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AN INSIGHT OF DRUG TARGETING TO COLON

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Abstract:

Step by step there are new advancements in field of colon explicit medication conveyance framework. Colonic drug delivery systems have expanded significance not only for the delivery of the medications for the treatment of diseases related with the colon like Crohn's disease, ulcerative colitis, and so forth. Yet additionally for the foundational delivery of proteins, helpful peptides, hostile to asthmatic medications, antihypertensive medications and hostile to diabetic specialists. New frameworks and advances have been created for colon focusing on and to beat pervious technique's constraints. Colon focusing on holds an incredible potential and still need increasingly imaginative work. This article talks about, to sum things up, introduction of colon, factor affecting colonic change, colonic ailments and the novel and rising advancements for colon focusing on.

Keywords: colon drug delivery, Crohn’s disease, inflammatory Bowel disease, Drug targeting

Introduction

Administration of drug via oral route is the most convenient and important method of administering drugs for systemic effect. Almost half of the drug delivery systems available in the market are oral drug delivery system and these systems have greater advantages in the form of patient acceptance and ease of administration [1, 2].

Drug targeting at the specific site gains importance since last decade and the study also extends to target

the drug at colon. Colonic drug delivery has earned extension in the significance not just for the delivery of the drugs for the treatment of local diseases associated with the colon like crohn's disease, ulcerative colitis, irritable bowel syndrome and constipation and also for the systemic delivery of proteins, therapeutic peptides, antiasthmatic drugs, antihypertensive drugs and antidiabetic agents[3, 4].

There are different strategies or methods through which colon tranquilize focusing on can be accomplished, for instance, arrangement of prodrug, covering with pH-delicate polymers, covering with bio-degradable polymers, structuring definitions utilizing polysaccharides, coordinated discharged frameworks, weight controlled medication conveyance frameworks, osmotic weight controlled frameworks[5, 6].

Covering of the medications with pH-touchy polymers gives basic way to deal with colon-explicit medication conveyance.

Advantages of colon targeting drug delivery system [7 – 9]

- Colon is an ideal site for the delivery of agents to cure the local diseases of the colon.
- Local treatment has the advantage of requiring smaller drug quantities.
- Reduces dosage frequency. Hence, lower cost of expensive drugs.
- Possibly leading to a reduced incidence of side effects and drug interactions.
- The colon is an attractive site where poorly absorbed drug molecules may have an improved bioavailability.
- Reduce gastric irritation caused by many drugs (e.g. NSAIDS).
- Bye pass initial first pass metabolism.
- Extended daytime or nighttime activity.
- Improve patient compliance.
- Targeted drug delivery system.
- It has a longer retention time and appears highly responsive to agents that enhance the absorption of poorly absorbed drugs [10].

It has low hostile environment, less peptidase activity so peptides, oral vaccines, insulin, growth hormones, can be given through this route [11].

Limitations of colon targeting drug delivery system

- Multiple manufacturing steps.
- The resident microflora could also affect co- lonic performance via metabolic degradation of the drug.
- Incomplete release of drug.
- Bioavailability of drug may be low due to potentially binding of drug in a nonspecific way to dietary residues, intestinal secretions, mu- cus or faecal matter.
- Drug should be in solution form before absorption and there for rate limiting step for poor soluble drugs.
- Non availability of an appropriate dissolution testing method to evaluate the dosage form in-vitro [12.]
- An important limitation of the pH sensitive coating technique is the uncertainty of the lo- cation and environment in which the coating may start to dissolve. Normal in patients with ulcerative colitis [13, 14].
- Limitations of prodrug approach is that it is not very versatile approach as it's formulation depends upon the functional group available on the drug moiety for chemical linkage. Furthermore prodrugs are new chemical entities and need a lot of evaluation before being used as carriers [15].

Anatomy and Physiology of Colon

Structure of Colon

Colon is the lower some portion of the gastrointestinal tract and keeps running from ileocecal intersection to the rear-end. It incorporates proximal part (climbing colon), transverse colon, sliding colon, sigmoid colon, rectum and butt (Figure 1). Interestingly with small digestive tract surface zone of colon is low yet powerful retention happen because of essence of villi, microvilli and long living arrangement time. The colon is round and hollow cylinder which is lined by soggy, delicate pink coating called mucosa and it is 2 – 3 creeps in breadth.

The colon and rectum have an anatomic blood supply. Lymph hubs are additionally present with veins. Action in the colon can be partitioned into sectioning and propulsive developments. Fragmenting developments, brought about by round muscle and causing the presence of the sac like haustra, pre-overwhelm and bring about blending of the luminal substance. Critical propulsive movement, related with defecation and affected by longitudinal muscle is less normal and happens at a normal of three or multiple times day by day [16].

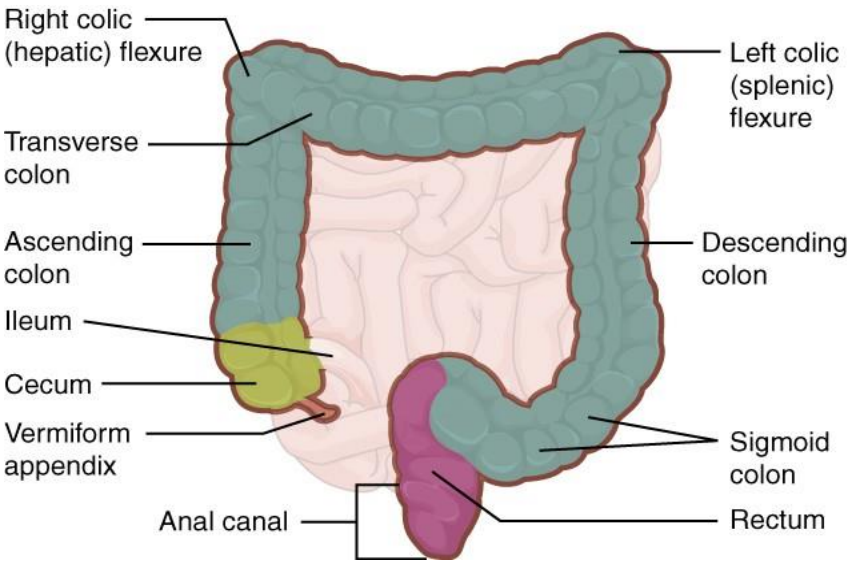


Fig 1: Structure of Colon.

Colonic Microflora

The moderate development of material through the colon enables an expansive microbial populace to develop there. More than 400 unmistakable bacterial species have been found. The vast majority of these secluded microorganisms are anaerobic in nature. Few parasites are likewise present. The main wellspring of nourishment for the colonic microorganisms is sugars touching base in intestinal toll. The carbocarbohydrates are corrupted by the activity of polysaccharidase and glycosidase catalysts and definitive results of aging are short chain unsaturated fats, sugar maturation prevails and results in a generally low pH. In the distal locales, there is little sugar aging, bringing about a higher pH. The microorganisms inside the colon are overwhelmingly anaerobic and are of low redox potential. Following table gives summery of colonic microorganism following up on the some part (Table 1).

Table-1: Effect of colonic microflora on the some component.

S.No.	Component	Converted to
1	Carbohydarate	CO2, organic acid
2	Cellulose	Carbonic acid, methane
3	Fat	Lower fatty acid and glycerol
4	Choline	Neurine
5	Protein	Amino acid, ammonia
6	Tryptophan	Indole, skatole (bad order of feaces)
7	Tyrosine	Tyramine
8	Histidine	Histamine
9	Arginine	Putrescine
10	Lysine	Codaverine

Functions of Colon

1. Suitable site and environment for the growth of colonic microorganism.

a.These bacteria are very rich in cytochrome. The normal flora of the large intestine prevents the growth of other pathogenic bacteria and serves a useful purpose.

b.Some bacteria can breakdown cellulose.It has been concluded that people suffering from constipation can breakdown cellulose more than normal ones, thus reducing the bulk [17].

2. Formation of stool and storage reservoir of facial contents.

3. Absorption of potassium and water from lumen resulting in formation of facial content. Saline, glucose, some anesthetics, amino acid are better absorbed here.

4. Secretion and excretion of potassium and bicarbonate, bismuth, mercury, arsenic, etc.

5. Synthesis function: microorganism in colon synthesizes vitamin k, folic acid. Large amount of vitamin B12 are also synthesis by these microorganism but are not absorbed.[18]

Adsorption of Drugs from the Colon

Drugs are ingested latently by paracellular or transcellular courses. Transcellular ingestion includes he entry of medications through cells and this is the course most lipophilic medications takes, though paracellular assimilation includes the vehicle of sedate through the tight intersections among cells and is the course most hydrophilic medication takes. The poor paracellular assimilation of numerous medications in the colon is seen because of the way that epithelial cell intersections are exceptionally tight. The moderate rate if travel in colon gives the medication a chance to remain in contact with the mucosa for a more drawn out period than in small digestive system which remunerates the much lower surface region. The colonic substance ends up being progressively thick with dynamic maintenance of water as one endeavors further through colon. This causes a diminished breaking down rate, moderate spread of split up prescription through the mucosa.[19,20]

pH of different sections of Gastrointestinal Region

In the stomach pH goes some place in the scope of 1 and 2 in the midst of fasting anyway increase in the wake of eating. From the ileum to the colon pH diminishes basically. It is about 6.4 in the caecum . (Table 2). Travel time under Normal conditions using a radiopaque marker strategy, the movement times in a social occasion of 73 strong adults has been assessed. The mean mouth-to-backside travel time was 53.3 hr. Result is ordered in table no.3. The surface zone of the colon for maintenance is more diminutive than that of the little stomach related tract, and this is reimbursed by the moderate travel time [21,22] (Tables 3, 4).

Table-2: pH of various regions in gastrointestinal Tract.

S.No.	Main Part	Sub Part	pH
1	Stomach		1-2
2	Small intestine	Proximal small intestine	6.5
		Distal small intestine	7.5
3	Large intestine	Ascending (proximal) colon	5.7
		Transverse colon	6.6
		Descending colon	7.0

Factor Effecting Colonic Transit

There are different elements which influences the colonic travel. These incorporate eating routine, versatility, stress and ailment state. Dietary fiber impacts enormously the colonic motility. Dietary fiber increments fecal weight, halfway by maintenance of water and somewhat by expanding bacterial mass and lessens colonic travel times. For instance, expansion of 20 g/day of grain to the eating routine of gathering of sound subjects expanded stool weight by 127% and diminished entire gut travel by 73 to 24 to 43 to 7 h. [23].

Table-3: Transit time in gastrointestinal tract under normal conditions.

S.No.	Main Part	Sub Part	Transit time (Hrs.)
1	Stomach		1-2
	Small intestine		3-4
3	Large intestine	Right (ascending + portion of transverse)	11.3
		Left (descending + portion of transverse)	11.4
		Rectosigmoid colon	12.4

Table-4: Length of various parts of large intestine.

Part	Length (cm)
Cecum	6 – 7
Ascending colon	20
Transverse colon	45
Descending colon	30
Sigmoid colon	40
Rectum	12
Anal canal	3

Colonic Diseases [24]

Angiodysplasia

frequently in the cecum or right colon, ordinarily after the age of 60. They are inclined to break and seep into lumen. Such sore record for 20% of critical lower intestinal beading. Angiodysplasia is a little vascular deformity of the gut. It is a typical reason for generally unexplained gastrointestinal dying furthermore, pallor. Sores are regularly different, and as often as possible include the cecum or rising colon, in spite of the fact that they can happen at different spots. Treatment might be with endoscopic intercessions, drug, or sometimes medical procedure. Analysis of angiodysplasia is regularly practiced with endoscopy, either colonoscopy or esophagogastroduodenoscopy (EGD) [25].

Inflammatory Bowel Disease

Crohn's disease may influence any segment of the gastrointestinal tract from throat to rear-end yet frequently includes the ileum. The reason for provocative inside illness is multi-factorial and it is because of the fiery reactions, anomalous neighborhood invulnerable reaction against the ordinary verdure of the gut, hereditary factors, for example, numerous hereditary variables, hopeful qualities, chromosome area, irresistible specialists like Escherichia coli, Measles infection, Cytomegalovirus, and so forth., dietary factors, for example, immersed fats, milk items, unfavorably susceptible sustenances and so on. Crohn's sickness and ulceration colitis are incessant backsliding aggravation issue of obscure inception, all in all known as idiopathic fiery gut malady (IBD).

The primary medications utilized in the treatment of ulcerative colitis and Crohn's illness are the amino salicylates and corticosteroids . These ailments and other provocative entrail infection have been connected with an expanded danger of colorectal malignant growth.[26]

Ulcerative colitis

Ulcerative colitis happens just in the internal organ. Ulcers structure in the internal coating of the digestive tract, or mucosa, of the colon or rectum, regularly bringing about looseness of the bowels, blood, and discharge. The aggravation is normally thorough in the sigmoid and rectum and as a rule diminishes in the colon.

Crohn's Disease

Crohn's illness, likewise called territorial enteritis, is a ceaseless irritation of the digestion tracts which is generally bound to the terminal part of the small digestive system, the ileum. (Table 5).

Colorectal cancer

Expansive inside malignancy incorporates carcinogenic developments in the colon, rectum and addendum. 98% of all cancers in the internal organ are adenocarcinomas. A few examinations proposed that utilization of headache medicine and different NSAIDs have a defensive impact against colon malignant growth. Colorectal diseases emerge from adenomatous polyps in the colon. These mushroom-formed developments are normally benevolent, yet some form into malignancy after some time. Confined colon malignant growth is normally analyzed through colonoscopy. Intrusive malignant growths that are bound to the mass of the colon (TNM stages I and II) are reparable with medical procedure. On the off chance that untreated, they spread to territorial lymph hubs (arrange III), where up to 73% are treatable by medical procedure and chemotherapy. Malignancy that metastasizes to removed destinations (organize IV) is generally not treatable, in spite of the fact that chemotherapy can broaden survival, and in uncommon cases, medical procedure and chemotherapy together have overseen patients to a fix. Radiation is utilized with rectal malignant growth [27,28].

Drugs used in colon cancer [29]

1) 5-fluorouracil;

2) 9-aminocamptothecin;

3) Capecitabine;

4) Cetuximab;

5) Trinotecan;

6) Levamisole hydrochloride;

7) Oxaliplatin;

8) Trimetrexate;

9) UFT (ftorafur and uracil);

10) Bevacizumab;

11) Cisplatin.

Constipation

Clogging (otherwise called costiveness, dyschezia, and dyssynergic defaecation) alludes to solid discharges that are rare and difficult to pass. Stoppage is a typical reason for excruciating poo. Extreme blockage incorporates obstipation and fecal impaction. Medicines incorporate changes in dietary propensities, intestinal medicines, bowel purges, biofeedback, and medical procedure. Since obstruction is a manifestation, not an infection, powerful treatment of clogging may require first deciding the reason [30].

Diarrhea

Looseness of the bowels is the state of having at least three free or fluid solid discharges every day. The loss of liquids through loose bowels can cause drying out and electrolyte awkward nature. Incendiary looseness of the bowels happens when there is harm to the mucosal covering or brush outskirt, which prompts an aloof loss of protein-rich liquids, and a diminished capacity to ingest these lost liquids. Highlights of each of the three of different sorts of loose bowels can be found in this kind of looseness of the bowels. It very well may be brought about by bacterial contaminations, viral diseases, parasitic diseases, or immune system issues, for example, incendiary gut illnesses. It can likewise be brought about by tuberculosis, colon malignancy, and enteritis [31].

Diverticulitis and Diverticulosis

A diverticulum is a visually impaired pocket that speaks with the lumen of the gut. Congential diverticula have every one of the three layers of the entrail divider and are particularly extraordinary. Procured diverticula may happen anyplace in the nutritious tract, yet by a long shot the most well-known area in the colon. Diverticulitis results if diverticula ends up excited. An underlying scene of intense diverticulitis is normally treated with gut rest (i.e., nothing by mouth), IV liquid revival, and expansive range anti-infection agents which spread anaerobic microscopic organisms and gram-negative bars. In any case, repeating intense assaults or entanglements, for example, peritonitis, ulcer, or fistula may require medical procedure, either quickly or on an elective premise [32].

Hirschsprung's disease (Aganglionosis)

Hirschsprung malady results while, amid advancement, the movement of nonpartisan peak determined cells along the nutritious tract captures at some print before achieving the butt. The basic sore in hirschspring malady is the absence of ganglion cells, and of ganglia, in the muscle divider and submucosa of the influenced portion [33]. Hirschsprung's Disease is an uncommon intrinsic (present at birth) variation from the norm that outcomes in obstacle in light of the fact that the digestive organs don't work ordinarily. It is regularly found in guys. It is generally found in Down disorder kids. It very well may be dangerous or a ceaseless issue. In an infant, the central signs and side effects are inability to pass a meconium stool inside 24 – 48 hours after birth, hesitance to eat, bile-recolored (green) regurgitating, and stomach distension. Amid early stages the kid experiences issues putting on weight, blockage, stomach distension, scenes of looseness of the bowels and retching. Unstable watery the runs, fever and weariness are indications of enterocolitis (aggravation of the colon) and are viewed as genuine and hazardous. On the off chance that these side effects happen, inform your kid's specialist right away. In more established youngsters, manifestations become perpetual and incorporate obstruction, entry of lace like, noxious stools, stomach distension and unmistakable peristalsis (wave-like development of the digestive organs). The more seasoned tyke is generally ineffectively supported and sickly [34].

Table-5: Advertised medication items for the treatment of different ailments of colon.

S. No.	Marketed name	Company name	Disease	Drug
1	Mesacol tablet	Sun pharma, India	Ulcerative colitis	Mesalamine
2	Mesacol enema	Sun pharma, India	Ulcerative colitis	Mesalamine
3	Asacol	Win-medicare, India	Ulcerative colitis, crohn's disease	Mesalamine
4	SAZO	Wallace, India	Ulcerative colitis, crohn's disease	Sulphasalazine
5	Intazide	Intas, India	Ulcerative colitis	Balsalazide
6	Lomotil	RPG Life, India	Mild ulcerative	Diphenoxylate

			colitis	hcl, atropine sulphate
7	BUSCOPAN	German Remedies, India	Colonic motility disorder	Hyoscine butylbromide
8	COLOSPA	Solvay, India	Irritable colon syndrome	Mebeverine
9	CYCLOMINOL	Neol, India	Irritable colon syndrome	Diclomine
10	Entofoam	Cipla, India	Ulcerative colitis	Hydrocortisone acetate

Ileus

It is characterized as intestinal obstacle. Ileus is an interruption of the ordinary propulsive gastrointestinal engine movement due to non-mechanical causes. Interestingly, motility issue that outcome from basic variations from the norm are named mechanical gut block. Ileus is of three kinds, i.e., Postoperative Ileus, Paralytic Ileus and Acute colonic pseudoobstruction [35].

Intussusception

An intussusception is an ailment in which a piece of the digestive tract has invaginated into another segment of digestive system, like the manner by which the pieces of a collapsible telescope slide into each other. The extended portion is known as the intussusceptum and lower accepting fragment is known as the intussuscipiens. This can frequently result in an impediment. The part that prolapses into the other is known as the intussusceptum, and the part that gets it is known as the intussuscipiens. The condition is most regular in newborn children and kids. The condition isn't typically quickly hazardous. The intussusception can be treated with either barium or water-dissolvable difference purification or an air-differentiate douche, which both affirms the analysis of intussusceptions and much of the time effectively decreases it. The achievement rate is over 80%. Be that as it may, roughly 5 – 10% of these repeat inside 24 hrs [36,37].

Irritable bowel syndrome

Irritable bowel syndrome (IBS) or spastic colon is a finding of prohibition. It is a practical gut issue portrayed by ceaseless stomach torment, distress, swelling, and change of gut propensities without any perceptible natural reason. IBS may start after a contamination, or an unpleasant life occasion. In spite of the fact that there is no solution for IBS, there are medicines that endeavor to mitigate side effects, including dietary alterations, drug and mental mediations.

Understanding instruction and a decent specialist persistent relationship are additionally significant. A few conditions may present as IBS including celiac ailment, Fructose malabsorption, mellow contaminations, parasitic diseases like giardiasis, a few incendiary gut illnesses, useful interminable obstruction, and ceaseless utilitarian stomach torment. In IBS, routine clinical tests yield no variations from the norm, however the guts might be progressively touchy to specific upgrades, for example, swell insufflation testing. The precise reason for IBS is obscure.

The most widely recognized hypothesis is that IBS is a turmoil of the connection between the mind and the gastrointestinal tract, in spite of the fact that there may likewise be variations from the norm in the gut greenery or the insusceptible framework [38].

Pseudomembranous colitis

Pseudomembranous colitis, otherwise called anti-microbial related loose bowels (AAD), is a contamination of the colon. It is regularly, however not generally, brought about by the bacterium Clostridium difficile. The sickness is described by hostile smelling looseness of the bowels, fever, and stomach torment. In serious cases, perilous inconveniences can grow, for example, dangerous uber colon [39].

Haemorrhoids

Hemorrhoids or heaps are the varicosities of the haemorrhoidal veins. They are regular injuries in older and pregnant ladies. They ordinarily result from expanded venous weight. The potential causes incorporate entryway hypertension, endless clogging and enduring stool, heart disappointment, venous stasis of pregnancy, genetic inclination, tumors of the rectum.

Polymers for Colon Targeting:

Polymers are macromolecules having very large chains contain a variety of functional groups, can be blended with low and high molecular weight materials. Polymers are becoming increasingly important in the field of drug delivery. Advances in polymer science have led to the development of several novel drug delivery systems. Use of polymeric material in novel drug delivery approaches has attracted the scientists.

Biodegradable Polymers:

Biodegradation is a natural process by which organic chemicals in the environment are converted to simpler compounds, mineralized and redistributed through elemental cycles such as carbon, nitrogenand sulphur cycles. Biodegradable polymers have been widely used in biomedical applications because of their known biocompatibility and biodegradability. Biodegradable polymers are intended for temporary aids, such as sutures, tissue-supporting scaffolds, and drug delivery devices[40].

Polymers within this group retain their properties for a limited period of time and then gradually degrade into soluble molecules that can be excreted from the body[41].

Biodegradable polymers are preferred for drug delivery applications, since the need for surgical removal of the depleted device is eliminated. Although the number of biodegradable polymers is large, only a limited number of polymers are suitable for drug delivery applications. Suitable candidates must not only be biodegradable but also fit the high prerequisites of biocompatibility.

In addition, a polymer should ideally offer process ability, sterilizability, and storage stability if it is to be useful for biomedical applications[42]. The greatest advantage of degradable polymers is that they are broken down into biologically acceptable molecules that are metabolized and removed from the body via normal metabolic pathways.

However, biodegradable materials do produce degradation by products that must be tolerated with little or no adverse reactions within the biological environment. These degradation products both desirable and potentially non desirable must be tested thoroughly, since there are a number of factors that will affect the biodegradation of the original materials.

Table-6: List of biodegradable polymers used in drug delivery.

Natural Polymers	Synthetic Polymers
Pectin	Eudragit L100
Chitosan	Eudragit S100
Guar Gum	Eudragit L30D
Chondroitin Sulfate	Eudragit RS 30D
Dextran	Eudragit L100-55
Cyclodextrin	Poly Vinyl Acetate Phthalate
Inulin	Hydroxy Propyl ethyl cellulose Phthalate 50
Xantahn Gum	Hydroxy Propyl ethyl cellulose Phthalate 55
Amylose	Cellulose Acetate phthalate
Locust Bean Gum	
Alginates	
Shellac	

Natural Polymers

Natural polysaccharides are extensively used for the development of solid oral dosage forms for colonic delivery of drugs[43]. Biodegradable polymers aregenerally hydrophilic in nature and have limited swelling characteristic in acidic pH. Various bacteria present in the colon secretes many enzymes which can cause hydrolytic cleavage of glycosidic bonds e.g. C-D-galactosidase, amylase, pectinase, C-Dglucosidase, dextranase, D-D-xylosidase.

These polymers are inexpensive and are available in a variety of structures. Pectin, starch, guar gum, amylase and karaya gum are a few polysaccharides commonly used in dosage forms. Linear polysaccharides remains intact in stomach and small intestine but the bacteria of human colon degrades them and thus make them potentially useful in colon targeted drug delivery systems[44].

Pectin:

Pectins are nonstarch linear, heterogeneous polysaccharides that consist of D-1, 4 D-galacturonic acid and 1, 2 D-rhamnose with D-galactose and Darabinose side chains. It is refractory to host gastric and small intestinal enzymes but is almost completely degraded by the colonic bacterial enzymes to produce a series of soluble oligalactorunates[45,46]. Pectins are soluble in pure water. Monovalent cations (alkali metal) salt of pectinic and pectic acids are soluble in water; di- and tri-valent cations salts are weakly soluble or insoluble. If used alone it swells, when it comes in contact with aqueous fluids of GI tract and causes the release of entrapped drug through diffusion mechanism. Pectin has been used in the pharmaceutical industry for a wide range of applications. Spray drying method has been employed to prepare pectin microspheres for oral colon delivery of indomethacin[47]. The prepared microspheres were cross linked with calcium chloride. The release of Indomethacin from the cross linked pectin microspheres was more suppressed than its release from non-cross linked microspheres. Drug release from pectin microspheres was increased by the addition of pectinase. Release of indomethacin from pectin microsphere was less in acidic pH while it was stimulated at neutral pH (pH 7.4). The resultsof the study clearly demonstrated that pectin microspheres prepared by spray drying and cross linking methods are potential carriers for colonspecific drug delivery.

Chitosan:

Chitosan is a high molecular weight polycationic polysaccharide derived from chitin by alkaline deacetylation. Chitosan is consisting of the repeated units of (2-amino-2-deoxy-D-gluco-pyranose) which are linked by (1-4) C-bonds[48,49]. Chitosan is a nontoxic, biodegradable, biocompatible and bioactive polymer. It is used for the colon targeted drug delivery because it has a tendency to dissolve in acidic pH of stomach but get swollen in the intestinal pH. Chitosan capsules were used for colonic delivery of an antiulcerative colitis drug. 5-Aminosalicylic acid (5-ASA) was used as model drug. A marked increase in the release of drug from chitosan capsule was observed in the presence of the rat cecal content. From the results of this study it was concluded thatchitosan capsules could be an effective carrier for the colon targeted delivery of anti-inflammatory drugs[50]. A chitosan dispersed system was newly developed for colon-specific drug delivery which was composed of

drug reservoir and the outer drug release-regulating layer dispersing chitosan powder in hydrophobic polymer. It was observed that the thickness of the outer layer controls the drug release rate. Since the dispersed chitosan dissolves easily under acidic conditions, an additional outer enteric coating was also provided to prevent the release of drug from chitosan dispersed system in the stomach[51]. Chitosan is used to provide controlled release of many drugs and to improve the bioavailability of degradable substances such as protein, as well as to improve the uptake of hydrophilic substances across the epithelial layers.

Guar gum:

Guar gum is a polysaccharide composed of the sugars galactose and mannose. The backbone is a linear chain of C 1, 4-linked mannose residues to which galactose residues are 1, 6-linked at every second mannose, forming short side-branches[52]. Guar gum is used in colon targeted drug delivery systems due to its drug release retarding property and susceptibility to microbial degradation in large intestine. Guar gum has a gelling property which retards the release of drug from the dosage form, making it more likely that degradation will occur in the colon. Guar gum was found to be a colon-specific drug carrier in the form of matrix and compressioncoated tablets as well as microspheres[53].

Guar gum-based matrix tablets of rofecoxib were prepared for their intended use in the chemoprevention of colorectal cancer[54]. A colonspecific guar gum–based tablet of 5-FU has also been reported[55]. Krishnaiah *et al* in their study performed the pharmacokinetic evaluation of guar gum-based colon-targeted tablets of mebendazole against an immediate release tablet in six healthy humanvolunteers. Colon-targeted tablets showed delayed tmax (9.4±1.7 h) and absorption time, and decreased Cmax (25.7±2.6 μg/ml) and absorption rate constant when compared to the immediate release tablets. The results of the study indicated that the guar gumbased colon-targeted tablets of mebendazole delivered the drug to the colon resulting in a slow absorption of the drug and making the drug available for local action in the colon[56].

Chondroitin Sulfate:

Chondroitin sulfate is a soluble mucopolysaccharide that is used as a substrate mainly by *B. thetaiotaomicron* and *B. ovatus* species in large intestine. Chondroitin sulfate is highly water soluble and this property act as a

barrier in the formulation of the colon targeted drug delivery. Rubistein *et al*. cross-linked Chondroitin sulfate and formulated a matrix form with indomethacin as a drug marker. Results of the study revealed that drug targeting to the colon may be achieved by varying the amount of cross linked Chondroitin sulfate in formulations[57]. Amrutkar *et al*. have prepared matrix tablet for colon specific delivery of indomethacin using Chondroitin sulfate and chitosan as carrier and binder. Chondroitin sulfate was used to form polyelectrolyte complexes (PEC) with chitosan, and its potential as a colon-targeted drug carrier was investigated. The study confirmed that selective delivery of drug to the colon[58]. Cavalcanti *et al*. characterized cross linked Chondroitin sulfate for specific drug delivery to colon. Chondroitin sulfate was cross linked with trisodium trimetaphosphate to reduce its hydro solubility[59].

Dextran:

Dextran is a polysaccharide consisting of D-1, 6 Dglucose and side chain of D-1, 3 D-glucose units. Dextran is a water soluble polymer. It gets degraded by microbial enzyme dextranases which is found in colon[60]. In pharmaceutics, dextran has been used as model of drug delivery due to its unique characteristics like water solubility, biocompatibility, and biodegradability. In recent studies, dextran has been regarded as a potential polysaccharide polymer that can sustain the delivery of proteins, vaccines, and drugs. Injectable and degradable dextran-based systems for drug delivery were generated by a crosslinking reaction with photo-polymerization or free radical polymerization. McLeod *et al*. synthesized glucocorticoid dextran conjugates in which dexamethasone and methylprednisolone were attached to dextran using dicarboxylic acid linkers (succinate and glutarate). Dextran conjugates resisted hydrolysis in upper GI tract contents but was rapidly degraded in cecal and colonic contents where the bacterial count is high. The results of this study indicate that dextran conjugates may be useful in selectively delivering glucocorticoids to large intestine for the treatment of colitis[61]. In a gene therapy study by Liptay and co-workers, it was reported that recombinant DNA (which contains chloramphenicol acetyltransferase) was successively encapsulated in cationic liposomes and then integrated within dextran. This system was reported to be a suitable delivery system since it could stop transfection efficiency within the colon epithelium wall *in- vivo.* Cyclodextrin: Cyclodextrin is a cyclic oligosaccharide

consisting of six to eight glucopyranose units joined by D-(1_4) glucosidic linkage. Cyclodextrins consist an internal lipophilic cavity, which can make complex with hydrocarbon materials. Cyclodextrins remains intact during their passage throughout the stomach and small intestine of the GI tract. However, in colon, they undergo fermentation in the presence of vast colonic microfloras into small monosaccharide and thus absorbed from these regions[62]. The *in vivo* drug release behaviour of these drug-cyclodextrin conjugates was investigated in rat. The results reveal that these conjugates were stable in stomach and in small intestine. The study suggested that Cyclodextrin can be used for colon specific delivery of drug[63].

Inulin:

Inulin is a naturally occurring glucofructan and consists of C 2-1 linked D-fructose molecule having a glycosul unit at the reducing end. It can resist the hydrolysis and digestion in the upper gastrointestinal tract. Inulin is not hydrolyzed by the endogenous secretions of human digestive tract[64]. However, bacteria harbouring in the colon and more specifically Bifidobacteria are able to ferment inulin. Vervoort *et al*, developed inulin hydrogels for colonic delivery of drugs and swelling property of these hydrogels was investigated[65]. In another study Vervoort and Rombaut, investigated the *in-vitro* enzymatic digestibility of the inulin hydrogels using an inulinase preparation derived from *Aspergillus niger*. It was concluded that the inulinase enzyme can diffuse into the hydrogels resulting in the degradation of the hydrogels[66].

Xanthan gum:

Xanthan gum is a high molecular weight extra cellular polysaccharide produced by the fermentation of the gram-negative bacterium *Xanthomonas campestris*. Xanthan is a free flowing powder soluble in both hot and cold water to give viscous solutions at low concentrations. It is a very effective thickener and stabilizer because it gives highly viscous solutions even at low concentrations as compared to other polysaccharide solutions. Xanthan gum solutions offer very good stability. They are least affected by changes in pH and are stable in both alkaline and acidic conditions[67]. Xanthan gum and hydroxypropyl methylcellulose were used as hydrophilic matrixing agents for preparing modified release tablets of diltiazem HCl. The amount of hydroxypropylmethylcellulose and xanthan gum exhibited significant effect on drugrelease from the tablets

prepared by direct compression technique. It was concluded that by using a suitable blend of hydroxypropylmethylcellulose and xanthan gum desired modified drug release could be achieved.

Amylose:

Amylose is unbranched linear polymer of glucopyranose units (D-1, 4-D-glucose) linked through D–D-(1-4) linkage. Amylose is resistant to pancreatic amylases but it gets degraded by the bacteroids, bifidobacterium[68]. Amylose can form film by gelation, which can be used for tablet coating purpose. But coating made up of amylose solely becomes porous and release the drug under simulated gastrointestinal conditions. To avoid this problem, water insoluble polymers are added to the amylose film as these water insoluble polymers control the amylose swelling. Addition of ethylcellulose to amylose gives a suitable polymer mixture for colon targeting. Cumming *et al*. used a mixture of amylase and ethocel (1:4) to prepare microspheres of [13C] glucose which was used as a surrogate for drug delivery. The results of the study revealed that combination of amylase and ethylcellulose can be used for coating of pellets which results in controlled release of contents for targeted delivery of drug to the large bowel during a period of 12–24 h[69].

Locust bean gum:

Locust bean gum contains natural polysaccharides which have a molecular weight of 310000. Locust bean gum is also known as 'Carob gum' as it is derived from the endosperm of the seed of the 'Carob' (*Ceratonia Siliqua Linne*, Fam: Leguminosae). It is irregular shaped molecule with branched C-1, 4- D-galactomannan units. This neutral polymer is only slightly soluble in cold water; it requires heat to achieve full hydration and maximum viscosity[70]. Studies on the polysaccharides done by Raghavan *et al*. proved that the combination of locust bean gum and chitosan, as a coating material, is capable of protecting the core tablet containing mesalazine during the condition mimicking mouth to colon transit. The coating was susceptible to the colonic bacterial enzymes which causes the release of drug. It was concluded that the formulation containing locust bean gum and chitosan in the ratio of 4:1 held a better dissolution profile, higher bioavailability and hence a potential carrier for drug targeting to colon[71].

Alginates:

Alginates are linear polymers that have 1-4'linked C- D-mannuronic acid and D-L-guluronic acid residue arranged as blocks of either type of unit or as a random distribution of each type. Alginate and their derivates have many unique properties such as biocompatibility, biodegradability, low toxicity, non-immunogenicity, water solubility, relatively low cost, gelling ability, stabilizing properties, and high viscosity in aqueous solutions[72]. A Eudragit L-30D–coated calcium alginates bead for colonic delivery of 5-aminosalicylic acid has been reported. Different enteric as well as sustained release polymers were applied as coat on calcium alginate beads.

Synthetic Polymers in Colon Targeting:

The polymers used for colon targeting, however, should be able to withstand the lower pH values of the stomach and of the proximal part of the small intestine and also be able to disintegrate at the neutral of slightly alkaline pH of the terminal ileum and preferably at the ileocecal junction. These processes distribute the drug throughout the large intestine and improve the potential of colon targeted delivery systems. There are various synthetic polymers which are use for colon targeted drug delivery. These can also be called as pH dependent polymers. The most commonly used pH dependent polymers are derivatives of acrylic acid and cellulose. For colonic drug delivery, drug core is coated with pH sensitive polymers. The drug are includes tablets, capsules, pellets, granules, micro-particles and nanoparticles[73]. The pH dependent in colon specific drug delivery are insoluble at low pH levels but become increasingly soluble as pH rises.

Table-7: List of synthetic/ pH dependent polymers[74].

Polymer	Threshold pH
Eudragit L100	6.0
Eudragit S100	7.0
Eudragit L30D	5.6
Eudragit RS 30D	6.8
Eudragit L100-55	5.5

Poly Vinyl Acetate Phthalate	4.5-4.8
Hydroxy Propyl ethyl cellulose Phthalate 50	5.2
Hydroxy Propyl ethyl cellulose Phthalate 55	5.4
Cellulose Acetate phthalate	5.0

Eudragit:

Eudragit products are pH-dependent methacrylic acid polymers containing carboxyl groups. The number of esterified carboxyl groups affects the pH level at which dissolution takes place. Eudragit are of three types: Eudragit L, Eudragit S, and Eudragit RS. Eudragit S is soluble above pH 7 and Eudragit L above pH 6. Eudragit S coatings protect well against drug liberation in the upper parts of the gastrointestinal tract and have been used in preparing colon-specific formulations. When sites of disintegration of Eudragit S-coated single-unit tablets were investigated using a gamma camera they were found to lie between the ileum and splenic flexure. Site specificity of Eudragit S formulations, both single- and multiple-unit, is usually poor. Eudragit S coatings have been used to target the anti-inflammatory drug 5-aminosalicylic acid (5-ASA) in single-unit formulations on the large intestine. Eudragit L coatings have been used in single-unit tablets to target 5-ASA on the colon in patients with ulcerative colitis or Crohn's disease[75]. The polypeptide hormone vasopressin and insulin have been administered to rats orally in Eudragit Scoated single-unit capsule. Eudragit S-coated insulin capsules have also been administered orally to hyperglycaemic beagle dogs. In the latter study it was concluded that plasma glucose levels were lowered gradually and reproducibly but that delivery by means of the oral route was not bioequivalent to delivery by means of parenteral route (SC). Eudragit S has been used in combination with another methacrylic acid copolymer, Eudragit L100-55, in colon-targeted systems to regulate drug delivery[76].

Shellac:

Shellac is the purified product of the natural resin lac which is the hardened secretion of the small, parasitic insect Kerria Lacca, popularly known as the lac insect. It is the only known commercial resin of animal origin. Shellac is a hard, brittle and resinous solid. It is practically odorless in the cold but evolves a characteristic smell on heating and melting. Shellac is water insoluble. Shellac coatings for food applications are commonly

applied from ethanolic solutions. Shellac is unsuitable for a conventional enteric coating it is of interest for colon targeting formulations[78]. The shellac coating layer remains intact during the passage of the stomach and the small intestine until it reaches the colon with its higher pH. This allows the transport of drugs into the colon for a topical treatment of colonic diseases. Moreover, the peptidase activity in the colon is lower than in the upper GI tract allowing for an oral delivery of peptide drugs such as insulin[79].

Methods Used For Drug Targeting to the Colon

Formation of prodrugs

(Example: azo-Prodrug, glucuronide conjugate, etc.)

Prodrug is characterized as a latent medication that winds up dynamic simply after it is changed or utilized by the body [80]. Covalent linkage is shaped among medication and bearer, which upon oral organization achieves colon without being consumed from upper piece of GIT. In the colon sedate discharge is activated by high action of specific catalysts in contrast with stomach and small digestive tract.

a) Azo bond conjugate: Sulfasalazine is chiefly utilized for the treatment of provocative bowl illnesses. It is 5-Amino Salicylic Acid (5-ASA) prodrug. 85% of oral portion of sulfasalazine compasses to the colon unabsorbed, where it is diminished by the anaerobic condition into 5-ASA what's more, sulphapyridine as appeared in Figure 2 [81]. Different investigations are led on sulphapyridine which lead to the development of other prodrug like Olsalazine, Balsalazine, 4-amino benzoyl-_-alanine [82]. Intestinal microflora produces glycosidase, one of unmistakable gathering of chemical. Colon explicit definition of flurbiprofen had been assessed by utilizing azo-sweet-smelling and pH-touchy polymer and it was inferred that azo-sweet-smelling polymer (poly-ethylmethacrylatehydroxy rthylmethacrylate:1:5) [83]. Common azo prodrug of 5-aminosalicyic corrosive with histidine, was orchestrated by coupling L-histidine with salicylic corrosive, for focused medication conveyance to the excited gut tissue. [84].

b) Glucuronide conjugate: Glucuronide and sulfate conjugation is the real components for the inactivation and planning for freedom of an assortment of medications. Microscopic organisms of the lower gastrointestinal tract discharge glucuronidase that glucouronidate an assortment of medications in the digestive system.Since the

glucuronidation procedure results in the arrival of dynamic medication and empowers its reabsorption, glucuronide prodrugs would be required to be unrivaled for colon focused on medication conveyance.8[45]

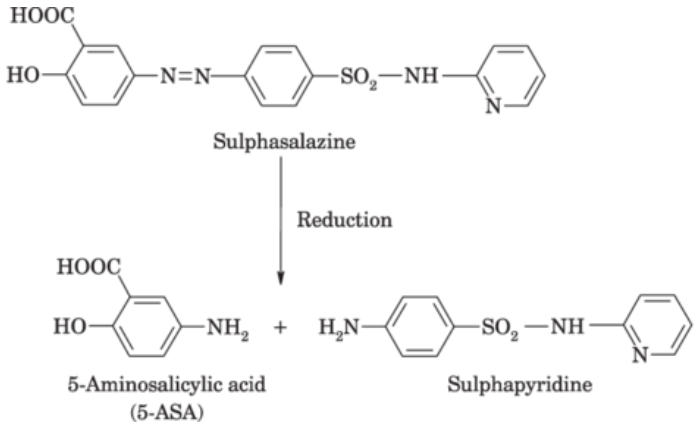


Fig. 2: Reduction reaction of sulphasazine in 5-ASA and sulphapyridine.

c) Cyclodextrin conjugates: The hydrophilic and ionisable Cyclodextrins can fill in as intense medicate bearers in the quick discharge and postponed discharge definitions, while hydrophobic Cyclodextrins can impede the discharge rate of water. Additionally, the most attractive trait for the sedate transporter is its capacity to convey a medication to a focused on hand. Conjugates of a medication with Cyclodextrins can be an adaptable methods for building another class of colon focusing on prodrugs solvent medications [86]. Ibuprofen prodrugs of alpha-, beta-and gama Cyclodextrins were explored.

Methotrexate prodrugs of alpha and gama Cyclodextrins were likewise orchestrated and result built up the essential point of veiling the ulcerogenic capability of free medication, by utilizing 12-overlay portion of the ordinary portion of methotrexate and identical dosages of the esters. [87,88].

d) Dextran conjugates: Dextran ester prodrugs of metronidazole have been arranged and described. Dextran ester prodrugs of dexamethasone and methyl prednisolone was combined and demonstrated the viability of the prodrugs for conveying medications to the colon. Methyl prednisolone and dexamethasone were covalently connected to the dextran by the utilization of a succinate linker. [89].

e) Amino-acid conjugates: Because of the hydrophilic idea of polar gatherings like NH2 and COOH, that is available in the proteins and their essential units (for example the amino acids), they lessen the film penetrability of amino acids and proteins. Different prodrugs have been set up by the conjugation of medication

atoms to these polar amino acids. Superfluous amino acids, for example, tyrosine, glycine, methionine and glutamic corrosive were conjugated to Salicylic corrosive. [90].

Hydrogels

Hydrogels can be utilized for site explicit conveyance of peptide and protein medicates through colon. The Hydrogels are making out of acidic ordinary people and enzymatically degradable azo fragrant cross-joins. In the acidic pH, gels demonstrates less swelling that ensure the medication against corruption in stomach. As the pH of condition increments for example become fundamental, swelling increments. This result is simple access of catalysts like azoreductase, which at last arrival of medication [91].

Covering with pH subordinate polymers The pH in the terminal ileum and colon in higher than in some other area of the gastrointestinal tract and in this way dose shapes which break down at high pH reaches can be focus into the locale. A dimension of pH is higher in the terminal ileum district then in the cecum. Measurement shapes are regularly postponed at the ileocecal intersection, cautious choice of enteric coat piece and thickness is expected to guarantee that crumbling does not happen until the dose from travels through the ileocecal intersection from the terminal ileum into the cecum. Equivalent words for eudragit are Eastacryl, Kollicoat MAE, polymeric methacrylates [92].

Deferred discharge tablets containing mesalazine and covered with eudragit S-100 were examined. These tablets disintegrated at a pH dimension of 7 or more prominent, discharging mesalazine in the terminal ileum and past for topical incendiary activity in the colon. The plan was fruitful in accomplishing site explicit conveyance of mesalazine, disappointment of the covering to break up has been accounted for [93]. The most ordinarily utilized pH subordinate polymers are subsidiaries of acrylic corrosive and cellulose. For colonic medication conveyance, sedate center is covered with pH delicate polymers. The medication are incorporates tablets, containers, pellets, granules, smaller scale particles and nanoparticles.

Disadvantages of this method are:

a) Lack of consistency in the dissolution of the polymer at the desired site.

b) Lack of site specificity of pH dependent systems.

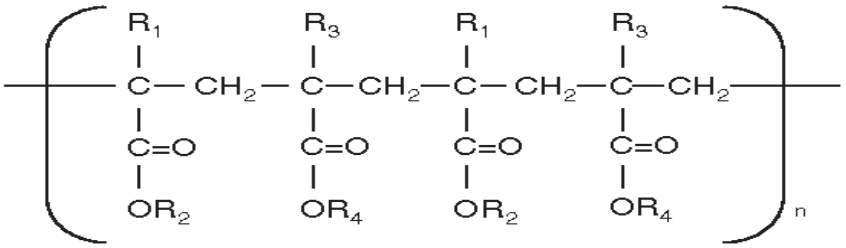
The disintegration of the polymer can be in the distal part of the colon or toward the end if ileum,

contingent upon the force of the GI motility [94]

pH-dependent microbeads of theophylline hydrochloride were created and assessed by utilizing alginate and chitosan by ionotropic gelation technique pursued by enteric covering with eudragit S100 [95]. Examination concentred with the plan of prednisolone containing 1% eudragit

RS PM had been done which indicates 100% medication discharge [96]. Tablet containing mesalazine were examined which was covered with two polymers eudragit L100 and eudragit S100 in blend 1:0, 4:1, 3:2, 1:1, 1:5, and 0:1 [97]. Chitosan microspheres contain Ondansetron

were set up by emulsion cross connecting strategy. Work joins eudragit S100 and chitosan polymers. Investigation relapse esteems propose that the conceivable medication discharge was Peppas model [98]. Mebeverine Hydrochloride microspheres defined utilizing eudragit S100 and L100 which demonstrated biphasic discharge design with non-fickian dissemination discharge in 12 hrs [99].



Eudragit Grade	R_1	R_2	R_3	R_4
E	CH_3	$CH_2CH_2N(CH_3)_2$	CH_3	CH_3, C_4H_9
L and S	CH_3	H	CH_3	CH_3
RL and RS	H, CH_3	CH_3, C_2H_5	CH_3	$CH_2CH_2N(CH_3)_3^+Cl^-$
NE 30D	H, CH_3	CH_3, C_2H_5	H, CH_3	CH_3, C_2H_5
L 30 D-55 and L 100-55	H, CH_3	H	H CH_3	CH_3, C_2H_5

Fig. 3: Structure of various grades of Eudragit polymers.

Timed released systems

(Example: pulsatile release, pulsincap, delayed release, sigmoidal release system)

It depends on the idea of forestalling the arrival of medication 3– 5 hrs in the wake of going into small digestive system. In this methodology, sedate discharge from the framework after a foreordained slack time as indicated by travel time from mouth to colon. The slack time relies on the gastric motility and size of the measurements

structure. One of the most punctual methodologies is the Pulsincap gadget. This gadget comprises of a non-crumbling half case body fixed at the open end with a hydrogel plug, which is secured by a water-solvent top. The entire unit is covered with an enteric polymer to stay away from the issue of variable gastric discharging. At the point when the container enters the small digestive tract, the enteric covering breaks down and the hydrogel plug begins to swell. The measure of hydrogel is balanced so it flies out simply after the stipulated timeframe to discharge the substance [100]. In another methodology, natural acids were filled into the body of a hard gelatin container as a pH-altering operator together with the medication substance. The joint of the container was fixed utilizing an ethanolic arrangement of ethylcellulose.

The case was first covered with a corrosive solvent cationic polymer, at that point with a hydrophilic polymer hydroxypropyl methylcellulose lastly enterically covered with hydroxy propyl methyl cellulose acetic acid derivation succinate. After ingestion of the case, the furthest enteric layer of the covering averts sedate discharge in the stomach. The enteric layer and the hydrophilic layers break up rapidly after gastric discharging and water begins entering the container. At the point when the natural pH inside the container diminishes by the disintegration of natural corrosive, the corrosive solvent layer breaks up and the encased medication is immediately discharged [101]. Chronomodulated sedate conveyance arrangement of salbutamol sulfate had been created for the treatment of nighttime asthma. The centers containing salbutamol sulfate were set up by direct pressure strategy utilization of microcrystalline cellulose and bubbly specialist (sodium bicarbonate) and afterward covered consecutively with an inward swelling layer containing a hydrocolloid (hydroxypropylmethylcellulose E5) and an external rupturable layer having eudragit RL/RS (1:1) [102]. Medication conveyance framework was examined which was based on the standards of the mix of pH and time affectability. Press-covered mesalamine tablets with a layer of HPMC E-15 were over-covered with eudragit S100 [103]. An epic time and pH subordinate framework was explored. The framework comprises of the center tablet of mesalamine which is pressure covered with hydroxypropyl methylcellulose (HPMC K4M). This is then covered with eudragit L100. The outcome uncovered that as the measure of HPMC builds, the slack time and t50 esteem additionally increments.

Osmotic pressure controlled systems: The unit achieves flawless to the colon where medicate discharge happens because of osmotic weight created by the passage of the dissolvable. It is otherwise called OROS. There are two OROS frameworks for colon tranquilize conveyance:

1. Osmet siphon: It comprises of an enteric covered semi-penetrable shell which encases an osmotic layer alongside a focal impermeable and collapsible repository loaded up with medication. The inside of this compartment is associated with the outside condition through a conveyance hole toward one side. After disintegration of the gastric-safe film, water is permitted to enter through the semi-porous layer, along these lines raising the weight inside the gadget. Which cause internal repository to therapists and medication detailing to siphon out?

2. OROS CT. Following ingestion, the hard gelatin container shell breaks down. The push furthermore, pull unit is kept from retaining water in the acidic mechanism of stomach by enteric covering. The osmotic siphoning activity results when the covering breaks down in the medication is conveyed out of the hole at a rate constrained by the rate of water transport over the layer [104]. Planning definitions utilizing polysaccharides (model: bacterial chemicals) Dosage frames appreciate the protecting impact of polysaccharide in upper piece of GIT and medication is discharged in the colon by swelling and biodegradable activity of polysaccharidases. Polysaccharides normally happening in plant (e.g., gelatin, guar gum, inulin), creature (e.g., chitosan, chondroitin sulfate), algal (e.g., alginates), or microbial (e.g., dextran) sources were examined for colon focusing on. These are separated by the colonic microflora to straightforward saccharides by saccharolytic species like bacteroides and bifidobacteria. Hydrolysis of the glycosidic linkages on landing in the colon triggers the arrival of the captured bioactive. Albeit explicitly debased in the colon, a large number of these polymers are hydrophilic in nature, and swell under presentation to upper GI conditions, which prompts untimely medication discharge. To defeat this issue, the regular polysaccharides are synthetically changed and blended with hydrophobic water insoluble polymers, though on account of plans they are typically covered with pH delicate polymers. A gelatin/chitosan-based colonic conveyance framework has been created [105]. The utilization of calcium pectinate as a transporter depended on the supposition that, similar to gelatin, it tends to

be deteriorated by explicit pectinolytic proteins in the colon however holds its respectability in the physiological condition of the little gut. Different subordinates, for example, methoxylated and amidated gelatins are likewise created. The detailing of Guar gum based grid tablets of metronidazole/tinidazole were created and the impact of the corresponding organization of these medications on the handiness of guar gum as a bearer for colon-explicit medication conveyance utilizing guar gum network tablets of albendazole was contemplated as a model definition . The quick breaking down center tablets of budesonide were covered with khaya gum pursued by further covering with eudragit S100 by plunge covering procedure. Khaya gum did not totally ensure the medication discharge in the upper stomach related tract and displayed diverse discharge profile in nearness and nonattendance of rodent cecal substance and it was reasoned that khaya gum alone can not be utilized for focusing on the medication to the colon. Tablet definition utilizing gelatin as bearer and diltiazem HCl and indomethacin as model medication had been created. The tablets were covered with inulin pursued by shellac. It was uncovered that polysac-charides as bearers and inulin and shellac as a covering as a covering material can be utilized viably for colon focusing of both water dissolvable and insoluble medications .

Redox touchy polymer covering Analogs to azo security cleavage by intestinal compounds, novel polymers that hydrolyzes nonenzymatically by enzymatically produced flavins are being created for colon focusing on [110]. A typical colonic bacterium, Bacteroidesfragilis was utilized as test living being and the decrease of azo colors amaranth, Orange II, tartrazine and a model azo compound, 4,4_-dihydroxyazobenzene were examined. It was discovered that the azo mixes were diminished at various rates and the rate of decrease could be connected with the redox capability of the azo mixes.

Bioadhesive systems

Bioadhesion is a procedure by which a measurement structure stays in contact with specific organ for an increased timeframe. This more drawn out living arrangement time of medication would have high nearby focus or improved ingestion qualities if there should be an occurrence of ineffectively absorbable medications. This technique can be connected for the plan of colonic medication conveyance frameworks. Different polymers

including polycarbophils, polyurethanes and polyethylene oxide polypropyline oxide copolymers have been researched as materials for bioadhesive frameworks[106].

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