IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, March 2026
Impact Factor: 8.2

Method for Targeting Medication Administration in the Colon

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Abstract: *"The oral route is generally the most preferred method for systemic drug administration. However, it is not suitable for delivering drugs intended to treat lower gastrointestinal (GI) diseases, as most orally administered drugs are released and absorbed in the upper GI tract (stomach and small intestine), their availability at the lower gastrointestinal tract''.*
"The colon's high water absorption capacity and viscous contents can reduce drug availability at the absorptive membrane".
"Targeting drug delivery to the colon can minimize systemic side effects". In order to successfully target medications to the colon, the dosage form should be created in a way that keeps the drug from leaking into the colonic region from the upper gastrointestinal system..

Keywords: Newly developed approach, Systemic drug administration, Gastrointestinal tract (GIT)

I. INTRODUCTION

The primary goal of any drug delivery system is to deliver a useful quality of the drug to a specific location in the body so that the necessary drug concentration can be quickly obtained and then maintained. The most suitable method for administering drugs is orally. Constipation, diarrhea, debilitating inflammatory bowel diseases, and colon cancer—the third most prevalent type of cancer in both men and women—are all examples of illnesses associated to the colon[1]
Anatomy and physiology of colon:-
The colon divided into a canal, caecum, and ascending colon rectum. A dilated,internally blinded portion of the caecum sits above the ascending colon.
A dilated, internally blinded portion of the caecum sits above the ascending colon. From the caecum, the ascending colon ascends to the liver's stage, where it abruptly merges to the left at the right colic flexure to produce a transverse colon.
The colon is a segment of the large intestine, which extends from the anus to the ileocecal junction. The major components of the large intestine are the colon, rectum, and anal canal. Because the colonic region has a considerable quantity of lymphoid tissue, the mast cells in the colonic mucosa create a lot of antibodies when the antigen is absorbed, which facilitates effective vaccine administration.

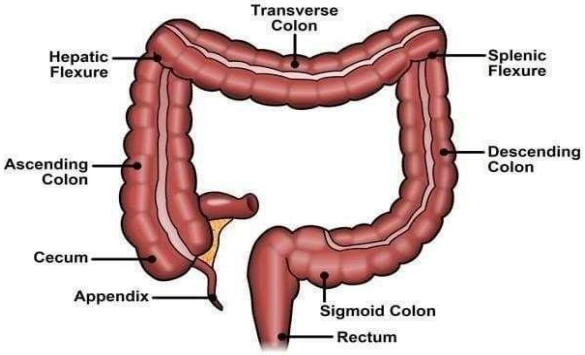

Fig 1- Anatomical view of colonic disease [1]

DOI: 10.48175/IJARSCT-31948

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Advantages of colon targeted drug delivery system

- Drug targeted to the colon can be attractive for several reason.
- Several manufacturing procedures are required to develop such delivery systems.
- Medication bioavailability may be low because of the drug's possible non-specific binding to intestinal fluids, mucus, fecal debris, or nutritional residues.
- The drug should be in solution form prior to absorption; hence, for poorly soluble medicines, this may be the rate-limiting stage.
- The colon is the best place to provide therapeutic medicines to address diseases unique to the colon. One of the advantages of using local treatment is that less medication is required.
- Due to the possibility of increased bioavailability, the colon is a desirable site for therapeutic molecules with poor absorption.[2]
- Boost patient aherence.[3]

Disadvantage:

1. Individual differences in variable gastric emptying time can be substantial, and it is impacted by the kind and quantity of food consumed.[4]

2. Movement of the gastrointestinal tract:-

The passage of the medication through the GIT may be changed by gastrointestinal movement, particularly peristalsis or stomach contractions. [5]

Evaluation techniques of colon targeted preparation:

1. In Vivo Evaluation:-

a) X-ray imaging

The x-ray approach was utilized to evaluate the dose form in vitro using dogs. Omnipause x- ray imaging was performed using 50 milliliters of radio diagnostic agent. 50 milliliters of water are then given with the units. The animals' radiographs were obtained at 0, 0.5, 2.5, 4, 5, 6, and 8 hours after the drug under test was consumed.[6]

1) In Vitro Evaluation:-

The basket method is typically used to undertake in vitro dissolution tests of a dosage form. Evaluation procedures include simulating the GIT's in vivo parameters, such as PH, volume, bacteria, enzymes, food particles, etc., under laboratory circumstances[7].

1. Thakur L.K., Rana S., Chaudhary A. et al , (2022)

In their article “Colon Targeted Drug Delivery System – A Novel Perspective”, the authors discuss physiological considerations of the colon and review conventional and novel approaches such as pH-dependent, time-dependent, prodrug, and microflora-activated systems. They highlight advances like nanoparticles and polysaccharide-based carriers for improved site specificity.

2. Thakur L.K, Pradwsh H, Rana S, Chaudhary A. et. al (2022)

In their review “Colon Targeted Drug Delivery System – A Novel Perspective”, the authors present an updated overview of colon-specific drug delivery methods and the physiological factors influencing them. They discuss major approaches such as pH-dependent systems, time-controlled formulations, microbial-triggered polysaccharide carriers, pressure-controlled systems, and prodrug strategies. The review also highlights the importance of colonic microflora, transit time, and pH variability in determining formulation success. Additionally, the authors emphasize novel technologies like nanoparticles, microspheres, hydrogels, and biodegradable polymers, noting that these systems enhance site-specific drug release, reduce systemic side effects, and improve therapeutic efficiency. Overall, the paper focuses on modern advancements and challenges in achieving precise delivery to the colon.

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3. Saxena S., Singh C. (Year Not Specified, Pharma Tutor, Vol. 6). et al., (2012)
Saxena and Singh provide a comprehensive review of novel approaches for colon-targeted drug delivery systems. Their work focuses on understanding the physiological environment of the colon, including pH, microflora, transit time, and enzymatic activity, as the basis for designing effective formulations.
4. Arora S, Ali J, Ahuja A, Baboota S, Qureshi J. et al. (2006)
The authors reviewed pulsatile drug delivery systems, emphasizing their role in providing time-controlled and chronotherapeutic drug release. They described various pulsatile approaches—such as time-dependent, stimuli-responsive, and multiparticulate systems—and highlighted their usefulness for diseases following circadian rhythms, improving therapeutic
5. Reddy G.J., Kokkula P.K. et al , (2024)
Reddy and Kokkula reviewed colonic drug delivery systems with a focus on biodegradable polymers for achieving systemic drug effects. They highlighted polymers such as pectin, chitosan, guar gum, and alginate, emphasizing their ability to protect drugs in the upper GIT and release them selectively in the colon through microbial degradation. The review concludes that biodegradable polymer-based systems enhance safety, stability, and targeted systemic absorption.

Novel drug delivery system for colon-targeted drug delivery:
The limitations linked to traditional dosage forms can be addressed by utilizing innovative drug delivery systems. Nanotechnology-based delivery systems offer numerous benefits, including the ability to overcome the challenges faced by conventional oral systems and providing an extensive area for interaction within the gastrointestinal tract.

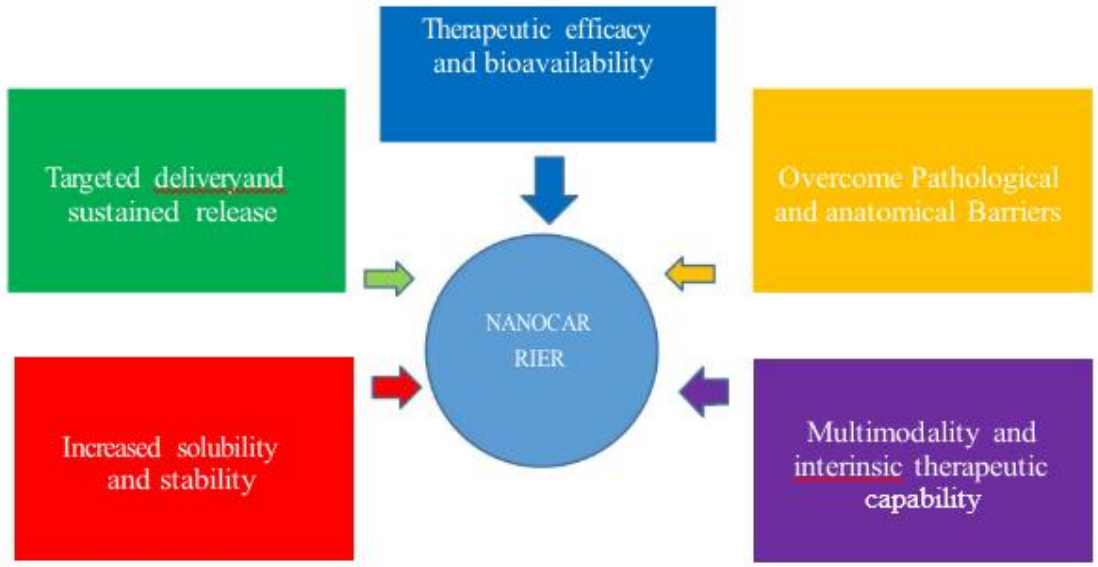

Fig. 2. Key advantages of colon targeted NDDS

The effectiveness of the treatment and the absorption of the cells are greatly affected by the nanoparticles' surface, shape, and size.
The field of medicine has transformed because of the unique and notable characteristics of nanoparticles. For example, research revealed a high susceptibility to pH and demonstrated enhanced encapsulation efficiency, as well as increased bioavailability, safety, and effectiveness of doxorubicin. The study discussed the use of a grafting strategy to silica incorporate doxorubicin into a pH-sensitive polymer (polyacrylic acid) combined with porous.[8]
Advances in noval drug delivery system for colon targeted drug delivery Advance:-

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Many obstacles and challenges must be overcome while developing innovative drug delivery systems for colon-targeted drug delivery in order to increase efficiency.

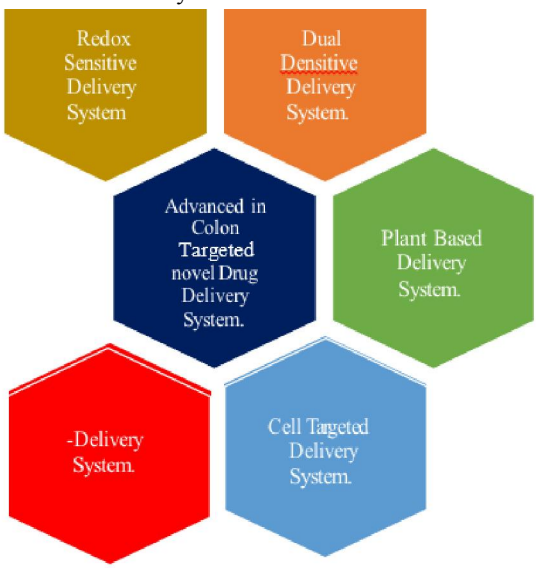

Fig 3- Advances in colon targeting noval drug delivery system.

Redox responsive noval delivery system:-

A drug formulation that responds to alterations in redox potential may serve as a beneficial approach for managing ulcerative colitis and colorectal cancer. A drug formulation that responds to alterations in redox potential may serve as a beneficial approach for managing ulcerative colitis and colorectal cancer.

Oxidative stress, which results in an overabundance of inflammatory reactive oxygen species (ROS), is linked to ulcerative colitis.

Dual stimuli noval delivery systems:-

Enzyme, PH, and time-dependent systems are the main methods used to transport drugs to the colon. However, each of these approaches has certain drawbacks that result in ineffective medication delivery. Premature drug release and lack of selectivity are linked to PH- dependent systems.[9]

Factor affecting on colon targeting drug:-

1. Physiological factor
2. Pharmaceutical factor

1. Physiological factor:-

a) Gastric emptying

The main factors influencing drug distribution to the colon following oral administration are stomach emptying and intestinal transit time. The dosage form's transit duration in the colon depends on the size of the particles; smaller particles have longer transit times than larger ones. Transit times are longer for persons with constipation and shorter for those with diarrhea. Each segment's transit time is as follows: 2-3 hours for the small intestine transit, 20-35 hours for the colon transit, 10 minutes to 2 hours for the fasted condition, and more than 2 hours for the fed state.[10]

B) Colon PH:-

Numerous factors, including diet, illness, and food consumption, affect the gastrointestinal tract's pH level, leading to both inter- and intra-subject differences. Targeted colon medication delivery has made use of these PH shifts.

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According to radio telemetry, the terminal ileum has the highest PH level (7.5+_0.5), whereas the PH decreases to 6.4 +_ 0.6 as one enters the colon.[11]

New approaches colon drug delivery system:-

Pressure control drug delivery system

The process of digestion is facilitated by the stomach's contractile movements and the peristaltic motions of the intestines. The contractions of the stomach help break down food particles into smaller sizes before they are passed on to the intestines. The peristaltic action of the intestines enables the movement of the bolus from one section of the gastrointestinal elevated luminal pressure plays tract to another. The peristalsis occurring in the ascending colon that moves the

bolus to the transverse colon is known as mass peristalsis. This specific type of peristalsis happens sporadically, approximately three to four times a day. The peristaltic movement in the intestines contributes to an increase in luminal pressure. membrane's thickness. The density and size of the capsules determine the system.[12]

CODES^TM

A novel technology called CODES^TM was created to solve the shortcomings of time- dependent medication delivery systems and PH. Lactulose, which functions as a trigger for the release of particular medications in the colon, was used to develop this technique. A tablet core with active compounds covered with acid-soluble polymers like Eudragit E and enteric components like Eudragit L makes up the CODES^TM system. Until the system is transferred to the small intestine, enteric polymers shield it inside the stomach. The enteric layer starts to dissolve due to the small intestine's higher pH.

Osmotic controlled drug delivery system (OROS-CT)

The medication is released through a thrust-pull device that dissolves in the gelatin capsule after consumption. An impermeable membrane covering the mechanism prevents the medicine from releasing at the stomach's acidic pH. The semipermeable membrane then starts to breakdown in the upper intestine region (PH>7), allowing water to enter. This causes the osmotic compartment to enlarge, forming a gel that can flow within the medication unit. Pulsative drug delivery system

Pulsincap system:-

The formulations used in this technique are created as capsules. To regulate the drug's release, the stoppered is inserted into the capsule. The drug's contents are sealed with an expandable hydrogel. When the capsules come into contact with the dissolving fluid, they swell. The medicine is then released when the stopper is forced out of the capsule after a brief delay. Hydrogel plugs are made of polymers like polyvinyl acetate, polymethacrylate, and hydroxypropyl methylcellulose (HPMC).

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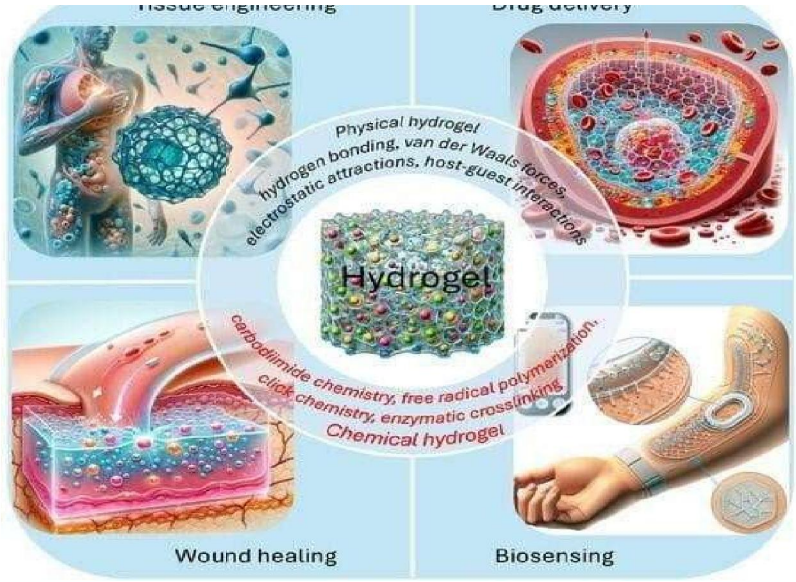

Fig.4. Advance in hydrogel-based drug delivery systems

Port System:-

The system operates on the principle of a delayed drug release. It comprises a gelatin capsule that is covered with a semipermeable membrane material (for instance, cellulose acetate), along with impermeable plugs (such as lipidic) and osmotically active substances, accompanied by drug formulations. The semipermeable membrane permits fluid to flow into the capsule as soon as it comes into contact with the dissolving fluid. This generates a pressure swelling in the capsule body, which releases the medicine when the stopper is removed.

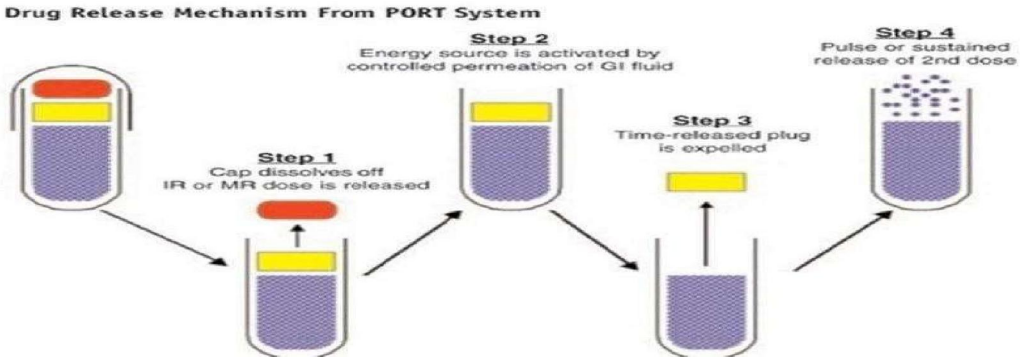

Fig 5 -Drug release mechsnism for PORT system[13]

In order to treat a number of colonic diseases, including inflammatory bowel disease (which is further subdivided into ulcerative colitis), Crohn's disease, amoebiasis, diarrhea, colon cancer, vaginal infection, and bacterial infection, among others, colon targeted drug delivery is an excellent drug delivery system that targets the lower parts of the GI tract . Target specificity for colonic disorders, including inflammatory bowel diseases (including ulcerative colitis and Crohn's disease), amoebiasis, colorectal cancer, and persistent constipation, is mostly provided by colon focused drug delivery. persistent diarrhea, etc.

Patient compliance was decreased by a colon-specific medication delivery system that had lower dose frequency and less enzymatic activity.[14]

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Colon-targeted drug delivery systems are used to treat both local and systemic conditions, and they work well with proteins and peptides. Because of their early release at the upper GI tract and the increased risk of adverse reactions from high dosages, targeting the transport of proteins and peptides to the colonic environment is extremely challenging. Drug therapy might be protracted and involve drug use during treatment. Colon-targeted drug delivery decreased stomach irritation (NSAIDs).

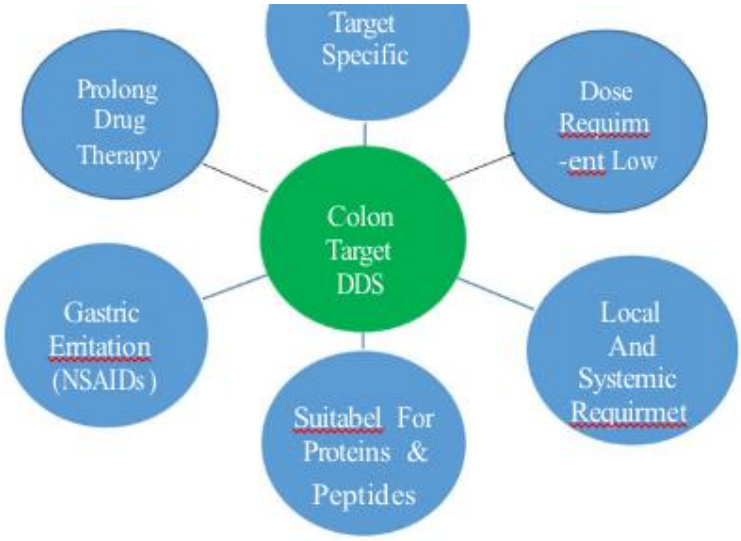

Fig 6. Imp of colon targeted drug delivery system[15]

Approaches to deliver intact molecule to colon:-

1) PH dependent approach:-

This approach utilizes the existence of PH gradient in the GIT that increases progressively from the stomach (PH 1.5-3.5) and small intestine (5.5-6.8) to the colon (6.4-7.0). By combining the knowledge of the polymers and their solubility at different PH environments, delivery systems can be designed to delivery drug at the target site. The most commonly used

PH dependent polymers are derivatives of acrylic acid and cellulose.[16]

2) Coating of the drug core with PH sensitive polymers.

By wrapping the medication molecule with the appropriate polymers, which only break down in the colon, the complete molecule can be transported to the colon without absorbing at the upper portion of the gut. However, the polymer utilized to target the colon should be able to tolerate the lower pH values of the stomach and the proximal portion of the small intestine.

Polymer	Threshold pH
Eudragit L 100	6.0
Eudragit 100	7.0
Hydroxypropylmethylcellulose phthalate 50	5.2
Hydroxypropylmethylcellulose phthalate 55	5.4
Cellulose acetate trimellate	4.8

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Covalent linkage of drug with carrier approach:-

Prodrug approaches

Prodrugs are pharmacological substances that are inactive but are transformed into active form by the body's natural enzymatic activity. They are intended to improve membrane permeability and absorption by decreasing adverse effects and metabolism and boosting the water solubility of medications. Carrier-linked prodrugs and bioprecursor prodrugs are the two primary categories of prodrugs. A drug covalently bonded to a carrier group makes up inactive carrier linked prodrugs. When the linker is cleaved, the drug and the linker—which might be an insert or an active molecule like an antibody—are freed. To improve prodrug activation by vectorization, a variety of tactics are used. Because of the importance of activation in the lower gastrointestinal tract, azo conjugates are often used in prodrug formulations meant for the colon. Instead of being hydrolyzed in the stomach and small intestine, these compounds are metabolically activated by azo reductase, a bacterial enzyme found in the colon.

PH dependent approach

A number of variables, like as diet, microbiota, and food transmission time, affect the coon's pH, which varies along its length. The proximal, ascending, and transverse colons have somewhat acidic PH values, which range from 5.5 to 6. The PH gradually grows increasingly alkaline as the gastrointestinal contents, including the descending and sigmoid colons, move toward the distal colon, reaching about 7.0.The PH of the colon is an important aspect, even though PH sensitivity is important for drug release, especially when it comes to enteric coatings and other components. But in recent decades, questions have been raised about the in vivo dependability of PH-sensitive formulations.[18]

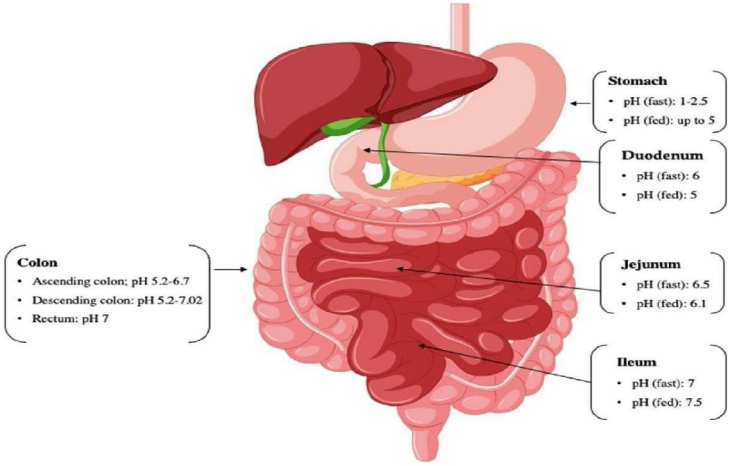

Fig 7. Human digestive system

There are more than a thousand different types of bacteria in the human body. Despite being distributed throughout the gastrointestinal tract, the majority of bacteria are concentrated in the colon; estimates place the number of colonic bacteria alone at about 1012 cells per milliliter of colonic fluid. Free DNA, viruses, archaea, bacteria, fungi, and a variety of enzymes and metabolites make up the microbiome. In order to facilitate digestion in the upper gastrointestinal tract, colonic bacteria, which are primarily anaerobic, release enzymes that break down substrates. They can break down complex carbs and have a strong metabolic capability. Microbiotactivated delivery systems have showed potential in colon focused medication administration because of the lower GI tract's rapid rise in microbiota and related enzyme activity.[19]

Drug absorbtion mechanism in colon:-

(CTDDS) was created to ensure that the formulation remains intact in the small intestine while also achieving the intended and efficient medication concentration in the colon. The majority of medications either follow paracellular or transcellular routes. in routes that are transcellular. Lipophilic drug molecules go via a pathway by penetrating the cell

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membranes in a transcellular pathway. The hydrophilic medicines moved between cell junctions via the paracellular route. A well-defined barrier prevents a portion of the medicine from being absorbed in the small intestine.

Drugs can remain in the colon for longer because of its shorter transit time, which lengthens the time they are in contact with colonic mucusa. Additionally, the colon's more viscous content causes a slower rate of dissolution, which slows the diffusion of drugs through the colon. These characteristics vary depending on the colon's length and fluid content. Although medications can theoretically be absorbed throughout the GIT, they are typically absorbed in the small intestine's duodenum and proximal jejunum.The purpose of the delayed release dosage forms is to provide the colon with an efficient release of the medicine. A "burst release, a sustained or prolonged release, or a targeted release" is demonstrated by this colon- targeted formulation. Single unit colon targeted medication formulations fall into two primary categories: multi-T particle dosage form systems and single unit colon targeted drug delivery systems. Single unit CTDDS's drawbacks include the formulations' perceived inadequacy. Am

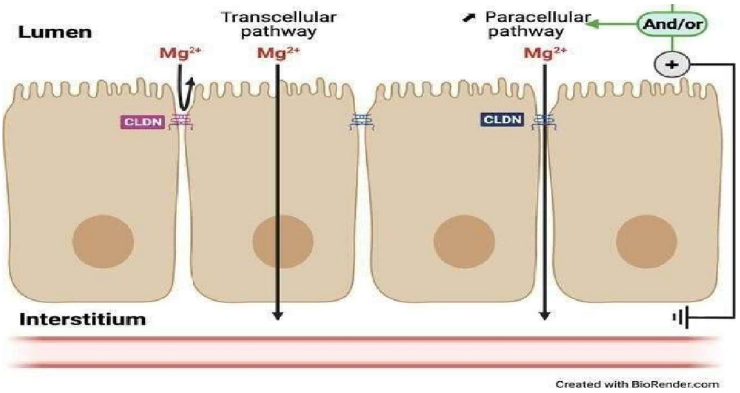

Fig 8. Colonic crypt protects stem cells .

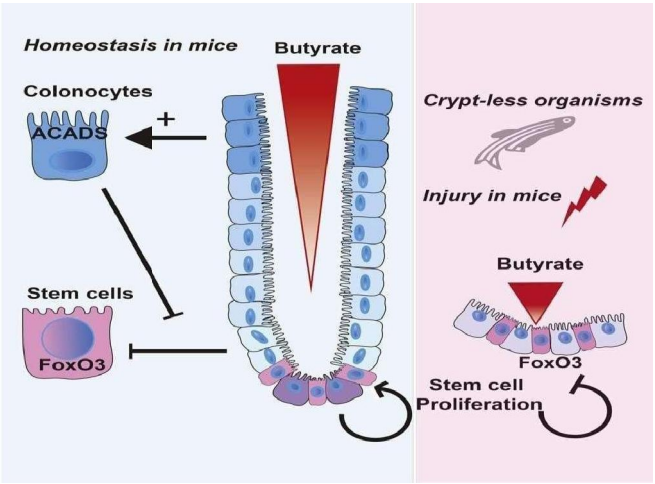

Fig 9 :-Drug uptake pathways in the cell. [20]

Table 2:- Drug used for colon targeting

Drug	Indication	Dosage form	Absorption	Sources
Bisacodyl	Constipation	Suppository, Enema	Local	[6]
Glycerol	Constipation	Suppository	Local	[1,6]

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Saline laxatives	Bowel preparation	Enema	Local	[6]
Mesalazine	Inflammatory bowel disease	Enema, Rectal Foam	Local	[1,6]
Budesonide	Anti- inflammatory	Rectal Foam	Local	[1,6]
Prednisolone	Anti- inflammatory	Rectal Foam	Local	[6]
Hydrocortisone	Anti- inflammatory	Suppository, Enema	Local	[6]

Sulfonate Resins				
Glyceryl Trinitrate	Anal fissure, Hemorrhoids	Ointment	Local	[1,4,6]
Acetaminophan	Pain Fever	Suppository	Systemic	[1,4,6]
Oxycodone	Pain	Suppository	Systemic	[6]
Ondansetron	Nausea and Vomiting	Suppository	Systemic	[1,6]
Caffeine+ergotamine	Migraine	Suppository	Systemic	[6]
Prochlorperazine	Nausea and Vommiting	Suppository	Systemic	[6]
Promethazine	Antihistamine	Suppository	Systemic	[1,6]
Ibuprofen	Pain, Fever	Suppository	Systemic	[6]
Diclofenac	Pain, Fever	Suppository	Systemic	[6]
Indomethacin	Pain	Suppository	Systemic	
Diazepam	Seizures,Sedati on	Enema, Gel	Systemic	[6]

Table 3:-Different drug preprations and their benefits in treatment of different colon diseases.

Prepartions	Their benefits in treatment of diseases in colon arthritis.
Topical Preparations (Foams, suppositories, or enemas)	They play a key role in the treatment of ulcerative colitis, either alone or while combined with oral steroids.
Old Systemic and Topical	Synthetic glucocorticoids considered as the traditional corticosteroids used for the treatment of Ulcerative colitis.
Oral Preparations	Localized treatment of diseases and condition such as inflammatory bowel diseases, irrictable bowel syndrome and colon cancer mainly as well asothers. They can also put for use in the chronotherapy of diseases which affected by circulation biorhythms, such

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Structure and function of colon:-

The colon, rectum, and anal canal are the three divisions of the large intestine, which runs from the ileocecal junction to the anus. The cecum, ascending colon, hepatic flexure, transverse colon, descending colon, and sigmoid colon are the components that make up the colon. The colon's widest section, the cecum, is around 8.5 cm long. Its primary purpose is 1) to absorb liquids and any salts that are left over after intestinal digestion is finished. 2) To lubricate it by combining its contents with mucus. From the cecum, the ascending colon reaches the hepatic flexure, which is lateral to the right kidney and in contact with the liver's inferior side. [21]

Colonic structure:-

The serosa, external muscular region (muscularis external), submusoca, and mucosa are the four layers that make up the colon wall. Adipose tissue covers the squamous epithelium of the serosa, forming distended fat pouches called appendices epiplocicae, which are larger and more numerous in the distal half of the colon and are one of its defining characteristics.

The supply of blood the superior and inferior mesenteric vessels provide blood to the colon and upper rectum. arteries, and the inferior and superior mesenteric veins carry the venous return. As a component of the hepatic portal system, these connect to the splenic vein. Therefore, the liver must first eliminate any medication that is absorbed from the colon and upper rectum. Blood flow via the colon can be difficult to measure, with reported levels ranging from 8 to 75 ml/min.

Through water-filled channels, the colon is in charge of exchanging bicarbonate and potassium ions for sodium and chloride ions. The salt is subsequently transported into the intercellular space via a sodium potassium exchange pump system in the basolateral membrane, which operates against sharp concentration (14 mM to 140 mM) and electrical (30 mV to +20 mV) gradient.[22]

Inflammatory bowel disease (IBD):-

IBD, or inflammatory bowel disease, is a general term that includes similar but different Crohn's disease, ulcerative colitis (UC), indeterminate colitis, microscopic colitis, and collagenous colitis are examples of long-term inflammatory gastrointestinal illnesses. The two most prevalent conditions are ulcerative colitis and Crohn's disease. An additional long-term gastrointestinal condition is irritable bowel syndrome (IBS). The symptoms of IBD and IBS might linger for months or even years for the majority of individuals. As a result of inflammatory bowel disorders such ulcerative colitis and Chorn's disease, the colon may eventually need to be surgically removed. Although it can happen at any age, it is more prevalent in young adults.[23]

Pathogenesis-

We still don't fully understand the causes of IBD and IBS. Typical theories include, for instance, immune system problems. system and effects of pro-inflammatory cytokines, as well as the selective activation of subsets of lymphocytes, which sustain the intestinal inflammatory response's unchecked activation. Additionally, it has been proposed that an intolerance to the gut's natural flora (bacteria) causes inflammation and the pathology that results. Colonic bacterial microflora is believed to play a role in the pathophysiology of inflammatory bowel illnesses, at least in part.

Table 4:- Drug metabolizingenzmes in the human colonthat catalyze reductive reactions.

Enzymes	Microorganisms	Metabolic reaction Catalyzed
Nitroreductase	E. coli, Bacteroides	Reduce aromatic and hydrocyclic compounds
Azoreductase	Lactobacilli, E.coli	Reductive clevage of azo compounds
Sulfoxide reductase	E. coli	Reduce sulfoxides
Hydrogenase	Lactobacilli spp	Reduce carbonyl groups and aliphatic duble bonds
Esterase amidases and	E. coli	Clevage of ester or amidases of carboxylic acids
Glucosidase	Eubacteria	Clevage of beta- glycosidase of alcoholsand

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		phenols
Glucoronidase	E.coli	Cleavage of beta-blucoronidases of alcohols and phenols
Sulfatase	Eubacteria, stretptococci	Cleavage of O-sulfates and sulfamates

Ulcerative colitis:-

A persistent inflammation of the colon, or large intestine, is known as ulcerative colitis. This illness results in inflammation and lining sores known as ulcers.of the colon and rectum. Where inflammation has destroyed the cells that normally border the colon, ulcers develop. These ulcers subsequently bleed and create pus. Ulcerative colitis is closely related to another ailment of inflammation of the intestines called Crohn's disease. Together, they are usually referred to as inflammatory bowel disease (IBD). Both men and women are equally affected by ulcerative colitis, which can strike at any age but typically begins between the ages of 15 and 30 and less frequently between the ages of 50 and 70.[24]

Symptoms of ulcerative colitis:-

The most common symptoms of ulcerative colitis are abdominal pain and bloody diarrhea.

Patients also may encounter.

Anemia

Exhaustion weight loss appetite loss rectal bleeding loss of bodily fluids and nutrients

Table 5: Anatomical and physiological characteristics of the gastrointestinal tract.

Sr. No	Region	Length(m)	Surface Area	pH
1	Oesophagus	0.3	02	6.8
2	Stomach	0.2	0.2	1.8-2.5
3	Duodenum	0.3	0.02	5-6.5
4	Jejunum	3	100	6.9
5	Ileum	4	100	7.6
6	Colon	1.5	3	5.5- 7.8

these issues resolve when the colitis is treated. About half of those with ulcerative colitis have mild symptoms, while others experience frequent fevers, bloody diarrhea, nausea, and severe abdominal cramps.

It is unknown why ulcerative colitis causes problems like arthritis, inflammation of the eye, liver disease, and osteoporosis; these complications may be the result of inflammation triggered by the immune system.

Pathogenesis:-

There are numerous ideas on the etiology of ulcerative colitis.

Immune system abnormalities are seen in people with ulcerative colitis, but doctors are unsure if these abnormalities are a cause or an effect of the illness. It is thought that the bacteria in the digestive tract cause an aberrant immunological response in the body.

Emotional discomfort and sensitivity to specific foods or food products are not the cause of ulcerative colitis, but they may produce symptoms in certain individuals. A worsening of symptoms may also be caused by the stress of having ulcerative colitis.

Diagnosis:

Ulcerative colitis is diagnosed using a variety of assays. A medical history and physical examination are typically the initial step. Blood tests may reveal a high white blood cell count, which is an indication of inflammation somewhere in the body, or anemia, which could indicate bleeding in the colon or rectum. White blood cells, which are indicative of

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 5, March 2026 Impact Factor: 8.2

inflammatory illness or ulcerative colitis, can also be found in a stool sample. A stool sample also enables the physician to identify bleeding or infection in the colon or rectum that may be brought on by parasites, bacteria, or viruses.[25]

Treatment of ulcerative colitis:-

Ulcerative colitis has been treated with both drugs and surgery. Surgery, however, is reserved for for people who have life-threatening problems and extreme inflammation. Ulcerative colitis cannot be cured by medication. Patients with ulcerative colitis usually go through months to years of remission, or the resolution of inflammation, after times of relapse, or the worsening of inflammation. The symptoms of diarrhea, rectal bleeding, and abdominal pain became worse during relapses. Remissions typically result after medicine or surgery, but they can also happen on their own, that is, without any medical intervention.

Drugs for Colonic Delivery :-

Oral drug administration that targets the colon specifically is growing in popularity for the therapy for big intestinal disorders and for the systemic absorption of medications containing proteins and peptides. Selective local medicine delivery to the colon is necessary for inflammatory bowel diseases (IBD), including Crohn's disease and ulcerative colitis (UC). Oral or rectal administration can be used to deliver drugs to the colon. Due to the large degree of heterogeneity in the distribution of medications given by this route, traditional rectal delivery methods (suppositories and enemas) are not always effective. Since enema fluid can only be given topically to address conditions affecting the sigmoid and descending colon, suppositories work well in the rectum due to their limited distribution. As a result, the oral route is recommended.[26]

Modified release dosage forms

A modified release dosage form is one in which the time course and/or location of drug release properties are selected to achieve therapies or convenience goals not provided by traditional dosage forms such suspensions, solutions, and solid medication forms with quick release. Extended release and delayed release are two categories for modified release dose formulations.

1. Dosage formulations with delayed release

A dosage form that releases medications at a time other than immediately following
administration is known as a delayed release dosage form.

2. Dosage formulations with extended release

An extended-release dosage form is one that, when compared to conventional dosage forms (such as solutions or immediate-release solid dosage forms), permits at least a two-fold decrease in dose frequency or a notable improvement in therapeutic performance. Extended release is related with sustained release and controlled release lasting action.[27]

Limitation of colon targeting drug delivery system

1. several stages in the production process.
2. Colonic function may potentially be impacted by the indigenous microbiota through metabolic degradation of the medication.
3. Drug transport across the mucosa and into the systemic circulation may also be impeded by the colony's tight connections' reduced surface area and relative "tightness".
4. Prior to absorption, the drug should be in solution form; for poorly soluble medicines, this is the rate-limiting phase.
5. The unpredictability around the location and environment in which the coating may begin to dissolve is a significant drawback of the pH-sensitive coating technology.

Normal in ulcerative colitis patients .[28]

6. The prodrug method has the drawback of being less adaptable because its formulation relies on the functional group that the drug moiety has available for chemical bonding.[29]

Microbial environment and colon PH :-

The large intestine, sometimes referred to as the colon, has a distinct pH and microbial ecology that are habitat and colon pH:

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PH of the colon:- The colon's pH ranges from 6.7 to 7.6, which is somewhat alkaline. This pH range is greater than that of the small intestine, which is mildly acidic to neutral, and the stomach, which is acidic. The presence of bicarbonate ions released by the colon's lining epithelial cells is the main cause of the colon's alkaline pH.
Numerous physiological functions, including the development and metabolism of helpful microorganisms, depend on an alkaline environment.

Microbiological Environment:-
The gut microbiota, also known as the gut microbiome, is a complex and varied microbial community found in the colomicrobiome. It is made up of trillions of microorganisms, including as viruses, fungus, bacteria, and other microbes. The colon has a more varied and abundant gut microbiota than any other area of the digestive system.
The microbial habitat of the colon serves a variety of vital purposes, such as The process offermentation:-
The fermentation of undigested fibers and carbohydrates that make it to the colon is mostly influenced by the gut bacteria. Beneficial bacteria convert complex carbohydrates into simpler molecules by fermentation, resulting in the production of short chain fatty acids (SCFAs), such as butyrate, propionate, and acetate. These SCFAs support the integrity of the colon lining and give colonocytes a source of energy.
Production and Absorption of Nutrients:-
Certain vitamins, including vitamin K, biotin, and folate, are synthesized in part by the gut flora and are subsequently taken up by the body and used. Furthermore, the gut flora aids in the absorption of electrolytes and minerals like iron, calcium, and magnesium.
Immune System Management:-
The immune system's development and regulation are significantly influenced by the gut flora. It ensures proper immunological responses and reduces excessive inflammation by educating and training the immune system. Additionally, the gut microbiota supports the integrity of the gut barrier, which keeps dangerous pathogens from invading the body.

Metabolism and Disease Risk:-
The risk of pathogenic infections is decreased by beneficial bacteria in the colon that compete with and prevent the formation of harmful bacteria.
Disease and Metabolism Risk: Several facets of metabolism, such as glucose homeostasis, lipid metabolism, and energy control, have been connected to the gut microbiota. Gastrointestinal imbalances Dysbiosis, or
microbiota, has been linked to a number of illnesses, such as diabetes, obesity, inflammatory bowel disease, and even mental health issues. For general gut health and wellbeing, the colon's beneficial bacterial balance must be maintained. The makeup and diversity of the gut microbiota can be influenced by a number of factors, including lifestyle choices, drugs (particularly antibiotics), food, and certain illnesses. A favorable microbial habitat in the colon can be fostered by a balanced diet high in fiber, prebiotics, and probiotics as well as by adopting lifestyle choices that support gut health.[30]

POLYMER SELECTION FOR CTDDS:-
There is a lot of interest in treating various colonic diseases locally and systemically when medications are delivered to the colon.
illness due to the colon's many therapeutic benefits, such as its near neutrality and extended transit time. Effective drug transport to the colon depends on protecting the drug from breakdown or release in the stomach, which can be accomplished by employing polymers, as they can affect the medication's rate of release and absorption and play a significant part in creating CTDDS. For medication delivery applications, both natural and biodegradable polymers are favored.
Natural and biodegradable polymers have the following benefits:- They are costly and come in a range of structures.

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Biodegradable polymers decompose into physiologically acceptable chemicals that the body may metabolize and eliminate through regular metabolic processes.

Benefits of colon targeted drug delivery system:- Colon target DDS advantages include:

Minimizing side effects when treating colon disorders (ulcerative colitis, colorectal cancer,

By creating an environment that is "friendlier" for proteins and peptides than the gastrointestinal tract.

Reducing significant first-pass steroid metabolism.

Preventing the irritation of the stomach caused by NSAIDS taken orally.

Drugs used to treat rheumatoid arthritis, asthma, and angina are released gradually.[31]

Future Directions

- Biomarker-based smart systems that respond to disease-specific colonic signals.
- Combination approaches (e.g., pH + microbiome triggers) for higher reliability.
- Safety and long-term microbiome impact studies.
- Clinical validation in heterogeneous patient populations.

II. CONCLUSION

Targeted medication delivery to the colon offers significant advantages for treating colonic diseases (e.g., inflammatory bowel disease, colorectal cancer) and improving oral drug bioavailability, while minimizing systemic side effects. This review highlighted several promising approaches:

-pH-sensitive and time-delayed capsule systems exploit the alkaline colonic environment or transit time to release drugs site-specifically.

-Microbial-triggered systems release drugs in response to colonic bacterial enzymes.

- Nanocarrier and hydrogel-based carriers protect drugs during upper GI transit and enhance colonic retention or uptake.

-Colonic targeting prodrugs rely on bacterial azoreductases for activation.

-Despite advances, challenges remain in achieving precise localization, ensuring consistent drug release across variable colonic conditions (pH, transit, microbiota), and scaling up for commercial production. Most technologies are still in preclinical or early clinical stages.

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