Expert Opinion on Drug Delivery

ISSN: 1742-5247 (Print) 1744-7593 (Online) Journal homepage: informahealthcare.com/journals/iedd20

Getting into the colon: approaches to target colorectal cancer

Mayur M Patel

To cite this article: Mayur M Patel (2014) Getting into the colon: approaches to target colorectal cancer, Expert Opinion on Drug Delivery, 11:9, 1343-1350, DOI: 10.1517/17425247.2014.927440

To link to this article: https://doi.org/10.1517/17425247.2014.927440

Published online: 05 Jun 2014.

EXPERT OPINION

Getting into the colon: approaches to target colorectal cancer

Mayur M Patel
Nirma University, Institute of Pharmacy, Gujarat, India

Colorectal cancer (CRC) is the third most common cancer in the world and the second most common cause of cancer related deaths. Conventional treatment of CRC is comprised of drug (chemotherapeutic agents) administration by parenteral route, which delivers the drug to both normal as well as cancerous tissues, thus leading to numerous undesirable effects. Enormous research is going on worldwide for designing an alternative route of administration, among which oral colon-targeted drug delivery systems have gained immense attention amongst scientific community. Direct delivery of drugs at the site of action leads to an increase in the availability of drugs at the targeted region. This causes a reduction in the amount of drug required to exert same therapeutic effect, thus reducing the incidents of adverse effects. Various maneuvers (pH-dependent, time-dependent and microflora-activated systems) have been attempted by researchers for targeting drugs successfully to the colonic region by circumventing the upper part of gastrointestinal tract. This *Editorial* article aims to put forth an overview of the formulation technologies that have been developed for attaining colon specific drug delivery for the treatment of CRC.

Keywords: anti-cancer agent, chemotherapy, colon cancer, colon targeting, particulate drug delivery, receptor mediated transport

Expert Opin. Drug Deliv. (2014) 11(9):1343-1350

1. Introduction

Drug targeting is a useful tool for achieving selective and efficient delivery of active moiety at the anticipated site of action with minimized unwanted side effects. Colon-specific drug delivery system (CoDDS) has been attaining tremendous curiosity among scientific community. CoDDS denotes targeted delivery of active moiety to the lower part of gastrointestinal tract (GIT), that is, large intestine. CoDDS can be achieved either by rectal (suppositories and enemas) or oral administration of drugs. The latter is more preferred as the rectal routes displays high variability with respect to drug distribution. As far as oral route of administration is concerned, the conventional formulation will get dissolved in stomach and small intestine, thus leading to absorption of drugs from the respective sites. Hence, in order to achieve a successful oral CoDDS, the key area of concern is to overcome the absorption and degradation of drug in upper part of GIT. CoDDS has found its application for the treatment of both local diseases (viz., colon cancer, inflammatory bowel disease [IBD], irritable bowel syndrome [IBS] and so on) as well as for systemic delivery of proteins, peptides (viz., vasopressin, insulin, calcitonin, etc.) and vaccines [1]. Further, CoDDS has been reported to be useful for chronotherapy of various diseases like cardiac arrhythmias, rheumatoid arthritis, hypertension, nocturnal asthma, inflammation and angina pectoris [2]. This *Editorial* aims to put forth an overview of the formulation technologies that have been developed for attaining

informa
healthcare

10.1517/17425247.2014.927440 © 2014 Informa UK, Ltd. ISSN 1742-5247, e-ISSN 1744-7593

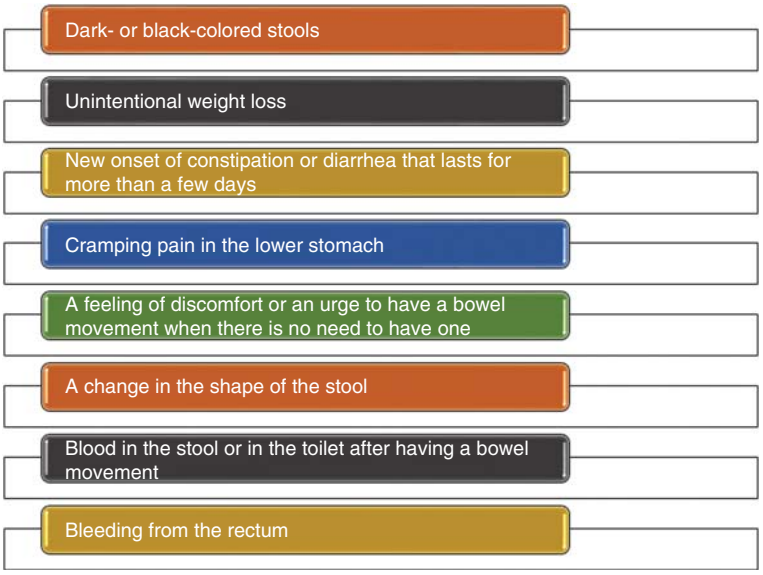

Figure 1. Warning signs depicting colorectal cancer.

CoDDS for the treatment of colorectal cancer (CRC) and not to provide a comprehensive review on drug delivery.

2. Colorectal cancer

CRC is the third most common cancer in the world and the second most common cause of cancer-related deaths [3]. In the USA, other than skin cancer, CRC was diagnosed as the third most common cancer in both men and women. It has been reported that estimated new CRC cases and deaths in the USA in 2014 will be 136,830 and 50,310, respectively [4]. Further, as occurrence of CRC is most frequent in countries like North America, Australia, New Zealand, Japan and Western Europe, it is considered to be a disease of affluence [5]. In India too, an increasing drift of CRC rates have been depicted through population based time trend studies. Bothersome are the studies which reports; Indians who have migrated to USA and UK are more prone to CRC. This could, thus, be attributed to modified dietary habits and lifestyles [6].

The development of CRC takes place slowly over a period of 10 – 15 years. Initially a noncancerous polyp develops on the lining of colon or rectum that can further grow as cancerous tissue. Adenomatous polyps (also called as adenomas) are certain kinds of polyps that are likely to become cancerous, although less than 10% of adenomas progresses to cancers. It has been reported that adenomas are common and about one-third to one-half of individual develops one or more adenomas. Further, about 96% of CRC are adenocarcinomas, evolving from glandular tissues. Most of these CRC ascends from adenomatous polyps. Once the commencement of growth of cancer takes place in the colonic region, it can further propagate through the lining and into the walls of the colon and rectum. Cancers propagated through walls can spread to distant parts (lungs, liver, abdominal cavity or ovary) of the body via blood or lymph vessels (this process is known as metastasis). Early stage of CRC often has no symptoms, leading to progression of disease. **Figure 1** shows some of the warning signs that depict risks of CRC. Further, several factors, both modifiable and nonmodifiable, exist that can either intensify or reduce the risk of CRC (**Figure 2**) [7-12].

Currently depending on the stage of cancer, CRC is been treated either by chemotherapy, surgery, radiation therapy or by immunotherapy. Further, it is a well-known fact that the conventional dosage form when used for the treatment of CRC delivers the drug to both normal and cancerous tissues, thus leading to undesirable adverse effects. Hence, targeted or site-specific delivery of drugs to the colonic region is gaining remarkable interest among scientific community. Direct delivery of drugs at the site of action leads to increment in availability of drugs at the targeted site, which further results into reduction in the amount of drug required to exert same therapeutic effect, thus reducing the incidents of adverse effects. The most commonly used drug candidates for the treatment of CRC comprises of 5-fluorouracil (5-FU), leucovorin, oxaliplatin and capecitabine. Moreover, apart from these, other drug candidates that have been reported to play a significant role in prevention of CRC are meloxicam, curcumin, valdecoxib, resveratrol, indomethacin and celecoxib [5,13].

3. Getting in to the colon: targeting CRC

Since the past two decades, remarkable research is going on in the field of oral CoDDS. A majority of these findings are focused on localized targeting of active moieties to the colonic region for the treatment of diseases like CRC, IBD, IBS, etc. The principal approaches applied for achieving localized

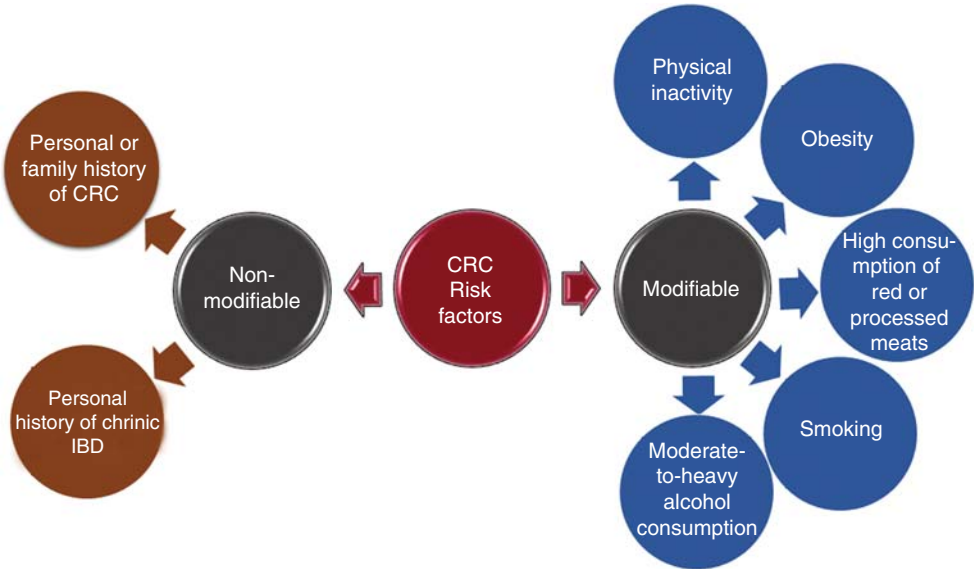

Figure 2. Factors intensifying or reducing the risk of CRC.
CRC: Colorectal cancer; IBD: Inflammatory bowel disease.

targeting to colonic region were pH-dependent systems, time-dependent systems and microbially and/or enzymatically driven drug delivery systems (consisting of biodegradable polymers [polysaccharides] and prodrugs-based CoDDS) [14]. As far as commercial availability is concerned, pH-dependent systems are supremely existing products. In this system, the formulation is been coated with enteric polymers (pH dependent), which protects the drug in the upper part of the GIT. However, the drawback associated with this system is that it lacks site-specific delivery of drug, which may either lead to no release in colonic region or premature release of drug in small intestine. In case of time-dependent systems, the site of preliminary drug release depends on the transit time of GIT. Despite the relatively constant small intestinal transit time (3 – 4 h), the gastric emptying time is highly variable and owing to this there are chances of either early drug release in small intestine or a deferred release of drug far down in the transverse colon. Microbially and/or enzymatically driven drug delivery systems is considered as the most accurate and precise strategy for achieving colon targeting of drugs. These systems employ the ecosystem of the specific microflora present in the colonic region. Naturally occurring polysaccharides are the most commonly used carriers that are specifically hydrolyzed by the microflora of colonic region. Unfortunately, due to hydrophilic nature of majority of natural polysaccharides, controlling the release of drug from these material possess a key challenge. As, as discussed, no single system is found to be precise and accurate enough to deliver active moiety into the colonic region, recently, a novel concept of using di-dependent drug delivery system has been proposed. In these systems, two factors, that is, pH and time, and pH and microflora of the colon controls the release of drug [15,16]. The formulation technologies that have been developed for the treatment of CRC are summarized in **Table 1**. In order to understand the maneuver of developed CoDDS for the treatment of CRC, the readers are requested to have thorough knowledge pertaining to different approaches used for colon targeting [1,2,16].

4. Expert opinion

CoDDS has proved its potential and has grown by leaps and bounds for the treatment of both local diseases and systemic therapies. The successful development of CoDDS encompasses usage of a triggering mechanism for delivery of drugs that answers only to the physiological conditions made available by the colonic region. Among the three primary approaches used for achieving CoDDS, microbially and/or enzymatically driven drug delivery systems seems to be more encouraging as it offers a unique advantage of sudden increment in bacterial population and associated enzyme activity in the colon (a noncontinuous event independent of GI transit time). Taking into accounts the above-mentioned facts of the microbially and/or enzymatically driven systems, among the two di-dependent approaches, the amalgamation of pH and microflora seems to be the supreme promising one. Further, despite such a massive amount of research work being reported in the pharmaceutical literature for achieving colon targeting of drugs by oral route, unfortunately very few of them have thrived in reaching the doors of clinical phase (the details of which have been discussed elsewhere) [16].

Currently, enormous research is going on worldwide for designing of oral CoDDS for localized treatment of CRC using anticancer agents (e.g., 5-FU, oxaliplatin, etc.).

Table 1. Recently developed colon-specific drug delivery system for the treatment of colorectal cancer.

Approach	Type of dosage form	Description	Drug candidate evaluated	Ref.
pH-dependent systems	Enteric-coated capsule filled with SMEDDS	Curcumin-loaded FSMEDDS was prepared in order to improve its solubility and achieve colonic targeting. This system was further filled into a capsular system, coated with Eudragit® S 100. The optimized formulation consists of 57.5% Cremophor® EL, 32.5% Transcutol® HP, 10% Capryol™ 90, and folate-polyethylene glycol-cholesteryl hemisuccinate (in small amount). The *in vitro* drug release studies revealed that the prepared formulation could deliver the drug efficiently to the colonic region. Cell uptake studies depicts that the system could bind efficiently with the folate receptors.	Curcumin	[18]
	Nanogels	A methacrylic acid and 2-ethyl hexyl acrylate copolymers were prepared by microemulsion polymerization technique. Drug entrapment within the polymeric backbone was achieved using solvent evaporation method. *In vitro* drug-release studies revealed pH dependent release of drug in a sustained manner. The cell proliferation assay performed using HCT-116 cell lines revealed that the prepared formulation demonstrated significant cytotoxic effect compared with free 5-FU.	5-FU	[19]
pH and time-di-dependent systems	Microparticulate system	A dually coated drug-loaded microparticulate system was prepared using a time- and pH-dependent approach. Poly-ε-caprolactone was evaluated as time-dependent coat and Eudragit® S100 as pH-dependent coat. *In vitro* drug release studies revealed that the double coat provides a satisfactory protection required for achieving colonic targeting. *In vivo* pharmacokinetic study revealed that the microparticles enhanced the bioavailability of drug and extended the duration of drug-plasma concentration in rats.	Celecoxib	[20]
	Tablets	A release modulated colon targeted system of meloxicam for potential application in the prophylaxis of colorectal cancer was prepared. Dually coated tablets containing polyethylene oxide as release retardant were prepared by direct compression technique. The out coat consists of Eudragit® FS 30D (pH-dependent layer) and inner coat consists of ethyl cellulose containing polyethylene glycol (time dependent layer). *In vitro* dissolution studies revealed that the developed system prevents premature drug release in upper part of GIT. *In vivo* pharmacokinetic and roentgenography studies in rabbits revealed that the prepared formulation remained intact until it reaches to the lower part of GIT.	Meloxicam	[3]
	Multiparticulate systems (pellets)	A multiparticulate (pellets) system dually coated with Eudragit® NE30D (time dependent layer) and Eudragit® FS30D (pH dependent layer) has been developed. Pellets were prepared by extrusion-spheronization technique using Avicel® PH101 as a spheronization	5-FU	[21]

5-FU: 5-fluorouracil; CoDDS: Colon-specific drug delivery system; FSMEDDS: Folate-modified SMEDDS; GIT: Gastrointestinal tract; MAMs: Mucoadhesive microspheres; MTX-FA-GGNP: Methotrexate-loaded folic acid modified guar gum nanoparticles; SMEDDS: Self-microemulsifying drug delivery system.

Table 1. Recently developed colon-specific drug delivery system for the treatment of colorectal cancer (continued).

Approach	Type of dosage form	Description	Drug candidate evaluated	Ref.
		aid and HPMC K4M as a binder. The *in vitro* drug release studies revealed that the system coated with 15% w/w of inner and outer coating level was found to be optimum for achieving colon targeting.		
Microbially and/ or enzymatically driven drug delivery systems	Microparticulate system	An Assam Bora rise starch has been evaluated for its efficiency as CoDDS. A MAMs were prepared by double emulsification solvent evaporation technique. *In vitro* dissolution studies revealed a minor drug release in upper part of GIT and a significant release in presence of rat caecal content. *In vivo* evaluation of the prepared formulation revealed that majority of drug got distributed to the lower part of the GIT depicting the potential of the developed system for colon targeting.	5-FU	[22]
	Nanoparticulate system	Paclitaxel-loaded chitin (amorphous) nanoparticulate system was prepared by ionic cross-linking reaction technique. *In vitro* drug release studies revealed sustained release behavior of the prepared nanoparticulate system. Cell uptake study of the developed system was confirmed by fluorescent microscopy and flow cytometry. Anticancer activity of the developed system was proven by determining toxicity toward colon cancer cell lines.	Paclitaxel	[23]
	Multiparticulate system	A multiparticulate system (pellets) consisting of pectin as both coat and core material was prepared and evaluated for colon targeting. Ethyl cellulose was employed as an *in situ* intracapsular coating material. *In vitro* evaluation revealed that less than 25% drug was released in upper part of GIT demonstrating the potential of the developed system for achieving colon targeting.	5-FU	[5]
	Nanoparticulate system	A MTX-FA-GGNP has been prepared by emulsification cross-linking technique. It has been reported that the percent growth inhibition of Caco-2 cells with MTX-FA-GGNP was higher than that of MTX-GGNP indicating folate receptor mediated uptake of the developed system.	Methotrexate	[24]
	Tableted – microsponges	A calcium pectinate matrix tablet for colonic delivery of meloxicam microsponges were prepared. Modified quassi-emulsion solvent diffusion technique was used to formulate the microsponges. The *in vivo* fluoroscopy in rabbits revealed that the calcium pectinate matrix released the drug-loaded microsponges selectively into the colonic region. The *in vivo* pharmacokinetic study revealed a lag time of 7 h for appearance of drug in plasma proving the potential of developed system for colon targeting.	Meloxicam	[25]
	Tablets	Compression-coated tablets containing 5-FU as drug candidate was evaluated as a potential alternative for achieving CoDDS.	5-FU	[26]

5-FU: 5-fluorouracil; CoDDS: Colon-specific drug delivery system; FSMEDDS: Folate-modified SMEDDS; GIT: Gastrointestinal tract; MAMs: Mucoadhesive microspheres; MTX-FA-GGNP: Methotrexate-loaded folic acid modified guar gum nanoparticles; SMEDDS: Self-microemulsifying drug delivery system.

Table 1. Recently developed colon-specific drug delivery system for the treatment of colorectal cancer (continued).

Approach	Type of dosage form	Description	Drug candidate evaluated	Ref.
		Granulated chitosan was employed as a compression coat. *In vitro* drug release studies revealed that the granulation of chitosan provides protective action against the acidic environment of the upper part of GIT. Roentgenography study in beagle dogs revealed that the developed system was resistant to the conditions prevailing in upper part of the GIT and selectively release the drug in the lower part of GIT.		
	Azo-conjugates	An azo-based polyphosphazene drug conjugates of methotrexate and gemcitabine has been prepared and evaluated for CoDDS. The conjugates were found to be stable in presence of acidic conditions and were reported to release more than 89% of drug in presence of rat cecal contents. The *in vitro* cytotoxicity study revealed that the prepared azo-conjugates are active against HT-29 and COLO 320 DM (human colorectal cancer cell lines), depicting the potential of the prepared system for colon targeting.	Methotrexate and gemcitabine	[27]
	Tablets	A novel microbially triggered CoDDS was developed using pectin and starch paste as biodegradable material. *In vitro* evaluation of the optimized formulation revealed negligible amount of drug release at pH 1.2 and 7.4, whereas significant amount of drug release was observed at pH 6.5 in presence of rat caecal content. *In vivo* pharmacokinetic and roentgenographic evaluation in rabbits revealed the potential of the developed formulation for colon targeting.	5-FU	[28]
pH and microflora-activated di-dependent systems	Microparticulate system	Eudragit® S 100 coated valdecoxib-loaded sodium alginate microspheres were prepared and evaluated for achieving CoDDS. The *in vitro* cell line studies revealed that the transport of valdecoxib microspheres across Caco-2 cell monolayers at pH 7.4 was found to be slower than that of solutions, thus providing a prolonged and sustained release profile.	Valdecoxib	[29]
	Microparticulate system	Eudragit® S 100 coated calcium pectinate microspheres were prepared by emulsification cross linking technique. *In vitro* evaluation of the developed system revealed that the drug release was significantly increased in presence of rat caecal content (1% w/v).	Curcumin	[30]
	Multiparticulate system	Eudragit® S 100 coated ginger extract-loaded alginate beads were prepared for treatment of CRC. *In vitro* evaluation of the developed systems revealed a super class II release mechanism, controlled by swelling and polymer relaxation. Preclinical evaluation in male Wistar rats revealed that the developed system could significantly reduce the growth of cancer after four weeks of treatment.	Ginger extract	[31]

5-FU: 5-fluorouracil; CoDDS: Colon-specific drug delivery system; FSMEDDS: Folate-modified SMEDDS; GIT: Gastrointestinal tract; MAMs: Mucoadhesive microspheres; MTX-FA-GGNP: Methotrexate-loaded folic acid modified guar gum nanoparticles; SMEDDS: Self-microemulsifying drug delivery system.

A handsome amount of money and time has been invested for the development of these systems. Despite such enormous research being conducted at academia as well as industrial level, the following are the major constraints associated with CoDDS developed for the treatment of CRC:

1) *Large intra- and interindividual variability in physiological conditions of GIT may lead to either premature release of drug in the small intestine or no drug release in colonic region, thus affecting targetability and availability of drug at tumor site.*
2) *Poor availability of drug at distal part of colon and rectal region.*
3) *High possibility of exposure of normal cells to antineoplastic agents.*
4) *Presence of efflux pumps on the tumor cells is not taken into consideration.*
5) *Reports of CoDDS pertaining to cell uptake and cell cytotoxicity studies are not available in majority of the published literature and hence it is not evident whether the targeting will result into drug uptake inside the tumor cells.*
6) *Further, studies pertaining to antitumor efficacy are not reported in most of the published literature and hence proof of concept of these studies are lacking.*

It is evident that unless and until the major constraints mentioned above are not overcome, selective and targeted delivery of drugs to the cancerous cells is difficult to achieve. Hence, it appears that the effective way of treating CRC is to employ the concept of receptor-mediated drug delivery approach (along with existing approaches, discussed in Section 3), which involves use of specific receptors present on the surface of cancerous cells [17]. Once reached to the target site (i.e., colonic tumor cells), the drug (loaded into carrier-like nanoparticles) will be taken up into the tumor cells 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 deadly disease of CRC!

Declaration of interest

The authors state no conflict of interest and have received no payment in preparation of this manuscript.

Bibliography

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Patel M, Shah T, Amin A. Therapeutic opportunities in colon specific drug delivery systems. Crit Rev Ther Drug Carrier Syst 2007;24:147-202

•• **A well-organized review article on colon-specific drug delivery systems.**

2. Patel M, Amin A. Recent trends in microbially and/or enzymatically driven colon-specific drug delivery systems. Crit Rev Ther Drug Carrier Syst 2011;28:489-552

3. Patel MM, Amin AF. Formulation and development of release modulated colon targeted system of meloxicam for potential application in the prophylaxis of colorectal cancer. Drug Deliv 2011;18:281-93

•• **Excellent paper on formulation of pH and time di-dependent systems.**

4. American Cancer Society. Available from: www.cancer.org/cancer/colonandrectumcancer/detailedguide/colorectal-cancer-key-statistics [Last accessed on 27 March 2014]

5. Elyagoby A, Layas N, Wong TW. Colon-specific delivery of 5-fluorouracil from zinc pectinate pellets through in situ intracapsular ethylcellulose-pectin plug formation. J Pharm Sci 2013;102:604-16

6. Mohandas KM. Colorectal cancer in India: controversies, enigmas and primary prevention. Indian J Gastroenterol 2011;30:3-6

7. Kelloff GJ, Schilsky RL, Alberts DS, et al. Colorectal adenomas: a prototype for the use of surrogate end points in the development of cancer prevention drugs. Clin Cancer Res 2004;10:3908-18

8. Levine JS, Ahnen DJ. Clinical practice. Adenomatous polyps of the colon. N Engl J Med 2006;355:2551-7

9. Bond JH. Polyp guideline: diagnosis, treatment, and surveillance for patients with colorectal polyps. Practice Parameters Committee of the American College of Gastroenterology. Am J Gastroenterol 2000;95:3053-63

10. Schatzkin A, Freedman LS, Dawsey SM, Lanza E. Interpreting precursor studies: what polyp trials tell us about large-bowel cancer. J Natl Cancer Inst 1994;86:1053-7

11. Stewart SL, Wike JM, Kato I, et al. A population-based study of colorectal cancer histology in the United States, 1998-2001. Cancer 2006;107(5 Suppl):1128-41

12. Colorectal cancer. Available from: www.cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-028323.pdf [Last accessed 27 March 2014]

13. Krishnaiah YS, Khan MA. Strategies of targeting oral drug delivery systems to the colon and their potential use for the treatment of colorectal cancer. Pharm Dev Technol 2012;17:521-40

•• **A comprehensive review article on colon-specific drug delivery system (CoDDS) for treatment of colorectal cancer.**

14. Patel MM. Drug delivery: oral colon-specific. In: Swarbrick J, editor. Encyclopedia of pharmaceutical science and technology. 4th edition. Taylor & Francis Group, LLC, UK; 2014. p. 1091-121

•• **A comprehensive book chapter on CoDDS.**

15. Patel MM, Amin AF. Process, optimization and characterization of mebeverine hydrochloride loaded guar gum microspheres for irritable bowel

syndrome. Carbohydr Polym 2011;86:536-45

16. Patel MM. Cutting-edge technologies in colon-targeted drug delivery systems. Expert Opin Drug Deliv 2011;8:1247-58

•• **Excellent review article on various technologies developed for colon-specific drug delivery systems.**

17. Jain A, Jain SK, Ganesh N, et al. Design and development of ligand-appended polysaccharidic nanoparticles for the delivery of oxaliplatin in colorectal cancer. Nanomedicine 2010;6:179-90

18. Zhang L, Zhu W, Yang C, et al. A novel folate-modified self-microemulsifying drug delivery system of curcumin for colon targeting. Int J Nanomedicine 2012;7:151-62

19. Ashwanikumar N, Kumar NA, Nair SA, Kumar GV. Methacrylic-based nanogels for the pH-sensitive delivery of 5-fluorouracil in the colon. Int J Nanomedicine 2012;7:5769-79

20. Ghorab DM, Amin MM, Khowessah OM, Tadros MI. Colon-targeted celecoxib-loaded Eudragit® S100-coated poly-ε-caprolactone microparticles: preparation, characterization and in vivo evaluation in rats. Drug Deliv 2011;18:523-35

21. Kulthe SS, Bahekar JK, Godhani CC, et al. Modulated release of 5-fluorouracil from pH-sensitive and colon targeted pellets: an industrially feasible approach. Drug Dev Ind Pharm 2013;39:138-45

22. Ahmad MZ, Akhter S, Anwar M, Ahmad FJ. Assam Bora rice starch based biocompatible mucoadhesive microsphere for targeted delivery of 5-fluorouracil in colorectal cancer. Mol Pharm 2012;9:2986-94

23. Smitha KT, Anitha A, Furuike T, et al. In vitro evaluation of paclitaxel loaded amorphous chitin nanoparticles for colon cancer drug delivery. Colloids Surf B Biointerfaces 2013;104:245-53

24. Sharma M, Malik R, Verma A, et al. Folic acid conjugated guar gum nanoparticles for targeting methotrexate to colon cancer. J Biomed Nanotechnol 2013;9:96-106

25. Srivastava R, Kumar D, Pathak K. Colonic luminal surface retention of meloxicam microsponges delivered by erosion based colon-targeted matrix tablet. Int J Pharm 2012;427:153-62

26. Yassin AE, Alsarra IA, Alanazi FK, et al. New targeted-colon delivery system: in vitro and in vivo evaluation using X-ray imaging. J Drug Target 2010;18:59-66

27. Sharma R, Rawal RK, Malhotra M, et al. Design, synthesis and ex-vivo release studies of colon-specific polyphosphazene-anticancer drug conjugates. Bioorg Med Chem 2014;22:1104-14

28. Dev RK, Bali V, Pathak K. Novel microbially triggered colon specific delivery system of 5-Fluorouracil: statistical optimization, in vitro, in vivo, cytotoxic and stability assessment. Int J Pharm 2011;411:142-51

29. Thakral NK, Ray AR, Bar-Shalom D, et al. The quest for targeted delivery in colon cancer: mucoadhesive valdecoxib microspheres. Int J Nanomedicine 2011;6:1057-68

30. Zhang L, Cao F, Ding B, et al. Eudragit® S100 coated calcium pectinate microspheres of curcumin for colon targeting. J Microencapsul 2011;28:659-67

31. Deol PK, Kaur IP. Improving the therapeutic efficiency of ginger extract for treatment of colon cancer using a suitably designed multiparticulate system. J Drug Target 2013;21:855-65

Affiliation

Mayur M Patel M Pharm PhD
Associate Professor,
Nirma University, Institute of Pharmacy,
Department of Pharmaceutics, SG Highway,
Chharodi, Ahmedabad, Gujarat, 382481, India
Tel: +91 79 30642718;
Fax: +91 2717 241916;
E-mail: drmayurmpatel@gmail.com