The Role of Nano-Polysaccharides in Colon-Targeted Therapeutic drugs

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ABSTRACT

One of the areas of the pharmaceutical sector that is now expanding at a rapid rate is colon targeting, which makes therapeutic agents for specific medication delivery regardless of the challenges. Patients may respond better to medicine administration that specifically targets the colon. In pharmaceutical formulations, several polysaccharides are utilised. In the development of colon-focused drug delivery systems, nano-polysaccharide materials have assumed a prominent role. Thus, pH-dependent systems, microflora-dependent systems, multi-matrix technology systems, and drug delivery systems combining nanoparticles and osmotic pressure control have all been reviewed. Additionally, this study critically analysed and attempted to determine the significance of nano-Polysaccharides in the gradual development of colon targeting techniques.

KEYWORDS: Colon-targeted drug delivery system, Nano-polysaccharides, Ulcerative colitis, Crohn's disease, Inflammatory Bowel Disease.

1. INTRODUCTION

Targeted distribution of drugs is one of the most unique methods of drug administration. In this method, the active pharmaceutical ingredient (API) for a cure is selectively carried to the targeted location, where the drug is absorbed in such a way as to increase the medicament concentration in a diseased area of any patient. Targeted drug delivery systems, also known as DDS, have as its primary objective to improve a medication's effectiveness while simultaneously reducing the negative effects that are caused by the drug's removal, breakdown, and inactivation. In addition to this, its primary concentration is on the management of the inclined therapeutic behaviour of a medicine in the targeted location[1]. When the intrinsic effects are taken into account, oral administration is among the most effective methods for the delivery of drugs. Oral administration is used for about half of all pharmaceutical products now on the market. This

method is preferred for a variety of reasons, including higher compliance and patient acceptability, lower levels of discomfort, and simpler procedures[2].

For the transport of medications to the large intestine of the GIT, certain classes of natural, artificial, and synthetic polymers were used. There have been reports that polysaccharide nanoparticles increase bioavailability and targeted medication delivery at the site of action. Because of their versatility, polymers are well-suited to fulfil the requirements of the drug delivery system. Nano-polysaccharides may be discovered to have a key part in the transportation of drugs to the colon. This involvement might extend beyond standard matrix tablets to composite and sophisticated osmotic-pressure control drug delivery systems. Indisputable evidence suggests that nanotechnology offers a promising approach to the treatment of issues associated with the colon. Because it has the capability of releasing the medicine into the intestinal section of the body. The colonic drug delivery system, also known as the CDDS, has been regarded as a key method during the course of the preceding two decades for the purpose of delivering medications to the colon, which is the large intestine (a site for both local and systemic action)[3-5].

There are a few distinct types of CDDS, the most common of which are oral and rectal administration. However, rectal dosage forms are not nearly as effective as oral administration when it comes to the delivery of drugs in this manner[6-7]. In view of these facts, this review mainly focuses on the novel procedures/technologies and the role of nano-polysaccharides in the colon-specific delivery of drugs.

2. COLON-TARGETED MEDICATION DELIVERY: AN ANATOMIC PERSPECTIVE AND CONTROLLING FACTORS

The stomach, in addition to the small and the large intestines, are the primary components of the GIT. The large intestine is a stretched structure that extends from the ileocolic junction all the way to the anus. This region of the intestine is called the jejunum. The large intestine, sometimes known as the whole intestine, is divided into three distinct regions: the colon, the rectum, and the anal canal and anus. The whole length of the colon is around 5 feet (150 cm) long, and it is divided into five distinct parts throughout its length. The peritoneal folds, sometimes referred to as the mesentery, are supported by the ascending and descending colon (which have the function to connect the organs to the abdominal wall). The cecum, the hepatic flexion, the ascending colon, and the right side of the bisected cross colon are all considered to be components of the right side of the colon. Aside from the left bisected cross colon, the left side of the colon is included in the descending colon, the sigmoid, and the splenic flexion. Before reaching the anus, the rectum is the most unusual and anatomically significant piece of the gastrointestinal system.

Figure 1 depicts the organisational structure of the intestinal tract:

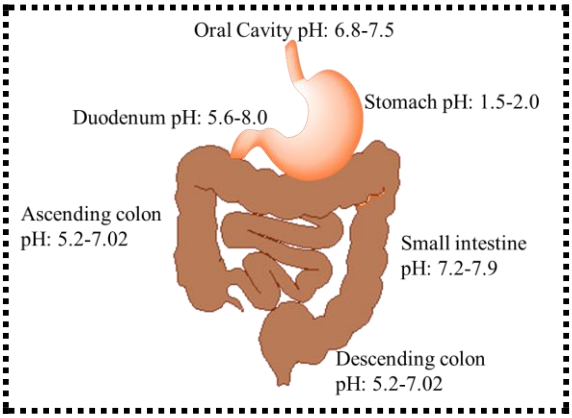


Figure 1: pH of the different region of digestive system.

As it provides an environment that is favorable to the development of colonic bacteria, the colon maintains a variety of activities. The intestinal lumen serves as a storage space for faeces, removing undesired material when necessary and absorbing vital potassium and water molecules. A maximum of 2000 ml of liquid may pass through the intestinal membrane and colon thanks to the colon's strong absorption abilities. The ileocecal valve, however, allows up to 90% of the fluid to be reabsorbed[8,9]. In addition, a number of other variables might have a direct or indirect impact on colon target drug delivery.

3. ASPECTS OF COLON DRUG DELIVERY

3.1. Alteration of pH in the colon region

The pH may change to 6.40.5 at the end of the small intestine. The pH in the middle of the colon is 6.6±1, whereas it is around 7.0±1 in the left colon. Different subjects have different digestive tract pH levels. The main idea behind treating the colon's illness location is to adjust pH. The variation in pH is significantly influenced by factors including nutrition, food consumption, and illness. The colon's pH drops as a consequence of the presence of short-chain fatty acid molecules (products of bacterial fermentation of polysaccharides)[10,11].

3.2 Colonic transit time in the intestines

A primary influence on one CDDS conduction with the intestinal drug bioavailability is the human intestinal transit time. The transit duration is influenced by gastrointestinal conditions including Ulcerative Colitis (UC) and Crohn's disease (CD). In contrast to healthy people (~52 h), those who are UC-tolerant have short colonic times (~24 h)[12]. The length of orofecal transit is taken into consideration when comparing patients with inflammatory bowel disease (IBD) to healthy individuals. The timing of administration, the kind of dosage form, and the presence or absence of meals are often taken into consideration while moving the delivery mechanism. Stubbs et al. looked at how day and night affected the mobility of drugs in the large intestine. A rresults indicate that sleeping and taking greater dosages are the factors that slow intestinal transit[13].

3.3 Volume of Colonic Fluid

Humans typically consume 1.5 kg of feed per day, most of it is made up of lipids, monosaccharides, and indigestible proteins. The intestinal substrate for the bacteria enzymes

may include the dietary material. The colon has a greater water-absorption capacity and can absorb around ~90% of the water that is introduced to it. The amount of intestinal fluid is estimated to be between 1 to 44 ml, with a comparative extent of around 13 ml. Low levels of intestinal fluids lead to drug disintegration, which in turn affects the drug's local bioavailability[14,15].

3.4 Colonic Luminal Contents' viscosity

The consistency of the content occupied lumen is superior to upper GIT due to superior or excessive water captivating function, which initiated an opposition for CDDS dissolution. In addition, the content's thickness steadily increased as it moved from the ascending artery to the descending colon, resulting in a reduced rate of drug disintegration and mucosal penetration. The viscosity has a stronger effect on the medication perforation in the microorganisms present in the colon. The viscosity of the intestinal contents affects how easily bacteria can be transmitted[16,17].

3.5 Enzymes and Metabolic Processes in the Colon

In addition to 400, non-identical genera of bacteria that are dependent on free oxygen (such as Escherichia coli) and microorganisms that are unaffected by oxygen (such as Clostridium) help to form the structure of the colon. These bacteria produce certain digestive and metabolising enzymes, and this catalyst speeds up a range of responses associated with the metabolic process of xenobiotics (such as drugs); more biological molecules (such as bile acid); deactivates damaging metabolites; and able to ferment carbohydrates and proteins[18]. Carbohydrate derivatives such as chitosan, guar gum, pectin, and other related compounds are often used in order to regulate the liberation rate in dosage forms that are intended for colon treatment. These familiar units of monomers have the ability to compete with the enzymes that are found in the GIT, but they are consumed by anaerobic bacteria in the large intestine[19]. It is also well known that the drugs are susceptible to the biotransformation that is caused by intestinal enzymes. This change resulted in the development of a pharmacologically active metabolite, which is an approach generally referred to as a "prodrug." Prodrugs are typically used for methods of administering medication that are particular to the colon[20].

4 Requirements for selecting a CDDS medication

The majority of drug delivery methods used to treat colitis, IBD, diarrhoea, and cancer release medication molecules called peptides that are poorly absorbed into the stomach region[21]. Another crucial aspect for CDDS is the drug carrier. Drugs carriers are selected based on the physicochemical characteristics of the drug (such as its chemical components, partition coefficient, and stability), the disease being treated, the absorption-enhancing agents, and the drug delivery method. Additionally, the existence of functional groups connected to the drug molecule affects the choice of drug carriers. For example, a medication containing an aniline or nitro group may also demonstrate linking to some other benzene group through an azo bond. The release profiles and effectiveness of these systems may be influenced by the carrier molecules comprising additives, particularly polymeric materials utilized in matrix and hydrogel-based systems or coating agents[22-23].

5 INFLAMMATORY BOWEL DISEASE: INFECTIOUS DISEASE AFFECTING THE LARGE INTESTINE

The development of inflammatory bowel disease (IBD), Crohn's disease (CD), and ulcerative colitis (UC) go hand in hand with chronic inflammatory problems (immune-mediated diseases). Immune-mediated diseases are syndromes that impact a considerable part of the human population and represent a number of severe hazards for the etiopathology, detection, and control of the condition. Both the CD and the UC include instances of these provocations. The replication of the immune system in response to certain components of the colon microbiota in infected hereditary hosts is one of the fascinating aspects of the GIT[24-25], Irritable bowel disease is characterised by a wide variety of problems, many of which are caused by a decrease in colonic microbiota.

6 THE HISTORICAL AND CONTEMPORARY PERSPECTIVES ON THE ETIOPATHOLOGY OF INFLAMMATORY BOWEL DISEASE

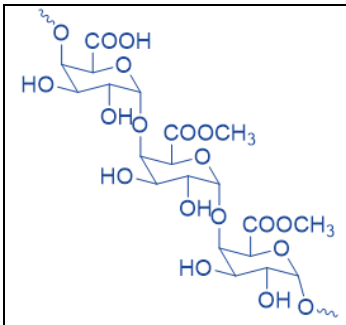
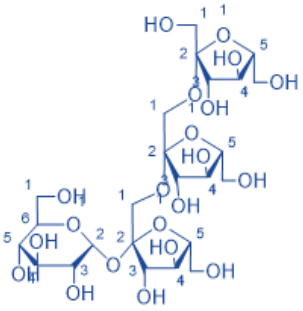
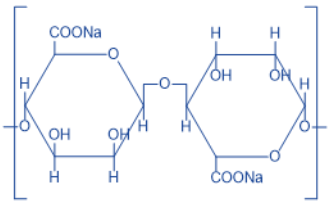
In the 1990s, considerable research was done on the pathophysiology of IBD. It was widely assumed that both CD and UC were associated with increased bacterial activity in their respective forms[26-36]. It has been given a lot of thought that inflammatory bowel disease might be caused by infectious pathogens. Along with the pro-inflammatory agents that were the primary contributors to the development of inflammatory bowel disease (IBD), it was also well known that factors such as humoral immunity, acquired immunity, traditional medication (such as immunosuppressants and corticosteroids), and other unusual responses could also play a role[37]. IBD is thought to be the result of a complex interaction between microbes, the environment, the immune system, and other microbes. It differs from Crohn's disease and ulcerative colitis in that it is characterised by ongoing inflammation of the small and large intestines[38].

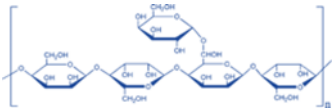
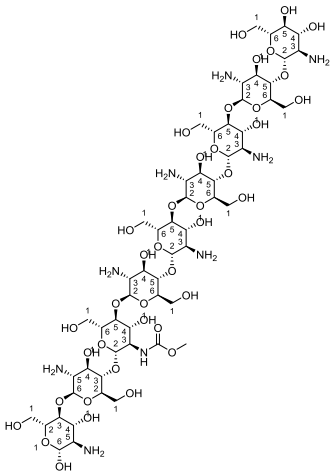
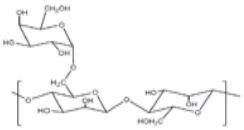
7 POLYSACCHARIDES SERVE AS A TARGETING CHANNEL FOR THE DELIVERY OF COLONIC ACIDS

Along with their particular variety in structure and chemical characteristics, naturally occurring polysaccharides provide an affordable option for target medication delivery to the large intestine. This is possible due to the polysaccharides' use[39]. These polysaccharides are also most beneficial after undergoing chemical and biochemical alteration and modification with certain groups, which results in stability, safety, and non-toxicity with occupational gel forming characteristics. The polysaccharides categorization includes naturally occurring polysaccharides that are derived from plants (such as guar gum and inulin), animals (such as chondroitin sulphate and chitosan), algae (such as alginates), or microbes (such as dextran)[40-42]. **Table 1** contains a discussion of some natural and modified polysaccharides that have been employed in drug delivery strategies.

Table 1: Polysaccharides' inherent qualities as well as those that have been altered[43-44]

Polysaccharide	Natural characteristics	Modified characteristics
Pectin	• Soluble dietary fibre. • Contains neutral sugars. Such as rhamnose (as a part of the polymer	• **Evolution in the structure to alter the solubility:** Calcium salts of

	backbone and galactose) • Liberate the entrapped agent through degradation of the glycosidic linkages by colonic microflora.	pectin showed a better protective effect to decrease the solubility. • **Degree of esterification:** The degree of esterification classifies the behavior of pectin in drug delivery as high-ester (HE) ≥ Low-ester pectin (LE).
Inulin 	• Indigestible by the human enzyme even as it passes intact through much of the digestive enzyme. • Vital bacteria are responsible for the fermentation of inulin. • Metabolization by bifidobacteria. • Metabolization only at the colon.	• Introduction of vinyl group by free radical polymerization to assist successful drug delivery.
Alginates 	• Capability of preventing drug release from the core in the gastric medium. • Alginates don't form gel due to presence of poly alpha-guluronic acids. • Alginates can be used as a colonic carrier only if they are accompanied by	• Alginate gelation occurs when divalent cationic bonds made with alpha-guluronic acid residues which result in ionic exchange in between sodium and calcium ions claimed to be

	Ca^{+} ions.	responsible for the swelling and degradation in the colonic region results in drug liberation.
Locust Bean gum 	• Solubilize in water. • Less hydration capacity in cold water needs heat for more hydration and viscosity.	• Cross linking led to the water insoluble film-forming product.
Chitosan 	• Natural polysaccharide obtained by the deacetylation of Chitin. • Degree of deacetylation helps to increase the solubility and rheological properties. • Low degree of deacetylation (<40%) soluble only upto the pH of 6.5. • Provides protection to therapeutic agents against the hostile environment of upper GIT.	• **Crosslinking of a chitosan solution with aldehyde:** Chemical cross linking with aldehyde can make it insoluble in acidic fluids. • **Effect of H-bond formation:** Development of hydrogen bonding between Polyvinylpyrrolidone (PVP) and chitosan led to a decrease the solubility in acidic medium.
Guar gum 	• Natural polysaccharides, a type of dietary fiber. • Specifically degraded in the presence of colon microflora by decreasing drug release in large intestine attributable to	• Modification in configuration by crosslinking it with sodium trimetaphosphate (STMP) to avoid premature drug

	hydration and swelling property.	release induced by rapid swelling.

8 SYSTEMS FOR DRUGS DELIVERY FOR COLONY-SPECIFIC TARGETING

3.2 pH-dependent delivery systems

The pH of a healthy stomach ranges from 1 to 4, although it may sometimes reach a value of 6 in the proximal small intestine while rising to a maximum of 7.4 in the distal small intestine. The pH gradually decreases from the ileum to the colon, then increases again in a continuous pattern. By coating the tablets, capsules, or pellets with pH-sensitive polymers[49], these devices are used to release active compounds that are targeted by the colon. The pH may be raised from neutral to a little alkaline pH to boost the solubility of certain types of polymers. Because of this feature, medications are better able to withstand the stomach's acidic pH, allowing for more precise colon delivery. However, intestinal pH is inconsistent and unstable, and it is regularly influenced by food and nutrition, illness, and a few other things, which further demonstrates a significant variation in individuals. As a result of the formulation's early disintegration in the small intestine, there may be non-targeted drug distribution[50].

The solubilization of therapeutic agents in the colonic fluid might be affected by the decreased pH of the colon caused by IBD, which will hinder penetration and disrupt the solubilization of the system's pH-sensitive coating. These patented targeted drug release polymers, Eudragit L (solubility at pH 5.5–6), Eudragit S (solubility at pH 7), and Eudragit FS (solubility at pH 7), are the most often used pH-sensitive polymers and have been used alone or in combination to provide the best coating dissolution. Eudragit is not the only pH-sensitive coating polymer for colon targeting; others include hydroxypropyl methylcellulose acetate succinate (HPMC-AS) and cellulose acetate phthalate (CAP)[51,52]. The Colon Pulse technology is a typical pH-sensitive system, but it includes an additional swelling disintegrant (croscarmellose sodium) in the coating material, which causes a speedier and more pulsatile release of the drug than other pH-dependent systems[53,54].

8.2 Microflora-activated release

The colonic microflora is a complex community made up of a variety of bacteria. Different kinds of fermented substrates that enter the colon undigested serve as the primary source of energy for colonic bacteria. To do this, microflora produces a variety of enzymes utilising different polysaccharides[55]. Many polysaccharides, such as guar gum, chitosan, amylose, xanthan gum, dextran, pectin, etc, have previously been used to their fullest extent as a CDDS[56]. Polysaccharides and other azo polymers have been categorised for colon-targeting. These kinds of chemicals are broken down by microflora-induced reductase enzymes[57]. The commercial microflora-activated delivery system COLAL^{TM} uses amylose, which is made from starch and is sometimes referred to as "glassy amylose," a carbohydrate that is not broken down by the enzyme (human amylase) in the GI tract. The polysaccharides also had ethyl cellulose added to them to help them swell and delay the premature release of the drugs[58]. Two further delivery systems, known as CODES^{TM} (Colon targeted system) and TARGIT (enteric coated injection

moulded starch capsules), employ a combination of microflora-activated and pH-responsive processes to prevent active ingredient release in the small intestine[59]. Following that, a dual layered coated colon-targeted delivery system was developed. It consists of a chitosan-created micro protective layer of both the dosage form comprising citric acid for ambient acidification, followed by an enteric coating. The system was designed to deliver the medication to the colon. Using chitosanase, which is produced by the microbiota, this strategy shows promise for maintaining a slow release of medicine in the colon[60]. In recent years, a multitude of researchers have become aware of the GIT microbiota as a method for the release of drugs. The genus Bacteroides, which is a member of the family Bacteroidaceae, is responsible for 20–30% of the microflora that is found in the GIT (Gram-negative rod shape anaerobic bacteria without endospores or pigments that live in human and animal guts). The distal region was formerly home to a community of GIT microflora, which may still be found throughout the gut. The microfloral enzymes in the colon may be responsible for the release of the drug. This results in the release of the drug from the pro-drug, as well as the digestion and elimination of endogenous and foreign proteins and carbohydrates that are not digested in the upper part of the gastrointestinal tract (GIT)[61,62]. According to the information shown in **Table 2**, the enzymes that promote the destruction of bacteria in the colonic area may be divided into two categories: reducing enzymes and hydrolytic enzymes[63].

Table 2: Different enzymes responsible for the microbial breakdown in the colon

S. NO.	Reduction	Hydrolytic
1.	Nitro reductase Enzymes	Esterase Enzymes
2.	Azoreductases Enzymes	Amidases Enzymes
3.	N-oxide reductase Enzymes	Glycosidases Enzymes
4.	Sulphoxidoreductase Enzymes	Glucuronidase Enzymes
5.	Hydrogenase Enzymes	Sulfatase Enzymes

8.3 Time-dependent drug releasing system

These technologies predict the timing of medicine release using GI transit time. Because individuals have greater differences in the amount of time it takes for their stomachs to empty, these techniques have their limitations owing to the fact that they announce an unexpected flow of the medicine to the colon. Patients who have inflammatory bowel disease typically suffer symptoms including short intestinal transit time and diarrhoea, which may result in premature medication release and quick drug clearance from the colon. Patients with IBD also regularly have other symptoms like abdominal pain and bloating[64]. The Chrono cap is a time-dependent delivery device that comprises of a drug with a solid dosage core that is laminated with a water-soluble adhesive covering and an interior layer of a hydrophobic surfactant. Following the

disintegration of the water-soluble coating, the inner layer will start to decompose. As a consequence of this, the length of time that it takes for medicine to be released is dependent on the hydrophobicity of the layers[65].

8.4 Multimatrix technology

When numerous layers are combined into one for colon-specific targeting, this method is referred to as "multimatrix technology." The multimatrix delivery technology ensures that medications are distributed evenly and in a controlled way throughout the colon. The pH-dependent polymer in the outermost layer of the dosage form protects the core until it reaches the gut, which is when the predetermined breakdown process starts[66-68]. In addition to an inert polymeric matrix, the primary core is made up of hydrophilic material. The inert matrix covers and protects the drugs and ingredients within of a mesh made of an amphoteric polymeric substance. This improves drug solubility and relaxes the hydrophilic material that is primarily utilised for swelling, hence reducing the rate at which pharmaceuticals are released into the body. This sort of event indicates that the implanted drug is exposed to the whole intestinal mucosa in a consistent and prolonged way[69-71].

Figure 2 illustrated the multimatrix drug delivery system and Table 3 depicts the transit timings, pH, and microbial composition of .

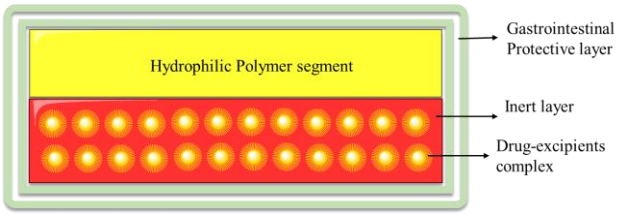


Figure 2: Impression of Multi matrix segments drug delivery system

Table 3: Transit timings, luminal pH in the Gut specifically in active IBD and in a healthy condition

	Transit time		**Luminal pH**	
	Healthy condition	**In active IBD**	**Healthy condition**	**In active IBD**
Stomach	--	--	1-4	1.5-4
Duodenum	2-6h	--	6	7.4
Jejunum	2-6h	15-30%	7	7
Ileum	2-6h	--	7.4	7.4
Large intestine(colon)	6-70h	Varying usually decreased but can be increased	6-6.8	2.3-5.5

9 NEW COLON-TARGETING METHODS

9.1 Osmotic controlled drug delivery (ORDS-CT)

Drugs may be administered to the large intestine using the OROS-CT device from the ALZA firm. These ALZA companies may take the form of a single absorbent assembly or a grouping of many push-pull assemblies (5–6) surrounded by an enteric coating material and housed within a stiff gelatin capsule that dissolves in the small intestine. The osmotic medication delivery method is shown in **Figure 3**. An individual assembly consists of a spongy push sheet and a medication coat, both of which are encircled by a permeable membrane. Following that, an opening must be drilled in the drug sheet by the membrane[72]. The stomach's natural aqueous acid medication dissolves right away once the gelatin capsule interacts with it. However, because the gastro resistant coating makes it difficult for H2O to pass through, no medication is disseminated as a consequence of the individual push-pull assembly. When the units reach the jejunum, the coated layer starts to diffuse there in a high pH environment (pH > 7), and water enters the push-pull assemblies, invading the section containing osmogenes and causing flowable gel in the pharmaceutical agent portion to swell. Bulging of the osmogene-containing push sections forces out thicker drug production from the entrance at specified rates together with the quantity of water transit by semipermeable sheet[73]. To prevent medication transportation in the small bowel during UC treatment, a specific unit device is used with a 3–4 hour post-gastric delay. The OROS-CT units can deliver drugs in as little as 4 hours or support a constant release rate in the large intestine for up to 24 hours. Recently, new phase-transitioned systems with excellent potential for colon drug delivery have appeared. To assess the potential and stability of CDDS, several in-vitro/in-vivo evaluation methods have been proposed[74,75].

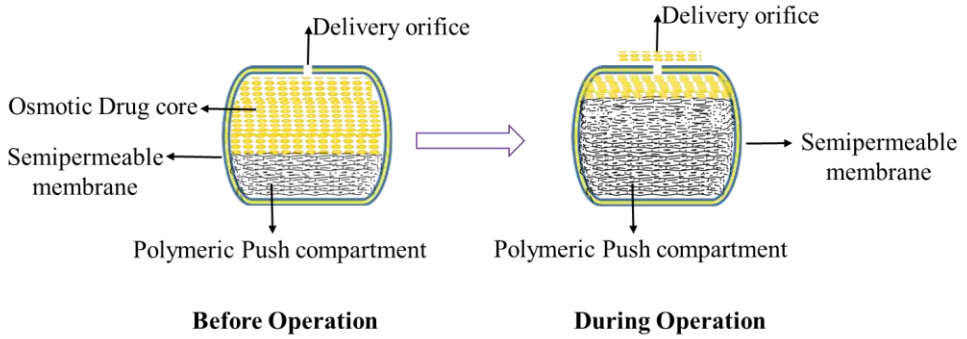


Figure 3: Osmotic drug delivery system

9.2 Pressure Controlled Drug-Delivery Systems

Due to the presence of peristaltic waves, excessive pressures manifest themselves in the big bowel rather than the jejunum. It has been possible to create ethyl cellulose-based pressure-controlled large intestine-targeting capsules that are insoluble in water[76]. Similar to how the H_2O insoluble polysaccharides capsule collapsed under luminal pressure in the large intestine, allowing the medication to be released, The most important element affecting formulation breakdown is the width of ethyl cellulose[67,78]. The density and size of the capsule seem to be key factors in the arrangement. Colonic water reassimilation thickens the large intestine's lumen

content relative to the small intestine. As a result, it would be done with the idea that the large intestine drug dissolving would provide a problem for colon spotting oral drug delivery methods. In pressure-controlled ethyl cellulose individual assembly, the medication is administered as a liquid. Log periods of 3 to 5 hours for medication absorption were acclaimed whenever these pressure-controlled capsules were given out to individuals[79].

9.3 Nanoparticles delivery systems

Nano formulations are used to distribute and regulate therapeutic ingredients in these novel systems. Nanomaterials are better for drug delivery systems due to their chemical, physical, and biological properties. Nanoparticles may interact with biomolecules to increase cell membrane absorption, have a high surface area/volume ratio, and be geometrical and chemical tuned. Pharmaceuticals and smaller molecules like ligands and antibodies are also attracted to the large surface area for targeting and release regulation solve the delivery system's flaw. Guidance for nanotechnology-based delivery systems[80]. Nanoparticles do not build up above physiologic conditions and bacterial configuration of the GIT concerning illness state. Nanoparticles-based delivery systems targeting the gut leverage the differences between normal and abnormal mucosa or tumour cells to target infection or cancer. In discriminated nanoparticles complexes could be utilized to destinate the colon possessing specific mechanisms such as:

i. Nanoparticles made of triglycerides have fascinating biological properties, including compatibility, biodegradability, and the ability to trap water-soluble and hydrophobic drugs[81,82]. E.g. Liposome systems and solid lipid nanoparticles change the therapeutic agent's outer perimeter for colon targeting.
ii. PLGA poly (lactic-co-glycolic acid) is used to make colon-targeted nanoparticles for IBD therapy[83]. It would be investigated in such a way that only the measurement of nano-particles exists as an influential factor to spot unhealthy mucosa. Besides the dimension of a particle, the charge on its surface is furthermore salient in the intercommunication of mucus sheet and epithelial cells, a sore tissue network that contains an elevated concentration of positively charged protein that can captivate anionic PLGA[84].
iii. The nano-particulate in micro-particles oral delivery system (Nimos) is an uncommon delivery system for colon targeting. By combining plasmids and proteins into gelatin based nanoformulations, which are then enclosed in poly (caprolactone) microparticles, these systems are developed for oral ingestion of plasmids and proteins (a synthetic hydrophobic polyester that shields nanoparticles from the hostile environment of the stomach during transit)[85,86].

9.4 Biopharmaceuticals

Colon disease is treated using biopharmaceuticals. These biologics have revolutionised colonic disease therapy, although pharmaceutical applied sciences disagree on their formulation and transport to inflammatory sites[87]. Parenteral biopharmaceuticals offered a benefit, but it was toxic and caused immunological and oversensitive reactions. Targeting the medicine to the colon may decrease the clinical risk of systemic exposure[88]. Oral intake is better for the colon. Low mucus permeation and GIT degradation are powerful edges. Drying technology have made solid

oral formulations of numerous biopharmaceuticals (different healing microorganisms' proteins) for colon medication possible[89-91]. **Figure 4** depicts the method of preparation of biopharmaceuticals formulations and favourable route of delivery.

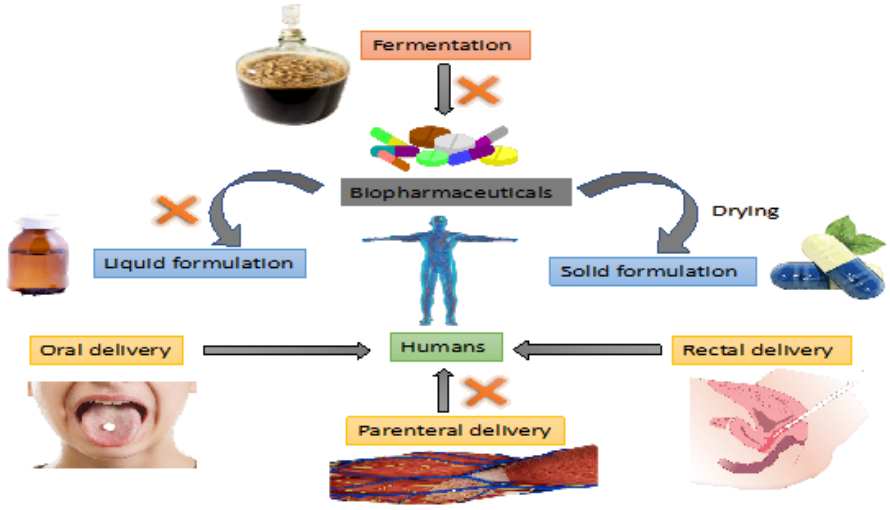


Figure 4: Biopharmaceuticals formulations and their effective route of delivery

10 FUTURE PROSPECTIVES

Polysaccharides and micro/nano fabrications will improve drug delivery to diseased regions in large intestine diseases. Replication of colonic disorganisations requires focused conveyance with minimal side effects. Novel methods improve effectiveness with oral delivery. Drugs specifically for the large intestine achieved these desirable properties. Given results, a combination of methods is needed to treat colon diseases. To promote productivity and health, concerned with transport must also be modified over time. Therefore, identifying various strategies. Following study may need for optimizing variables for drug delivery. Improving the feasibility analysis of a delivery method for diseases with a specific route of administration is important.

CONCLUSION:

Despite the limitations of colon-targeted delivery systems, oral administration of pharmacological agents for colon targeting is one of the most promising IBD therapy methods in terms of safety, effectiveness, and patient compliance. As colon disease prevalence increase, the pharmaceutical industry is interested in moulding an agent in an oral formulation with a polymer covering. Pharmaceutical companies may recognize this trend, which is likely to continue, and show that research in this area can help develop new IBD and colon-affecting disease treatments. This article analyzes oral drug and pharmaceutical administration to the colonic area and market-available biopharmaceutical formulations. It has a polysaccharide structure for colon release of drugs. A drying technology technique to stabilise biopharmaceutical liquid formulations has been explored, and its limits and uses have been fully informed by their distinction of key characteristics.

CONFLICT OF INTEREST:

The authors declared no conflict of interests.

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