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REVIEW ARTICLE: FUTURE ASPECTS OF COLON DRUG DELIVERY SYSTEM

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Abstract:

The colon serves as a site where drugs can be delivered either locally or systemically. Local delivery is used for the topical treatment of inflammatory bowel disease. However, for more effective treatment, drugs should be delivered directly into the colon, which helps in reducing the side effects that affect the whole body. This review focuses on comparing the main methods used for colon-specific drug delivery, known as CDDS. These methods include prodrugs, pH and time-dependent systems, and microbially triggered systems, which have had limited success and face certain challenges. In comparison, newer methods such as pressure-controlled colonic delivery capsules (CODEST) and osmotic-controlled drug delivery systems are more effective. These newer approaches are unique because they offer better site-specific drug delivery in the body and are more feasible to manufacture.

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1. INTRODUCTION

Colon-targeted drug delivery has been the focus of numerous studies in recent years due to its potential to improve treatment of local diseases affecting the colon, while minimizing systemic side effects. Some examples of disease states which impact the colon include Crohn's disease (CD), ulcerative colitis (UC), and irritable bowel syndrome (IBS) [1]. Some of the frequently used drugs for the treatment of these ailments include sulfasalazine, dexamethasone, hydrocortisone, metronidazole, prednisolone, and others[2] The delivery of these drugs specifically to the colon without being absorbed first in the upper gastrointestinal (GI) tract allows for a higher concentration of the drug to reach the colon with minimal systemic absorption [3]. The colonic contents have a longer retention time (up to 5 days), and the colonic mucosa is known to facilitate the absorption of several drug can be delivered to the colon via the oral, or the rectal route. Oral dosage forms are the most preferred delivery route for colon-specific delivery due to their convenience.

Oral dosage forms also allow for a greater degree of flexibility in their manufacturing, design, improved patient adherence, relatively safe administration, and they do not require sterile preparation. Direct rectal delivery of drugs is challenging with respect to targeting a drug to specific sites within the colon. Additionally, the extent of drug distribution varies for different rectal dosage forms depending on their spreading capacity and retention time. The success of a colon-specific drug delivery system (CDDS) depends on the drug's physic-chemical properties, the type of delivery system, all other factors which may influx once the GI transit time, as well as the degree of interaction between the drug and the GI tract. It is essential for oral CDDS to protect the drug from being released in the stomach and small intestine [4].

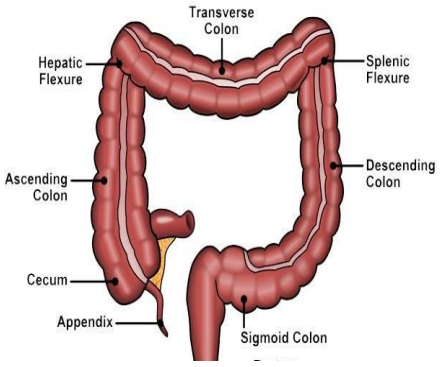

Figure 1: Anatomy of Colon

1. APPROCHES TO DRUG DELIVERY SYSTEM OF COLON

This section provides an overview of the major formulation strategies developed for colon-targeted drug delivery. These approaches are broadly categorized based on their underlying release mechanisms, including p^H responsiveness, time dependency, microbial activation, prodrug strategies, and pressure-controlled systems.

1.1 pH-RESPONSIVE POLYMER-COATED COLON DRUG DELIVERY

The p^H-responsive polymer-coated colon drug delivery system provides numerous benefits for colon drug delivery, including targeted drug administration, decreased adverse effects, increased bioavailability, and improved patient compliance. Additionally, it reduces adverse effects associated with systemic drug delivery, prevents drug degradation in the stomach and small intestine, and improves patient compliance. While fasting, the stomach acidity is between 1 and 2, but it elevates to around 3 after ingesting. (show in fig 3).

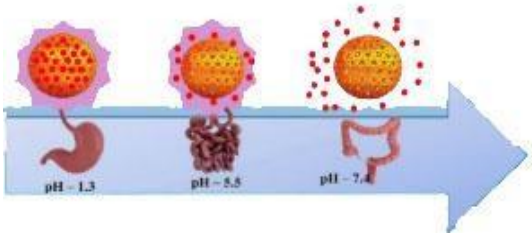

Figure 2: P^H-Responsive

1.1.1 Polymer-Coated Colon Drug Delivery

Compared to the ileum, the p^H of the colon is significantly lower. p^H-dependent polymers are employed to respond to these variations. [30] Polymers used for intestinal targeted deliveries are highly insoluble in acidic environments and even more so in basic environments. The p^H at which a polymer dissolves corresponds to the solubility of the polymer. For drug delivery in the ileum and colon, high-p^H-tolerance polymers are utilized.[12,13]

Example: CAP /HPMCP coated formulation

1.2 TIME-DEPENDENT COLON DRUG DELIVERY SYSTEM

Time-dependent drug delivery systems (TDDS) are drug delivery systems designed to discharge medications at a predetermined rate over a specific period. Typically, these systems are used to administer medications that must be steadily released over an extended period to accomplish therapeutic effects or to prevent toxicity. Colon-specific drug delivery is one area where time-dependent drug delivery systems have been extensively studied. Improved therapeutic efficacy, decreased dosing frequency, targeted drug delivery, and decreased systemic exposure are advantages of time-dependent drug delivery systems for the colon. Overall, time-dependent drug delivery systems have several advantages for colon-specific drug delivery, and ongoing research in this area holds great promise for developing

more effective treatments for colon diseases. (show in fig 5) Time-controlled release devices are another option for administering medicine. [14,15]

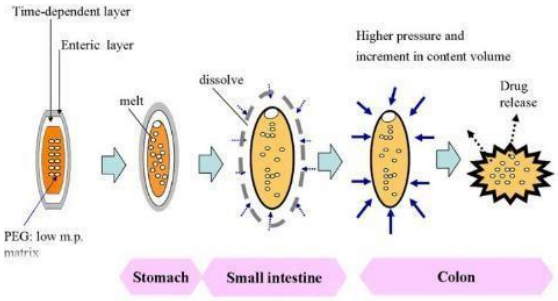

Figure 3: Time-Dependent Colon Drug Delivery System

2. FUTURE ASPECTS OF COLON DRUG DELIVERY SYSTEM

a) Targeted personalized therapy
- Involves specific drug delivery tailored to the patient-specific gut microflora in the colon.

b) Advanced polymer development
- Focuses on new biodegradable P^H -sensitive polymers.
- Uses enzyme-responsive polymers for controlled drug release.
- Employs natural polymers like pectin, chitosan, or guar gum with improved modifications.

c) Microbiota-responsive drug delivery
- Utilizes a colon microflora/sensitive system (probiotic-triggered delivery).
- Gut bacteria enzymes trigger drug release and control it.
- Nanotechnology & Smart Systems
- Uses nanoparticles, microspheres, and liposomes for enhanced colon targeting.

d) Smart drug delivery system
- stimuli-responsive (P^H, enzyme, time) to reduce adverse side effects.

e) Chronotherapeutic Drug Delivery
- Targets disease rhythm (night-time symptoms) for timed drug release.
- Involves colon-specific chrono modulated formulation.

f) Gene & Protein Delivery
- Enables colon-targeted gene therapy for peptide/protein delivery.
- Protects against enzyme degradation.
- Promising approach for targeted cancer therapy.

g) Improved Treatment of Colon Diseases
- Applies to colorectal cancer, IBS, and colon infections with higher efficacy.
- Reduces systemic side effects and suits long-term therapy with suitable formulations.

h) Commercial & market growth
- Increasing prevalence of colon-related disease
- High oral drug demand for targeted delivery → strong Pharma industry market expansion.

i) Combination drug deliver
- -Anti-inflammatory + probiotic + anticancer drug combination delivery in a multi-unit system (pellets, capsules, tablets).

3. CONCLUSION:

colon-targeted drug delivery, highlighting that the colon has become an important site for drug absorption with strong targeting to diseased colon tissue. This approach reduces systemic side effects and ensures drug release only when the drug is proximal to the target site in its intact form. It provides treatment for local colon disease or systemic absorption of poorly absorbable drugs. The varying P^H and enzymes throughout the GI tract complicate formulation and targeting efficiency because the dosage form must travel through the GIT before reaching the colon. CDDS offers considerable therapeutic benefits to patients in terms of both local and systemic treatment. Colon specificity is more likely to be achieved with system that utilize natural materials that cure degraded by colonic bacterial enzymes considering the sophistication of colon specific drug delivery system and the uncertainty of current dissolution methods in establishing possible in-vitro / in-vivo correlation, challenges remains for pharmaceutical scientists to develop and establishing possible in-vitro / in-vivo validated dissolution method that incorporates the physiological features of the colon and yet can be used routinely in an industry setting for the evaluation of CDDS.

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