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Various Aspects of the Colon Specific Drug Delivery System

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ABSTRACT

The best place where both local and systemic delivery of drugs can take place is colon. Most of the conventional drug delivery systems for treating the colonic disorder such as Inflammatory bowel diseases, Ulcerative colitis, Cohn's diseases, Colon cancer and Amoebiasis are failing as drug do not reach the site of action in an appropriate concentration. A drug delivery system which is used to deliver the substances that are degraded by the digestive enzymes in the stomach like-proteins, peptides is known as colon targeted drug delivery system. Colon targeted drug delivery system increases the absorption of poorly absorbable drugs due to the high retention time of the colon. Colon targeted drug delivery plays a vital role in novel drug delivery systems. The colon as a site for drug delivery offers distinct advantages on account of near neutral pH, a much longer transit time, relatively low proteolytic activity and offers a much greater responsiveness to absorption enhances. This review focus on various aspects of aspects of the Colon targeted drug delivery system, like advantages, disadvantages, model drug selection criteria and evaluation of colon targeted drug delivery system.

INTRODUCTION

Oral route is the most convenient and extensively used route for drug administration in body. It is probable that at least 90% of all the drugs given by oral route .[1]

Oral route is most preferred route & it received more attention in pharma sector because it offers more flexibility in designing of dosage form as compared to other routes. However, this route has certain problems such as unpredictable gastric emptying rate, short gastrointestinal transit time, inter-subject variability leads into less bioavailability & it is not applicable for drugs which having narrow absorption window. The goal of any drug delivery system is to provide a therapeutic amount of the drug to the proper site in the body to achieve promptly, and then maintain, the desired drug concentration, to ensure safety of drugs as well as patient compliance which is not achieved by conventional oral drug delivery [2,3] So there is need of controlled release drug delivery systems to overcome this problem. The best place where both local and systemic delivery of drugs can take place is colon. Most of the conventional drug delivery systems for treating the colonic disorder such as Inflammatory bowel diseases inflammatory bowel disease., Ulcerative colitis, Cohn's diseases, Colon cancer and Amoebiasis are failing as drug do not reach the site of action in appropriate concentration .[4,5] A drug delivery system which is used to deliver the substances that are degraded by the digestive enzymes in the stomach like-proteins, peptides is known as colon targeted drug delivery system. Colon targeted drug delivery system increases the absorption of poorly absorbable drugs due to the high retention time of the colon. Colon targeted drug delivery plays a vital role in novel drug delivery systems. Most popular approach of oral controlled drug delivery for management of colon diseases is colon targeted drug delivery.[6,7]

ANATOMY AND PHYSIOLOGY OF COLON

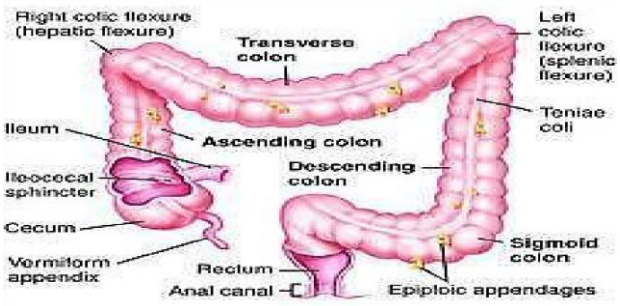

Fig.1: Showing anatomy of colon

The GI tract is divided into stomach, small intestine and large intestine. The large intestine extending from the ileocecal junction to the anus is divided into three main parts. These are the colon, the rectum and anal canal. The entire colon is about 5 feet (150 cm) long and is divided into five major segments. 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 contains the left half of the transverse colon, descending colon.[8]

NEED OF COLON TARGETED DRUG DELIVERY

1. For lower dosing and fewer systemic side effects, there is need of Targeted drug delivery of the colon.

2. 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

3. Colon targeting is use full for site specific treatment of number of others diseases of the colon, e.g. colorectal cancer,

4. Colonic delivery needed for drugs which are polar and/or susceptible to chemical and enzymatic degradation in the upper GI tract, highly affected by hepatic metabolism, in particular, therapeutic proteins and peptides.

5. Targeted drug delivery system needed for oral administration of peptide and protein drugs, colon-specific formulation could also be used to prolong the drug delivery.[9,10]

ADVANTAGES OF COLON TARGETING DRUG DELIVERY SYSTEM

1. Colon targeted drug delivery reduces dosage frequency. Hence lower cost of costly drugs.

2. It is used for the effective treatment of inflammatory bowel diseases like ulcerative colitis, Colon cancer Crohn's disease, etc.

3. The colon is an attractive site where poorly absorbed drug molecules may have an improved bioavailability.

4. Limited risk of local irritation.

5. No risk of dose dumping.

6. Improve stability.

7. High level patient compliance associated with colon targeted drug delivery.

8. Achieve a unique release pattern bypass initial first pass metabolism.

9. Extended daytime or night-time activity.

10. Prevents gastric irritation resulting due to the administration of NSAIDs.[11,12]

LIMITATIONS OF COLON TARGETING DRUG DELIVERY SYSTEM

1. The resident microflora could also affect colonic performance.

2. The non-specific interactions of drug with the colonic content e.g., dietary residues, intestinal secretions, mucus, or fecal matter

3. Lower surface area and relative tightness of the tight junction in the colon can restrict drug transport across the mucosa into the systemic circulation.

MODEL DRUG SELECTION CRITERIA FOR COLONIC DRUG DELIVERY SYSTEM[1]

1. Drugs poorly absorbed from upper GIT like Ibuprofen, Isosorbide

2. Drugs for colon cancer like Antineoplastic drugs

3. Drugs that degrade in stomach and small intestine like Insulin, 5-fluorouracil, Doxorubicin

4. Drugs that undergo extensive first pass metabolism like Bleomycin

5. Drugs poorly absorbed from upper GIT

6. Drugs for targeting like 5- Amino-Salicylic acid, Prednisolone, Hydrocortisone,[13,14]

POLYMERS USED IN COLON TARGETED DRUG DELIVERY

1. Natural polymer

Guar gum, Inulin, Pectin, Cyclodextrin, Dextran, Amylase, Chitosan, Chondroitin sulphate, Locust bean gum.

2. Synthetic polymer

Shellac, Ethylcellulose, Cellulose acetate phthalate, Hydroxypropyl methylcellulose, Eudragit, Polyvinyl acetate phthalate.[15]

FACTORS INFLUENCING COLON TARGETED DRUG DELIVERY

1) **Physiologic factors:** Gastric emptying, PH of the colon, Colonic microflora and enzymes

2) Pharmaceutical factors: Drug candidates, Drug carriers [16,17,18]

APPROACHES OF COLONIC DRUG DELIVERY SYSTEM

Following are the most popular approaches of colon targeting

1. Transit time dependent colonic DDS

2. pH Dependent colonic DDS

3. pH- and time-dependent colonic DDS

4. Bacterial enzyme dependent colonic DDS

5. Prodrug based

6. Colonic pressure controlled DDS

7. Osmotic pressure controlled colonic DDS [19,20,21,22]

EVALUATION TESTS FOR COLON DRUG DELIVERY SYSTEM

***In-vitro* evaluation**

The *in-vitro* evaluation of colon targeted drug delivery systems includes the *in-vitro* dissolution study & *in-vitro* enzymatic test[1].

In-vitro dissolution test:

The dissolution testing is done using the conventional basket method. The dissolution testing is done in different buffers to characterize the behaviour of formulations at different pH levels. The different media that are used for the dissolution testing of colon targeted drug

delivery are pH 1.2 to simulate gastric fluid, pH 6.8 to simulate small intestine, pH 7.4 to simulate large intestine. The colon targeted drug delivery systems are tested for 2hr in 0.1N HCl, 3hr in pH 6.8 phosphate buffer and finally at pH 7.4 phosphate buffer. Buffers of the above pH are prepared to evaluate the colon targeted drug delivery systems.2. In-vitro enzymatic test:

There are 2 tests for the *in-vitro* enzymatic test.

The carrier drug system is incubated in fermenter containing suitable medium for bacteria. The amount of drug released at different time intervals is determined.

Drug release study is performed in buffer medium containing enzymes pectinase, dextranase or rat or guinea pig or rabbit cecal contents. The amount of drug released at a particular time is directly proportional to rate of degradation of polymer carrier. *In-vivo* evaluation.

The *in-vivo* evaluation of the CDDS is done in dogs, guinea pigs, rats & pigs as they resemble the anatomic and physiological conditions, microflora of human GIT. The distribution of various enzymes in GIT of rat and rabbit is comparable to that in human [23,24,25,26].

CONCLUSION

Colon targeted drug delivery is used to deliver the substances that are degraded by the digestive enzymes in the stomach such as proteins and peptides. During the past decade's research is going on in developing the methods to target the drug to the specific region. The goal of targeted drug delivery is to deliver the drug to the specific organ1. Colon targeted drug delivery of drugs reduces the systemic side effects. Colon targeted drug delivery system increases the absorption of poorly absorbable drugs due to the high retention time of the colon. Colon targeted drug delivery system offers benefits of local and systemic effects thereby enable sustained and prolonged input of the drug to the upper part of the GIT.

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