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COLON TARGETED DRUG DELIVERY APPROACH

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ABSTRACT

Targeted drug distribution towards the colon remains extremely anticipated meant for indigenous management of a variability of bowel ailments particularly for instance (ulcerative colitis, crohns disease) colon malignancy, and for indigenous management of indigenous colonic illness. The colon specific drug distribution system ought to remain adept of protecting the medication on path to colon aforesaid as medication discharge and absorption must not ensue in the stomach and the small intestine and vitality means must not remain degenerated and towards consent medication discharge merely in the colon. The localization of various medications towards colon has been found to be very helpful for many pharmacotherapies, including the supervision of inflammatory bowel syndromes, crohns ailment, ulcerative colitis, diverticulus, anaerobic bacterial infections and mainly colon cancer.

KEYWORDS: Colon, Colon cancer, Targeted drug delivery, Inflammatory bowel disorders.

1. INTRODUCTION

Colon is the preceding portion of digestive tract which starts from ileocecal junction and ends at anus. It has a length of about 1.5 m. It remains alienated into four main segments i.e. the ascending colon, the transvers colon, the descending colon, and the sigmoid colon.[1]

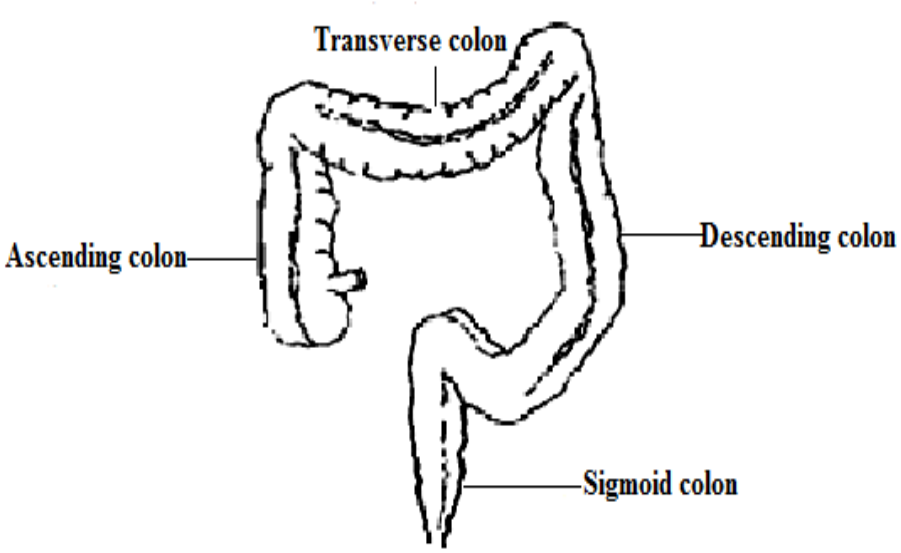

Fig. 1: Different sections of colon.

The chief purpose of the colon remains the association of the intestinal fillings obsessed through faeces through the concentration of water and electrolytes and to stock the faeces till excretion. In a well human colon, sodium and chloride ions remain typically absorbed and potassium and bicarbonate ions remain typically concealed. There remains a liberal absorption of fluid by means of the substantial permits laterally the colon. This outcomes in solidifying the mass.[2]

Colon disorders

Table 1: Common disorders of colon.

S. No.	Name of the disease	Pathophysiology	Affected area	Signs and symptoms	Medications practiced in the handling of these ailments	References
1.	Crohn's disease	A disorderly guideline of mucosal and systemic immune retort ensuing in the endurance of the inflammatory cascade.	Affects any part of the GIT, from anus to mouth.	Diarrhoea, fever, abdominal pain, blood in stool, weight loss.	Antibiotics, aminosalicylate, anti-inflammatory drugs and corticosteroids.	Sathiyasekaran *et al.*, 2006.
2.	Ulcerative colitis	Sub category of IBD. Inflammation of the colonic mucosa.	Any part of the inner most lining of the colon	Bloody diarrhoea, weight loss.	Vincomycin, Metronidazole.	Kathleen, 2003.
3.	Inflammatory bowel disease	It implicates relations amid the host liability, mucosal immunity and intestinal microflora.	Distal ileum, proximal regions of the colon	Abdominal pain, vomiting, diarrhoea	Sulfasalazine, 5-ASA, Budesonide.	Friend, 2005, Rolhion *et al.*, 2007,
4.	Diarrhoea	The loss of fluids through diarrhea cause dehydration and electrolyte imbalance.	Affects some share of the GIT, from mouth to anus	Frequently watery, loose bowel movements	Prednisolone, Aspirin, Omeprazole	Spreux *et al.*, 1993, Chassny *et al.*, 2000
5.	Colon cancer	Genetic modifications remain allied through progression after premalignant lesion (adenoma) towards invasive adenocarcinoma	Small intestine, colon	GIT bleeding, digestive complication,anaemia	5-fluorouracil, Irinotecan	Kelly *et al.*, 1996, Banoob *et al.*, 2002, Sibilia *et al.*, 2003

Colon cancer

The majority of colon cancers develop from pre-existing colonic adenomas. These include the tumors of the islet's cells and Bruner's glands as well as polyploid adenomas. They develop slowly in the colon over a period of many years. Slow movements of bowel matters might consequence in adaptation of indefinite ingredients extant to carcinogenic agents.[3]

The tumor developed may be

1. A soft polypoid form, protrusive into lumen of the colon through a penchant to ulceration, contagion and haemorrhage.
2. A rigid fibrous frame enclosing the colon, initiating compact pliability and peristaltic, constricting of the lumen and impediment.

Predominance of colon malignancy in the Asian nations has improved in last little years. Elizabeth *et al.* (2009) described the statistically substantial upsurge in the prevalence of colorectal malignancy rates for both males and females from 1983-87 to 1998-2002 in emerging nations of Asia and designated nations of Europe and South America. These surges remained initiate towards remain further noticeable in men as associated towards women.[4]

2. Site Specific Delivery of Drugs To The Colon

Site specific delivery of drugs to the ailment site i.e. the colon remains probable towards diminish their side properties and towards surge the pharmacologic response.[5], [6–9] For precise discharge method, oral course of management remains the first prime since the physiology of our GIT permits us towards proposal further diverse dose forms as linked towards the further means. Furthermore, oral course remains the utmost adaptable and frequently engaged route for systemic achievement, owing towards its simplicity of management, patient amenability and elasticity in preparation. Consequently, it performs such colon besieged medicines through an applicable discharge design could remain precise expedient in providing active healing for colonic ailments.[10]

To decrease the side effects and upsurge the ability, innumerable methods have stood practiced for targeting the medications towards the colon. These embrace development of prodrugs[11], time-dependent distribution organizations[12], coating through pH-sensitive polymers.[13–15]

Nevertheless, as a site for medication distribution, the colon proposals an adjacent inert pH, compact intestinal enzyme action and an extended transit period. The side-effects of medications remain curtailed through exploiting their resident attentions at the target location. Nevertheless, the targeting of the medications towards the colon remains precise intricate since:

1. Colon remains located at the distal portion of the alimentary canal and remains, therefore, demanding towards entrance.[11,16]
2. In GIT, altered enzymes and an extensive sort of pH values remain extant. When dose method remains assumed, it has towards portable over these pH sort and enzymes, formerly attainment the target site, auxiliary obscuring the consistency and delivery efficacy.[17]

Numerous approaches remain obtainable to aim the discharge of medications in colon. Distribution methods for targeted distribution towards the colon can remain considered into four classes

1. Time-based colonic drug delivery.
2. pH dependent colonic drug delivery
3. Prodrugs approach for colonic drug delivery.
4. Polysaccharides based colonic drug delivery.

Time-based colonic drug delivery

This method remains centered on the source of deferring the issue of medication till it arrives into the colon. Therefore, it is also called time dependent delivery system. The residence period in the colon (> 24 h) enables the fascination of medications from this extent.[18] The transit period in the small intestine is almost 3-5 h. It has stood initiate such together single unit preparations and small multi-unit preparations proceeds three to four hours towards permit over the small intestine.[19] However, the arrival period of designs addicted to the colon is not predictable owing towards the prodigious distinction of transit time in the stomach. The strategy to design the timed release system remains towards resist the acidic environs of the stomach and allow the discharge of medication at specific site at predetermined lag time and rate. These formulations are solid dose systems coated by hydrophobic surfactant film to such water-soluble polymer remains auxiliary to expand the linkage of the core. The outer film redisperses in aqueous environs in a time proportionate towards the width of the film and the core remains offered for dispersal.[20] After the gastric

emptying, the medication distribution system discharges the medication subsequently a predetermined lag time.

pH dependent colonic drug delivery

Practice of pH-dependent polymer remains centered on the variance in pH stages laterally the GIT. The polymer designated as pH-dependent in colon explicit distribution remain insoluble at low pH levels nevertheless develop progressively soluble as pH upsurges.[21] This can be utilized in manipulating the release of drug from the delivery system at various sites in the GIT. For the development of pH based colonic formulations, enteric polymers are used. These remain insoluble in the substances of stomach and avert medication dissolution till the preparation permits into the small intestine. The polymer used in the formulation depend on the chemical configuration and liquefy for instance the pH upsurges from 5 to 7 subsequent gastric emptying.[20] Preparations centered on pH-responsive polymer need stood probed in edict towards aim the colon.[22]

Prodrugs approach for colonic drug delivery

A prodrug remains a pharmacological constituent (medication) such remains directed in an inactive (or considerably less active) method. Formerly overseen, the prodrug remains processed *in vivo* into an active metabolite. For aiming medications towards the colon, medication remains towards remain endangered from the inimical environs of the stomach and small intestine. This defense in the upper GIT remains precious through conjugation through importer moieties, developing prodrugs. These prodrugs endure enzymatic cleaving in the colon and reinforce the medication. A effective prodrug-based distribution organization remains unique in such the promoiety curtails absorption till the active constituent remains unconstrained proximate the target location.[23] However, the side effects can remain curtailed by exploiting local medication deliberations at the target site.

Polysaccharides based colonic drug delivery

Polysaccharides remain polymers of monosaccharides (sugars). They remain originate in environment in profusion, have varied obtainability, remain economical and obtainable in a diversity of structures through a variability of possessions.[24] The practice of naturally happening polysaccharides for colon targeted medication distribution remains chosen owing to the subsequent details[25]:

1. They can remain certainly amended chemically and biochemically.
2. They remain vastly stable.

3. They are safe.
4. They are nontoxic.
5. They are hydrophilic.
6. They are gel forming.
7. They are biodegradable.

These natural polysaccharides can be from algal source (alginates), plant source (pectin, guar gum), microbial source (dextran, xanthan gum) and animal origin (chitosan, chondroitin). If they deed for instance substrata towards the bacterial residents of the colon, they can be used for colon targeting. Owning to their proven safety profiles, they are included in the category of generally regarded as safe (GRAS) substances.[26] In colon, a large number of microflora are present, which fulfill their vitality desires by fermenting several sorts of carriers such have stood gone undigested in the small intestine like many di- and tri-saccharides, polysaccharides etc. Intended towards the ferment of aforesaid polysaccharides, the microflora of the GIT produce an immense sum of enzyme certainly β-xylosidese, α-arabinosidese, β-galactosidese, nitroreductase, azoreductese and urea dehyroxylse.[27] Due to the incidence of this microflora solitary in the colon, the practice of these biodegradable polymers for colon-targeted medication distribution appears to remain further site-specific as related towards further methodologies. These polymers guard the medication after the environs of stomach and small intestine, and stand capable to distribute the medication towards colon. Proceeding accomplishment the colon, such endure adaptation through micro-organisms or deprivation through enzymes, prominent towards an ensuing lessening in their molecular weight and thus defeat of powered forte. They remain then impotent to clench the medication article every extended and discharge the medication in colon.[28]

CONCLUSION

The colonic expanse of the GIT has developed a progressively imperative locate for medication distribution and absorption. CDDS compromises substantial beneficial profits to patients in relations of together local and systemic management. Colon specificity remains further probable towards be accomplished through systems such employ expected constituents such remain degraded by colonic bacterial enzymes. Amended medication delivery methods remain vital for medications presently in practice to delight confined ailments of the colon. The benefits of aiming medications precisely to the unhealthy colon

remain abridged frequency of systemic sideways properties, subordinate quantity of medication.

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