COLON TARGETED DRUG DELIVERY SYSTEM: A SYSTEMIC REVIEW

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Abstract:

Day by day there are new developments in field of colon specific drug delivery system .colon is a site where both local and systemic delivery of drugs can take place. The colon is also receiving significant attention as a portal for the entry of drugs into the systemic circulation. Due to the lack of digestive enzymes, colon is considered as suitable site for the absorption of various drugs. Colon in recent days offers great advantages for drug its physiological condition enriched for prolonging drug release time for successful colon targeted drug delivery, the drug needs to be protected from absorption and/or the environment of the upper gastrointestinal tract and then be abruptly released into the colon. Local delivery allows topical treatment associated with the colon like Crohn's disease, ulcerative colitis etc. but also for the systemic delivery of proteins, therapeutic peptides, anti-asthmatic drugs, antihypertensive drugs and anti-diabetic agents. However, treatment can be made effective if the drugs can be targeted directly into the colon thereby reducing the systemic side effects. A variety of delivery strategies and systems have been proposed for colonic targeting. Hence continuous efforts have been made on designing colon targeted drug delivery systems with improved site specificity and versatile drug release kinetics to fulfill different therapeutic needs. This article gives an overview on anatomy of the colon and approaches utilized for colon specific drug delivery.

Keywords: Colon, Colon specific drug delivery, Inflammatory Bowel Disease,

DOI Number: 10.14704/nq.2022.20.12.NQ77009 **NeuroQuantology 2022; 20(12): 84-90**

INTRODUCTION

The oral route is considered to be most convenient for the administration of drugs to patients. Where drug normally dissolves in the gastro-intestinal (GI) fluids and is absorbed from these regions of the gastro-intestinal tract (GIT), and both process depends upon the physicochemical properties of the drug.[1]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. [2, 3, 4] The site-specific delivery of drugs to lower parts of the GI tract is advantageous for localized treatment of several colonic diseases, mainly inflammatory bowel disease. Other potential applications of colonic delivery include chronotherapy, prophylaxis of colon cancer and treatment of nicotine addiction. [5,6] Formulations that deliver drugs into the colonic region rather than the upper GI tract offer a number of advantages. In certain conditions, oral delivery of drugs to the colon is valuable in the treatment of

eISSN 1303-5150

certain diseases, such as ulcerative colitis, Crohn's disease, carcinomas, infections and colon cancer. [7] It has also gained increased importance not just for the delivery of drugs for the treatment of local diseases but also potential site for the systemic delivery of therapeutic proteins and peptides which are being delivered by injections. These delivery systems when taken orally, allow drugs to release the drug from the delivery system once the delivery system arrives into the colon. These delayed mechanisms are designed to improve the efficacy of the drug by concentrating the drug molecules where they are need most, and also minimize the potential side effects and drug instability issues associated with premature release of drug in the upper parts of the GIT, namely stomach and small intestine. [8]

Necessitate Of Colon Targeted Drug Delivery

- Targeted drug delivery to the colon to ensure that direct treatment at the disease site (local delivery), at lower dosing and fewer systemic side effects. [9]
- Site-specific or targeted drug delivery system would allow oral administration of peptide and protein drugs, colon-specific formulation could also be used to prolong the drug delivery. [10]
- Colon-specific drug delivery system is considered to be beneficial in the treatment of colon diseases. [10]
- The colon is a site where both local or systemic drug delivery could be achieved, topical treatment of inflammatory bowel disease, e.g. ulcerative colitis or Crohn's disease. Such inflammatory conditions are usually treated with glucocorticoids and sulphasalazine. [11]
- A number of 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. [12]
- Formulations for colonic delivery are also suitable for delivery of drugs which are polar and/or susceptible to chemical and enzymatic degradation in the upper GI tract, highly affected by hepatic metabolism, inparticular, therapeutic proteins and peptides. [12]

Anatomy of Colon

The GI tract is divided into stomach, small intestine and large intestine. The large intestine is wider and shorter than the small intestine. The large intestine extending from the ileo-cecal junction to the anus is divided in to three main parts as shown in Figure 1.0. These are the Colon, the rectum and anal canal. The entire Colon is about 5 feet long, and is divided into five major segments. The cecum forms the first part of the Colon and leads to the right Colon or the ascending Colon (just under the liver) followed by the transverse Colon, the descending Colon, sigmoidal Colon, rectum, and the anal canal. Peritoneal folds called as mesentery which is supported by ascending and descending Colon. The right Colon consists of the cecum, ascending Colon, hepatic flexure and the right half of the transverse Colon. The left Colon contain the left half of the transverse Colon, descending Colon, splenic flexure and sigmoid. The rectum is the last anatomic segment before the anus. Unlike the small intestine, the Colon does not have any villi. However, because of the presence of plicae semilunares, which are crescentic folds, the intestinal surface of the Colon is increased to approximately 1300 cm. The Colon is a cylindrical tube lined by a moist, soft pink lining called mucosa; the pathway is called the lumen

eISSN 1303-5150

and is approximately 2 to 3 inches in diameter. CTDDS is very important system for reach the drug to the specific site. In this system drug targeted to the local site and used for the local colonic disease and number of GIT disease. [13] Number of polymers are used to prevent degradation of drug in stomach because some drugs are degraded in acidic pH so drug coated by polymers then the drug degrade only colon not in acidic pH. [14] Drug are administered through rectum because this is shortest route for CTDDS by proximal part. But rectal route is a very difficult and painful then patient compliance decrease. [15]50% drugs are administered through oral route because this route has more advantages and high patient compliance [13] But when drug is administered through oral route then drug pass through the GIT due to presence of enzymes and acidic pH are reduce the absorption or the drugs then absorption of drug decreases so bioavailability of drug also decreased. To overcome this problem by new system are developed this system is called colon targeting drug delivery system. They are new targeting system. Colon targeting drug delivery system comes in the category of control release and sustain release of drug example of drugs for the treatment of the colon disease are sulfasalazine, dexamethasone, hydrocortisone, metronidazole, prednisolone etc. [16]

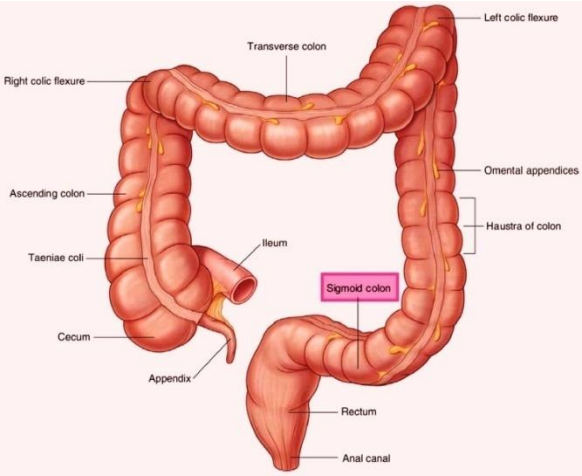

Figure 1: Anatomy of Colon

Criteria for Selection of Drug

The criteria for colon drug delivery system are drugs which show poor absorption from the stomach or intestine including peptides. The drugs used in the treatm ent of IBD, ulcerativecolitis, diarrhea, and colon cancer, for local colon delivery. [17] The selection of particular drugs depends on the physiochemical nature of drug as well as disease such as chemical nature, stability and partition coefficient of drug and type of absorption enhancer. [18] It also depends on the functional groups of 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 hydro gels or coating agents) may influence the release properties and efficacy of the systems. [19]

eISSN 1303-5150

Advantages of Colonic Drug Delivery System

• Chronic colitis, namely ulcerative colitis, and Crohn'sdisease are currently treated with glucocorticoids, and other anti-inflammatory agents.

• Administration of glucocorticoids namely dexamethasone and methyl prednisolone by oral and intravenous routes produce systemic side effects including adenosuppression, immunosuppression, cushinoid symptoms, and bone resorption. Thus selective delivery of drugs to the colon could not only lower the required dose but also reduce the systemic side effects caused by high doses.

• Drugs are directly available at the targeted site.

• Decreased side effect.

• Improved drug utilization.

• Comparatively lesser amount of required dose. [20, 21]

Disadvantages of Colonic Drug Delivery System

• One challenge in the development of colon-specific drug delivery systems is to establish an appropriate dissolution testing method to evaluate the designed system *in-vitro*.

• As a site for drug delivery, the colon offers a near neutral pH, reduced digestive enzymatic activity, a long transit time and increased responsiveness to absorption enhancers; however the targeting of drugs to the colon is very complicated.

• In addition, the stability of the drug is also a concern and must be taken into consideration while designing the delivery system. The drug may potentially bind in a nonspecific way to dietary residues, intestinal secretions, mucus or faecal matter. The resident microflora could also affect colonic performance via metabolic degradation of the drug, Lower surface area and relative 'tightness' of the tight junctions in the colon can also restrict drug transport across the mucosa and into the systemic circulation.

eISSN 1303-5150

Table 1: Marketed Formulation of Colon Drug Delivery

Trade Name	Drug	Dose	Dosage Form
Azulfidine	Sulfaasalazine	Either 1-2 or 2-4g/day	500mg tablets
Salazopyrin	Sulfaasalazine	Either 1-2 or 2-4g/day	500mg tablets
dipentum	olsalazine	1g/da1g/day	250 mg capsule and 500mg tablets
pentaza	mesalazine	1.5-4 mg/day	250 mg tablets
Asacol	mesalazine	1.5-4 mg/day	250 mg tablets
salotalic	mesalazine	1.5-4 mg/day	250 mg tablets
claversal	mesalazine	1.5-4 mg/day	250 mg tablets and 400 mg tablets
mesazal	mesalazine	1.5-4 mg/day	250 mg tablets and 400 mg tablets
Entocost	Budenoside	9mg/day	250 and 400 mg capsules

FUTURE PROSPECTS:

Recent reports indicate interest in colon as a site where poorly absorbed drug molecules may have improved bioavailability. The distal colon is considered to have less hostile environment as well as enzyme activity compared to stomach and small intestine. The development of a dosage form that improves the oral absorption of peptide and protein drugs whose bioavailability is very low because of instability in the GI tract (due to pH or enzymatic degradation) is one of the greatest challenges for oral peptide delivery in the pharmaceutical field. Colon targeted multiparticulate systems like microspheres and nanoparticles can provide a platform for spatial delivery of candidates like peptides, proteins, oligonucleotides and vaccines. However, drug release is not the end point of oral delivery. The bioavailability of protein drugs delivered at the colon site needs to addressed. The use of drug absorption enhancers into the drug delivery systems is likely to enhance therapeutic efficacy. Studies on drug absorption by the intestinal system have focused on drug transporters that mediate drug influx and efflux and agents which can enhance drug absorption. The colon segment is

eISSN 1303-5150

designed by nature mainly to expel metabolism products rather than to absorb nutrients. Therefore, more research that is focused on the specificity of drug uptake at the colon site is necessary. Such studies will be significant in advancing the cause of colon targeted delivery of therapeutics in future.

Reference:

1. Qureshi MA, Momin M, Rathod S, Dev A, Kute C. 2013. Colon targeted drug delivery system: A review on current approaches. Indian J. Pharm. Biol. Res 1(4):130-147.
2. Kumar Sp, D.Prathibha, R.Parthibarajan, C.Rubina Reichal. 2012. Novel Colon Specific Drug Delivery System: A Review. International Journal of Pharmacy And Pharmaceutical Sciences. 4(1):22-29.
3. Philip AK, Dabas S, Pathak K. 2009. Optimized prodrug approach: A means for achieving enhanced anti-inflammatory potential in experimentally induced colitis. J Drug Target. 17:235-241.
4. Oluwatoyin AO, John TF. 2005. In vitro evaluation of khaya and albizia gums as compression coating for drug targeting to the colon. J Pharm Pharmacol. 57: 63-168.
5. Abdul B, John B. 2003. Perspectives on Colonic Drug Delivery, Business Briefing, Pharmatech. 185–190.
6. Bajpai S K, Bajpai M, Dengree R. 2003. Chemically treated gelatin capsules for colontargeted drug delivery: a novel approach, J. Appl. Polym. Science. 89:2277–2282.
7. Rhodes J., Evans B.K. 2004. US20046734188.
8. Edith mathiowitz (ed.). 2003. Encyclopedia of controlled drug delivery. John wiley and sons, Inc. Newyork.:698-726.
9. Malik K, Goswami L, Kothiyal P, Mukhopadhyay S. 2012. A Review on Colon targeting Drug Delivery System: Novel Approaches, Anatomy and Evaluation. The Pharma Innovation. 1(9):1-12.
10. Encyclopedia of controlled drug delivery. John wileyand sons, Inc. Newyork. 2003: 698-726.
11. Sarasija S, Hota A. 2000. Indian J Pharmaceutical Sci.: 62: 1-8.
12. Reena Sharma, Nimrata Seth. 2013. Colon Targeted Drug Delivery System: A review. 4(4): 66-77.
13. Akhil, Mittal Anuj, Gupta Alok Kumar. 2011. Colon targeted drug delivery system A review. RussianJournal of Biopharmaceutics. 3(4): 3-13.
14. Rajpurohit H, Sharma P, Sharma, Bhandari A (2010). Polymers for colon targeted drug delivery system. Indian Journal of Pharmaceutical Sciences. 72(6): 689-969
15. Campieri Mas``simo, Corbelli Claudio, Gionchetti Paolo, Brignola Corrado (1992). Spread and distribution of 5-ASA colonic foam and 5-ASA enema in patient with ulcerative colitis. Digestive diseases and sciences. 37(12): 1890-97.
16. Leuva VR, Patel BG, Chaudhary DJ, Patel JN, Modasiya MMK. 2012. Oral colon-specific drug delivery system. JPharm Res. 5(4):2293 – 7.
17. Hiremath S.N., Godge G.R. (2011). Recent advances in pharmaceutical approaches to colon specific drug delivery. Inventi impact. 4: 277-285

eISSN 1303-5150

18. Philip Anil K., Philip Betty. (2010). Colon Targeted Drug Delivery Systems: A Review on Primary and Novel Approaches. Oman Medical Journal. 25(2): 70-7812.
19. Newton John Maria A. Kabilan P. (2011). Drug deliveries to colonic region, The Indian Pharma: 19-23.
20. Tortra, G J, Derrickson B: Principles of anatomy and physiology. John Wiley and sons, New York, 2007.
21. Chaurasia M K, Jain SK. 2003. Pharmaceutical Approaches to Colon Targeted Drug Delivery Systems. J Pharm Sci : 33-66.
22. Reddy M S, Sinha RV, Reddy DS. 1999. Colon targeted systems. DrugsToday .35: 7: 537.