Strategic Approaches for Targeted Drug Delivery System in Colon Cancer

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ABSTRACT

Colon-focused drug delivery systems have drawn a lot of attention as prospective vehicles for the local treatment of colonic disorders with fewer systemic side effects as well as for the improved oral delivery of numerous treatments vulnerable to acidic and enzymatic degradation in the upper gastrointestinal tract. The importance of colonic drug delivery as a noninvasive delivery method for macromolecules is highlighted by the recent expansion of the global pharmaceutical industry for biologics and the rising desire for a more patient-friendly drug administration system. For macromolecules, colon-targeted drug delivery systems can offer therapeutic advantages such as higher patient compliance (because they are painless and self-administrable) and reduced costs. Therefore, a variety of techniques, including pH-dependent systems, enzyme-triggered systems, receptor-mediated systems, and magnetically-driven systems, have been investigated to produce more effective colonic drug delivery for local or systemic medication effects. This study covers current developments in several methods for developing colon-targeted drug delivery systems and their pharmaceutical applications, with a focus on formulation technology.

INTRODUCTION

The dangerous cancer form known as colorectal cancer (CRC) has considerable incidence and survival rates in developed nations. When it comes to cancer diagnoses in both men and women, colorectal cancer (CRC) comes in third in the US.[1] Due to their many affinities, rectal cancer and colon cancer are usually mixed. Rectal, colorectal, and other cancers related to colon cancer were gathered and examined in this study under the category of colon cancer. Polyps are the preliminary stages of colon cancer, which later develop into malignant cells. The most common and useful method for finding these polyps and screening for colon cancer is colonoscopy. This article aims to review and summarise the impact and effectiveness of the mentioned deep learning on colon cancer, which ranks third among the most common and fourth in cancer-related deaths worldwide.[2]
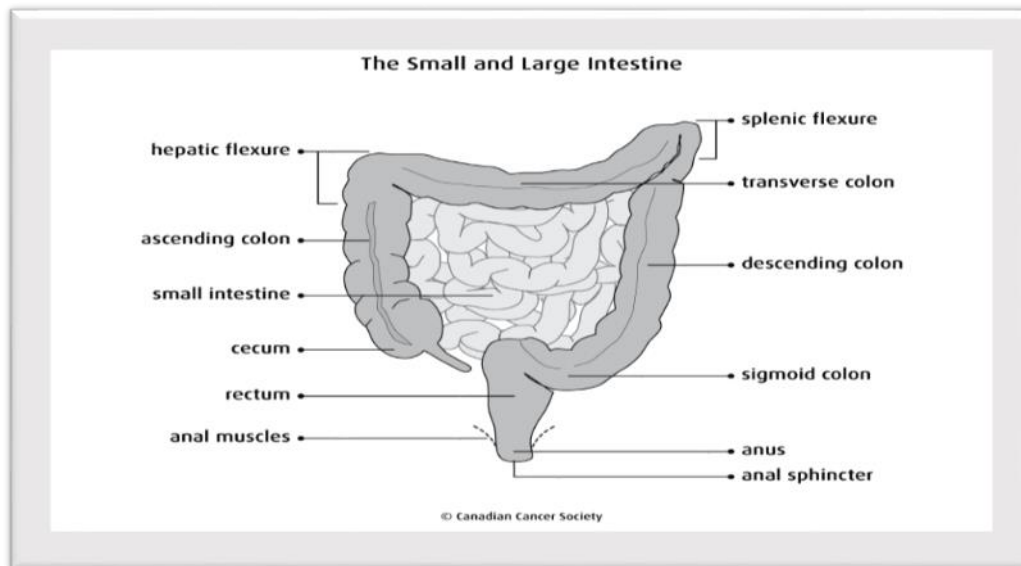

Fig 01: **Anatomy of the colon.**

Today, one of the main illnesses that impair human health and have a high mortality rate is cancer. Malignant tumors are caused by cancers.[3] Because benign tumours frequently do not recur, they are frequently removed and rarely pose a threat to health. Somebody cells begin to divide and spread into the surrounding structures in all forms of cancer.[4] Based on a National Cancer Institute (NIH) figure, the USA would encounter 1,806,950 million new cases of cancer in 2020, destroying 606,520 individuals. That's why scientists have presented many studies for the early detection of cancer. In addition, if physicians' misinterpretation of data is taken into consideration in the detection of diseases, the accuracy rate decreases sharply and the duration of early detection is prolonged.[5]

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2

The third most frequent malignancy in oncologic pathology is colorectal cancer. Currently accounting for 13% of all malignant tumours, it is the most prevalent cancer of the gastrointestinal tract.[6] It is also the second most common cause of cancer-related death worldwide, affecting both men and women equally in both industrialized and developing nations, and it is prophesied to surpass heart disease mortality rates in the years to come. It affects a lot of people aged 65 to 74, with women being more at risk than males. Due to risk factors such obesity, sedentarism, poor eating habits. smoking, and population aging, this condition is, nonetheless, detected more commonly in younger individuals. The clinical presentation includes symptoms such as abdominal pain, alteration of chronic bowel habits, changes in bowel movements, involuntary weight loss, nausea, vomiting, malaise, anorexia, and abdominal pain.[7]

Lung cancer accounts for 11.6% of all cancer diagnoses in both sexes, followed by breast cancer in women (11.6%) and prostate cancer in men (7.9%).[8] CRC ranks second in terms of mortality (9.2%) and third in terms of recognition (6.1%). Rectal and colon cancer-related fatalities are anticipated to rise by 60% and 71.5%, respectively, by the year 2035. The likelihood of developing the illness rises with increased consumption of red and processed meat as well as alcoholic beverages.[9] The development of civilization and economic prosperity not only result in better socioeconomic conditions but also "westernization" of lifestyles, or modifications in eating habits. This entails consuming more animal fats, processed meats, refined grains, and sweets, as well as less fruit, vegetables, and dietary fibre, and engaging in less physical activity. A lifestyle like this frequently leads to overweight or obese. Secondary prevention is also significant based on follow-up exams and nutrition prevention based on a balanced diet.[10] Considering all the aspects, we made efforts to systematize the available literature data in terms of epidemiology, risk factors, type and nature of symptoms, stages of development and available diagnosis of colorectal cancer.[11]

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3

Table 1: Colon targeting drugs, diseases and sites.

Target sites	Disease conditions	Drug and active agents
Topical action	Inflammatory Bowel Diseases, Irritable bowel disease and Crohn's disease. Chronic pancreatitis	Hydrocortisone, Budenoside, Prednisolone, Sulfasalazine, Olsalazine, Mesalazine, Balsalazide
Local action	Pancreatectomy and cystic fibrosis, Colorectal cancer	Digestive enzyme supplements 5-Fluorouracil
Systemic action	To prevent gastric irritation To prevent first-pass metabolism of orally ingested drugs. Oral delivery of peptides Oral delivery of vaccines	NSAIDS Steroids Insulin Typhoid

1. Criteria for Selection of Drug for CDDS

The best candidates for CDDS are drugs that show poor absorption from the stomach or intestine including peptides. The drugs used in the treatment of IBD, ulcerative colitis, diarrhea, and colon cancer are ideal candidates for local colon delivery. Drug Carrier is another factor that influences CDDS. The selection of carriers for particular drugs depends on the physiochemical nature of the drug as well as the disease for which the system is to be used. Factors such as chemical nature, stability and partition coefficient of the drug and type of absorption enhancer chosen influence the carrier selection[12] Moreover, the choice of drug carrier depends on the functional groups of the drug molecule. For example, aniline or nitro groups on a drug may be used to link it to another benzene group through an azo bond. The carriers, which contain additives like polymers (may be used as matrices and hydrogels or coating agents) may influence the release properties and efficacy of the systems.[13]

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4

Table 2: Criteria for selection of drugs for CDDS

Criteria	Pharmacological class	Nonpeptide drugs	Peptide drugs
Drugs used for local effects in colon against GIT diseases	Anti-inflammatory drugs	Oxprenolol, Metoprolol, Nifedipine	Amylin, Antisense oligonucleotide
Drugs poorly absorbed from upper GIT	Antihypertensive and antianginal drugs	Ibuprofen, Isosorbides, Theophylline	Cyclosporine, Desmopressin
Drugs for colon cancer	Antineoplastic drugs	Pseudoephedrine	Epoetin, Glucagon
Drugs that degrade in stomach and small intestine	Peptides and proteins	Brompheniramine, 5-Flourouracil, Doxorubicin	Gonadoreline, Insulin, Interferons
Drugs that undergo extensive first-pass metabolism	Nitroglycerin and corticosteroids	Bleomycin, Nicotine	Protirelin, sermorelin, Saloatonin

1.1 Approaches used for Site-Specific Drug Delivery to Colon (CDDS)

Several approaches are used for site-specific drug delivery. Among the primary approaches for CDDS, these include:[14]

1.2 Primary Approaches for CDDS

a. pH-Sensitive Polymer Coated Drug Delivery to the Colon:

During a fast, the stomach's pH is between 1 and 2, but after eating, it rises. The proximal small intestine has a pH of around 6.5 and the distal small intestine has a pH of around 7.5. There is a significant pH drop from the ileum to the colon. In the cecum, it is around 6.4. However, in the ascending colon of healthy volunteers, pH levels as low as 5.7 have been seen. The pH in the descending colon is 7.0, while it is 6.6 in the transverse colon. These variations in pH levels form the basis for the use of pH-dependent polymers.[15] When it comes to colon-specific drug delivery, the polymers that are defined as pH-dependent are insoluble at low pH levels but become progressively soluble as pH rises. Although a polymer that is

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5

pH-dependent can shield 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.[16]

b. Delayed (Time Controlled Release System) Release Drug Delivery to Colon:

Sustained or delayed-release dosage forms are examples of time-controlled release systems (TCRS), which hold great promise for drug delivery. However, in these approaches, the colon arrival time of dose forms cannot be properly predicted, leading to low colonical availability because of the possibly significant variability in gastric emptying time of dosage forms in humans.[17] By extending the lag period by approximately 5 to 6 hours, the dosage forms may also be used as colon-targeting dosage forms. However, this system has the following drawbacks:

i. The amount and type of food consumed influence the gastric emptying time, which differs significantly between participants.

ii. Gastrointestinal motility, particularly peristalsis or contraction in the stomach, might alter how the medicine was absorbed by the digestive tract.

iii. Patients with ulcerative colitis, IBD, and conditions causing diarrhoea and carcinoid syndrome have all been seen to move through the colon more quickly than normal.[18]

In order to deliver medications to the colon precisely for the treatment of disorders related to the colon, time-dependent systems are not optimal. The site specificity of medication administration to the colon may be improved by properly integrating pH-sensitive and time-release characteristics into a single dosage form. Due to the small intestine's less variable small intestine transit period, which is approximately 3–1 hour, in comparison to the stomach, the small intestine should act more effectively as a time-release mechanism (or timer). [19]The target side of the small intestine will receive the drug carrier, and the drug release will start at a predefined time following stomach emptying. On the other hand, in the stomach, the drug release should be suppressed by a pH sensing function (acid resistance) in the dosage form, which would reduce variation in gastric residence time. A drug-containing core tablet (rapid release function), a press-coated swellable hydrophobic polymer layer (hydroxy propyl cellulose layer (HPC), time-release function), and an enteric coating layer make up enteric coated time-release press coated (ETP) tablets (acid resistance function). [20,21.]

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6

1.3 Microbially Triggered Drug Delivery to Colon:

The colon's microflora is composed primarily of anaerobic bacteria, such as bacteroides, bifidobacterial, eubacteria, clostridia, enterococci, enterobacteria, and ruminococcus, and is in the range of 1011 -1012 CFU/mL. Various substrates, such as di- and tri-saccharides, polysaccharides, etc., that have been left undigested in the small intestine are fermented by this massive microflora to meet its energy requirements.[22] Numerous enzymes, including glucoronidase, xylosidase, arabinosidase, galactosidase, nitroreductase, azareducatase, deaminase, and urea dehydroxylase, are produced by the microflora for this fermentation. Because of the presence of the biodegradable enzymes only in the colon, the use of biodegradable polymers for colon-specific drug delivery seems to be a more site-specific approach as compared to other approaches.[23]These polymers shield the drug from the environments of the stomach and small intestine, and can deliver the drug to the colon. On reaching the colon, they undergo assimilation by micro-organisms, or degradation by enzyme or breakdown of the polymer backbone leading to a subsequent reduction in their molecular weight and thereby loss of mechanical strength. They are then unable to hold the drug entity any longer.[24]

1.4 Prodrug Approach for Drug Delivery to Colon:

The term "prodrug" refers to a pharmacologically inert derivative of a parent drug molecule that needs to undergo spontaneous or enzymatic transformation to release the active drug in vivo[25]. The prodrug is intended for enzymatic hydrolysis in the colon, which releases the active drug moiety from the drug carrier, and minimum hydrolysis in the upper tracts of the GIT for colonic delivery. One of the most thoroughly investigated bacterial metabolic processes is the digestion of azo compounds by gut bacteria. Other connections that are made with the medication are connected to hydrophobic moieties such amino acids, glucuronic acids, glucose, galactose, cellulose, etc[26]. are susceptible to bacterial hydrolysis, particularly in the colon. The prodrug strategy has drawbacks in that it is not highly adaptable because of its formulation depends upon the functional group available on the drug moiety for chemical linkage. Furthermore, prodrugs are new chemical entities and need a lot of evaluation before being used as carriers.[27]
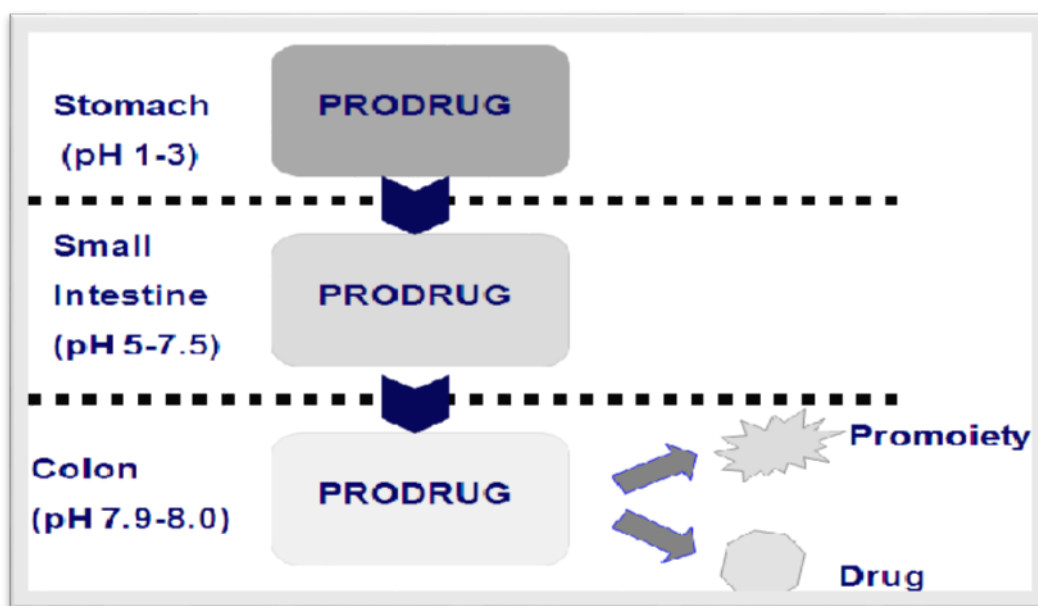
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7

Fig 02: Action of prodrugs

Table 3: Prodrugs evaluated for colon-specific drug delivery with there in vitro/in vivo performance.

Carrier	Drug investigated	Linkage hydrolyzed	In vitro/in vivo model used	Performance of the Prodrug/conjugates.[28]
Azo conjugates Suphapyridine (SP) 5-ASA	5-ASA 5 ASA	Azo linkage Azo linkage	Human Human	Site-specific with a lot of side effects59 associated with SP Delivers 2 molecules of 5-ASA as compared to sulphasalazine.[29]
Amino acid conjugates glycine Tyrosine/methionine	Salicylic acid Salicylic acid	Amide linkage Amide linkage	Rabbit	Absorbed from upper GIT, though metabolized by the microflora of lrge intestine.[30]

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8

				Salicylic acid-l-alanine was hydrolyzed to salicylic acid by intestinal microorganisms but salicylic acid-D-alanine showed negligible hydrolysis thereby showing enantiospecific hydrolysis.[31]
L – Alanin/D Alanine	Salicylic acid	Amide linkage	In vitro	
Glycine	5-ASA	Amide linkage	In vitro	Prodrug was stable in upper GIT and was hydrolyzed by caecal content to release 5-ASA.[32]
Saccharide carriers	Dexamethasone/ prednisolone	Glycosidic linkage	Rat	Dexamethasone prodrug was site specific and 60% of oral dose reached the cecum. Only 15% of prednisolone prodrugs reached the cecum.[33]

2. Formulation Approaches for Colon-Targeted Drug Delivery

2.1 pH-Dependent Drug Delivery System:

Given that the colon has a pH that is noticeably higher than that of the upper GI tract, colonic medication administration can be targeted using this fact.[34] In light of this, a colon-targeted drug delivery system is created using pH-dependent polymers, such as cellulose acetate phthalates (CAP), hydroxypropyl methyl-cellulose phthalates (HPMCP) 50 and 55, and

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9

copolymers of methacrylic acid and methyl methacrylate (e.g., Eudragit® S 100, Eudragit® L, Eudragit® FS, and Eudragit® P4135 F) [For colonic drug administration, Eudragit® polymers in particular are the most popular synthetic copolymers because they offer muco adhesiveness and pH-dependent drug release[35]. The ideal polymer should be able to withstand the low pH of the stomach and the proximal part of the small intestine but be dissolved by the pH of the terminal ileum and the colon. As a result, drug delivery systems coated with pH-dependent polymers having a dissolution threshold of pH 6.0–7.0 are expected to delay the drug dissolution and prevent premature drug release in the upper GI tract before reaching colonic sites [36]. However, this pH-dependent system has demonstrated significant variability in drug release and failure in vivo due to the vast inter- and intra-subject variability in critical parameters including pH, fluids volumes, GI transit times, and motility[37]. Furthermore, nutrition, illness condition, water intake, and microbial metabolism can all have a major impact on the pH ranges of the GI tract. For instance, compared to healthy people, patients with ulcerative colitis have more acidic intestinal pH, which causes inadequate drug release from enteric-coated systems to the target location[38,39]. Therefore, the dynamic pH shift caused by numerous internal and external events may reduce the effectiveness of pH-dependent drug release systems, frequently resulting in drug release that is not site-selective[40]. Eudragit® S coating was not acceptable for the colon-targeted drug release, according to Ibekwe et al., either because the target site did not disintegrate or because the drug was released prematurely before the target site[41]. Ibekwe et al.'s later experiments on humans supported the lack of site-selective drug release of Eudragit® S coated tablets, suggesting that disintegration of these tablets is affected by multiple physiological factors including gastrointestinal pH, feed status, and intestinal transit time.[42,43]
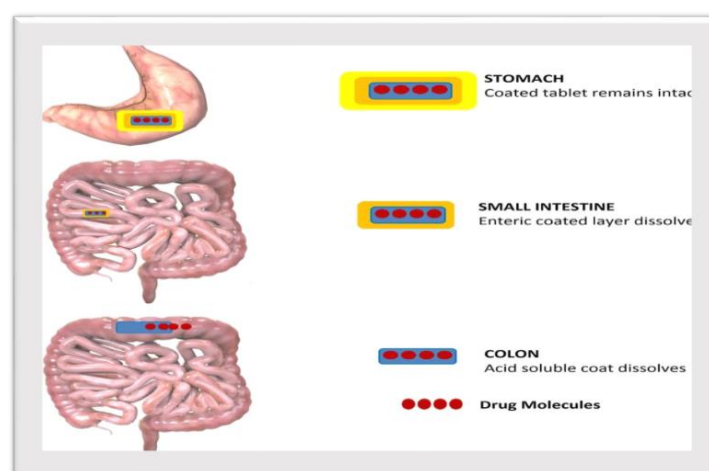

Fig 03: PH dependent drug delivery system

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10

2.2 Polymer-Based Nano-/Micro-Particles

pH-dependent polymeric nanoparticles have been successfully used in numerous investigations to transport drugs to the colon[44]. To transport curcumin nanoparticles specifically to the colon, Mutalik et al. employed a brand-new, pH-sensitive hydrolyzed polyacrylamide-grafted-xanthan gum (PAAm-g-XG). In acidic environments (pH 1.2 and 4.5), the amount of drug released from the PAAm-g-XG-modified nanoparticles was negligible, but at pH 7.2, increased and faster drug release was seen[45]. The nanoparticles were therefore successful in reducing intestinal inflammation and weight loss in IBD rat models. Additionally, the medication release rate can be regulated using a mixed combination of two distinct pH-sensitive polymers[46]. In order to create the HBsAg-loaded nanoparticles for efficient colonic immunization, Sahu and Pandey combined Eudragit® L100 and Eudragit® S100 distribution of nanoparticles at the colon along with the improved immune response[47]. Budesonide-loaded pH-/time-dependent nanoparticles were created by Naeem et al. for the efficient treatment of colitis in order to increase the site-specificity to the colon[48]. Using an oil-in-water emulsion solvent evaporation technique, these nanoparticles were created using Eudragit® FS30D and Eudragit® RS100.[49,50]

Table 4: Advantages and Disadvantages of Natural and synthetic polymers.

Natural Polymers	Synthetic Polymers
Advantages	
• Less toxic • Biocompatibility • Biodegradable • Easily available	• Biocompatibility • Good flexibility, and strength.
Disadvantages	
• High degree of variability in natural materials derived from animal sources • Structurally more complex • Extraction process very complicated and high cost	• Toxic • Non-degradable • Synthetic

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11

2.3 Lipid-Based Formulations

Double-layered phospholipids make up the drug delivery system known as a liposome. Drugs that are hydrophilic or lipophilic can be added to liposomes since they are biodegradable, biocompatible, and conducive to doing so.[51] To prevent liposome disintegration in acidic environments and to increase site-specificity, ligands and pH-dependent polymers can be coated on the surface of liposomes[52]. By coating the surface of anionic liposomes with glycol chitosan and pH-dependent Eudragit® S100, Zhao et al.for instance, created colon-targeted liposomal formulations for sorafenib[53]. The systemic exposure of sorafenib in rats was increased by these liposomes' great stability at acidic and neutral pHs and negligible drug leakage[54].In terms of entrapment effectiveness, drug protection, and boosting the amount of drug released at certain areas, solid lipid nanoparticles are also a superior technology[55]. Solid lipid nanoparticles' delayed lipid matrix degradation permits prolonged drug release. The development of colon-targeted drug delivery systems may benefit from the use of self-micro emulsifying drug delivery systems (SMEDDS), which have enormous potential for improving the oral bioavailability of a variety of hydrophobic medicines[56,57]. Folate-modified SMEDDS Pharmaceutics 2020, 12, 68 4 of 19 (FSMEDDS) containing curcumin were created by Zhang et al. and then put into soft capsules coated with Eudragit® S 100. This version of the FSMEDDS, which contains curcumin, effectively bound to the folate receptors on colon cancer cells.[58]

2.4 Tablets and Capsules

Despite the limited number of commercially available products, film-coated tablets or capsules can be used to deliver drugs specifically to the colon. The Eudragit L100-coated tablets for the colonic distribution of a new anti-tumor necrosis factor domain antibody were recently created by Crowe et al (V565). This tablet showed a sustained drug release at a pH greater than 6, but not during a 2-hour incubation in an acidic environment. The persistent release of V565 in the colon for the topical treatment of IBD was further validated by in vivo experiments in monkeys. Additionally, the drug release characteristics can be changed by combining copolymers in different ratios. This combination system may be superior to tablets coated with a single polymer for colon-targeted drug delivery. However, the tablets coated only with pH-sensitive enteric polymers still face the issues of premature drug release due to the variability of pH in GI tract In addition, variability in the GI fluid composition, feeding status, and GI transit time affect the site-specific drug release from the pH-dependent system.

Citation: Suchitra Patil et al. Ijppr.Human, 2023; Vol. 27 (1): 1-21.

12

Therefore, there have been continuous efforts to improve the targeting effectiveness via the multi-unit formulations based on the integration of the different mechanism-based systems with pH-dependent coating. A bisacodyl-loaded multi-unit tablet, for instance, was created by Park et al. by covering the tablet with various combinations of pH-dependent polymers (Eudragit S and Eudragit L) and time-dependent polymers (Eudragit RS)[59]. In simulated gastric and intestinal fluids, drug release from the optimized tablet was barely detectable, whereas significant drug release was seen in the colonic fluid . In a recent study, Foppoli et al. also described an efficient method for delivering 5-aminosalicylic acid to the colon through the combination of time-dependent and pH-dependent techniques[60]. This method involved coating a tablet core repeatedly with low-viscosity HPMC and Eudragit® L. Additionally, based on a human-scintigraphy research, they were able to show that, in both fed and fasting phases, there was no premature drug release before the colon.

The targeting effectiveness of pH-dependent delivery systems has recently been actively improved by novel coating technology. Colo Pulse technology, for instance, is a cutting-edge pH responsive coating technique that combines super-disintegrant in the coating matrix to hasten the disintegration at the target site[61].A more consistent and pulsatile drug release results from the integration of a super-disintegrant in a non-percolating manner. Previous research showed that ColoPulse pills allowed for the site-specific administration of the active ingredient to both Crohn's patients and healthy volunteers in the ileo-colonic region. Additionally, food and the timing of eating had no impact on the efficiency of ColoPulse delivery systems' targeting[62]. The ileo-colonic-targeted zero-order sustained release budesonide tablets for the topical treatment of IBD were recently created using this technique by Gareb et al. According to the findings, medication release from the designed tablet started in the simulated ileum and continued at a steady pace throughout the duration of the simulated colon[63]. Infliximab oral tablets coated with Colo Pulse technology were also developed and validated for the local treatment of ileocolonic IBD. Another method for site-specific drug distribution is the fabrication of capsule shell with built-in gastroresistance.[64]

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13

Fig 04: Action of tablets and capsules

3. Benefits of colon target DDS

• Lessening side effects associated with the treatment of colon disorders (such as ulcerative colitis, colorectal cancer, and Crohn's disease).

• By creating a "friendlier" environment than the upper gastrointestinal system for peptides and proteins.

• Limiting the first pass of steroids' substantial metabolism.

• Avoiding stomach irritability brought on by NSAIDS taken orally.

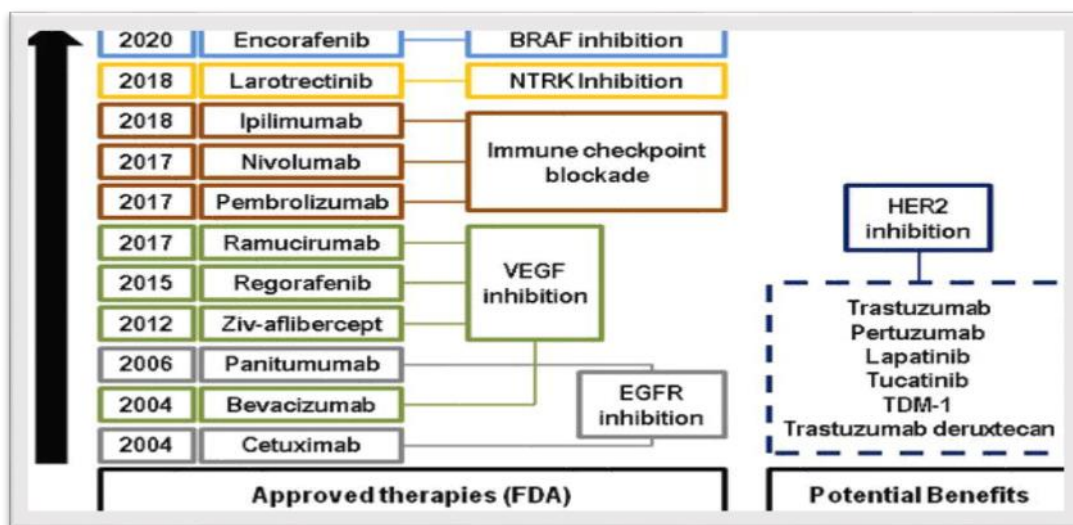• The postponed release of medications for rheumatoid arthritis, angina, and asthma.[65]

Fig 05: Approved therapies for colon cancer

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14

4. Limitation of colon target DDS

•Difficult to access the colon.

• For effective delivery, the medicine must be in solution before it reaches the colon, but the colon's fluid content is lower and more viscous than that of the upper gastrointestinal tract, which is the limiting factor for poorly soluble medications.

• Drug transport across the mucosa into the systemic circulation may be hampered by the lower surface area and relative tightness of the tight junctions in the colon.[66]

5. Need for colon-targeted drug delivery

• Drugs are sent specifically to the colon to ensure local delivery, direct treatment at the illness site, reduced dosage, and fewer systemic side effects.

Oral administration of peptide and protein medications would be possible using site-specific or targeted drug delivery systems, and colon-specific formulations might also be employed to extend drug delivery.

• It is thought that colon-specific medication delivery systems are helpful in the treatment of colon disorders.

• The colon is a location where topical therapy of inflammatory bowel illness, such as ulcerative colitis or Crohn's disease, could be accomplished through local or systemic drug delivery. Sulphasalazine and glucocorticoids are typically used to treat such inflammatory disorders.[67]

• Several others serious diseases of the colon, e.g., colorectal cancer, might also be capable of being treated more effectively if drugs were targeted to the colon.

• Formulations for colonic delivery are also suitable for the delivery of drugs that are polar and/or susceptible to chemical and enzymatic degradation in the upper GI tract, highly affected by hepatic metabolism, in particular, therapeutic proteins and peptides.[68]

6. Drug candidates for colon targeting

• It must be difficult to biotransform in the large intestine and compatible with carrier molecules, with limited absorption from the stomach and small intestine.

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15

• At an alkaline pH of the GIT, it should be stable.

• It needs to have both local and widespread effects.

• The use of drugs to treat a variety of intestinal conditions, including ulcerative colitis, amoebiasis, colon cancer, inflammatory bowel disease, and diarrhoea.[69,70]

7. Evaluation of colon-targeted drug delivery system

A. In-vitro assessment

As an ideal in vitro model should possess in-vivo conditions of the gastrointestinal tract, such as pH, volume, stirring, bacteria, enzymes, enzyme activity, and food components, there is no standardized evaluation technique available for CDDS. Diet & physical stress both have an impact on these diseases. The in-vitro dissolution study and in-vitro enzymatic test are used to evaluate colon-targeted medication delivery systems.

B. In-vitro dissolution test

The traditional basket method is used to conduct the dissolving testing. Dissolution testing is carried out in various buffers to describe how formulations behave at various pH levels. To assess the solubility of colon-targeted drug delivery, three distinct media—pH 1.2 to simulate gastric fluid, pH 6.8 to model the small intestine, and pH 7.4 to model the large intestine—are used. The colon-targeted drug delivery systems are put to the test for two hours in 0.1N HCl, three hours in pH 6.8 phosphate buffer, and finally for an hour in pH 7.4 phosphate buffer. Buffers with the aforementioned pH are ready to test colon-targeted medication delivery methods.[71]

C. In-vitro enzymatic test

The in-vitro enzymatic test consists of two assays.

a) The carrier drug system is cultured in a fermenter with a bacteria-friendly media. It is calculated how much drug will be released at each interval of time.

b) Drug release research is carried out in a buffer medium that contains the enzymes pectinase, dextranase, or caecal contents from rats, guinea pigs, or rabbits. The rate at which the polymer carrier is degrading directly relates to the amount of medicine delivered at any one time. Galactomannase enzyme presence, caecal rate content, and in vitro enzymatic

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16

dissolution study of tablets manufactured of natural guar gum and xanthan gum were all investigated.

D. In- vivo evaluation

Dogs, guinea pigs, rats, and pigs are used for the in-vivo evaluation of the CDDS because their anatomical and physiological circumstances and microbiota are similar to those of the human GIT. The distribution of different enzymes in the GI tracts of rats and rabbits is similar to that in humans.[72]

CONCLUSION:

Conclusion and a Look into the Future Although surgical and adjuvant therapy breakthroughs have been made quickly, there has been no improvement in colorectal cancer-related mortality, which clearly shows that there is still an opportunity for therapeutic progress. The focus of the current review on colorectal cancer is mostly on modern drug delivery techniques that are effective in the successful therapy of colon cancer. The overall collection and compilation of this systematic review concluded that the employment of various cutting-edge nanotechnology-based drug delivery systems, both alone and in combination with conventional chemotherapy regimens, is the only effective treatment method. Combining tumor targeting and cutting-edge localized drug delivery techniques may be the best strategy for the effective management of colon cancer. Therefore, novel carrier-mediated formulations comprising anti-cancer drugs can address the issue of localization and site-specific delivery. Such delivery systems can obstruct the progression of cancer cells and can effactually lead to their apoptosis. Concisely, the novel-cum-advanced drug delivery systems lead to a proficient and successful treatment of colon cancer and offer great promises.

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17

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19

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21