



A Review on Colon Targeted Drug Delivery System

Anwarulhaqq. N. Shaikh ^{*1}, Quereshi S. I. ², Nandkishor B. Bavage ³, Shyamli B. Bavage ⁴,

¹B.Pharmacy Final Year Student, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512, Maharashtra, India

²Department of Pharmaceutical Chemistry, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512 Maharashtra, India

³Department of Pharmaceutical Analysis, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512 Maharashtra, India

⁴Department of Pharmacology & Toxicology, Latur College of Pharmacy Hasegaon, Tq. Ausa, Dist. Latur-413512 Maharashtra, India

ABSTRACT

Despite such countless enhancements inside the cure, colon malignancy regardless stands 1/3 in many tumors related passings global. Poisonousness related with customary medications is one of the principle issues identified with chemotherapy. Centered transportation works by means of amassing the medication in the tissues of diversion and diminishing the mindfulness in leftover tissues. This conveyance machine empowers the medication atom to achieve preferably to the favored site. The focused on will diminish the prerequisite of a higher portion of the medication thus diminishing the measurement recurrence. the current assess has practical experience in the various boundaries of centered medication transport which incorporates the norms for decision of medication and variables influencing the designated drug conveyance and furthermore incorporates the short exchange about unmistakable focused medication conveyances for colon disease treatments.

KEYWORDS : Colon cancer, Targeted drug delivery, Chemotherapies

INTRODUCTION:

Colon delivery refers to centered delivery of drugs into the decrease GI tract, which happens primarily within the massive gut (i.e. Colon). (1) The website precise shipping of drugs to lower elements of GIT is high-quality for localized remedy of several Colonic diseases, particularly inflammatory bowel disease (Croh's sickness and ulcerative colitis), and Irritable bowel syndrome and colon cancer. The colon is believed to be a suitable absorption site for peptides and protein drugs for the subsequent reasons; (i) less variety, and depth of digestive enzymes, (ii) Comparative proteolysis interest of colon mucosa is tons much less than that observed within the small intestine, therefore CTDDS protects peptide tablets from hydrolysis, and enzymatic degradation in duodenum and jejunum, and eventually releases the drug into ileum or colon which leads to more systemic bioavailability. Oral controlled release formulations for the small gut and colon have obtained extensive attention within the past 25 years for a variety of reasons along with pharmaceutical superiority and clinical blessings derived from the drug release sample that aren't completed with traditional on the spot or sustained launch products. (2). Colon drug delivery has additionally won multiplied significance not just for the systemic shipping of drugs for the treatment of nearby diseases, however additionally capability website online for the systemic transport of therapeutic proteins and peptides that are being brought by injections. These transport structures whilst taken orally, allow capsules to launch the drug from the delivery gadget as soon as the drug reaches in to the colon. ^[3,4]

Need of Colon Targeted Drug Delivery

Focused drug transport into the colon useful in remedy of diseases at that website, fewer systemic side results and dose may be minimized. Colon specific components are beneficial for the administration of proteins, peptide drugs and also to prolong the drug transport. Colon focused drug shipping is suitable for delivery of drugs that are polar and/or susceptible to the Chemical and enzymatic degradation in the top GI tract, pretty affected by hepatic metabolism Serious illnesses of the colon are treated greater efficaciously if pills were targeted to the colon.

Instance Colonic cancers like colorectal most cancers. ^[5,6]

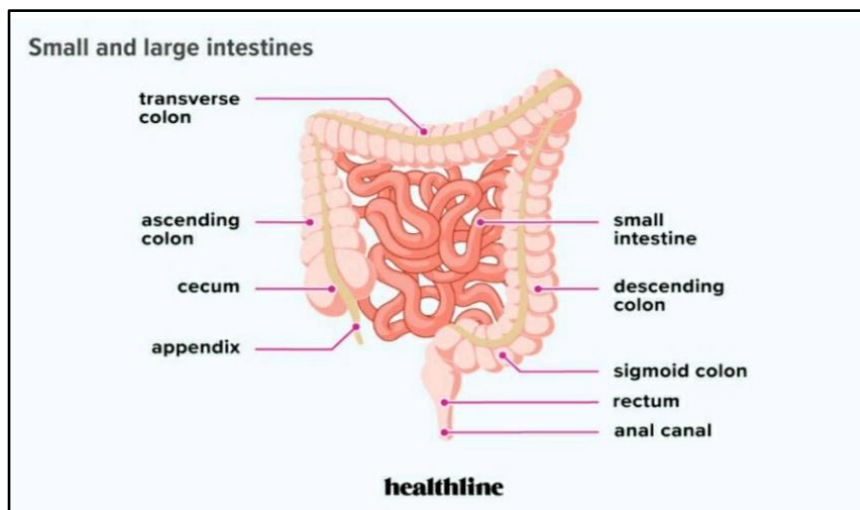


Fig 1: Colon and its Segment

The complete colon is nearly five feet (150 cm) long and is divided into 5 major segments. The GI - tract is divided into the belly, small gut, and large gut. Large gut extending from the ileocecal junction to the anus and it is divided into 3 main parts. (Figure - 1) They are the colon, rectum, and anal canal. Peritoneal folds are known as mesentery that is supported via ascending and descending colon. The right colon consists of the cecum, ascending colon, and hepatic flexure. The left colon includes descending colon, splenic flexure, and sigmoid. The rectum is the ultimate anatomic phase earlier than the anus. The colon tissue contains the villi, lymph, muscle, nerves, and vessels. The absorptive capability may be very excessive; each approximately 2000ml of fluid enters the colon through the ileocecal valve from which ninety% of fluid is absorbed. The grownup colon is a line by way of at least 8 wonderful epithelial cell types, viz columnar or absorptive cells, deep crypt secretory cells, vacuolated cells, microfold or M cells, undifferentiated crypt cells, multivesicular or caveolae cells, goblet cells, and kind of endocrine cells. (3, 5, 7).

ADVANTAGES

The web site-precise transport of medication to decrease parts of the GI tract is fantastic for localized treatment of numerous colonic illnesses, particularly inflammatory bowel ailment, irritable bowel syndrome, colon cancer.

Used within the treatment of nicotinic dependency, beneficial for the shipping of proteins, peptides which are being introduced with the aid of injections delayed mechanisms are designed to improve the efficacy of the drug by using concentrating the drug molecules where they're wanted most and also limit the ability facet effects and drug instability, used in direct remedy of disorder at that website, low dosing and less systemic aspect results. Molecules which can be poorly absorbed in the upper intestine, together with peptides, proteins,

Perhaps higher absorbed from the decrease GIT.

The colon is a website wherein both nearby and systemic shipping of drugs can take region. Nearby shipping permits topical treatment of inflammatory bowel ailment.

The colon is having excessive water absorption ability, the colonic contents are significantly viscous and consequently the provision of maximum pills to the absorptive membrane is low.

The metabolic tactics like azo reduction and enzymatic cleavage take place in the colon that is Chargeable for the metabolism of many drugs and peptides like insulin. (7, 8, 9)

Disadvantages

A longer house time of 3-five days outcomes in accelerated plasma levels of the medication and therefore higher bioavailability in popular, but specially for tablets that are substrates for this class of enzyme.

Single unit colon targeted drug shipping gadget has the downside of UN intentional disintegration of the components because of production deficiency or unusual gastric body structure

development of colon specific drug is tough because of many organic limitations Cytochrome (P450) class of drug metabolizing enzymes has decrease affinity in the colonic mucosa. (8,10)

Limitations

Colon gives a near impartial pH, on the website online of drug transport, reduced enzyme hobby, a protracted transit time and expanded responsiveness to absorption enhancers.

Wide variety of pH values and distinctive enzymes present during the gastro intestinal tract, through which dosage form has to journey before achieving goal web site For better drug transport it ought to be in solution form before it arrives inside the colon Fluid content material in the colon is tons decrease and it's far extra viscous than within the upper part of GI tract.

Balance of drug is also a subject and need to be considered at the same time as designing the shipping system. The drug may potentially bind in a non-precise way to nutritional residues, Intestinal secretions mucus or fecal count number.

The resident microflora may also affect colonic performance thru metabolic degradation of the drug Decrease floor region and relative tightness additionally influences the bioavailability of medicine. (7, 8)

Factors Governing the Colon Drug Delivery

Factors which influence colon drug delivery are mainly divided into 2 types;

- Pharmaceutical factors
- Physiological Factors

Gastrointestinal Transit

Gastrointestinal motility in fasted kingdom proceeds via four phases over a period of 2-3 hours. The feeding nation impacts the regular pattern through irregular contractile pastime.

Small Intestinal Transit

Small intestinal transit is not influenced by the physical state, size of the dosage form and the presence of food in the stomach. The mean transit time of the dosage form is about 3-4 hours to reach the ileocecal junction and the time period is consistent.

Colonic Transit

The bioavailability of drugs released from the dosage forms may be rather stimulated by using the colonic transit time. various factors like gender and size of the dosage shape and physiological situations such as pressure, presence of food and diseased country influence the colonic transit time. Small debris and answers bypass slowly thru the proximal colon and in individual, guys shows shorter colonic transit time than ladies. The colonic transit time of pill in adults is 20-35 hours; the transit time of tablet is unbiased of the tablet density and volume.

Gastric Emptying

Gastric emptying is fastest and most consistent. Emptying completes from 5-10 min up to 2Hrs, depending on phase of stomach at the time of drug administration. Gastric emptying can be considerably slowed by fed state.

Stomach and Intestinal pH

Release and absorption of orally administered capsules are influenced by means of the gastro intestinal ph.

Colonic Micro flora and Enzymes

The human alimentary canal is noticeably populated with microorganism and other micro flora at both ends, are oral hollow space and the colon /rectum. Azoreductase produced by means of the colonic micro flora plays an critical function in development of a number of transport structures, particularly in catalyzing the release of five-amino salicylic acid, from a the diffusion of prod rugs. Different enzymes are glycosidase and glucuronidases produced by using lactobacilli, bacteroids and bifid bacteria. The interest of enzyme is associated with the concentration of microorganism mainly location.

Colonic Absorption

The floor area of the colon is much less in comparison to the small gut, and for this reason no longer ideally suited for absorption. Colon is considered for drug delivery because the environment is dividing of endogenous enzymes apart from microbial or is in. Resident time of colon is 10-24 hours. Little blending inside the colon makes it feasible to create neighborhood environments with top-rated absorption. Absorption is motivated by way of the transport of water, electrolytes, and ammonia throughout the mucosa and it is more in the proximal colon and distal colon.

Mechanisms of Absorptions

Passing through colonocytes (Trans-cellular shipping)

Passing among adjacent colonocytes (Para-cellular delivery)

Absorption enhancers facilitate effective absorption through various mechanisms.

They may be disruption of the intracellular occluding junction complicated opens the

Para cellular course, amendment of epithelial permeability by means of denaturing membrane proteins and change of lipid-protein interactions, and disruption of the integrity of lipid barrier with the aid of colonic enterocytes.

Colonic Absorption of Macromolecules

The absorption property of Bovine serum albumin is 0.13% from colon and 1.7% through small intestine. This is due to surface area difference.

Gastrointestinal Diseased State:

Crohn's sickness, constipation, diarrhea, and gastroenteritis can also have an effect on the release and absorption properties of the colon particularly drug transport structures.

Pharmaceutical Factors

DrugMolecules

Drugs which show poor absorption from the stomach or intestine including peptide

Drugs are most suitable for colon-specific drug delivery systems. Sulphasalazine and 5-ASA is widely used drugs for the treatment of IBD and other diseases.

Drug Carriers

The choice of carrier for a unique drug candidate relies upon on physicochemical nature of the drug in addition to the ailment for which the system is to be used. Chemical nature, balance, and partition coefficient of the drug and type of absorption enhancer selected impact the provider choice.

Targeting Approaches to Colon

Colon-specific drug shipping is taken into consideration as useful inside the treatment of colon-associated diseases and the oral delivery of protein and peptide tablets. Various mechanisms following for colon targeted drug shipping are:

- i) Coating with pH-dependent polymers.
- ii) Osmotic control system.
- iii) Strain delivery systems.
- iv) Coating with pH-independent biodegradable polymers.
- v) Delivery structures based totally at the metabolic activity of colonic microorganism
- vi) Pulsatingdrug transport gadget.
- vi) Timecontrolled or time-based system.

Conclusion

Drug delivery to the diseased colon is fine in reducing systemic aspect results; decrease the dose of the drug, supply of the drug most effective when it is required and maintenance of the drug in its intact form as near as feasible to the goal website. Better colonic shipping could be achieved by protecting the drug from absorption and/the environment of the higher GIT and then all of sudden launched into proximal colon, which is the website online for colonic focused shipping of dry is. all of the procedures provide means for the treatment of local diseases related to the colon or for systemic absorption of poorly absorbed pills. The colon is rich in micro flora which may be used to goal the drug launch in the colon.

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