RESEARCH PAPER

COLON-TARGETED NANOFORMULATIONS OF HERBAL COMPOUNDS: PHARMACOGNOSTIC BASIS, FORMULATION STRATEGIES, AND PHARMACOLOGICAL OUTCOMES

Mr. Tadikonda Sandeep[1], C.L. Sindhura[2], K. Sampath Kumar[3], Nimmala Raviteja[4], Thirumalaikumaran.R[5], Pradeep Kumar Reddy Siddavatam[6], Arey Vaishnavi[7*]

[1,7*]Assistant Professor, Crescent School of Pharmacy, B.S. Abdur Rahman Crescent Institute of Science & Technology, Vandalur, Chennai-48, India-600048.
[2]Associate professor, Department of pharmacy practice, Narayana Pharmacy College, Chinthareddy Palem -Nellore, Andhra Pradesh-524 004.
[3]Department of Pharmaceutics, Malla Reddy Institute of Pharmaceutical Sciences, Mallareddy Vishwavidyapeeth (Deemed to be University), Maisammaguda, Hyderabad 500100, Telangana, India.
[4]Associate Professor, Jagan's College of Pharmacy, Nellore, Andhra Pradesh
[5]Professor & Head, Department of Pharmacognosy, Saveetha institute of Medical and Technical sciences, Chennai.
[6]Research Scholar, Department of Pharmacy Practice, Saveetha Institute of Medical and Technical Sciences, Chennai.

Corresponding Author
Arey Vaishnavi
Mail ID: areyvaishnavireddy1993@gmail.com

ABSTRACT
Colon-targeted herbal therapeutics have emerged into the limelight as a consequence of their natural safety profile and multi-target pharmacology being applied in the treatment of inflammatory bowel disease, colorectal cancer and microbial-infections. However, most of the herbal compounds are typified by poor stability, low solubility and degradation in the upper gastrointestinal system thus restricting their treatment ability. Nanoformulations strategies offer the possible solution of maintaining phytochemicals during delivery, increasing adhesion at the mucus, and delivering to the colon with controlled delivery or stimuli-sensitive delivery. The phytochemical composition and bioconversion with colonic microflora are the most important knowledge of the pharmacognostic properties of the botanical identity of the plant, which is essential to select the appropriate actives of the plant. Polymeric nanoparticles, lipid-based carriers and polysaccharide-triggered systems are such sophisticated nanotechnology platforms that have demonstrated improved delivery efficacy and bioavailability. These nanoformulations have been demonstrated as having a higher anti-inflammatory, anticancer, antimicrobial and antioxidant activity in in vitro and in vivo studies that render these nanoformulations next-generation therapeutic in colon-targeted therapy.

Keywords: Colon targeting, herbal compounds, nanocarriers, pharmacognosy, controlled release, phytochemicals.

How to cite this article: Sandeep T, Sindhura CL, Kumar KS, Raviteja N, Thirumalaikumaran R, Siddavatam PKR, Vaishnavi A. Colon-Targeted Nanoformulations of Herbal Compounds: Pharmacognostic Basis, Formulation Strategies, and Pharmacological Outcomes. Int J Drug Deliv Technol. 2026;16(13s): 564-577. DOI: 10.25258/ijddt.16.13s.64

1. INTRODUCTION

1.1 Burden of Colon-Related Diseases (IBD, CRC, Infections)

Inflammatory bowel disease (IBD), colorectal cancer (CRC), irritable bowel syndrome and microbial infections are some of the leading health issues that cause significant health burden in the whole world. IBD, ulcerative colitis, and Crohn disease are long-term illnesses that impact thousands of people every year and affect millions of people across the globe. Colorectal cancer is the third most frequently diagnosed cancer and the level is increasing among the young people. Colon parasitism and bacterial colonies also play a major role in causing serious morbidity in developing nations(1). These are usually chronic, recurrent and hard to treat using conventional therapies. Thus, there is growing interest in the creation of localized, targeted and efficacious therapeutic approaches with safe herbal compounds(2).

1.2 Limitations of Conventional Herbal Formulations

Even though herbal medicines were traditionally applied in treating colon disorders, the conventional formulations are also confronted with great challenges. Majority of phytochemicals are poorly soluble in aqueous phase, insoluble, unproductive and unstable in acidic or enzyme-rich stomach and small intestine. Numerous herbal substances are broken down in the small intestines and are not present in sufficient amounts at the site(3). Moreover, high metabolism, inadequate bioavailability, and high dose are factors that decrease clinical efficacy. Uncertainty on the source of plants and inability to standardize formulations also add to reproducibility problems. These constraints underscore the importance

of sophisticated delivery mechanisms that will be in a position to shield actives in the herbs and guarantee precise discharge in the colon(4).

1.3 Advantages of Colon-Targeted Delivery

Colon-targeted delivery possesses several therapeutic advantages on herbal compounds in colonic disease treatment. It allows direct delivery to the location of inflammation, infection or tumour development that will lead to a higher concentration of the drug in the area and a higher treatment effect. By attacking the colon, also the breakdown in the stomach and small intestine is prevented and enhances the stability and bioavailability of the labile herbal actives. Site-specific and controlled release reduces systemic side effects as well as dosing schedule that improves patient compliance. Besides, the elevated transit time, neutral pH, and dense microbial population of the colon also provide favourable conditions to initiate the action of some of the pro-herbal components through microbiota-mediated bioconversion(5).

1.4 Role of Nanotechnology

Nanotechnology has a transformational effect of enhancing delivery of herbal compounds to the colon. Nanocarriers preserve the phytochemicals, increase their solubility, and enhance the adhesion to the mucosal. Nanocarriers can be modified in terms of particle size, surface charge, and polymeric coats to stay intact in the upper GI tract and degrade to release their cargo only in colonic pH, enzymatic activity, or in the presence of microbes. Polymeric nanoparticles, lipid-based systems and polysaccharide coated carriers have all shown increased therapeutic activity in IBD, colon cancer and infection models. Nanotechnology is therefore able to deliver herbal actives to the colon specifically, with a high level of control and efficiency(6, 7).

This review gives a blanket outline of colon targeted nanoformulations of herbal compounds, where pharmacognostic principles, development methods, and pharmacological results are incorporated. The first one addresses the applicability of herbal therapeutics in the treatment of colon disorders and the necessity of the local delivery. The review then looks at the different nanotechnology platforms that have been developed to target the colon, such as pH-responsive, enzyme-responsive, microbiota-responsive, and ligand-modified platforms. Also mentioned are in vitro and in vivo techniques of evaluation, pharmacokinetic behavior and therapeutic efficacy. Lastly, the paper discusses the current problems, technological innovations, and opportunities in the future of standardizing, effective, and clinically translatable nano-herbal preparations to colon therapy.

2. Pharmacognostic Basis of Herbal Compounds for Colon Disorders

2.1 Importance of Pharmacognosy in Colon Therapy

2.1.1 Traditional Use of Herbs in GI Disorders

Pharmacognosy forms the basis of the traditional herbal remedies that are used in gastrointestinal disorders in Ayurvedic herbal remedies, Chinese herbal remedies and folklore herbal remedies(8). Herbs Turmeric, aloe vera, bael (*Aegle marmelos*), liquorice, and boswellia have been traditionally used in the treatment of diarrhoea, colitis, abdominal pain, and microbial infections. They have therapeutic benefits that are associated with the presence of bioactive phytochemicals that have anti-inflammatory, antispasmodic, and mucosal-healing properties. The use of traditional knowledge in making modern choices of plant species used in treatment and care is safe and effective. This historical application will provide an insight into dose forms, preparation processes and therapeutic indications that can be used in the development of colon-targeted nanoformulations(9).

2.1.2 Correlation Between Botanical Identity and Efficacy

Species, part of plant and chemotype are direct impacts of botanical identity in relation to the therapeutic effects of herbal drugs. Phytochemical variation, which is determined by the dissimilarity in the environment, genetic and also harvesting seasons, affects clinical outcomes. Pharmacognostic authentication is used to ensure proper identification is carried out through the macroscopic, microscopic and phytochemical analysis. When the botanical characterization is performed properly, the contamination is avoided, stability and preserved pharmacological activity is maintained. The activity of curcumin, quercetin, berberine, or boswellic acids in the colon-targeted therapy lies in the integrity and quality of the starting plant material and, therefore, pharmacognostic validation is an essential step in the synthesis of viable nanoformulations(10).

2.2 Bioactive Phytoconstituents with Colon-Specific Activity

2.2.1 Polyphenols

Curcumin and quercetin are polyphenols that have a strong anti-inflammatory, antioxidant, and anticancer action and can be used in the treatment of colon disorders, including IBD and colorectal cancer. Their low solubility, high metabolism and instability in the GI tract are however limiting therapeutic potentials. Nanoformulations ensure that these compounds are not degraded and increase their localization in the colon. Nanoparticles of curcumin and quercetin-nanocarriers have been shown to have better mucosal penetration, inflammatory cytokines inhibition and tumour pathways inhibition. They also interact with gut microbiota, which also contributes to synergistic therapeutic effects(11, 12).

2.2.2 Flavonoids

.

Rutin, kaempferol and naringenin are popularly known as great anti-inflammatory and antioxidant properties of flavonoids. They control oxidative stress-responses, prevent inflammatory mediators and assist mucosal repair-dominant activities that are useful in IBD and ulcerative colitis. The composition of the gut microbiota is also regulated by flavonoids, which enhances the functionality of the barriers and reduces the inflammation. They will be insoluble in water and will be unstable, on the other hand, requiring advanced delivery systems. The nanoformulations, which are colon-targeted, enhance the absorption and therapeutic transfer into the lower GI tract(13).

2.2.3 Terpenoids

Boswellic acids, ginsenosides as well as thymol are terpenoids which have anti-inflammatory, antimicrobial, and anticancer properties which are applicable to colon therapy. As an example, boswellic acids (5-lipoxygenase inhibitors) reduce colonic inflammation, whereas ginsenosides have an immunomodulatory and cytoprotective effect. Their lipophilicity leads to their low oral bioavailability and they require nanoencapsulation to delivery. Nanoparticles, loaded with terpenoids, have demonstrated improved stability, tissue location and therapeutic effects in colon disease models(14, 15).

2.2.4 Alkaloids

The alkaloids including berberine and piperine are very active in IBD, cancer of the colon, and microorganisms' infection. Berberine maintains gut microbiota, reduces inflammatory cytokines, and induces pathogenic cell apoptosis(16). The efficacy limits, however, to the high absorption and degradation by the GI tract characteristics. Its stability is enhanced by the use of nanoformulations and it releases selectively to the colon. Piperile having a bioavailability behavior is also antimicrobial and, its incorporation in nanocarriers, forms an efficient targeted delivery to the colon(17).

2.2.5 Polysaccharides

The herbal polysaccharides like inulin, pectin, aloe polysaccharides, and guar gum have the prebiotic effect, immunomodulatory and anti-inflammatory effect. In the upper GI tract, they are not easily digested and are fermented by colon microbiota, which are ideal carriers or active agents of colon targeting. Enzyme-triggered and microbiota-responsive nanoformulations rely on their inherent properties of creating gels or matrices. Nanoparticles made of polysaccharides can be used to improve mucosal recovery and to prevent oxidative stress and inflammation(18).

2.3 Stability and Bioconversion in the GI Tract

2.3.1 Enzymatic Degradation

Most of the herbal compounds are digested by the digestive enzymes: esterases, proteases and glycosidases before they reach the colon. This makes them substantively less therapeutically available. Nanoencapsulated phytochemicals are protected by enzymes in the stomach and small intestine by nanoencapsulation. Also, pectin/chitosan nanocarriers that respond to enzymes can be used and are intact until colonic microbial enzymes are present, and then they degrade(19).

2.3.2 pH Sensitivity

The GI tract has different PH levels, which are as follows: acidic (pH 1-3) in the stomach and almost neutral (pH 6-7) in the colon. Most phytochemicals are sensitive to acidic or alkaline environments, pH-sensitive polymers such as Eudragit protect the nanoformulations in the stomach, and only dissolve in the colonic pH. This is a localized delivery that enhances stability and therapeutic concentration of the colon(20).

2.3.3 Microbiota-Mediated Activation of Herbal Compounds

Gut microbiota requires herbal compounds to react into their active metabolites. An example is that the metabolism of curcumin into tetrahydro curcumin with a better antioxidant effect and ginsenosides into more active ones by bacterial deglycosylation. It should also be mentioned that these bioconversion routes have been identified such that nanoformulations can be formulated with such a characteristic that drugs are strategically released in the colon with significant concentration of microbiota. The nano-polysaccharide systems particularly use this mechanism of activation(21).

2.4 Pharmacognostic Challenges

2.4.1 Variability in Herbal Raw Materials

The material of herbs differs extensively because of the plant species, geographical of the source, mode of cultivation, time of harvest and storage. This variability causes inconsistency in phytochemical concentrations as well as variation in therapeutic effects. Pharmacognostic assessment such as botanical verification, macroscopic and microscopic study and chemical profiling are crucial in quality and reproducibility of colon-targeted herbal nanoformulation(22).

2.4.2 Lack of Standardization

One of the biggest problems with herbal medicine is standardization. Reproducibility is deterred by variability in the methods of extraction, absence of validated biomarkers and inconsistent processing methods. In the absence of standardization, it is hard to provide the appropriate dosing and therapeutic reliability. Nanoformulations need the same starting material in order to ensure good encapsulation and predictable

pharmacological behavior. There is thus a need to homogenize extraction protocols, phytochemical profiles, in order to develop colon target nano-herbal systems successfully(23).

The basis of colon-targeted development of herbal drugs is pharmacognostic evaluation that will guarantee proper botanical identity, therapeutic relevance, and biochemical behavior of herb-derived compounds. In order to achieve better clarity and give a comparative perspective, the following table is a summary of significant groups of herb phytoconstituents used in colon diseases, their pharmacologic potential, GI stability properties, and formulation issues associated with the same. This systematic review assists in the comprehension of why certain compounds are selected to be targeted to the colon utilizing nanoformulation and the significance of the pharmacognostic understanding in the achievement of optimality in therapeutic results **as shown in Table 1**.

Table 1: Pharmacognostic Characteristics of Herbal Compounds Used in Colon-Targeted Nanoformulations

Phytochemical Class	Key Herbal Compounds	Colon-Relevant Pharmacological Activity	GI Stability / Bioconversion Behavior	Pharmacognostic/ Formulation Challenges
Polyphenols	Curcumin, Quercetin	Anti-inflammatory, antioxidant, anticancer	Unstable in acidic pH; degraded by enzymes; converted by microbiota into active metabolites	Poor solubility, rapid metabolism, low bioavailability
Flavonoids	Rutin, Naringenin, Kaempferol	Anti-inflammatory, mucosal healing, antioxidant	Moderate stability; partial degradation in upper GI; enhanced activity after microbial fermentation	Low permeability, variable content in raw material
Terpenoids	Boswellic acids, Ginsenosides	Anti-inflammatory, anti-cancer, antimicrobial	Sensitive to gastric and intestinal enzymes; microbiota-mediated deglycosylation enhances activity	Lipophilicity, poor oral absorption
Alkaloids	Berberine, Piperine	Antimicrobial, anti-IBD, anti-cancer	Degraded by intestinal enzymes; limited absorption; microbial metabolism influences efficacy	Bitter taste, low solubility, instability in GI fluids
Polysaccharides	Pectin, Inulin, Aloe polysaccharides	Prebiotic, immunomodulatory, anti-inflammatory	Resistant to stomach/intestinal digestion; fermented by colonic microbiota	High molecular weight; requires specific nano-carrier techniques
General Herbal Extracts	Turmeric, Boswellia, Aloe vera	Multi-target GI therapeutic benefits	Variable stability; influenced by extraction method	Raw material variability, lack of standard markers

.

Complex Extract Mixtures	Polyherbal formulations	Synergistic anti-inflammatory + antimicrobial effects	Differing stability among constituents; diverse bioconversion pathways	Difficult standardization; batch inconsistency

3. Rationale for Colon Targeting in Herbal Medicine

3.1 Localized Treatment Needs

3.1.1 Inflammation

IBD and ulcerative colitis are inflammatory bowel diseases that involve the mucosa of the colon to inflammatory diseases that can potentially require long-term treatment. Herbal products like curcumin, boswellic acids, quercetin have very high anti-inflammatory and antioxidant effects that are unable to circulate at therapeutic levels when given systemically via conventional modes of administration. Colon-targeted delivery can also be employed to guarantee that high local concentration of these phytochemicals is delivered to the inflamed area, and the delivery results in high local concentration, rapid mucosal healing, minimal systemic adverse effects and the patient complies. Nano formulations can also be considered a further step in targeting the herbal actives by protecting them during GI transit and releasing them during a controlled release in the colon milieu(24).

3.1.2 Colon Cancer

The colorectal cancer is one of the most prevalent causes of cancer deaths in the world. Many natural products which include curcumin, resveratrol, berberine and quercetin exhibit pronounced anti-proliferation and pro-apoptotic effects on colon cancerous cells. Colon-specific nanoparticles enable the localization of drugs to tumour lymphoid tissue improving the selectivity of the therapeutic as well as reducing the systemic toxicity of the therapeutic. The system of nano-delivery can be used to enhance the bioavailability and the local concentration of anticancer phytochemicals through bypassing metabolic breakdown and high mucosal retention. This very particular design enhances the escalation of apoptosis, tumour-promoting inflammatory pathway blockage, and long-term inhibition of chemoprevention(25).

3.1.3 Parasitic Infections (Amoebiasis)

Entamoeba histolytica causes amoebiasis which can cause serious cases of dysentery and tissue injury especially in the colon. Herbal extracts like berberine, neem extracts and garlic extracts are highly anti-parasitic and antimicrobial. Their efficacy however reduces when ruined in the upper GI tract. Colon-targeted formulations are meant to see these active molecules located to the infected area to maximise parasite elimination and minimise systemic contact. Nano formulations increase the efficacy of therapy, by increasing retention time, speeding up the rate of action, and decreasing the frequency of recurrence following chronic parasitic infections(26, 27).

3.2 Systemic Delivery Through Colon Absorption

3.2.1 Avoiding First-Pass Metabolism

They include herb compounds that degrade highly or hepatic first-pass degrades when absorbed across the stomach or the small intestines leading to inefficiency systemic availability. Effects of the colon specific delivery is that the early metabolism pathways are avoided because drug-metabolizing enzyme concentration is less in the colon, and permits a slower and longer absorption. The plan improves the systemic exposures of bioactive herb-based compounds that have low bioavailability i.e. curcumin or ginsenosides. The nano formulations are also better in enhancing absorption because of increased solubility and also the route of absorption through the colonic mucosa(28).

3.2.2 Controlled Release for Chronic Conditions

Controlled therapeutic exposure is a requirement in many colon related diseases such as IBD and irritable bowel syndrome. Colon target nano preparations allow longer release of herbal compounds, thus maintaining therapeutic levels in the colon at prolonged levels. This slow delivery helps to reduce the frequency of dosing, have a consistent level of drug exposure and lowers the variation in plasma concentrations, which might trigger a flare-up. These systems can respond to pH, enzyme, or microbiota activity, and they can release drugs under certain conditions only, which makes them a good solution to the continuous management of chronic diseases with greater adherence to therapies(29).

3.3 Advantages of Nano formulations Over Conventional Approaches

3.3.1 Improved Solubility

The majority of herbal actives such as curcumin and boswellic acid are poorly soluble in water and this inhibits their absorption and pharmacologic effects. Nanoparticle formulations enhance solubility by reducing the size of the particles, thereby increasing their surface area and dispersion of the biological fluids. Lipid-based and polymeric nanoparticles encapsulate hydrophobic phytochemicals enabling their dissolution with a high degree of solubility ensuring a greater bioavailability. This is because this solubility is enhanced in colon-targeted systems and therefore, the appropriate levels of drug can reach the site of action(30).

.

3.3.2 Better Mucosal Permeation

Nanocarriers adhere to colonic mucosal surface easily and tight junctions are permeated by nanocarriers easily thus enhancing herbal actives permeation which is normally signified by low absorption. Mucoadhesive nanoparticles, systems whose surfaces have been modified to facilitate local uptake and retention are examples of polysaccharide-based carriers. The impact of this is increased pharmacological effects particularly on diseases of inflammation which need penetration of deep tissues. It is also more mucosally permeated hence fewer doses with greater therapeutic results(31).

3.3.3 Protection from Gastric Degradation

Phytochemicals can be destroyed by acidic gastric pH, or by digestive enzymes, e.g. flavonoids, terpenoids, alkaloids. Nano formulations have a protective shell that serves to block early degradation to ensure that the payload is transported intact across the stomach and small intestine. pH-sensitive polymers, polysaccharide matrices, and enteric-coated nanocarriers release their cargo only in the neutral pH conditions of the colon. This focused protection increases the therapeutic efficacy as well as minimizes the drug wastage in the GI tract(32).

4. Nanotechnology Platforms for Colon-Targeted Delivery

4.1 Polymeric Nanoparticles

4.1.1 Natural Polymers

Because of their biodegradability, biocompatibility and responsiveness to colonic microflora, natural polymers are extensively employed to form colon-specific nanoformulations. Chitosan is mucoadhesive and controlled release and only dissolves in acidic conditions, so chitosan is appropriate to use in the upper GI protection. Pectin and guar gum are not digested in the stomach and small intestine but digested in the colonic bacterium, and released through the action of enzymes. These polymers enhance stability, shield herbal actives against adverse environments as well as increase localized therapeutic levels. Their natural derivation also reduces toxicity and hence they are the best vectors of chronic colon diseases such as IBD(33).

4.1.2 Synthetic Polymers

Synthetic polymers can be easily controlled in terms of particle size, release kinetics and rate of degradation. PLGA (poly lactic-co-glycolic acid) is approved by FDA and provides prolonged release and great resistance to enzymatic damages(34). Eudragit polymers are also pH responsive and dissolve in neutral to alkaline pH of the colon to avoid early release of drug. These polymers guarantee the high encapsulation efficacy, stability during the GI transit, and targeted drug delivery. They are also permitting surface modification to permit better targeting and permeation. The use of synthetic polymer nanoparticles in the treatment of colon cancer and inflammatory disorders is because of its reliability and reproducibility(35).

4.2 Lipid-Based Nanocarriers

4.2.1 SLN and NLC

Nanostructured lipid carriers (NLC) and Solid lipid nanoparticles (SLN) are stable and are biocompatible in the delivery of lipophilic herbs. SLNs carry out controlled release and phytochemical oxidation and hydrolysis protection. NLCs can use mixed solid and liquid lipids, which gives it a superior drug loading and removes drug expulsion during storage. Both systems enhance adhesion of the mucosal region, and ensure that the deep tissue of the colon is penetrated. Their lipid matrix will be more useful in dissolving their hydrophobic compounds of curcumin, boswellic acids and berberine. They find wide usage in the treatment of colon cancer and inflammatory illnesses(36).

4.2.2 Nano emulsions

Nano emulsions are oil-in-water or water-in-oil systems whose diameter is usually less than 200 nm. They enhance immensely the solubility, absorption, and dispersion of low solubility herbal compounds. With an excellent Stability, easy scaled, and fast-acting characteristics, nanoemulsions are excellent. In the case of colon targeting, they are disposed of together with an enteric coating, or polysaccharide gel to ensure protection of the upper GI. They have a small droplet size increasing mucosal permeation, and therefore they are very effective at delivering lipophilic phytochemicals. Anti-inflammatory and antimicrobial herbals that are delivered locally to the colon are particularly beneficial to have as nanoemulsions(37).

4.3 Polysaccharide-Based Nanocarriers

4.3.1 Dextran

Dextran is a natural polysaccharide, which is resistant to the digestive system of the stomach and small intestine and can be digested by the colonic enzyme, hence is ideal in colon-pointed drug delivery. Dextran as a nanocarrier has high water solubility, biocompatibility and capable of creating stable nanoparticles with herbal actives. It is microbiologically degradable and this provides it with site-specific release. Nanoparticles made of dextran, as carriers of antioxidants and anti-inflammatory agents, have proven to have a high level of efficacy when delivering their contents to the colon (particularly in ulcerative colitis models)(38).

4.3.2 Inulin

Inulin is an anti-digestive prebiotic polysaccharide that is a precursor to microbiota fermentation in the colon. This attribute renders it very appropriate in colon-targeted

nanoformulations. Inulin nanoparticles help stabilize herbal compounds and stimulate the growth of beneficial microbiota, which helps in the healing of the mucosa. Short-chain fatty acids are produced during their fermentation process and this also decreases inflammation. Phytochemicals such as quercetin and curcumin have a wide application in inulin-based systems of delivery in the management of IBD(39).

4.3.3 Cellulose Derivatives

There are a wide range of cellulose derivatives, including hydroxypropyl methylcellulose (HPMC), ethyl cellulose and cellulose acetate phthalate, which have been widely applied in colon-directed technologies. They offer a good film-forming behavior, pH-reactive behavior as well as mechanical strength. These derivatives ensure that the gastric degradation of herbal actives is prevented and they are released in the colon selectively. They are commonly used together with other biodegradable polysaccharides in order to obtain enzyme-based release. Nanocarriers of cellulose can be used especially in chronic colonic inflammation and oxidative stress(40).

4.4 Hybrid and Multifunctional Nanocarriers

4.4.1 Polymer–Lipid Hybrids

Polymer-lipid hybrid nanoparticles are a crossbreed of polymeric nanoparticles excellence and lipid carriers' excellence as far as stability and drug-loading capacity are considered respectively. The phytochemicals are entrusted by the polymer core, and biocompatibility and solubility is enhanced by the lipid shell. Some of the hybrid nanocarriers include controlled delivery, enhanced mucoadhesion and colon-specific accumulation. They have particularly been applied in the treatment of colon cancer and IBD using hydrophobic herbal components(41).

4.4.2 Mucoadhesive Nanoparticles

Mucoadhesive nanocarriers are constructed in such a way that they stick to the colonic mucosal table against prolonged durations to enhance drug retention and local absorption. The adhesion is usually enhanced with polymers like chitosan, Carbopol as well as thiolated derivatives. The nanoparticles would guarantee that the inflamed or diseased colon tissue is in contact over a long period, enhancing therapeutic efficacy. Mucoadhesive herbal nanoformulations have demonstrated better results of reducing inflammation, improving mucosal repair as well as anticancer phytochemicals(42, 43).

5. Strategies for Colon-Targeted Nanoformulations

5.1 pH-Responsive Systems

Due to the pH-sensitive solubility, Eudragit polymers are highly effective in colon targeting. Based on the neutral-alkaline pH of the colon (6-7.5), Eudragit L, S, and FS dissolve, which makes sure that no drugs are released in the acidic stomach or slightly acidic small intestine. The Eudragit-coated nanoformulations are safe throughout the upper GI and depolymerize to release their herbal cargo at the colon. It offers some of the most dependable site-specific delivery especially of volatile phytochemicals such as curcumin and quercetin(44).

pH-responsive polymers are designed to dissolve under special conditions of GI pH so that the drug can be released selectively in the colon. HPMCP, cellulose acetate phthalate and Eudragit variants are only dissolved at higher PH levels which are characteristic of the colonic environment. When used on nanoparticles, these polymers can be used to control drug release in time and space. This reduces the premature drug leakage, increases bioavailability and assures therapeutic concentrations at the site of disease. The pH-dependent systems are particularly effective in the treatment of ulcerative colitis and colorectal cancer(45).

5.2 Enzyme-Triggered Systems

Pectin, guar gum, inulin and dextran are non-digestible polysaccharide in the upper GI that will be readily degraded by colonic microflora. Ready-to-wear nanocarriers composed of these polymers do not degrade until they reach the colon at which point they are degraded into enzymes such as pectinases, xylanases, and b-galactosidases, which breakdown the polysaccharide matrix. This is the degradation promoted by this enzyme which ensures a uniform, localized release of herbal actives. The systems resemble natural physiological processes highly and therefore enhance precision of the therapeutic system and decrease systemic exposure(46).

5.3 Time-Dependent Delivery

Time-controlled delivery systems are designed to liberate drugs following a given lag interval that is equal to GI transit time (usually 5-6 hours). This makes sure that the active compound is released in the colon because the nanoformulation will evade the stomach and the small intestine. Pulsatile systems use polymers that swell or erode over time and the release of the drug will occur only when the target time has passed. The approach is helpful during chronotherapy of colonic conditions, in which the activity of a drug is synchronized with the onset of symptoms, including early-morning exacerbations in ulcerative colitis(47).

5.4 Ligand-Targeted Nanocarriers

Ligand-targeted nanocarriers improve specificity with overexpressed receptors on diseased colon cells. Cells of colorectal cancer express the highest levels of folate receptors and CD44 receptors (targeted by hyaluronic acid). Receptor-mediated endocytosis of the nanoparticles by functionalizing them with folate or hyaluronic acid leads to increased uptake of herbal compounds like curcumin, resveratrol and berberine.

This will augment therapeutic efficacy, minimize systemic toxicity, and enhance tumour-site accumulation and thus ligand-targeted systems are very effective in the treatment of colon cancer(48, 49).

5.5 Microbiota-Responsive Nanocarriers

Microbiota-responsive nanocarriers exploit microbiome metabolic activity on the intestines to deliver drugs. These systems consist of the materials developed to be designed such as azo-polymers, polysaccharides or biomimetic coating that are cleaved by bacterial enzymes, such as azoreductases, glycosidases and reductases. These levels of enzymes are so high in the colon, such that it is ensured that the activation is site-specific. This kind of smart systems suit best herbal compounds which are best transformed by microbiota or which require local action in inflammatory and infectious colitis diseases(50).

6. Formulation Considerations for Herbal Nanoformulations

The different physicochemical and biopharmaceutical parameters should be optimum to design effective colon-targeted nanoformulation of herbal compounds. These parameters influence the loading capacity, stability during the GI transit, behaving release in colon and therapeutic performance at target site. The efficiency of encapsulation of phytochemicals, their stability, release kinetics, particle size and surface charge are the outcome of the ability of a nanoformulation to preserve the phytochemicals, release them intact at the colon and interact with the mucosa of the colon(7) **as shown in Table 2**.

Table 2: Key Formulation Considerations for Colon-Targeted Herbal Nanoformulations

Formulation Parameter	Importance	Impact on Colon-Targeted Delivery
Encapsulation Efficiency	Determines how much herbal active is successfully loaded into the nanocarrier. Influenced by polymer/lipid selection and drug–carrier compatibility.	High encapsulation ensures adequate dose reaches the colon, minimizes drug loss during GI transit, and enhances therapeutic efficacy.
Stability and Degradation Protection	Prevents phytochemical degradation from gastric acid, enzymes, and oxidative conditions. Uses protective polymers, coatings, and lipid matrices.	Ensures intact delivery to the colon, preserves biological activity, reduces premature release, and improves shelf-life.
Controlled and Sustained Release Profiles	Achieved through polymer composition, cross-linking degree, and nanocarrier structure. Controls where and how fast drug is released.	Enables site-specific release in the colon, maintains therapeutic levels, reduces dosing frequency, and minimizes systemic side effects.
Particle Size Optimization for Colon Uptake	Nanoparticles between 100–300 nm show optimal mucus penetration and retention. Particle size influences absorption and biodistribution.	Ensures better colon permeability, enhances mucosal penetration, and promotes accumulation at inflamed or cancerous sites.
Surface Charge and Mucoadhesion	Surface charge affects nanoparticle interactions with mucosal surfaces. Mucoadhesive polymers such as chitosan improve retention.	Enhances adhesion to colonic mucosa, prolongs residence time, improves local drug uptake, and strengthens therapeutic outcomes.

7. *In Vitro* Evaluation of Colon-Targeted Herbal Nanoformulations

In vitro testing is essential in establishing the ability of colon-targeted herbal nanoformulations to survive gastrointestinal passage, deliver its cargo to the right location, traumatize colonic tissues and generate therapeutic effects without being toxic. Simulated GI fluids, release, simulated colon cell lines as well as cytotoxicity studies are standardized in vitro tests that enable researchers to make predictions about formulation performance prior to making in vivo predictions. The approaches aid in the evaluation of stability, aimed at efficiency, permeability, and safety of herbal nanoformulations meant to be delivered to the colon(51). The table provided below gives a summary of the major in vitro assessment methods and the specific reason why they are crucial in the development of a colon-targeted herbal drug **as shown in Table 3**.

.

Table 3: In Vitro Evaluation Methods for Colon-Targeted Herbal Nanoformulations

Evaluation Method	Purpose	Relevance to Colon-Targeted Nanoformulations
Simulated GI Transit Studies (SGF, SIF, SCF)	Assess nanoparticle stability in stomach (SGF), small intestine (SIF), and colonic fluid (SCF) conditions.	Ensures formulation survives upper GI tract and releases drug specifically in SCF; confirms pH- or enzyme-triggered behavior.
Release Kinetics	Measures rate and pattern of herbal drug release from nanocarriers under controlled conditions.	Determines controlled/sustained release in colon, prevents premature leakage, and ensures therapeutic levels at target site.
Permeation Studies (Caco-2, HT-29 Cell Lines)	Model intestinal and colonic epithelial barriers to evaluate nanoparticle permeability and uptake.	Predicts colon mucosal penetration, absorption, and enhancement of bioavailability; useful for targeting inflamed tissues or cancer cells.
Cytotoxicity Studies	Uses cell viability assays (MTT, SRB, LDH) to assess safety of formulation.	Ensures herbal nanoformulations are non-toxic to healthy colon cells; essential for selecting safe concentrations for in vivo studies.

8. *In-Vivo* Evaluation and Pharmacokinetics

There is also the need to do in-vivo testing in order to determine the level on which the colon-targeted herbal nanoformulations are exhibiting the desired biological behavior in the body. Animal models allow testing of tissue distribution, efficacy of colon specific targeting, pharmacokinetic activity and systemic safety(52). The parameters prove the survivability of the gastrointestinal tract, positioning of the target, efficient delivery of an active ingredient and tolerable safety levels of a particular formulation **as shown in Table 4**.

Table 4: *In-vivo* Evaluation and Pharmacokinetic Assessment of Colon-Targeted Herbal Nanoformulations

Evaluation Parameter	Purpose	Relevance to Colon-Targeting and Nano-Herbal Delivery
Animal Models for Colon Disorders	Use of mice/rats with induced IBD (DSS, TNBS), colon cancer models, parasitic infection models.	Enables evaluation of therapeutic effectiveness, inflammation reduction, tumor regression, or parasite clearance in realistic disease conditions.
Biodistribution of Nanoformulations	Tracks nanoparticle distribution across organs using fluorescence, radiolabels, or imaging.	Confirms minimal systemic spread and higher localization in the colon; evaluates targeting ability and safety.
Colon-Specific Accumulation	Measures nanoparticle retention and penetration in colon tissue.	Demonstrates successful colon targeting, improved mucosal adherence, and enhanced therapeutic residence time.
Pharmacokinetic Parameters (Cmax, Tmax, AUC)	Determines absorption rate, peak concentration, and total drug exposure.	Helps evaluate whether nanoformulations improve bioavailability of herbal actives while sustaining drug levels in colon tissue.
Toxicological Assessment	Includes histopathology, biochemical markers, organ weight, and safety profiling.	Ensures the formulation does not induce colonic irritation, systemic toxicity, or organ damage, supporting clinical safety.

9. Pharmacological Outcomes

The normal nanoformulations of herbs have been proved to show enormous pharmacological effects as they help to deliver directly to the disease place; phytochemicals augment the medicine concentration, stability as well as the biological activity of the phytochemicals.

.

Nanoformulations have been shown to increase natural anti-inflammatory, anticancer, antimicrobial, and antioxidant effects of herbs in the natural environment by preventing biodegradation in the upper gastrointestinal tract and increasing colonic content. Such effects are enhanced by improved drug kinetics, increased absorption by the mucosa and optimum association with cellular pathways. Nanotechnology combination hence facilitates nano-herbal systems to attain high therapeutic effects and low systemic toxicity of herbal actives at minimum dosage of herbal actives, thus nano-herbal systems promises as a colon therapeutic agent of the future(53, 54).

9.1 Anti-Inflammatory Effects in IBD Models

9.1.1 Cytokine Modulation

Colon-targeted herbal nanoparticles are also demonstrated as effective in the regulation of such inflammatory cytokines as TNF-a, IL-1b, IL-6, and IFN-g which play a key role in ensuring the pathogenesis of mucosal inflammation in IBD. The availability of the anti-inflammatory phytochemicals (curcumin, quercetin, boswellic acids) at the local level is increased through nanoencapsulation to avoid the expression of pro-inflammatory genes and provoke the generation of anti-inflammatory cytokines (IL-10). Nanoformulations reduce neutrophil inflammation, prevent NF-kB signaling and re-epithelial repair by targeting herbal actives to foci of inflammation. The effect of this regulated cytokine is increased therapeutic response and early healing of cytokines in colitis models(55).

9.1.2 Reduced Oxidative Stress

Another major cause of IBD pathogenesis is oxidative stress since it causes the destruction of epithelial cells and inflammation. Herbal compounds having antioxidant properties such as polyphenols and flavonoids respond to reactive oxygen species (ROS), enhance endogenous antioxidant enzymes, such as SOD, CAT and GPx. These phytochemicals can be encased by nanoformulations to prevent degradation and improve the penetration of the phytochemicals at inflamed areas of the colon. This results into reduced lipid peroxidation, improved performance of the mitochondria and protection of the mucosa. These antioxidants are very important in repairing the tissues and suppressing oxidative damages in IBD models(56, 57).

9.2 Anti-Cancer Effects in Colon Cancer Models

9.2.1 Apoptosis

The anti-cancer effects of colon-specific herbal nanoformulations induce apoptosis in cancerous cells through multiple mechanisms that is, destabilization of mitochondria, activation of caspases, and blockage of the survival pathway, such as PI3K/Akt and STAT3. Nanoencapsulation has been applied in enhancing the delivery of anticancer herbals such as curcumin, berberine and resveratrol and their intracellular absorption and retention. These nanoformulations mediate the mechanism of DNA fragmentation, anti-apoptotic protein (Bcl-2) down-regulation, and pro-apoptotic up-regulation (Bax). Enhanced bioavailability will give effectual activation of programmed cell death procedures within tumours tissues and enhanced tumours regression(58, 59).

9.2.2 Tumour Inhibition

Inhibitory effect on the tumour development through the lowering of angiogenesis, iHS oncogenic signalling and interference with metastasis is also an effect of herbal nanoformulations. Nanocarriers are used to direct the concentration in tumors tissue, as a result of high permeability and retention (EPR) effect and ligand-mediated targeting. Phytochemicals that are delivered with the help of nanoparticles down-regulate the synthesis of cytokines and prostaglandins comprising of VEGF, MMP-9, and COX-2 thereby suppressing tumor growth and invasion. They are also anti-inflammatory and antioxidant effect and this poses an undesirable situation when cancer cells are developing. As a result, the nanoformulations have a better ability to inhibit tumors as compared to the uncooked herbal extractions on colon cancer models(60).

9.3 Antimicrobial and Anti-Parasitic Effects

Nanoformulations of herbs have stronger antimicrobial and anti-parasitic effect against the pathogenic E. histolytica, Clostridium difficile and bacterial overgrowth of the colon. The phytochemicals berberine, the garlic compounds and the neem constituents are antimicrobial and are highly soluble and encapsulate well. Nanoformulations are better to avoid microbial biofilm and serve as a lasting concentration of drugs in the colon. Their delivery system is meant to maximize the number of the pathogen in order to replenish the equilibrium of microbes and reduction of recurrence. Colon-specific release can be applied in parasitic infections such as amoebiasis where local effect is required in the infected site more effective in the destruction and healing of mucosa(61).

9.4 Enhancement of Systemic Bioavailability

Nanoformulations have profound effects on the enhancement of the systemic bioavailability of herbal compounds; they increase their solubility, inhibit their degradation in the GI tract, and improve their uptake by the mucosal area. The lower enzymatic activity and increased transit time of the colon enable the nanoformulations to release phytochemicals in a slow manner to provide increased absorption. Nanocarriers enhance permeability of colonic epithelium by mucoadhesion and optimal particle size. Thus, the poorly orally bioavailable compounds, like curcumin, resveratrol, and ginsenosides, have a high plasma

concentration and an enhanced therapeutic efficacy. Systemic treatment of chronic inflammatory and metabolic disorder is also facilitated by this improved bioavailability(47).

10. Challenges and Future Perspective:

Significant therapeutic potential is associated with the emergence of colon-targeted herbal nano formulations, but these advancements are coupled by various challenges associated with variations in raw materials, formulation stability, scale-up, regulatory analysis, and lack of complete knowledge of interactions between the gut microbiota. The solution to these problems lies in new scientific methods and new technologies(62). Smart drug delivery systems, optimization based on artificial intelligence, custom herbal therapy, and multi-omics system integration will be the future of this field to improve understanding of drug-microbiota-host interactions **as shown in Table 5**.

Table 5: Challenges and Future Perspectives in Colon-Targeted Herbal Nanoformulations

Challenges	Description	Future Perspectives	Potential Impact
Raw Material Variability	Variability in plant species, chemotypes, cultivation conditions, and extraction processes affects phytochemical consistency.	Personalized colon-targeted herbal therapy	Enables individualized herbal dosing based on patient response and phytochemical profiles.
Stability Issues	Herbal compounds degrade due to pH, enzymes, heat, oxidation, and poor compatibility with nanocarriers.	Smart microbiota-responsive nanocarriers	Ensures selective drug release, enhanced stability, and precise targeting within the colon.
Scale-Up Difficulties	Nano formulation techniques like high-pressure homogenization or microfluidics face reproducibility and cost barriers at industrial scale.	AI-driven formulation optimization	Reduces trial-and-error, improves reproducibility, and accelerates commercial manufacturing.
Regulatory Complexities	Combined challenges of herbal variability, nano-specific safety concerns, and lack of harmonized guidelines.	Integration of multi-omics (genomics, metabolomics, microbiomics)	Provides mechanistic understanding, supports regulatory documentation, and improves credibility.
Incomplete Understanding of Microbiota Interactions	Microbiota influence drug activation, degradation, and therapeutic outcomes, but these pathways remain poorly defined.	AI + multi-omics approaches	Reveals host–microbe–drug interactions, enabling rational design of colon-targeted systems.

Conclusion

Much has been done concerning the development of colon-targeted herbal nano formulations, where pharmacognostic information is incorporated in the most advanced nanotechnology platforms, to counter the shortcomings of the conventional herbal treatments. Lipid-based, polysaccharide-responsive, polymeric and hybrid nano formulation strategies have improved the stability, solubility and targeted delivery of phytochemicals resulting in an improvement in the anti-inflammatory, anticancer, antimicrobial and systemic therapeutic effects. Regardless of these developments, there is an urgent need to have a standardized herbal raw material, reproducible production processes, and greater insightfulness into the microbiota-mediated processes so that clinical performance can be consistent. Nanotechnology remains critical in the contemporary modernization of herbal medicine through the provision of controlled release, site specific drug delivery as well as improved pharmacokinetics. Colon-targeted herbal nanomedicines have a great potential to become safe, effective and personalized treatments in the future with integration of smart microbiota-responsive carrier, AI-based optimization and multi-omics tools.

.

References:

1. Ashbolt NJ. Microbial contamination of drinking water and disease outcomes in developing regions. Toxicology. 2004;198(1-3):229–38.
2. Quaglio AEV, Grillo TG, De Oliveira ECS, Di Stasi LC, Sassaki LY. Gut microbiota, inflammatory bowel disease and colorectal cancer. World journal of gastroenterology. 2022;28(30):4053.
3. Palombo EA. Phytochemicals from traditional medicinal plants used in the treatment of diarrhoea: modes of action and effects on intestinal function. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives. 2006;20(9):717–24.
4. Latif R, Nawaz T. Medicinal plants and human health: a comprehensive review of bioactive compounds, therapeutic effects, and applications. Phytochemistry Reviews. 2025:1–44.
5. Kumar P, Mishra B. Colon targeted drug delivery systems-an overview. Current drug delivery. 2008;5(3):186–98.
6. Bonifácio BV, da Silva PB, Ramos MAdS, Negri KMS, Bauab TM, Chorilli M. Nanotechnology-based drug delivery systems and herbal medicines: a review. International journal of nanomedicine. 2014:1–15.
7. Shree D, Patra CN, Sahoo BM. Emerging Nanoparticle-Based Herbal Drug Delivery Systems for Colon Targeting Therapy. Internat Journal of Gastroent and Hepatology Diseases. 2024.
8. Dhami N. Trends in Pharmacognosy: A modern science of natural medicines. Journal of herbal medicine. 2013;3(4):123–31.
9. Kumar M, Verma I, Sindhu RK, Srivastava R. Herbal Bioactives for the Treatment of Gastrointestinal Tract Disorders. Herbal Drugs for the Management of Infectious Diseases. 2022:133–55.
10. Smillie T, Khan I. A comprehensive approach to identifying and authenticating botanical products. Clinical Pharmacology & Therapeutics. 2010;87(2):175–86.
11. Ojo OA, Adeyemo TR, Rotimi D, Batiha GE-S, Mostafa-Hedeab G, Iyobhebhe ME, et al. Anticancer properties of curcumin against colorectal cancer: a review. Frontiers in Oncology. 2022;12:881641.
12. Vecchi Brumatti L, Marcuzzi A, Tricarico PM, Zanin V, Girardelli M, Bianco AM. Curcumin and inflammatory bowel disease: potential and limits of innovative treatments. Molecules. 2014;19(12):21127–53.
13. Al-Khayri JM, Sahana GR, Nagella P, Joseph BV, Alessa FM, Al-Mssallem MQ. Flavonoids as potential anti-inflammatory molecules: A review. Molecules. 2022;27(9):2901.
14. Sharma SH, Thulasingam S, Nagarajan S. Terpenoids as anti-colon cancer agents–A comprehensive review on its mechanistic perspectives. European journal of pharmacology. 2017;795:169–78.
15. Trivedi VL, Soni R, Dhyani P, Sati P, Tejada S, Sureda A, et al. Anti-cancer properties of boswellic acids: mechanism of action as anti-cancerous agent. Frontiers in pharmacology. 2023;14:1187181.
16. Cao J, Chen M, Xu R, Guo M. Therapeutic mechanisms of berberine to improve the intestinal barrier function via modulating gut microbiota, TLR4/NF-κ B/MTORC pathway and autophagy in cats. Frontiers in microbiology. 2022;13:961885.
17. Raghunath I, Koland M, Narayanan AV. Piperine: A possible permeation enhancer for oral protein delivery. Journal of Applied Pharmaceutical Science. 2024;14(4):035–45.
18. Yuan D, Li C, Huang Q, Fu X, Dong H. Current advances in the anti-inflammatory effects and mechanisms of natural polysaccharides. Critical Reviews in Food Science and Nutrition. 2023;63(22):5890–910.
19. Ling JKU, Hii YS, Jeevanandam J, Chan YS, Danquah MK. Nanoencapsulation of Phytochemicals and in-vitro Applications. Phytochemistry: An in-silico and in-vitro Update: Advances in Phytochemical Research: Springer; 2019. p. 315–30.
20. Manickam V, Sundar V, Panchangam RL, Amiti, S KA, Tamizhselvi R. Nanotechnology in delivery and targeting of phytochemicals. Nanopharmaceuticals: Principles and Applications Vol 2: Springer; 2020. p. 211–64.
21. Peterson CT. Gut Microbiota-Mediated Biotransformation of Medicinal Herb-Derived Natural Products: A Narrative Review of New Frontiers in Drug Discovery. J. 2024;7(3):351–72.
22. Aljabali AA, Obeid MA, Bashatwah RM, Qnais E, Gammoh O, Alqudah A, et al. Phytochemicals in cancer therapy: a structured review of mechanisms, challenges, and progress in personalized treatment. Chemistry & Biodiversity. 2025;22(8):e202402479.
23. Kunle OF, Egharevba HO, Ahmadu PO. Standardization of herbal medicines-A review. International journal of biodiversity and conservation. 2012;4(3):101–12.
24. Wehkamp J, Götz M, Herrlinger K, Steurer W, Stange EF. Inflammatory bowel disease: Crohn's disease and ulcerative colitis.

Deutsches Ärzteblatt International. 2016;113(5):72.
25. McCubrey JA, Lertpiriyapong K, Steelman LS, Abrams SL, Yang LV, Murata RM, et al. Effects of resveratrol, curcumin, berberine and other nutraceuticals on aging, cancer development, cancer stem cells and microRNAs. Aging (Albany NY). 2017;9(6):1477.
26. Etewa SE, Abaza SM. Herbal medicine and parasitic diseases. Parasitol United J. 2011;4(1):3–14.
27. Upadhyay RK. Antiparasitic potential of plant natural products against protozoans, nematodes and cestodes: A review. Gen Med Clin Pract. 2024;7:1–5.
28. Zhang RX, Dong K, Wang Z, Miao R, Lu W, Wu XY. Nanoparticulate drug delivery strategies to address intestinal cytochrome P450 CYP3A4 metabolism towards personalized medicine. Pharmaceutics. 2021;13(8):1261.
29. Chavda VP, Patel AB, Mistry KJ, Suthar SF, Wu Z-X, Chen Z-S, et al. Nano-drug delivery systems entrapping natural bioactive compounds for cancer: recent progress and future challenges. Frontiers in oncology. 2022;12:867655.
30. Jia L. Nanoparticle formulation increases oral bioavailability of poorly soluble drugs: Approaches, experimental evidences and theory. Current nanoscience. 2005;1(3):237–43.
31. Talegaonkar S, Bhattacharyya A. Potential of lipid nanoparticles (SLNs and NLCs) in enhancing oral bioavailability of drugs with poor intestinal permeability. Aaps Pharmscitech. 2019;20(3):121.
32. Ejazi SA, Louisthelmy R, Maisel K. Mechanisms of nanoparticle transport across intestinal tissue: an oral delivery perspective. ACS nano. 2023;17(14):13044–61.
33. Hejazi R, Amiji M. Chitosan-based gastrointestinal delivery systems. Journal of controlled release. 2003;89(2):151–65.
34. Lu Y, Cheng D, Niu B, Wang X, Wu X, Wang A. Properties of poly (lactic-co-glycolic acid) and progress of poly (lactic-co-glycolic acid)-based biodegradable materials in biomedical research. Pharmaceuticals. 2023;16(3):454.
35. Gvozdeva Y, Staynova R. pH-Dependent drug delivery systems for ulcerative colitis treatment. Pharmaceutics. 2025;17(2):226.
36. Fathi F, Machado TO, de AC Kodel H, Portugal I, Ferreira IO, Zielinska A, et al. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) for the delivery of bioactives sourced from plants: part I–composition and production methods. Expert opinion on drug delivery. 2024;21(10):1479–90.
37. Cui M, Zhang M, Liu K. Colon-targeted drug delivery of polysaccharide-based nanocarriers for synergistic treatment of inflammatory bowel disease: A review. Carbohydrate polymers. 2021;272:118530.
38. Ghosh D, Jain A, Tyagi M, Katiyar D, Mittal A. Nutriose, a Dextrin-based Natural Polysaccharide Polymer with Beneficial Activities as a Candidate for Future Drug Delivery: A Review. Combinatorial Chemistry & High Throughput Screening. 2025;28(7):1112–24.
39. Tian X, Yang Y, Wang Y, Liu X, Wang B, Xu Y, et al. Recent Advances in Processing Methods and Utilization of Hulless Barley and Its Nutritional Components: A Review. Comprehensive Reviews in Food Science and Food Safety. 2025;24(5):e70245.
40. Sarkar R, Biswas P, Mukherjee DR, Tanbir S, Biswas B, Rahaman MM, et al. Chrono-Colonic Delivery in Engineering Time-Responsive Systems for Site-Specific Therapy. Journal of Drug Delivery and Therapeutics. 2025;15(10):148–71.
41. Sivadasan D, Sultan MH, Madkhali O, Almoshari Y, Thangavel N. Polymeric lipid hybrid nanoparticles (plns) as emerging drug delivery platform—A comprehensive review of their properties, preparation methods, and therapeutic applications. Pharmaceutics. 2021;13(8):1291.
42. Subramanian DA, Langer R, Traverso G. Mucus interaction to improve gastrointestinal retention and pharmacokinetics of orally administered nano-drug delivery systems. Journal of nanobiotechnology. 2022;20(1):362.
43. Desai V, Ashok PA, Kulkarni P, Ahmed KA, Raikar PK. Enhancing drug bioavailability through mucoadhesive technologies: A comprehensive review of delivery systems. Biomedical Materials & Devices. 2025:1–19.
44. Singh J, Nayak P. pH-responsive polymers for drug delivery: trends and opportunities. Journal of polymer science. 2023;61(22):2828–50.
45. García MA, Varum F, Al-Gousous J, Hofmann M, Page S, Langguth P. In vitro methodologies for evaluating colon-targeted pharmaceutical products and industry perspectives for their applications. Pharmaceutics. 2022;14(2):291.
46. Ansari Z, Goomer S. Natural gums and carbohydrate-based polymers: Potential encapsulants. Indo Glob J Pharm Sci. 2022;12:01–20.
47. Das A, Adhikari S, Deka D, Baildya N, Sahare P, Banerjee A, et al. An updated review on the role of nanoformulated phytochemicals in colorectal cancer. Medicina. 2023;59(4):685.
48. Abdellatif AA, Alshubrumi AS, Younis MA. Targeted Nanoparticles: the Smart Way for the Treatment of Colorectal Cancer. AAPS PharmSciTech. 2024;25(1):23.

.

49. Sultana N. Small Molecules Conjugated Silica Nanoparticles for Dual Targeting of Colon Cancer: Auburn University; 2022.
50. Khurana A, Hartmann P. Gut microbiome-specific nanoparticle-based therapeutics for liver diseases. World Journal of Gastroenterology. 2025;31(27):109105.
51. Kumar A, Vaiphei KK, Singh N, Datta Chigurupati SP, Paliwal SR, Paliwal R, et al. Nanomedicine for colon-targeted drug delivery: strategies focusing on inflammatory bowel disease and colon cancer. Nanomedicine. 2024;19(15):1347–68.
52. Deshmukh R, Prajapati M, Harwansh RK. Management of colorectal cancer using nanocarriers-based drug delivery for herbal bioactives: Current and emerging approaches. Current Pharmaceutical Biotechnology. 2024;25(5):599–622.
53. Oliveira da Silva L, Assunção Ferreira MR, Lira Soares LA. Nanotechnology Formulations Designed with Herbal Extracts and Their Therapeutic Applications–A Review. Chemistry & Biodiversity. 2023;20(8):e202201241.
54. Sun K, Wu L, Wang S, Deng W. Antitumor effects of Chinese herbal medicine compounds and their nano-formulations on regulating the immune system microenvironment. Frontiers in oncology. 2022;12:949332.
55. Jafarzadeh A, Jafarzadeh S, Nemati M. Journal of Traditional Chinese Medical Sciences. pathogenesis. 2021;10:11.
56. Rao MJ, Zheng B. The role of polyphenols in abiotic stress tolerance and their antioxidant properties to scavenge reactive oxygen species and free radicals. Antioxidants. 2025;14(1):74.
57. Mihailović M, Dinić S, Arambašić Jovanović J, Uskoković A, Grdović N, Vidaković M. The influence of plant extracts and phytoconstituents on antioxidant enzymes activity and gene expression in the prevention and treatment of impaired glucose homeostasis and diabetes complications. Antioxidants. 2021;10(3):480.
58. Biganeh H, Dizaji SM, Taghipour YD, Murtaza G, Rahimi R. Nanoformulations of plant-derived compounds as emerging therapeutic approach for colorectal cancer. Current Drug Delivery. 2023;20(8):1067–94.
59. Chaudhuri AD. Baicalein modulates colorectal tumor microenvironment to suppress growth, metastasis, and immune escape. 2025.
60. Wang W, Li J, Wu H, Xie M, Xu H. Targeting tumor angiogenesis with traditional Chinese medicine: mechanisms, challenges, and future directions. Tradit Med Res. 2026;11(5):35.
61. Asif M, Ch AS, Ubaidullah Z-U, Hussain N, Saleem MH, Azhar M, et al. Therapeutic Effect of Nanoparticles as Anti-inflammatory, Antibacterial and Anti-parasitic.
62. Jain A, Bhattacharya S. Recent advances in nanomedicine preparative methods and their therapeutic potential for colorectal cancer: a critical review. Frontiers in oncology. 2023;13:1211603.