery.
Key Words: *Novel drug delivery systems of colon targeted*

INTRODUCTION

Drug administration through an oral route is the most convenient and important method of administering drugs for systemic effect. Nearly 50% of the drug delivery systems available in the market are oral D.D.S. and these systems have more advantages due to patient acceptance and ease of administration. During the last decade there has been interest in developing site-specific formulations for targeting drug to the colon. 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, ulcerative colitis, irritable bowel syndrome and constipation but also for the systemic delivery of proteins, therapeutic peptides, antiasthmatic drugs, antihypertensive drugs and antidiabetic agents. The colon specific drug delivery system (CDDS) 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.[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] And finally, because the colon has a long residence time which is up to 5 days and is highly responsive to absorption enhancers[5]. Oral route is the most convenient and preferred route but other routes for CDDS may be used. Rectal administration offers the shortest route for targeting drugs to the colon. However, reaching the proximal part of colon via rectal administration is difficult. Rectal administration can also be uncomfortable for patients and compliance may be less than optimal.[6] Drug preparation for intrarectal administration is supplied as solutions, foam, and suppositories. The intrarectal route is used both as a means of systemic dosing and for the delivery of topically active drug to the large intestine. Corticosteroids such as hydrocortisone and prednisolone are administered via the rectum for the treatment of ulcerative colitis. Although these drugs are absorbed from the large bowel, it is generally believed that their efficacy is due mainly to the topical application. The concentration of drug reaching the colon depends on formulation factors, the extent of retrograde spreading and the retention time. Foam and suppositories have been shown to be retained mainly in the rectum and sigmoid colon while enema solutions have a great spreading capacity.[7]

Kowanko I.C *et al.,* (1981) studied the circadian variations in the signs and symptoms of rheumatoid arthritis and in the therapeutic effectiveness of flurbiprofen at different times of the day. Results concluded taking long acting NSAIDs like flurbiprofen, at bedtime optimizes their therapeutic effect and minimizes or averts their side effects[8].

Bruguerolle. B., (1998) reviewed the current status of Chronopharmacokinetics. Chronokinetic studies have been reported for many drugs in an attempt to explain chronopharmacodynamic phenomena and demonstrate that the time of administration is a possible factor of variation in the kinetics of a drug. Illustrated with the chronopharmacokinetics of cardiovascular and nonsteroidal anti-inflammatory drugs. Drug chronopharmacokinetic knowledge may be clinically relevant as it may have implications for drug prescription by modulating the distribution of the total daily dose along the 24 h scale[9].

Valentine C Ibekwe *et al.,* (2004) reviewed the advantages and different approaches of colonic drug delivery via oral route. In their review they quoted that colon can be site of drug targeting to synchronize the circadian rhythm of asthma, arthritis etc[10].

Brahma N Singh., (2007) reviewed on modified release solid formulations for colonic delivery and discussed about the various benefits of solid formulations intended for targeted drug release into the colon. The author discussed that the colon targeted drug delivery systems can be utilized for chemotherapy of diseases which are affected by circadian rhythms (e.g., asthma, hypertension and arthritis). He summarized the recent patent literatures concerning various modified release formulation technologies that are claimed to provide colonic delivery of drugs[11].

Michael H. Smolensky and Nicholas A. Peppas., (2007) has been studied circadian (24 h) time structure and shows

great importance to the practice of medicine and pharmacotherapy of patients. Rhythmicity in the pathophysiology of disease is one basis for chronotherapeutics purposeful variation in time of the concentration of medicines in synchrony with biological rhythm determinants of disease activity to optimize treatment outcomes. Great progress has been realized with hydrogels, and they offer many advantages and opportunities in the design of chronotherapeutic systems for drug delivery via the oral, buccal, nasal, subcutaneous, transdermal, rectal, and vaginal routes[12].

Veena S Belgamwar *et al.,* (2008) designed a system for chronopharmacotherapy which is based on circadian rhythm. The principle rationale for the use of pulsatile release is for the drugs where a constant drug release, i.e., a zero-order release is not desired. Various systems like capsular systems, osmotic systems, pulsatile system based on the use of soluble or erodible polymer coating, use of rupturable membranes and pulsatile system based on membrane permeability are summarized in this article[13].

Kinget. R *et al.,* (1998) aimed at providing insight into the design considerations and evaluation of colon drug delivery. They surveyed the anatomy and physiology of the lower GI tract and biopharmaceutical aspects in relation to the drug absorption in the colon by various approaches[14].

Ashford M and Fell JT., (1994) reviewed the approaches taken to achieve a universal system for delivery. The design of such a system requires the identification and exploitation of a unique feature of the colonic environment. The use of transit times, pH and bacterial enzymes are critically assessed. In addition, the system must provide protection for the drug during transit to the colon. Upper gastrointestinal physiology and the transit of pharmaceuticals through these regions are reviewed with reference to their relevance in achieving site specificity[15].

S.Sarasija and A.Hota., (2000) studied the Colon specific delivery of drugs for the treatment of colonic diseases, so as to maximize the effectiveness of these drugs. Oral delivery of peptides and proteins are possible because colon provides a more friendly environment than the upper GI tract. This review deals with the anatomy and physiology of colon and various aspects of formulations by which colon targeting of drugs can be achieved[16].

Jack Aurora *et al.,* (2006) reviewed the various challenges and opportunity in colonic drug delivery systems. The necessity of such systems is to protect the drug from absorption from the upper GI tract then enable selective release of drugs in in the proximal colon. This article reviewed the surge of research focus, potential opportunity and challenges available in the new area of colon targeted drug delivery systems[17].

Rubinstein. A., (1995) reviewed on the approaches and opportunities in colon-specific drug delivery. The two approaches studied were protective coats that bring the dosage form as close as possible to the colon after oral administration and prodrugs, polymeric drugs, and biodegradable polymers that are degraded mostly by the unique enzymes of the colon. Various opportunities include bypassing small intestine metabolism, achieving constant absorption rates for small molecules, and delivering cationized antioxidant enzymes to the colonic epithelium[18].

Yang. L *et al.,* (2002) reviewed the primary approaches like prodrugs, ph and time dependent systems and microflora activated systems to obtain colon specific drug delivery and found that triggering mechanism delivery system only respond to the physiological conditions particular to the colon. They suggested that four different systems (Pressure Controlled Colon Delivery capsules (PCDCs), Colonic Drug Delivery System (CODDS) based on pectin and galactomannan coating and azohydrogels) for colon targeting were unique[19].

Akhgari A *et al.,* (2006) evaluated the combination of pH dependent and time dependent polymers as a single coating for design of colon delivery system of indomethacin pellets. They used Eudragit S 100 and Eudragit L 100 as pH dependent polymers and Eudragit RS as a time dependent polymer. Dissolution studies of pellets were conducted in the media with different pH, simulating the GI tract. They found that the lag time prior to drug release was affected by coating level. They also found that optimum formulation containing 20% Eudragit RS, 64% Eudragit S and 16% Eudragit L and a coating level of 10% was useful to prevent the drug release in the upper GIT[20].

Sinha V.R, Kumria. R., (2001) studied the development if solid dosage forms using the natural polysaccharides for the delivery of drug to colon. The rationale for the development of a polysaccharide based delivery system for colon is the presence of large amounts of polysaccharides in the human colon is inhibited by a large number and variety of bacteria which secrets many enzymes[21] e.g. beta-D- glucosidase, beta-D-galactosidase, amylase, pectinase etc.

Rajendra Kotadiya., (2008) studied the various properties of guar gum for usage as better polysaccharide for colonic drug delivery. It includes general properties and chemistry of guar gum. The author also reviewed the various application of guar gum as a carrier for colon drug delivery systems[22].

Reddy SM *et al.,* (1999) reviewed on novel oral colon specific drug delivery systems for pharmacotherapy of peptide and non-peptide drug which was found to be obvious advantage over parentral administration. Sustained release colonic drugs are used in the treatment of nocturnal asthma, angina, and arthritis. Peptides, proteins, oligonucleotides and vaccines are the potential candidates for colon specific drug delivery. Sulfasalazine, ipsalazide and olsalazine are used for the treatment of inflammatory bowel disease. Recent developments in pharmaceutical industries including coating drugs with pH sensitive and bacterial degradable polymers, embedded in bacterial degradable matrices and designing into new prodrugs, have provided renewed hope to effectively target drug to colon. Polysaccharide and azopolymer coating have been used for colon specific targeting, which provides for the refinements in pharmacotherapy of colon specific drug delivery[23].

Sinha.VR, Kumria R., (2003) has reviewed about microbially triggered drug delivery to the colon. They have emphasized that protein and peptide based drugs necessitates an investigation into the suitability of various sites for their administration. They reviewed various microbially activated drug delivery system for colon specific drug delivery with specific reference to microflora

of the various segments of the GI tract and their role in targeting drug delivery in the colon[24].

Hogvaard. L and Cahdsted. H., (1996) reviewed current applications of polysaccharides in colon targeting which are used in the areas of controlled released coatings, matrices, macromolecular, and biodegradable carriers. They gave an overview of various approaches to obtain colon-specific drug delivery by using polysaccharides and a summary of available *in vitro* and *in vivo* testing methods and concluded that polysaccharides are very promising compounds for colon-specific drug delivery[25].

Wong D. *et al.,* (1997) evaluated several guar-based colonic formulations using apparatus III in simulated gastric fluid (pH 1.2), simulated intestinal fluid (pH 7.5) and simulated colonic fluids containing galactomannanase. When compared with drug release in simulated gastric and intestinal fluids, results showed that drug release was accelerated in the colonic fluid due to the presence of the galactomannanase that could hydrolyze the guar gum[26].

M. K. Chourasia *et al.,* (2003) proposed that colon targeting is naturally of value for the topical treatment of diseases of colon such as chron's disease, ulcerative colitis, colerectal cancer and amoebiasis. Microbially degradable polymers especially azo cross linked polymers have been investigated for use in targeting of drugs to colon. Certain plant polysaccharides such as amylose, inulin, pectin and guar gum remains unaffected in the presence of gastrointestinal enzymes and pave the way for the formulation of colon targeted drug delivery systems[27].

Amnon Sintov *et al.,* (1995) prepared a series of cross-linked products of chondroitin sulfate with 1, 12-diaminodecane. The water solubility of the modified polymers were low. The swelling of films made of the cross-linked polymers were measured in water and they found that an exponential- like dependency between the degree of swelling and extent of cross-linking. They prepared indomethacin tablets using two types of cross-linked polymers of chondroitin sulfate. Based on the physiochemical properties, water uptake and drug release characteristics, an optimal product with a potential to serve as a colon-specific drug carrier was suggested[28].

Y.S.R. Krishnaiah *et al.,* (1998) evaluated guar gum matrix tablets for colonic drug delivery in healthy human volunteers by conducting gamma scintigraphic studies using technetium 99m DTPA as traces. The colon arrival time of the tablets was found to be 24 h and the tablets were found to be degraded, thereby releasing a larger amount of traces on entering the colon. Thus the study clearly demonstrated that guar gum in the form of directly compressed matrix tablets was a potential carrier for colon-specific drug delivery[29].

Y.S.R. Krishnaiah *et al.,* (2001) developed colon targeted drug delivery system for metronidazole using guar gum as a carrier, matrix, multilayer and compression coated tablets of metronidazole containing various proportions of guar gum were prepared. All the formulations were evaluated for the thickness, hardness, drug content uniformity and were subjected to *in vitro* drug release studies. They found that the compression coated metronidazole tablets with either 275 or 350 mg of guar gum coat is most likely to provide targeting of metronidazole for local action in the colon[30].

Y.S.R. Krishnaiah et al., (2003) investigated the *in vivo* availability of guar gum-based colon-targeted tablets of tinidazole in comparison with immediate release tablets of tinidazole in human volunteers. The immediate release tablets of tinidazole produced a peak plasma concentration (C_{max} of 3239 ± 428 ng/ml) at 1.04 ± 0.32 h (T_{max}), whereas colon-targeted tablets produced peak plasma concentration (C_{max} of 2158 ± 78 ng/ml) at 14.9 ± 1.6 h. The delayed T_{max}, decreased C_{max}, and Ka, and unaltered bioavailability and elimination half-life of tinidazole from guar gum-based colon-targeted tinidazole tablets, in comparison with the immediate tablets, indicated that the drug was not released in the stomach and small intestine but delivered to the colon[31].

Sinha. VR and Kumria. R (2002) developed single unit colon specific drug delivery with polysaccharides and synthetic polymers as binders like xantham gum, guar gum, chitosan and eudragit E. Indomethacin was used as the model drug. Enteric coated tablets with eudragit L 100 containing 3% chitosan as a binder was prepared and tested for *in vitro* drug release in simulated stomach pH 1.2 for 2 h followed by small intestine environment at pH 6.8.the results showed only 12.5% drug release in the first 5 h, which is the usual upper gastrointestinal transit time. Tablets prepared by using guar gum as binder were unable to protect drug release under similar conditions. Preparations with xanthan gum as binder formed time-dependent release formulations and when used in concentration of 5.92% in the tablets, 28% drug release was observed in the usual upper GI tract conditions. Enteric-coated preparation with 8.88% of Eudragit E as binder could be used to carry water insoluble drug molecules to the colon especially in IBD. The studies showed that chitosan as a successful binder and chitosan with Eudragit E would be highly site specific since drug release would be at a retarded rate till microbial degradation or polymer solubulization takes place at the colon[32].

V.R. Sinha *et al.,* (2004) designed compression coating for colonic drug delivery of 5-fluorouracil for the treatment of colerectal cancer. Rapidly disintegrating core tablets containing 5 mg of 5-fluorouracil were prepared and compression coating with 175 mg of granules containing a mixture of xanthan gum (XG) and guar gum (GG) in varying proportions was done. Studies of XG:GG (10:20) tablets in presence of colonic contents showed an increased cumulative percent drug release of 67.2 ± 5.23 % in presence of 4% w/w caecal content after 19 h of incubation[33].

Ashutosh Mohapatra *et al.,* (2008) prepared, orally disintegrating tablets using direct compression and wet granulation method. First, the tablets of metformin were prepared using starch RX1500 and microcrystalline cellulose by direct compression. The tablets showed erosion behavior rather than disintegration. The optimized batches prepared by direct compression and wet granulation showed 85% drug release at 4 and 8 min, respectively[34].

Ravi V *et al.,* (2008) developed a novel colon targeted tablet formulation using pectin as carrier and diltiazem HCl

and indomethacin as model drugs. The tablets were coated with inulin followed by shellac and were evaluated for average weight, hardness and coat thickness. The study revealed that polysaccharides as carriers and inulin and shellac as a coating material can be used effectively for colon targeting of both water soluble and insoluble drugs[35].

Liu. L *et al.,* (2003) reviewed recent developments in pectin derived formulations for colon specific drug delivery via oral route. Their studies include gelation of pectin, calcium crosslinked pectinate, composites of pectin and other polymers, technologies to fabricate pectin into useful drug delivery vehicles, methods to evaluate release kinetics of incorporated drugs, advantages, limitations and possible further developments in pectin based formulations for colon specific drug delivery[36].

Rubinstein. A *et al.*, (1993) studied the *in vitro* evaluation of calcium pectinate, a potential colon specific drug carrier. Compressed and indomethacin were analyzed for degradation in the presence of pectinex 3XL, a typical pectinolytic enzyme mixture and in the presence of the human colonic bacterium, Bacteroids ovatus. Their findings indicate the potential calcium pectinate; compressed into tablets with insoluble drug, serve as a specific drug delivery system to colon[37].

Sverre Arne Sande (2005) overviewed oral formulations intended for site-specific drug delivery to the colon with pectin as the main excipient. Scintigraphic methods demonstrating the functionality of pectin formulations are discussed. The main focus is on the various formulations reported, including matrix tablets, multiparticulate formulations as pellets and hydrogel beads, and pectin-based coatings. Also included is an evaluation of common excipients employed to improve colon specificity by crosslinking or increasing the hydrophobicity. Finally, properties of the pectin molecules that are important for successful formulations are examined. The conclusion is that the studies found in the literature provide an excellent platform for the development of pectin-based colon delivery systems[38].

Gang cheng et al., (2004) (investigated time and pH dependent colon-specific drug delivery systems (CDDS) for oral administration of diclofenac sodium (DS) and 5-amino salicylic acid (5-ASA), respectively. The prepared DS tablets and 5-ASA pellets were coated with ethyl cellulose (EC) and methacrylic acid copolymers (Eudragit S-100 and L-100) respectively. They conducted the *in vitro* release behaviour of both ES coated tablets (DS) and Eudragit S-100 and L -100 coated pellets (5-ASA) in various dissolution medium simulating the GI tract. They studied the *in vivo* absorption kinetics of DS coated tablets in dogs. They found that the release profile of time-dependent DS coated tablets was not influenced by pH of the dissolution medium but the time of DS release was controlled by the thickness of the coating layer. The release of the 5-ASA from coated pellets depend upon both the combination ratio of Eudragit L100 and S100 and the thickness of the coating layer. They concluded that the coating of the tablets and pellets with ES and pH dependent polymers provided a promising strategy to target the colon[39].

Munira Momin, K. Pundarikakshudu., (2004) proposed colon targeted drug drug delivery systems for sennosides using guar gum as a carrier. The matrix tablets containing 50% of guar gum were found to be suitable for targeting of sennosides for local action in the colon. Thus it was concluded that matrix tablets containg 50% guar gum and coated with 10% HPMC are most suitable for drugs like sennosides which are mainly active in the lower GIT[40].

Yeole PG *et al.,* (2006) made an attempt, to increase therapeutic efficacy, reduce frequency of administration, and improve patient compliance, by developing sustained release matrix tablets of diclofenac sodium. Sustained release matrix tablets of diclofenac sodium and xanthan gum, were developed by using different drug: polymer ratios, such as F1 (1:0.12), F2 (1:0.16), F3 (1:0.20), F4 (1:0.24) and F5 (1:0.28). The kinetic treatment showed that the release of drug follows zero order kinetics (R^2 = 0.9758). Korsemeyer and Peppas equation gave value of n = 0.9409 which was close to one, indicating that the drug was released by zero order kinetics. Thus, xanthan gum can be used as an effective matrix former, to extend the release of diclofenac sodium[41].

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[42].

Aiedeh. K and Taha. M., (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[43].

M. A. Nasra *et al.,* (2007) prepared multilayer and compression coated tablets of metronidazole[44] to reach the colon intact has been investigated *in vitro*, using pectin as a carrier. *In vitro* release studies indicated that matrix and multilayer tablets failed to control the drug release in the physiological environment of stomach and small intestine. On the other hand, compression coated formulations were able to protect the tablet cores from premature drug release, but at high pectin coat: core ratios 4: 1 (F13) and 5: 1 (F14). Inclusion of chitosan 3 and 5% w/w (F12) in the pectin coat offered better protection at a lower coat: core ratio (3: 1). When the dissolution study was continued in pH 6.8 PBS containing 1.5% w/v rat caecal contents, compression coated tablet formulations F13, F14 and F12 released about 70.25 ± 9.9%, 51.3 ± 5.45% and 20 ± 5.01% drug respectively at the end of 24 h.

Khan MZ *et al.,* (1999) prepared lactose-based placebo tablets were coated using various combinations of two methacrylic acid copolymers, Eudragit L100-55 and Eudragit S100, by spraying from aqueous systems. The

Eudragit L100-55-Eudragit S100 combinations (w/w) studied were 1:0, 4:1, 3:2, 1:1, 2:3, 1:4, 1:5 and 0:1. The coated tablets were tested *in vitro* for their suitability for pH dependent colon targeted oral drug delivery. The same coating formulations were then applied on tablets containing mesalazine as a model drug and evaluated for *in vitro* dissolution rates under various conditions. The results also demonstrated that a combination of Eudragit L100-55 and Eudragit S100 can be successfully used from aqueous system to coat tablets for colon targeted delivery of drugs and the formulation can be adjusted to deliver drug at any other desirable site of the intestinal region of the GI tract on the basis of pH-variability[45].

Valluru Ravi *et al.,* (2008) developed A novel colon targeted tablet formulation using natural polysaccharides such as chitosan and guar gum as carriers and diltiazem hydrochloride as model drug. The prepared blend of polymer-drug tablets were coated with two layers, inulin as an inner coat followed by shellac as outer coat and were evaluated for properties such as average weight, hardness and coat thickness. The drug release from the coated system was monitored using UV/ Visible spectroscopy. *In vitro* studies revealed that the tablets coated with inulin and shellac have controlled the drug release in stomach and small intestinal environment and released maximum amount of drug in the colonic environment. Among the polymers used, chitosan was found to be the suitable polymer for colon targeting[46].

Mura P *et al.,* (2003) developed a new colonic drug delivery system which takes advantage of the combined approaches of a specifically enteric coated colon-biodegradable 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 over come the problems of pectin solubility in the upper GI tract and low site-specificity of simple pH-dependent systems[47].

Turkoglu Murat; Ugurlu Timucin., (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[48].

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-coats for 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[49].

Sajeev chandran *et al.,* (2004) developed a multiparticulate drug delivery system for the treatment of local disease associated with the colon. Reports suggest that drug carrier system larger than 200 μm possess very low gastric transit time due to physiological condition of the bowel in colitis. Studies suggest that approach based on pellets, granules, microsphere or nanoparticle type formulation is expected to have better pharmacological effect in the colon[50].

Watts P.J. *et al.,* (1992) studied the transit rate of different sized model dosage forms through the human colon and the effects of a lactulose induced catharsis. It has been shown that drug carrier systems with a size larger than 200 μm would be subjected to speedy bowel evacuation due to diarrhoea, resulting in a decreased GI transit time and decreased efficiency. Therefore, a multiparticulate system in the micron size range could be a useful option in the design of a suitable dosage form for inflammatory bowel disease[51].

Hua Zhang *et al.,* (2002) proposed a multiparticulate system of chitosan hydrogel beads for colon-specific delivery of macromolecules using fluoroscein isothiocyanate - labelled bovine serum albumin as a model protein. Polyelectrolytic complexation of chitosan its counterion, Tripolyphosphate (TPP). The results showed that the hydrogel beads in the presence of rat caecal and colonic enzymes indicated the potential of this multiparticulate system to serve as carriers to deliver macromolecules especially to the colon[52].

CONCLUSION

The colonic area of the GIT has become an increasingly significant site for drug delivery and absorption. CDDS offers extensive therapeutic benefits to patients in terms of both local and systemic treatment. Colon specificity is more likely to be achieved with systems that consume natural materials that are degraded by colonic bacterial enzymes. Considering the sophistication of colon-specific drug delivery systems, and the uncertainty of current dissolution methods in establishing possible in-vitro/in-vivo correlation, challenges remain for pharmaceutical scientists to develop and validate a dissolution method that incorporates the physiological features of the colon, and yet can be used routinely in an industry setting for the evaluation of CDDS.

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