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Review Article

# Recent Advances in Colon-Specific Drug Delivery with NSAID-Loaded Nanoparticles in Microparticles for Enhanced Efficacy and Minimized Side Effects

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**ABSTRACT**

Colon-specific drug delivery is utilized in disease conditions such as colorectal cancer, Ulcerative Colitis, and irritable bowel syndrome and to improve oral delivery and provide local treatment. It minimizes the need for numerous doses, permits precise treatment at the disease area, and lessens the possibility of systemic adverse effects, hence it provides better patient compliance and lowers costs. The strategies for colon targeting consist of magnetically driven, pH-dependent, enzyme-triggered, receptor-mediated systems, polysaccharides-based, and pressure-controlled drug delivery systems. Recent developments in formulation technologies for colon-targeted drug delivery systems include microencapsulation of nanoparticles. Recent research involves studies using model categories of drugs such as Ibuprofen and Triptorelin acetate that can reduce the burst release in controlled-release formulations, the advantage being that composite microparticles show lower burst release when compared to classical microparticles. This review gives insights into the fabrication methods, mechanisms of action, and potential therapeutic purposes of nanoparticles in microparticles.

**Keywords:** NSAIDs, nanoparticles in microparticles, Colon-Specific Drug Delivery, Ulcerative Colitis, Inflammatory Bowel Disease

## INTRODUCTION

Advanced colon-targeted drug delivery is needed and can be highly effective in treating conditions associated with the colon, primarily inflammatory bowel disease (IBD), irritable bowel syndrome, and colorectal cancer (CRC). The carrier-specialized delivery systems for the colon can minimize the chance of systemic adverse effects, and the need for frequent dosing, and allow direct treatment at the disease site. The colon, also known as the large intestine, is a 160 cm long tube that stretches from the ileocecal junction to the anus. Its main function is to absorb water and salt from the solid waste so that the body can expel it as faces [1,2].

### Colon-specific medication delivery considerations

The stomach, small intestine, and large intestine are the three primary parts of the gastrointestinal tract. An extension of the large intestine is the small intestine that connects the ileum and anus. The large intestine also known as the whole intestine, is made up of three different parts: the colon (the large part of the intestine), the rectum (the small part of the intestine), and the anus. Peritoneal folds (sometimes called mesentery) are supported by ascending and descending colons (which help to connect the organs with the abdominal wall). The colon's right side comprises the hepatic lesion, ascending colon, caecum, and right side of the bisected cross colon, the left portion of the bisected colon comprises the sigmoid descending colon and splenic flexion. Anatomically the rectum is a significant part of the GIT before / reaching the anus and is considered an environment conducive to the growth of colonic bacteria. The colon has a variety of functions. The intestinal lumen stores faeces, removes unwanted material when needed, and absorbs important potassium and water molecules [3,4,5].

The lungs, gastrointestinal tract, and liver are among the organs affected by the disease's severe inflammatory symptoms (GI tract), by dissolving mucosal barriers, releasing damage-associated molecular patterns, and conditioning regimens that

have a significant impact on the gastrointestinal system [6]. Several physiological systems are involved in drug distribution to the colon, which ensures the effectiveness of the therapy after oral administration. During formulation design, consideration should be given to the duration of drug residence in GIT, its effects in the GIT environment, and the dissolution of the drug [7].

### *Physiology of colon and colon microflora*

The mucosa, submucosa, serosa, and muscularis propria are the four layers that form the wall of the colon, which are made up of lamina propria, muscularis mucosa, and epithelium. There are several microorganisms in the GIT that play a role in its physiology and function, as well as in meal digestion periods. The upper GIT has very few bacteria while the colon contains about 1011 to 1012 cfu/ml of bacteria, mostly anaerobic bacteria, including Bacteroides (Bacteria), Bifidobacterium (Bacteria), Eubacteria, Gram (Gram-positive cocci), Clostridia, Enterococci, and Enterobacteria. Various substrates, like polysaccharides, are fermented by colonic microflora, which results in the generation of gases (methane, carbon dioxide) and end products of short-chain fatty acids [8]. Microbiota is created through interactions between the host's physiological system and externally introduced bacteria [9].

Human health and illness are significantly influenced by the gut microbiota. Not only do gut microbes absorb energy from food but they also play a role in generating signals, GIT function, immunity, infection, and inflammation responses. Gut microbiota is a communication channel between the microbial host ecosystem and the immune system that is naturally present. Therefore, changes to the gut microbiome's environment may raise the chance of acquiring bowel disorders [10]. Because of the gut microbiota's horizontal transfer, researchers suggest that it contributes significantly to the metabolic advantages of G. lucidum [11].

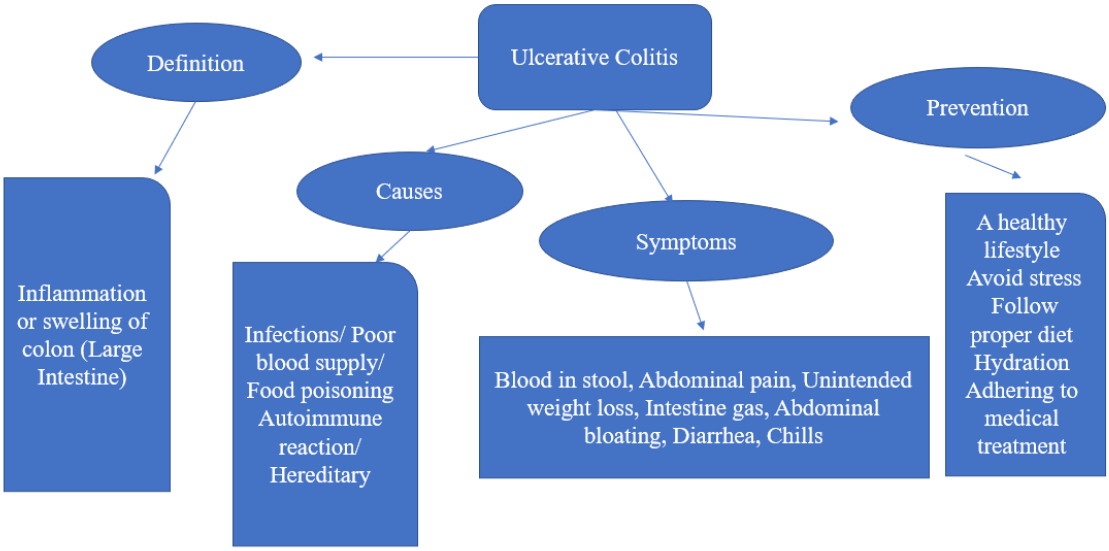


***Fig. 1 Schematic illustration of ulcerative colitis with causes and treatment***

### *Colonic fluid volume*

Colonic fluid volume can range from 1 to 44 mL approximately with an average volume of 13 ml. The colon absorbs over 90% of the water that enters the human body. Due to its large surface area, it highly contributes to water absorption capacity. This low volume can interfere with drug dissolution in the colon and may affect the systemic and local bioavailability of the drug.

Inflammatory bowel disease (IBD) includes ulcerative colitis (UC), and Crohn's disease (CD). The colon and small intestine are affected by both UC and CD, such as persistent mucosal

inflammations that primarily affect the colon and the rectum. [12,13,14].

To reduce the therapeutic agent's dose and enhance the drug's site-specific delivery, it is essential to develop a polymer with multi-stimulus-responsive properties. Recent research describes the preparation and characterization of a co-polymer that reacts to pH and temperature, as well as their application in vitro in colonic environments at pH 6-8 [15].

**Physiological Features of the Human GIT**

| Anatomical portion | *pH* | | *Time for residence* |
|---|---|---|---|
| Stomach | *Fed state* | *3.0-5.0* | 1–3 h |
| | *Fast state* | *1.5-2.0* | |
| *Jejunum* | *5.5-7.0* | | 1.5–2.0 h |
| *Ileum* | 7.0–7.5 | | 5–7 h |
| *Duodenum* | 4.0-5.5 | | *30-40 min* |
| *Cecum* | 5.5–7 | | - |
| Transverse colon | 5.8–7.4 | | 16–35 h |
| Descending colon | 6.3–7.7 | | |
| *Ascending colon* | *5.7-6.9* | | |
| Rectum | 7.0 | | - |

## NSAIDs and their Mechanism of action

Nonsteroid anti-inflammatory drugs are commonly involved in treating rheumatic disease and relieving pain but they cause side effects in many organs. The lower and upper GIT are considered the primary areas where side effects can occur [16]. Generally, NSAIDs are classified by their chemical structure, half-life in plasma, and selectivity (COX-1 vs. COX-2) [17].

NSAIDs function by stopping the production and release of prostaglandins by the enzymes COX-1,2. This results in analgesia, anti-inflammatory and antipyretic effects [18]. COX-2 has a slightly larger active site than COX-1, so selectivity can be achieved by using drugs that are too large to access COX-1 [19,20]. Selective COX-2 (Coxibs) are characterized by COX-2 inhibition, examples including Celecoxib whereas Ibuprofen, Naproxen, and Diclofenac all block both COX isoenzymes in a non-selective manner. The inhibition of selective COX-2 is designed to reduce the incidence of adverse reactions in GIT ( bleeding of upper GIT ) but is linked to an increased cardiovascular risk [21,22].

The enzyme COX-1 is widely expressed in the kidneys and gastrointestinal lining, which plays a role in homeostasis. It also plays a vital role in platelet aggregation [23]. Dose-dependent damage is demonstrated for prescribed NSAIDs that are used for less than 14 days. The damage is dose-dependent and acid-dependent and not seen in selective COX-2 inhibitors with a pKa > 7.0. A long-term (3 months or longer) endoscopy study in patients shows ulcer rates ranging from 15% to 35% with different NSAIDs [24]. NSAIDs are frequently used as anti-inflammatory and pain relievers, but their association with inflammatory bowel diseases remains a topic of concern. pH-sensitive nature and variable particle size make it easier to use them for regulated gene and medication delivery [25].

**An overview of recent NSAIDs and polymers used for colon-specific drug delivery**

| API | Polymer | Finding | References |
|---|---|---|---|
| Indomethacin | Azo-Aromatic Polymers | These polymers protect the drugs from degradation by peptidase enzyme | 26 |
| Sulindac | Carboxymethyl cellulose (CMC)Eudragit L100 | Minimized GIT | 27 |
| Lornoxicam | Polylactic-co-glycolic acid (PLGA), Chitosan | Reduced systemic exposure, improved anti-inflammatory effect | 28 |
| Rofecoxib | HPMC, Eudragit FS30D | Controlled release in the colon, reduced side effects, and improved therapeutic efficacy | 28 |
| Aspirin | Cellulose Derivatives | The time-released formulation ensures the delivery of the drug to the colon | 29 |
| Mesalamine | Ethylcellulose, Chitosan | Effective colon-specific delivery with no drug release in the stomach/small intestine | 29 |
| Meloxicam | Pectin, Eudragit L 100-55 | Minimized release in upper GIT, reduced gastric irritation | 30 |
| Naproxen | Acrylic polymer | Enhanced colon targeting with pH-sensitive coatings | 31 |
| Sulfasalazine | Pectin | Effective for both water soluble and insoluble drug | 32 |

## Treatment options

About 3 million persons in the United States suffer from inflammatory bowel disease, a condition that has been linked to low standard of living, serious complications, hospitalizations, and surgery [26]. Traditionally, treating inflammatory bowel disease has focused on blocking or inhibiting the pathogenetic pathway in the inflammatory cascade. However, recent discoveries suggest that nanotechnology may offer incredible benefits as particles with dimensions on a nanometer scale can alter the pharmacokinetic step of biological and traditional therapeutics agents with improved drug delivery inside the intestinal inflammatory cells [33].

Enhanced anti-UC action of Curcumin hydrogel via chitosan or alginate microparticle encapsulated with hyaluronic acid (HA) or zein nanoparticle has been observed. These utilized Nano in a Microparticle system of hydrogel zein NPs encapsulated with HA for modification of CD44 receptors [34]. Because IBD is persistent, it necessitates follow-up by medical specialists who specialize in this pathology [35]. The immunological and inflammatory dynamics of patients with IBD can be understood using Peripheral blood routine parameters (PBPRPs) [36].

Recent research has shown that the rapid breakdown caused by premature medication release in the GIT region of single nanoparticles makes them inefficient for controlling ulcerative colitis [37]. According to several studies and meta-analyses, using biologics people with ulcerative colitis may see progress in their Health-related quality of life. Although there isn't as much information to support the effectiveness of infliximab, golimumab, and adalimumab, as maintenance therapy, it was found that there is an induction in treatment with these drugs to improve

the quality of living standard compared to placebo [38]. The safety, effectiveness, and mode of administration of treatments for ulcerative colitis (UC) vary; the patient's treatment decisions should be considered for certain treatment characteristics into account [39].

### The European Center for Disease Prevention and Control (ECCO) Guidelines

Therapeutic Options for Ulcerative Colitis provides an in-depth overview of the treatment options available to patients with this condition. The key recommendations include:

5-aminosalicylates (5-ASA) were recommended as first-line therapy of UC for moderate to severe pain. Corticosteroids induce remission when UC is mild to severe. Thiopurines/Methotrexate keep patients in remission with steroid-dependent conditions or frequent relapse. Furthermore, if the patients not responding to the standard therapy, the guidelines suggest biologic medicines such as anti-tumor necrosis factor (Anti-TNF) medications, Ustekinumab, Vedolizumab, and Tofacitinib. The guidelines also emphasize the need for tailored treatment plans, regular disease activity monitoring, and consideration of non-steroidal corticosteroids to reduce long-term use of corticosteroids [40].

One of the benefits of natural polyphenols is their antioxidant and anti-inflammatory properties. Polyphenols such as EGGC (Epigallocatechin Gallate) present in green tea were seen to reflect anti-inflammatory and antioxidant properties [41,42]. These properties make it an excellent candidate for reducing oxidative stress and inflammatory responses in those patients suffering from ulcerative colitis. Natural polyphenols also regulate gut microbiota, boost beneficial bacteria levels, and create functional short-chain fatty acids (SCFA), which can help slow the progression of ulcerative colitis [43]. Recent studies using EPC (Chondroitin Sulfate Functionalized Natural Polyphenol) NPs showed high cellular uptake and were abundant in inflamed colon tissue. This is because chondroitin sulfate has negatively charged characteristics that target CD44. Furthermore, in vitro studies showed remarkable scavenging ability of EPC nanoparticles and anti-inflammatory properties [44].

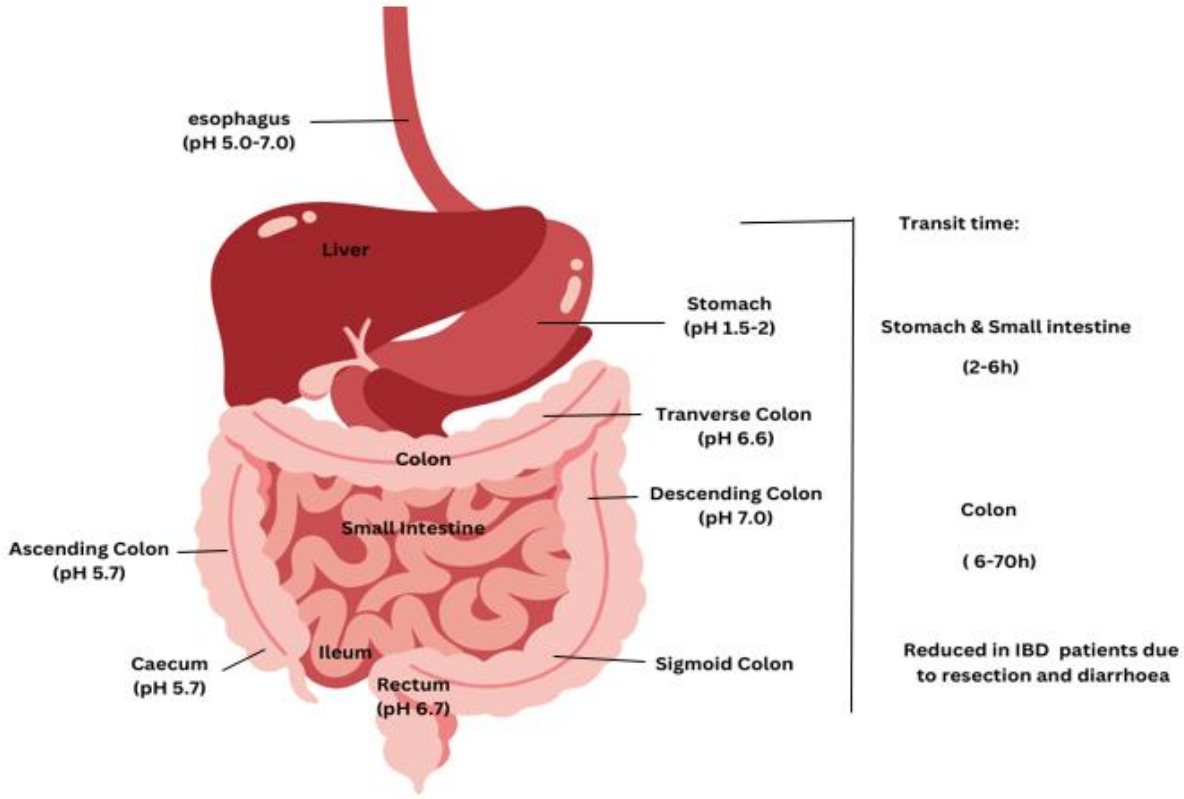


**Fig. 2 Schematic illustration of various Physiology and pathological factors for the colon**

**Drug delivery strategies focused on the colon:**

**(A) Traditional methods for delivering colon targets:**

- Microbial-triggered drug delivery
- pH-sensitive coated polymer system
- Time controlled system

**(B) Advanced colon approaches drug delivery system**

- CODES technology
- Osmatic controlled release delivery system
- Pressure-controlled release delivery system

**(C) Polymeric Approaches for CDS**

- Eudragit L-100-55
- Eudragit L-30D
- Reservoir system with rupturable polymeric coating
- Reservoir system with soluble or Eroding polymer coating

**Conventional drug delivery for the colonic system:**

The Conventional drug delivery for colon disease includes the parenteral route, the rectal route, and the oral route. More specifically, the main drug delivery system for conventional oral colon disease includes pH-sensitive polymer coating, Time-dependent polymers, Bacterial enzymes (pro-drugs), and polysaccharides [45]. Polysaccharides' distinct and adaptable properties result in significant interest in medication delivery as vehicles [46].

Conventional approaches are limited because their transport time and pH through the GIT ( upper gastrointestinal tract) differ significantly between individuals and diseases. Most people have a steady small intestine transit time of ( 3-4). Gastric emptying changes due to factors such as dosage form (fed vs. fasted), co-administered fluid, and motility cycle stage at the time of ingestion [47]. A key factor in guaranteeing the focused and

efficient administration of medications is the use of efficient drug delivery systems (DDSs) [48].

Colon pH can also be affected by inflammatory bowel diseases (e.g., colorectal cancer). Patients with acute colorectal disease show significantly lower colorectal pH levels, These variations in colon pH may raise concerns regarding the effectiveness of colon-specific pH-dependent delivery techniques. The goal of these approaches is to release drugs into the colon to enhance drug effectiveness and reduce systemic adverse reactions. However, conventional approaches are limited due to pH changes and transit times within the GIT that affect how medications are absorbed and released [49].

**Nanoparticles and microparticles in Drug Delivery:**

Cutting-edge, innovative drug delivery technologies like nanoparticles and microparticles have significantly improved the methods of drug delivery allowing for the controlled and highly precise release of medications [50,51]. This leads to lessening the side effects of drugs, and increases the effectiveness of medication therapy, due to its unique characteristics, which include surface chemistry, customizable size, a high volume-to-surface area ratio, and the capacity to contain a broad variety of treatments, such as polymeric NP PLGA with several uses in medication delivery and emerged as effective carriers in the drug delivery. For use in medication delivery, various nanoparticle forms, including liposomes, polymeric nanoparticles, and solid lipid nanoparticles, have been thoroughly investigated [52,53,54,55].

The drug molecules and other carriers that support the active components make up the NP for the dispersion and transport of the medication to its targeted site of action. examples of these carriers include polymeric nanoparticles, liposomes, nanotubes, inorganic silver and gold nanoparticles, and micelles [56]. selenium nanoparticle is utilized to target the colon with a bioactive carrier that is administered orally [57]. In the biomedical field, metal nanoparticles are employed in biosensors, gene delivery systems, bioimaging tools, and infection targeting and suppression [58]. Molecularly imprinted polymer (MIPs) is another outcome of nanotechnology utilized in developing biosensors and in providing methods to deliver different medications or new separation of phase. MIPs are essential "recognition" materials [59].

There has been a noticeable increase in research focused on micro- and nanotechnologies as innovative platforms for delivering different medicinal compounds with precise targeting and control. Multiple unit formulations of microparticulate delivery systems for topical, parenteral, or oral administration are thought to be potent therapeutic tools in the management of a different category of disorders, delivering accurate dosage, increased drug stability, prolonged drug release, and targeted delivery of the active ingredient to particular body locations [60,61].

Microparticles made of polymers have a size range from 1-100nm, composed of a polymeric structure, In terms of structure, microparticles can be categorized into two primary classes: microspheres and microcapsules [62,63].

**Novel delivery systems for colon drug targeting**

Research is now focusing on introducing dosage forms particularly oral for colon-specific drug delivery formulation is becoming increasingly popular such as Polysaccharides that cannot be digested and are not well permeable to GIT for various drug delivery systems, However, once they enter the colon are broken down by the enzymes generated by the colonic microbiota. Various polysaccharide carriers have been studied, but resistant starch was found to be the most effective [64]. Using biopolymers is a potential strategy to raise drug carriers' safety. Polysaccharide biopolymers are the most prevalent type, which consist of inulin, starch, chitosan, sodium alginate, and pectin [65]. The naturally occurring cyclic oligosaccharides are renowned for their capability to encapsulate various moieties within cavities and for having a safe profile [66].

The most prevalent polymeric approaches to colon drug delivery are Reservoir systems with rupture-resistant polymeric coating and reservoir systems with soluble or degradable polymeric coating. Pressurized controlled drug delivery utilizing a capsule to raise the pressure of the colon's luminal contents, the CODES technology combines a colon-specific medication delivery that is triggered by microbes and pH-dependent, involving lactulose as a trigger for medication release. A controlled osmatic delivery system is a formulation of a colonic target drug that is released through osmotic pumping actions [67]. The pressure-controlled colorectal drug delivery system capsules are used to increase the colonic luminal pressure. When water is reabsorbed in this region, the luminal pressure increases [68]. With the advancement of pharmacology and pharmacokinetics, which demonstrated the importance of drug release in affecting therapeutic success, the concept of controlled release was developed [69].

New strategies for targeted drug administration have been put forth, by combining the characteristics of natural or biomimetic materials with those of conventional synthetic carriers and surface functionalization to bind certain target cell receptors [70]. These systems were designed to deliver colon-specific delivery systems, facilitating enhanced local therapy for colonic disorders with minimized systemic adverse consequences, Moreover, ligand/receptor systems that interact between target ligands expressed on specific receptors at disease sites and on the carrier surface have been designed to increase target sensitivity [71]. There are certain restrictions and difficulties related to the development of a delivery mechanism tailored to the colon. The colon's location in the distal portion of the GITt is significant and might be an evident challenge [72]. Alginate-based drug delivery systems can be formulated as nanoparticles, microbeads, and other forms, and have a different range of medicinal applications [73].

Pulsatile drug delivery, a preprogrammed drug delivery system, describes the connection between a delivery system's actions and the body's internal operations. As a result, the introduction of a novel therapeutic known as "chrono-pharmacotherapy" [74].

Electronic drug delivery systems (EDDS) are also seen as a new way to deliver controlled drugs at targeted locations, although they have some drawbacks such as high costs, manufacturing challenges, and device failure [75,76]. The goal of these approaches is to determine the site specificity in vivo and the feasibility of colonic drug administration. Overall, these new drug delivery systems provide promising opportunities for more effective and safer drug treatments for colonic conditions, such as colorectal carcinoma and inflammatory bowel disease [77].

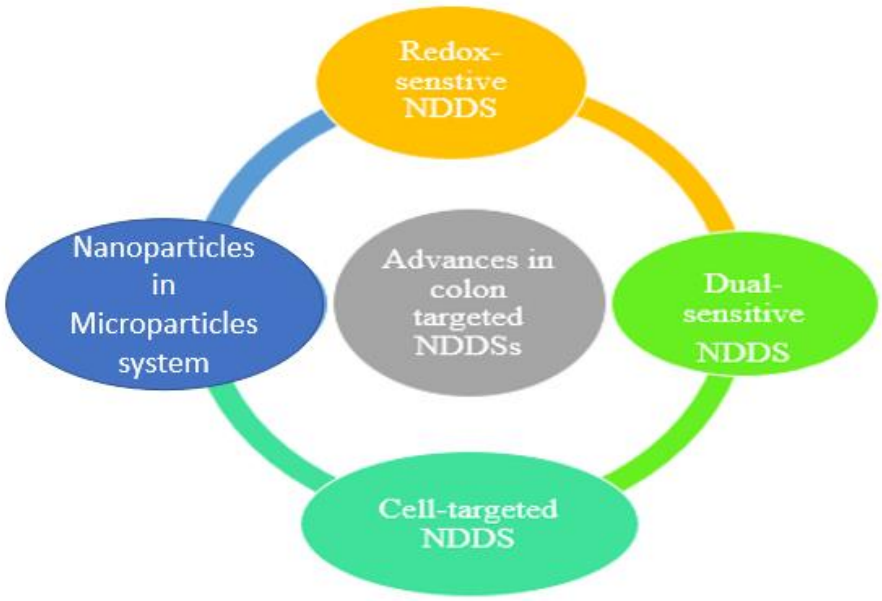


**Fig. 3 Schematic illustration for advances in colon-targeted drug delivery system**

## Marketed products available for colon-specific drug delivery system [13,93,94]:

| Sr. No | Drug | Brand name | Dosage form |
|---|---|---|---|
| 1 | Mesalazine | Asacol | Tablet |
| 2 | Prednisone | Deltasone | Entric-Coated Tablet |
| 3 | Budesonide | Entocort EC | Capsule |
| 4 | Sulfasalazine | Azulfidine | Tablet |
| 5 | Olsalazine | Dipentum | Capsule |
| 6 | Tofacitinib | Xeljanz | Tablet |
| 7 | Ustekinumab | Stelara | Injectable |
| 8 | Vedolizumab | Entyvio | Injectable |
| 9 | Linaclotide | Linzess | Capsule |
| 10 | Fidaxomicin | Dificid | Tablet |
| 11 | Rifaximin | Xifaxan | Tablet |
| 12 | Celecoxib | Celebrex | Capsule |
| 13 | Hydrocortisone | Solu-Cortef | Injectable |
| 14 | Vancomycin | Vancocin | Capsule |
| 15 | Metronidazole | Flagyl | Tablet |
| 16 | Oxaliplatin | Eloxatin | Injectable |
| 17 | Bevacizumab | Avastin | Injectable |
| 18 | Adalimumab | Humira | Injectable |
| 19 | Prucalopride | Resolor | Tablet |
| 20 | Balsalazide | Colazal | Capsule |

## Methods of preparation of Nanoparticles in microparticles:

Polymeric materials encompass the majority of microparticles, which can be developed via various physical and chemical techniques.

**Single emulsion technique:**

Hydrophobic drugs are encapsulated in a single emulsion using the O/W technique. copolymers (PLGA), the drug, and a solvent (benzyl alcohol, dichloromethane, ethyl acetate) in which the organic phase is dissolved, then the liquid becomes precipitated into the aqueous phase with sodium cholate, PVA as surfactant. After that, a mixture is sonicated, shaken, and evaporated to remove the organic solvent to produce emulsion droplets, which are then converted into polymer nanoparticles [78].

**Spray Drying Method:**

Polymeric mixed microspheres with a diameter range from 1-100nm are made using this technique. Organic solvents like DCM or acetone are added to dissolve the polymers. Next, the polymeric solution is mixed with polymer core materials, then the dispersed phase is kept under the spray chamber hot air, the end product is a fine mist that instantly evaporates the solvent, as a result, cyclone separation which is located directly adjacent to the spray chamber is used to separate microparticles [79,80].

**Precipitation Method:**

Precipitation methods are considered the easiest, most straightforward process used to create structure and function as needed for the formulation of micro/nanoparticles. Poly lactic-co-glycolic acid ( PLGA ) Micro/nanoparticles are produced by this technique that encapsulates the drug by dissolving PLGA copolymers with the drug in a polar solvent, which is subsequently mixed with a significant amount of aqueous phase. The organic volatile solvent can be eliminated by evaporation as the system goes through phase separation [81]. Using the nano-precipitation method, Razan et al. were to create PLGA-Paclitaxel nanoparticles that effectively prevent the growth of breast cancer cells called MCF-7. The paclitaxel-loaded PLAGA-NPs were highly effective against MCF-7 cells and did not cause any harm to normal MCF-10A cells [82,83].

**Coacervation Method:**

The coacervation method is used to formulate nano-sized or micro-sized biodegradable polymer substances by liquid and liquid phase separation techniques. It is the polymer's interaction with altering the ionic strength in the system, adding a non-solvent, or changing the temperature for the polymer to precipitate. Mono-coacervation and Complex-coacervation are the two main categories of coacervation techniques. when using the Mono-coacervation approach, the nano-materials are reduced in solubility with the help of a hydrophilic electrolyte (e.g., electrolyte) or a nonelectrolyte. The microparticles are agglomerated into microparticles by the formation of vesicles. Two polymer molecules are used in the complex coacervation process with opposite charges to create vesicles. The vesicle reabsorbs the solubility of the microparticles and causes agglomeration and precipitation from the solvent [84,85,86].

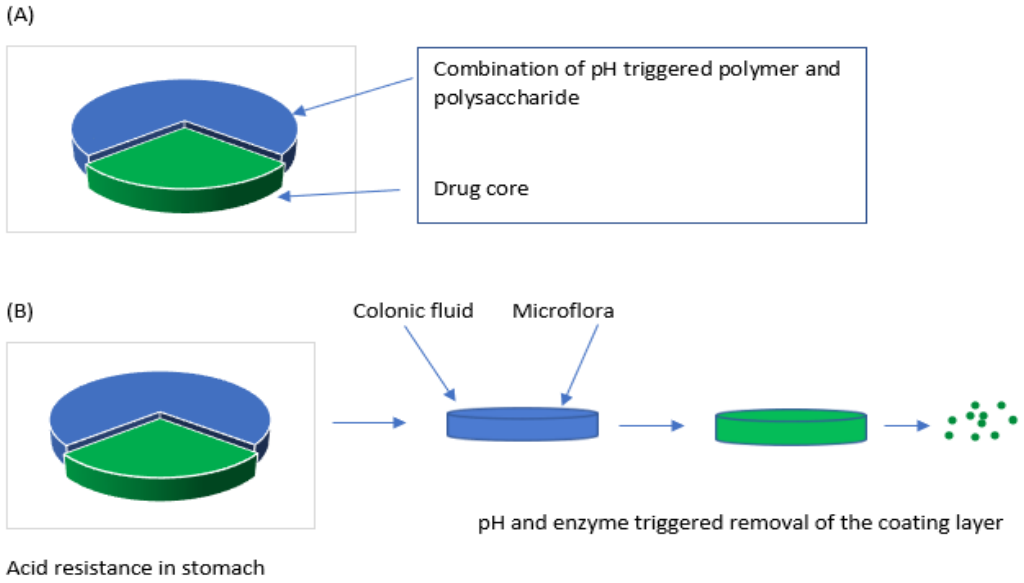


**Fig. 4 Schematic showing tablet and its release, (A) is the tablet and (B) the release of API from tablet**

**Ionotropic Gelation Technique:**

chitosan (CS) nanoparticle preparation followed a recognized ionotropic gelation process. Briefly, 25 mL of a 2% v/v acetic acid aqueous solution pH 4.5 containing the appropriate quantity of chitosan were dissolved to make a solution that contained chitosan 0.8% w/v. BUD is mixed with the chitosan solution in the smallest amount of ethanol necessary and at final concentrations of various weight ranges from 10%, 20%, and 30% in BUD to the chitosan polymer solution, then kept for 30 min in a magnetic stirrer. Under magnetic stirring, a dropwise addition of an aqueous TPP solution of 2 mg/mL was made, and the final concentration was made by adding 25 mL of chitosan in BUD [87, 88].

**Solvent evaporation method:**

A certain volume of DCM was used to dissolve ethyl cellulose to form the inner phase of the emulsion; it was also used to formulate the microparticle-loading AZI. To create a homogenous solution, add AZI to the mixture and ultrasonicate it for 15 minutes at 25 °C. To eliminate DCM, the inner phase was mixed with the polyvinyl solution in water (the outer phase) and stirred for 120 minutes at 1200 rpm using an electronic mechanical stirrer. After filtering, the produced microparticles were cleaned using deionized water and kept for drying for 48 hours at room temperature. The microparticles were then collected and stored [90, 91, 92].

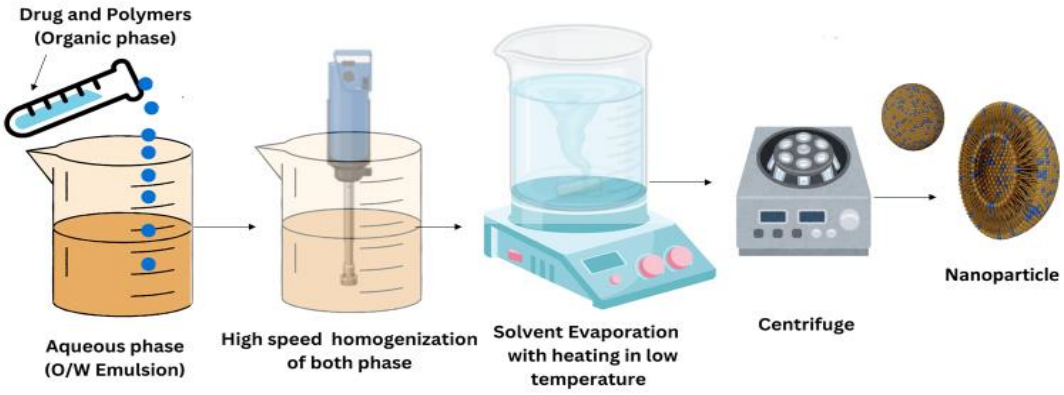

**Fig. 5 Schematic illustration for the preparation of nanoparticles by solvent evaporation method**

## CONCLUSIONS

Numerous approaches to colon-targeted medication delivery have been investigated. The methods discussed include receptor-mediated, enzyme-triggered, pH-dependent, and magnetically-driven systems. Composite microparticles can alter the release patterns of medications, lessen the burst impact, and demonstrate the potential for controlled medication release in vitro. the prospects for targeted drug delivery for the colon involving NSAID-based nanoparticles loaded in microparticles include increased therapeutic efficacy, decreased systemic side effects, better patient adherence, customized drug release profiles, the possibility for combination therapies, and diagnostic/theranostic uses.

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