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A REVIEW OF THE COLORECTAL DRUG DELIVERY SYSTEM

Pradip Paul, Sandeep Bag, Debasish Singha, Anuradha Shyam* and Dr. Kavitha P. N.

(K.R College Pharmacy, Kanakapura Main Road, Gantakana Doddi Bus Stop, Bangaluru, India– 560082).

***Corresponding Author: Anuradha Shyam**

(K.R College Pharmacy, Kanakapura Main Road, Gantakana Doddi Bus Stop, Bangaluru, India– 560082).

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ABSTRACT

The oral route is the most preferred for administration but it is not suitable for lower GIT disease. Because oral route administration drugs are released at the upper GIT tract(stomach, small intestine), they will not reach the lower GIT and minimize the accessibility of drugs at the lower GIT. To overcome this difficulty specific drug delivery has been properly analyzed last two years. Colonic drug delivery systems are of enhanced importance not just for the delivery of drugs but for the treatment of several colon local diseases such as Crohr's disease, ulcerative colitis, etc., and also other substances like protein, therapeutic peptides, anti-asthmatic drugs, anti-hypertensive drugs, anti-diabetic agents can be possible. This review article discusses, in brief, the introduction of the colon, factors affecting the colonic transition, colonic diseases, and novel and emerging technologies for colon targeting.

KEYWORDS: To overcome this difficulty specific drug delivery has been properly analyzed last two years.

INTRODUCTION

Colonic drug delivery is experiencing a renaissance due to a multitude of associated pharmaceutical benefits and opportunities discovered in recent years. It may follow the concept of a sustained or controlled drug delivery system.[11] For CIDDS the route of administration has received the most attention this is because of flexibility in dosage form designed for oral than the parenteral route because –

1. patients' acceptance of the oral administration of the drug is quite high.
2. It is the relatively safe route of drug administration compared with the parenteral route and potential damage at the site of administration is minimal.[1]

A targeted drug delivery system aims to provide a desired drug concentration in the body by delivering a therapeutic amount of the drug to a target site, it is suitable and requires for the drug having instability, low solubility, short half-life, a large volume of distribution, poor absorption, low specificity, and therapeutic index, targeting may provide maximum therapeutic activity. Meanwhile, it can also minimize adverse effects, and the toxicity of potent drugs by reducing dose.[2]

ADVANTAGE[11,12]

1. Ideal side for the delivery of an active agent to cure colon disease.
2. small drugs can be used.
3. less drug interaction and also fewer side effects.
4. cost-effective, very low dose can show action.
5. reaction time is long, due to poorly absorbed drug improved bioavailability.
6. due to preventing absorption in upper GIT many drugs (NSAID) reduce gastric irritation.
7. no nfrist pass metabolism.
8. both day and night can show the activity of the drug.
9. The presence of microflora easily degrade drug metabolism and improve colonic performance.

DISADVANTAGE[3,4]

1. Sometimes drug action can be terminated by microflora.
2. The surface area of the colon is small and the relative tightness of the junction in the colon for systemic absorption will be delayed and one set action slow.
3. Binding of the drug to dietary residues, and intestinal secretion.
4. It can reduce the concentration of free drugs.
5. Water-soluble drug dissolution rate is slow due to less fluid present in the colon compared to the small intestine.

ANATOMY AND PHYSIOLOGY OF THE COLON

A. STRUCTURE(ANATOMY)

GIT is a major part of the digestive system. IT IS a tube-like structure which extends from mouth to anus. it helps to digest the food and absorb the nutrients and fluids of food. It is divided into two parts (large and small intestine).[8] The small intestine is longer compared to the large intestine colon is the upper five feed of the large

intestine and is mainly situated in the abdomen.[11] The colon is a cylindrical tube that is lined by a moist, soft pink lining called mucosa.

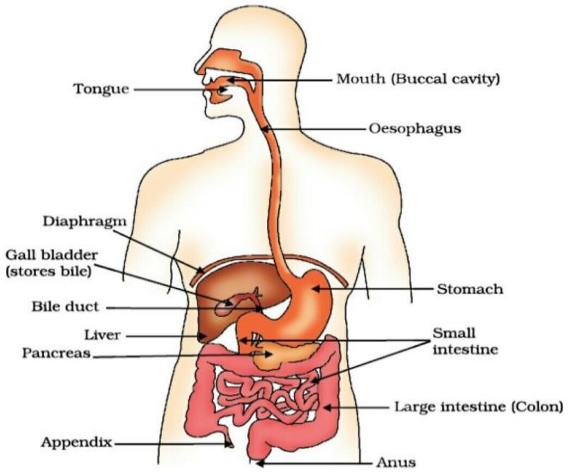

Fig. 1: Gastroinstional Tract.

Parts of the small intestine are the duodenum, jejunum, and ileum. parts of the large intestine are the ascending colon, descending colon, and transfer colon. The surface of the colon is about 1300 cm2.[5]

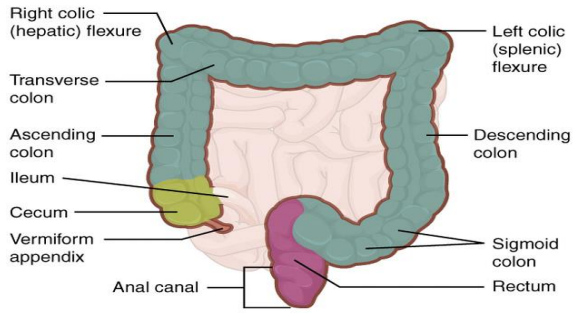

Fig. 2: Structure Of Colon.

B. Function of the colon[11,7,6]

1. It makes a favorable environment which helps to grow colonic microorganisms and increase the digestive power.

2. absorbtion of H2O and Na+ from lumen and scrate K+ and HCO.

3. the consolidation of the intestine content into feces by the absorption of the water and electrolytes and storage of feces until excreted from the body.

Factor effecting on colonic drug delivery system.

1. PHYSIOLOGICAL FACTOR[10,8,9]

a. COLONIC PH: colonic target drug delivery can be affected by colonic pH and can influenced by some factors like diet, disease state, and food intake.

b. ANATOMY AND PHYSIOLOGY OF COLON: the GIT tract is divided into so many parts like – the anus, large intestine, small intestine, and stomach. further small intestine(Ilium, jejunum, duodenum) and large intestine (ascending colon, descending colon, transfer colon) are divided into different parts. different parts have different digestive power, for a reason it can be effective

c. COLONIC MICROFLORA AND THEIR ENZYME: every 400 distinct colons have 10^{11}-10^{12} CFU/ml concentration bacteria can be found, of which 20-30% belong to the genus Bacteroides. They produce a different enzyme that helps metabolism activity such as – decarboxylation, hydrolysis, and dealkylation. So, it can also affect the action of drugs.

d. TRANSMIT OF MATERIAL IN THE COLON: The presence of food increases gastric resistance and sometimes regular feeding, and dosage forms have been shown to reside in the stomach periods over 12 hours. so, it can also be effective.

2. PHARMACEUTICAL FACTOR

a. DRUG CARRIER: it directly depends on the physiological nature of the drug. It also depends on the disease for the system to use it. It can also be affected by the nature, stability, and partition coefficients of the drug.

b. COLONIC ABSORPTION OF DRUG

drug absorbed in the colon in different mechanisms such – as transcellular, paracellular, and endocytosis. for different drugs having different mechanisms.

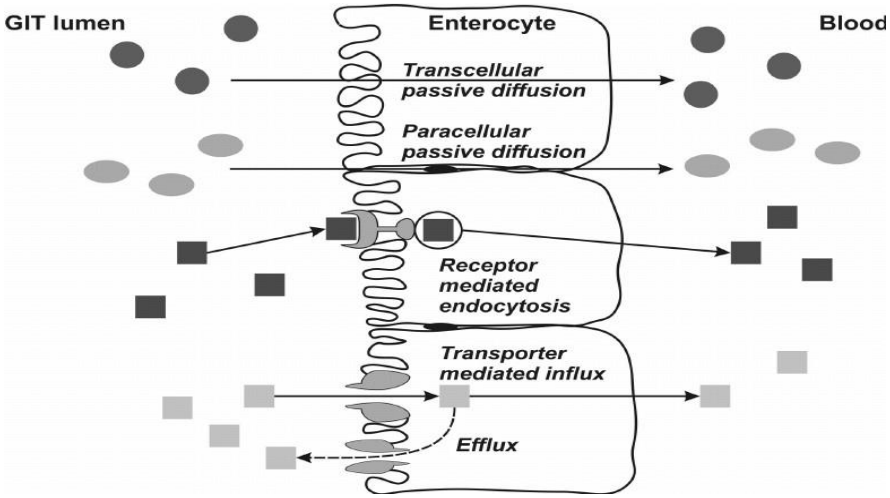

Fig. 3: Primary Routes Of Drugs Absorption From The Gastrointestinal Track.

APPROACHES USED FOR SITE-SPECIFIC COLORECTAL DRUG DELIVERY SYSTEM[5,6,7,8,9]

A. DELAYED (TIME-CONTROLLED RELEASE SYSTEM) RELEASE DRUG DELIVERY TO COLON: time-dependent colonic DDS such as sustained or delayed release dosage formed one of the important drug release systems. It should be released after predefer mined time. i.e. - delivery of drug should reach the right site and the proper amount. Fig 5 was proved to be a potential coating material for a delayed release of drugs to the colon. Different types of enteric-coated tablets have delayed the release process.

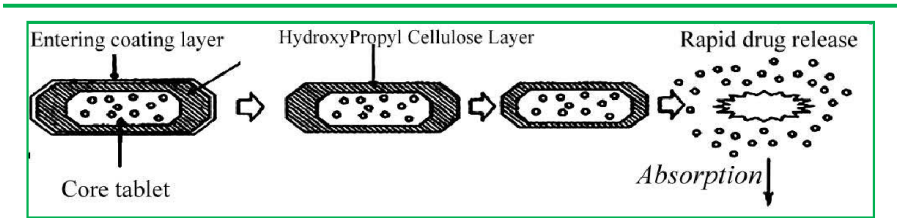

Fig. 4: Design Of Enteric Coated Timed-Release Press Coated Tablet.

B. MICROBIALLY TRIGGERED DRUG DELIVERY SYSTEM: the presence of different types of microorganisms (flora) in the colon it easily biodegradable the polymer coating. but it was safe in the upper GIT because very little microbial activity was present which is insufficient for cleavage of the polymer coating.

C. PH-DEPENDENT COLONIC DRUG DELIVERY SYSTEM: The p^H of the human GIT increases progressively from the stomach (p^H -1.2 up to 4), small intestine (p^H6-7) at the site of digestion and increase to 7-8 the distal ileum. coating of tablets and capsules by a polymer can be pH-sensitive. Polymers used for colon drug delivery systems should be able to withstand lower p^H of the stomach and small intestine. also, be able to disintegrate at the neutral or slightly alkaline p^H of the terminal ileum and preferably at the ileocecal junction.

D. PRODRUG APPROACHES FOR DRUG DELIVERY TO COLON: for colon delivery, prodrug (the inactive form of the parent drug) is designed to undergo minimal hydrolysis in the upper tracts of GIT. It undergoes enzymatic hydrolysis in the colon thereby releasing the active drug moiety from the drug carrier.

a. AZO POLYMERIC PRODRUG: sub-synthetic polymer from of polymeric prodrug with azo linkage between the polymer and drug moiety.

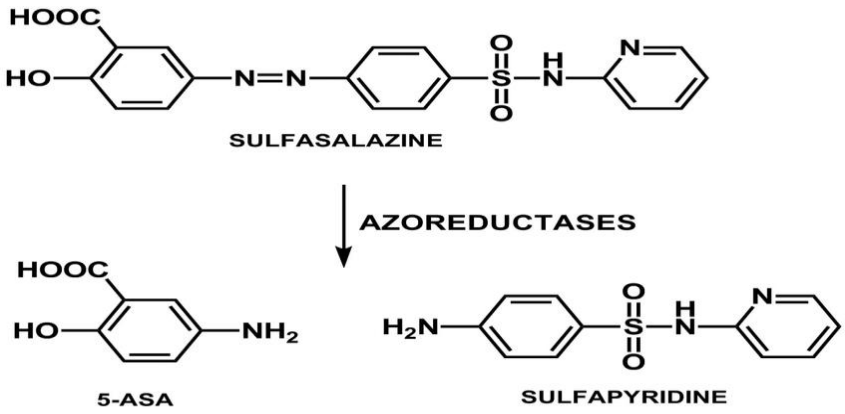

Fig. 5:

i. **HYDROLYSIS OF SULPHASALAZINE**
ii. **5-AMINO SALACYLIC ACID**
iii. **SULPHAPYRIDINE**

b. AZO PRODRUG: the azo linkage exhibits a wide range of thermal chemicals and photochemical and pharmaceutical properties. azo compound is metabolized by both intracellular enzymatic compounds and extracellular reduction most used azo compound is as a form of hydrogel to coat the drugs to form a prodrug. i.e-sulphasalazine.

SUMMARY

The colon-specific drug delivery systems (CDDS) should be capable of protecting the inside of the colon. For-drugs should not be absorbed or released in the stomach and small intestine, and the active pharmaceutical agent should not degrade in the dissolution site but only be released and absorbed once the system reaches the colon. The oral route is the most convenient preferred route but it does not show proper effect in lower GIT. due to this colonic drug delivery is introduced.

CONCLUSION

The colonic part of GIT become the most important site for drug delivery and absorption. CDDS have therapeutic benefits to patients for both local and systemic treatment. The presence of bacterial enzymes in the colon can utilize natural materials that have more colon specificity.

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