Novel Approaches For Colon Targeted Drug Delivery System

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Abstract: The oral route considered to be the most preferred method for the administration of drugs that have a systemic effect; however, the oral course is not suitable for administering medicines for a disease of the lower gastrointestinal tract disease. That occurred due to their release at the upper gastrointestinal tract (stomach, small intestine), which further reduced their accessibility to the lower gastrointestinal tract. Both local and systemic delivery of drugs can occur in the colon. For example, topical delivery of drugs can be used to treat inflammatory bowel disease. A colon-targeted drug delivery system has been gaining popularity because of its ability to act locally as well as systemically. As a part of this method, the upper gastrointestinal tract is protected from the drug, which is crucial to ensuring the drug reaches the colon intact. Colonic drug transport has gained accelerated, just for the transportation of the medication for the treatment of nearby sicknesses associated with the colon like Crohn’s disorder, ulcerative colitis, and so forth. This overview article discusses the creation of the colon, factors affecting the colonic transition, colonic sicknesses, and the novel and emerging technologies for the colon concentrated on.

Keywords: colon drug delivery system, primary approaches, drug carrier, Inflammatory Bowel disease.

Introduction: A targeted drug transport system intends to offer a desired drug concentration in the body via turning in a healing quantity of drug to a target site, and it is enormously applicable for neighborhood treatment of bowel diseases which include (ulcerative colitis, croghan’s disease) amebiosis, colonic most cancers, and for neighborhood remedy of neighborhood colonic pathologies, and the systemic transport of protein and peptide pills. The colon is a suitable for absorption of peptides and protein capsules for the following reason:
The colon has near residence time (up to 5 days) and is incredibly attentive to absorption enhancers. Colon unique systems can be used in situations where a circadian rhythm is evident, e.g., allergies, rheumatic disorder, ulcer ailment, large intestine than in the small gut.

A pharmaceutical scientist today understands that the overall action of a drug molecule is dependent not only on its inherent therapeutic activity, but also on the efficiency of its delivery at the site of action. A growing appreciation for the latter has resulted in the evolution and development of several drug delivery systems (DDS) aimed at improving the performance of potential drug molecules.

A survey of the literature found that recent technological breakthroughs have resulted in the creation of several Novel Medication Delivery Systems (NDDS) that have the potential to revolutionize drug delivery and hence give certain therapeutic advantages. It is true that standard immediate-release drug delivery methods, when used often throughout the day, may keep drug concentration levels in the therapeutically efficacious range. This, however, causes modest variations in plasma drug levels. Most diseases have been cured, but research is continually being conducted to enhance existing treatments. (41)

Bringing a novel medicinal molecule to market requires much more than a financial and time investment. Patents on medication molecules/formulations are expiring in the pre-GATT period. The new method of patenting the medicine is to employ "novel drug delivery systems," or NDDS with better bioavailability (BA). Formulating or re-formulating a medicine in the form of NDDS is not a Herculean process if done gradually and professionally. This is when formulation development studies come into play. (42)
Factors to Be Considered in the Design of Colon-Specific Drug Delivery System

Anatomy and Physiology of GIT:

The GIT divided into the belly, small intestine, and large intestine. The big gut extending from the ileo-cecal junction to the anus divided into three main elements. These are the colon, the rectum, and the anal canal. The entire colon is about five feet (150 cm) long, split into five essential segments. The right colon includes the cecum, ascending colon, hepatic flexure, and the good half of the transverse colon.

Colon pH:

The pH of the GIT is subject to each inter and intra-issue variation. Weight loss program, diseased kingdom, and meal consumption impact the pH of the gastrointestinal fluid. The adjustments within the pH along the gastrointestinal tract used for targeted colon drug delivery. Radio telemetry indicates the highest pH (7.5 ± 0.5) inside the terminal ileum. On access into the colon, the pH drops to 6. four ± zero.6. The pH in the mid colon is 6.6 ± 0.8, and within the left colon, 7.0 ± 0.7. There is a fall in pH on entry into the colon due to the presence of quick chain fatty acids arising from bacterial fermentation of polysaccharides. For example, lactose is fermented via the colonic microorganism to supply large quantities of lactic acid, ensuing in pH drop to about 5.0.

Gastro Intestine Transit:

The motion of substances through the colon is slow than in other regions of the gastrointestinal tract. The total time for transit tends to be highly variable and encouraged by a range of things together with food regimen, in particular nutritional fiber content material, mobility, pressure, sickness, and pills. Colonic transit instances ranged from 50 to 70 h. Stool weights improved significantly with active disease, possibly because of exudates from infected epithelium, enhanced mucus secretion, and discount in reabsorption of fluid and electrolytes.

Advantages of Colon Targeting Drug Delivery System

- The Colon is an ideal site for the delivery of agents to cure the local diseases of the colon.
- Reduces dosage frequency. Hence, lower the cost of expensive drugs.
- Possibly leading to a reduced incidence of side effects and drug interactions.
- The colon is an attractive site where poorly absorbed drug molecules may have improved bioavailability.
- Reduce gastric irritation caused by many drugs (e.g., NSAIDs).
- Bye pass initial first-pass metabolism
- Extended daytime or nighttime activity.
- Improve patient compliance.
Fig: 1 Anatomy of colon

Criteria for Selection of Drug for CDDS

Drug Candidate:
Tablets which display inadequate absorption from the belly or gut, inclusive of the peptide are maximum appropriate for CDDS. The drugs used in treating IBD, ulcerative colitis, diarrhea, and colon cancers are perfect applicants for the local colon drug delivery system.

Drug Carrier
The variety of carriers for exacting drug candidates depends on the physiochemical nature of the drug as well as the illness for which the system is used. The factors such as chemical nature, stability, and partition coefficient of the drug, and the type of absorption enhancer chosen influence the carrier selection. Moreover, the choice of drug carrier depends on the functional groups of the drug molecule.

Approaches used for colon drug delivery system (CDDS)

Primary approaches for CDDS

1. pH perceptive polymer coated drug delivery to the colon.
2. Delayed release drug delivery to the colon.
3. Microbial-triggered drug delivery to the colon.

Recently developed techniques for CDDS

1. Pressure-controlled drug delivery system
2. Osmotic managed drug delivery to the colon

pH perceptive polymer coated drug delivery to the colon

Fasting stomach acid has a pH between 1 and 2 but increases after eating. The pH is 6.5 in the small intestine's proximal region and 7.5 in the distal small intestine. The pH of the ileum is significantly lower than that of the colon. In the ileum, the pH is about 6.4, but in the ascending colon, it is sometimes as low as 5.7. The pH in the transverse colon is 6.6, and the pH in the descending colon is 7.0. Based on these differences in pH levels, the use of pH-dependent polymers is recommended for transverse colons and not recommended for descending colons.

pH-dependent polymers are insoluble at low pH levels but become increasingly soluble as pH rises. Although a pH-dependent polymer can protect a formulation in the stomach and proximal small intestine, it may start to dissolve even in the lower small intestine. The site-specificity of formulations can be poor.

A decrease in pH from the end of the small intestine to the colon can result in several problems. Long lag times at the ileocecal junction and rapid transit through the ascending colon can also cause poor site-specificity of enteric-coated single-unit formulations.
Delayed release drug delivery to the colon
There are several potential benefits to using a time-controlled release system (TCRS), such as sustained or delayed release dosage forms. For example, improved colonic availability of dosage forms may reduce the number of doses necessary for patients to achieve their desired result. However, due to the potentially significant variation of gastric emptying time of dosage forms in humans, in this approach, colon arrival time of dosage forms cannot be accurately predicted, resulting in poor colonial availability. The colon targeting dosage forms used as prolonging the lag time of about 5.5 h (range 5 to 6 h).

Microbial-triggered drug delivery to the colon
The microflora in the colon is a heterogeneous group of bacteria that includes anaerobic bacteria, some of which ferment undigested sugars and other carbohydrates to produce energy. This vast ecosystem provides nutrients for the host, prevents infections, and helps to maintain the health of body. The microflora of the colon produces a vast number of enzymes like glucuronidase, arabinoside, galactosidase, nitro reductase, deaminase, and urea dehydroxylates. Because of the presence of these biodegradable enzymes only in the colon, it seems to be a more site-specific approach compared to other techniques. To ensure that the drug entity stays in the colon and not be absorbed into the bloodstream. 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 microorganisms or degradation by enzyme or break down 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.

Pressure-controlled drug delivery system
The development of pressure-controlled delivery systems using ethyl cellulose has been a significant role in gastrointestinal drug delivery. The release of drugs occurs when the capsule dissolves due to tension in the colon’s lumen. The thickness of the ethyl cellulose membrane is an essential factor in this release. The luminal content in the colon is denser than that of the small intestine. Because of the reabsorption of water from the colon, which causes a higher viscosity in the luminal content of the colon than that of the small intestine. As a result, drug dissolution in the colon may present a problem concerning colon-specific oral drug delivery systems. In pressure-controlled ethyl cellulose single-unit capsules, drugs are in a liquid. Lag times of three to five hours noted when pressure-controlled tablets are administered to humans.

Osmotic controlled drug delivery to the colon
The Alza Corporation has developed a new treatment for digestive diseases and disorders, the OROS-CT (Osmotic Drug Release System). This device can target the drug locally to the colon for the treatment of illness or to achieve systemic absorption that is otherwise unattainable. The OROS-CT system can be a single osmotic unit or may incorporate as many as 5-6 push-pull units, each 4 mm in diameter, encapsulated within a hard gelatin capsule. Each bilayer push-pull unit contains an osmotic push layer and a drug layer, both surrounded by a semi-permeable membrane. An
orifice drill through the membrane next to the drug layer. Immediately after the OROS-CT swallow, the gelatin capsule containing the push-pull units dissolves. Because of its drug-impermeable enteric coating, each push-pull unit prevent from absorbing water in the acidic aqueous environment of the stomach, and hence no drug deliver.

**Conclusion:** Colon-targeted drug delivery systems generate both local and systemic effects. The main advantage of the colon drug delivery system is the long transit time, near neutral pH, reduced enzymatic activity, and increased responsiveness to absorption enhancers, and the colonic region of the GIT has become an increasingly important site for drug delivery and absorption. The wide range of pH values and different enzymes present throughout the gastrointestinal tract, through which the dosage form has to travel before reaching the target site, makes the reliability, delivery efficiency of formulation, and targeting to the colon complicated.

**CONFLICT OF INTERESTS**

The authors declare that they have no conflict of interest.

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