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Review Article

Overview: Review on colon drug delivery system

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ABSTRACT

The goal of this review is to comprehend existing methods for colon-targeting dosage forms that use microbially triggered (such as prodrugs and polysaccharide-based systems), pressure-dependent, pH-sensitive, osmotically controlled, and timed release systems. Over the past 20 years, colonic-focused drug transfer has become more and more significant due to the capacity to transfer therapeutic peptides and proteins as well as medications for the treatment of various colon disorders. With varying degrees of effectiveness, a sort of traditional approach that takes into account prodrugs, pH, time-dependent, and microflora-activated methods has been utilised in the past for colon-targeted delivery. Understanding current strategies for colon-targeting dosage forms that employ PH-sensitive, pressure-dependent, osmotically regulated, timed release, and microbially triggered (such as medicinal products and polysaccharide-based systems) systems is the aim of this review. Over the past 20 years, colon-focused drug delivery has become more significant due to its ability to administer medications for the treatment of numerous colonic disorders, as well as therapeutic peptides and proteins. A variety of traditional procedures, taking into account therapeutics, PH, time dependent on others, and microflora-activated, were all employed in previous years for colon-targeted dosing with varying degrees of success.

1. Introduction

To understand current approaches for colon-targeting dosage forms, this study focusses on systems that are timed release, osmotically controlled, pressure dependent, pH sensitive. Due to its ability to deliver therapeutic peptides and proteins, as well as pharmaceuticals management of various colon illnesses, colonic focused delivery of drug has gained importance during the past 20 years. In the past, a various of traditional method, considering prodrugs, pH, time-dependent, and microflora-activated method, use generally for purpose of colon-targeted delivery, with differing degrees success.[1] The majority of medications are not readily available to the absorptive membrane because more capacity absorption of water by colons, and highly viscous composition, & its ineffective mixing. The lymphoid tissue associated to colon; for example, the colorectal mucosa's mast cell populations rapidly produce antibodies in response to a substance, which facilitates the efficient delivery of vaccinations.[2]

1.1. Anatomy & physiology of colon

The digestive tract, small intestinal tract, and large intestine comprise the gastrointestinal system. The lining of the colon, rectum, and inner canal are the three primary portions that make up the large intestine, which runs from the junction of the ileocecal tube to the anus.[3] The colon is separated into five main sections and measures approximately 5 feet (150 cm) in length. The upward and

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downward movement of the colon support the mesentery, which is a type of peritoneal fold. The liver flexure, upward colon, the caecum, & the front half of the longitudinal colon make up the right colon. The sigmoid functions downward colon, splenic flexion, and left part of the lateral colon are all located in the left colon. The final anatomical segment before reaching the anus is the rectum.[3,4] Basically anatomy of colonic system is shown in (Figure 1).

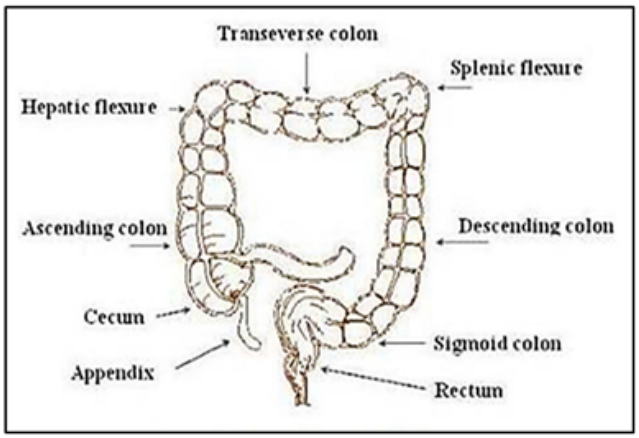

Figure 1: Anatomy structure of colonic part of body.[1,3]

The development of a colonic microorganism-friendly environment, a faecal storage reservoir, the prompt expulsion of colon contents, and the hydration and potassium intake through the luminal.[5] Such ileocecal valve allows each 2000 ml of fluid to enter the colon, where over 90% of the fluid is absorbed, indicating a very high absorptive capacity. Approximately 220 grammes of moist material, or 35 gm of dry material, are thought to normally be present in the colon. The bulk of such dried substance is microbacteria. Such celltissue of the colon contains the veins, muscle, lymph, nerves, and villi.[5,6]

2. Approaches for CDDS

2.1. Initial approaches for CDDS

1. PH Sensitive Polymer Coated Drug Delivery
2. Delayed Release (Time Controlled Release System)
3. Microbially Triggered Drug Delivery

2.2. Prodrug approach for CDDS

Azo-Polymeric Prodrugs

2.3. Recently developed systems for CDDS

1. Pressure Controlled Drug Delivery Systems
2. Novel Colon Targeted Delivery System (CODESTM)
3. Osmotic Controlled Drug Delivery (ORDS-CT)[6,7]

3. Initial Approaches for CDDS

3.1. Coating of PH sensitive polymer drug delivery to the colon

pH level of the stomach rises after eating, but it is about one and two during a fast. Such pH of the close to and downstream down intestines approximately 6.5 and 7.5, respectively. The pH drops considerably due to intestines to the colonic. It is about 6.4 in the cecum. However, it has been discovered that the ascending colon in healthy individuals can have a pH as low as 5.7. The sidewall of the pH of the intestine is 6.6, and the bottom intestine has a pH of 7.0. These pH variations serve as the foundation for the use of pH-dependent polymeric. At low pH values, the so-called dependent on pH polymer compounds used to provide colon specified medications are resistant; but, when pH increases, they get more dissolve. A dependent on pH polymeric material, on the other hand, can shield an object. For example, the names such as Salofalk, Claversal, Rowasa and Mesasalâ are used to sell Eudragit L-100-coated mesalazine pills, which are also referred to as mesalamine, 5-aminosalicylic acid, or 5-ASA. In those with inflamed bowel illness, these pills efficiently carry mesalazine to the terminating ileum and adjacent intestine.[8–10] Given (Figure 2) shows the release of drugs from a pH-sensitive polymeric based device in the colon, which ultimately shows coating dissolve and drug release.

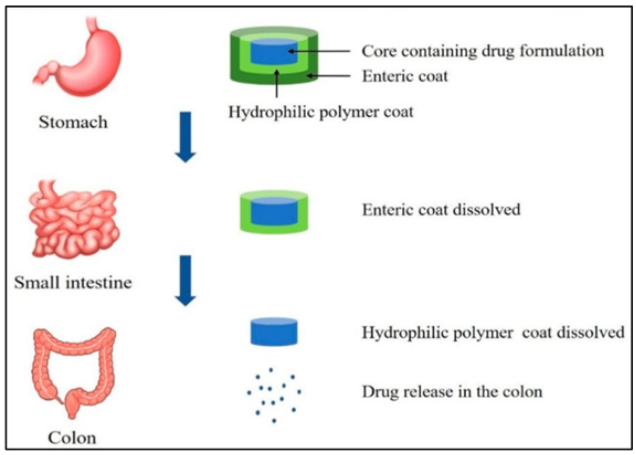

Figure 2: The release of drugsfrom a pH-sensitive polymeric based device in the colon.[3,7]

3.2. Delayed release

Time control method are helpful for Parallel drug transfer at certain times so that the patient gets the medication when they need it or at a predetermined GIT site. As a result, these devices are especially helpful in the treatment of illnesses that rely on circadian cycles. However, these methods are unable to forecast the colon arrival duration of dose

forms, which leads to lower colonial accessibility because of potentially wide Diversity among humans' medication stomach emptying rate.[6,8] Following (Figure 3) is details about Time-release press enteric coating pill (ETP tablet) design.

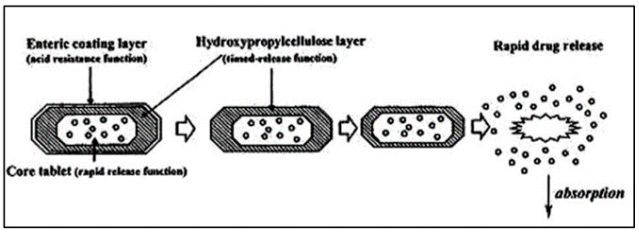

Figure 3: Design of time-releasepress enteric coating pill tablet. (ETP tablet)[3–7]

3.3. Microbially triggered drug delivery to colon

An Anaerobic microbes, including bacteroides, ruminococcus, bifidobacteria, clostridium, eubacteria, & enterococci that form the majority of the colon's microbes, typically has a concentration between 1011 and 1012 CFU/mL.[8] Such massive microbiota provides for its requirement for energy by digesting different materials, including a combination of poly, di- and tri-saccharides, and others, the fact that have been retained untreated in the smaller intestine. For this the process of fermentation, the microbial environment produces a variety of enzymes, such as xylosidase, glucoronidase, galactosidase, arabinosidase, azareducatase, nitroreductase, urea dehydroxylase and deaminase. Since these degradable enzymatic are unique to the the intestines the implementation of polymers that degrade for colon-specific drug delivery seems to be a more specific to the site approach than alternative techniques.[9] These polymer chains can carry the drug to the intestine while shielding it from gastric and small intestinal disorders. Their molecular mass decreases and, eventually, their rigidity is lost as a result of being dissolved up by the polymer core, absorbed by microbes, or destroyed by enzymes once they reach the colon.[10]

4. Drug Delivery Approaches of Prodrug to Colon

The order to release the active medication, a prodrug—an initial medication molecule's medicinally ineffective clone—must undergo Enzyme-based or unstructured change in vivo. Such prodrug is made to hydrolyse minimally in the GIT's upper tracts and enzymatically in the intestines, allowing the drug transporter to disgorge the active ingredient for colonic distribution.[10,11]

Some bacterial metabolic procedure that has been investigated the most is a method by which bacteria in the gut break down azo molecules.[12] Since the medication is connected to hydrophobic moieties such as protein molecules, glucoronic acids, carbohydrates, glactose, cellulose, etc., several have been now more connectors that are susceptible to pathogen hydrolysis, especially in the small intestine.[13]

4.1. Prodrug approach limitations

The way it expressed it flexible because it depends on the functional group. It is accessible for chemical attachment on the drug moiety. Prodrugs are also new chemical substances that need to be thoroughly tested before being used as carriers.[14]

5. Recent Approaches for CDDS

5.1. Pressure control DDS

Because movement of peristalsis, the colon is under more pressure than the small intestine. capsules of Pressure-controlled colon-delivery were developed by Takaya et al. through ethylcellulose, which happens to be insoluble in water.[15] In these devices, a water-insoluble copolymer capsule breaks down under pressure in colon lumen, releasing medicine. The primary component influencing the dosage collapse is the ethylcellulose membrane's strength.[16,17]

Furthermore, the mechanism appeared to be reliant on capsules' density and size. Water is reabsorbed from colon, such luminal material in the colon has a more viscous by the intestine. As a result, it shown been established API breakdown in the last colon will provide a condition for colon-specific

5.2. Novel type colon targeted DDS

The (Figure 4) describes the diagrams showing the CODES design concept in such order overcome the problems concerning time or ph dependent systems, a revolutionary CDDS method known as CODESTM developed.[18] Microbially mediated and pH-dependent CDDS are combined in the CODESTM technique.

It was make that uses such lactulose, which behave a catalyst to release medications at certain points within the colon. The process involves covering a standard tablet core with lactulose with an Eudragit E, followed by such enteric substance called Eudragit L. given method is based on the idea that the pill dissolves quickly once the stomach is empty and is shielded by the enteric barrier while in the stomach. After that, the preparation is protected while it moves through the coating of acid-soluble material.

5.3. Osmotic controlled drug delivery system

When treating a condition, the ALZA Corporation's OROS-CT utilised to obtain the medicine would as wise be impossible. such OROS-CT system are consist of a one osmotic unit or six push-pull units, one having a diameter

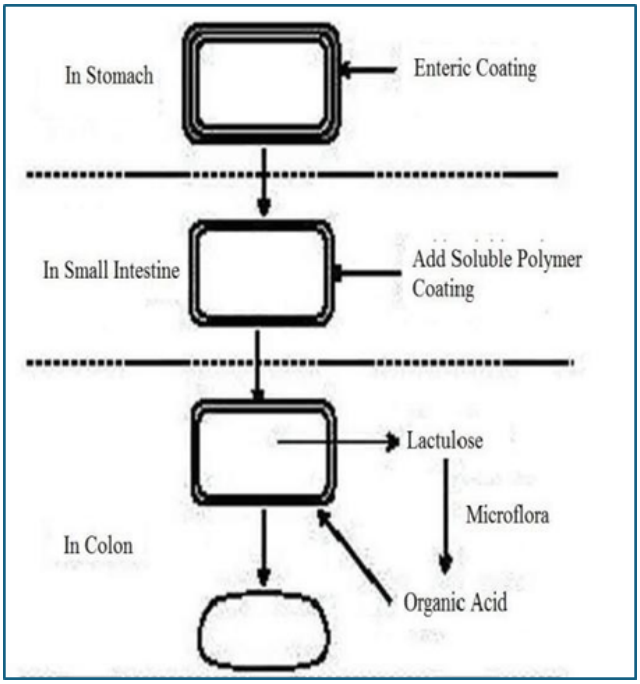

Figure 4: Diagrams showing the CODES design concept[2–9]

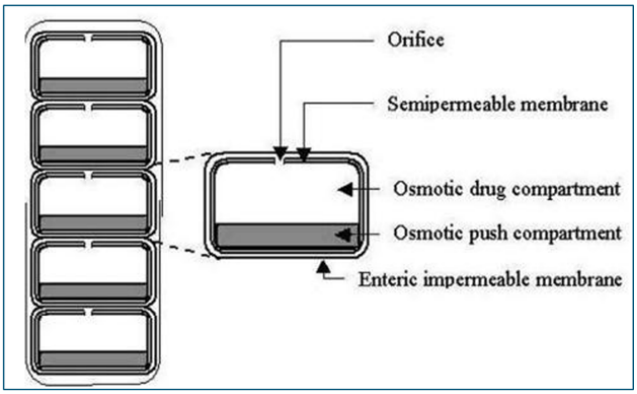

Figure 5: OROS-CT colonicfocused medication delivery device cross-sectional[4,7]

of 4 mm and closed in a gelatin hard capsule. Every two layer push unit has a API layer & osmotic push layer, both of which are cased in a semipermeable layer membrane. Such membrane adjacent to the API layer is punctured. Such gelatin capsule that contains push-pull units soluble as soon as OROS-CT is consumed.

One push-pull unit's medicine-impermeable enteric coating keeps it by collecting H2o in the stomach's aqueous acidic environment, preventing such delivery of any dosage. Once the film disappears in the small intestine's more acidic condition (pH >7), water enters unit, causing the osmotic push compartment to enlarge. This also causes a gel to form in drug compartment. Drug gel is forced out orifice by osmotic push swelling compartment by the rate at which H2O moves through the semipermeable Layer membrane. Every push-pull unit used to treat ulcerative colitis is made a 3–4 hour post gastric delay to avoid medication distribution in intestine. Given (Figure 5) elaborates diagrammatically OROS-CT colonic focused medication delivery device cross-sectional.

Whenever unit enters to colon, the API starts to discharge. In the colon, OROS-CT give medication over as little as four hours or sustain an ongoing dose 24 hours rate. latest phase-transitioned methods have updated emerged & show promise as a useful tool for colon medication delivery.[19,20]

6. Discussion

Colonic focused medicine delivery can deliver therapeutic peptides and proteins, as well as pharmaceuticals for the treatment of various colonic illnesses, it has gained importance during the last 20 years. With differing degrees of success, a type of traditional methods, considering prodrugs, pH, time dependently, and microflora-activated methods, have been used in the past for colon-targeted administration. It has many versatile potentials for future aspects to do work more on colon drug delivery system. Many drugs can use those diseases which are generally associated with colon system. Different types of coating are used for tablet to focused on colon targeted drug delivery. So, it has great bright future to do work.

7. Conclusion

For medications now used to treat localised colon disorders, better drug delivery mechanisms are needed. Drugs that are targeted specifically to the diseased colon have the following benefits: a lower risk of systemic adverse effects, a lower dosage, delivery of the medication to the biophase only when necessary, and preservation of the drug in its intact form as close to the target location as feasible. All of the methods offer ways to treat colon-related local illnesses or to help poorly absorbed medications enter the body. The right strategy must be chosen in order to distribute medications in a way that is safe, effective, and less costly while causing the least amount of variation in the release of the medications at the intended location.

8. Source of Funding

None.

9. Conflict of Interest

None.

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