Nano Nexus & Applications

www.nna.reapress.com

Nano. Nex. App. Vol. 1, No. 2 (2026) 106–126.

Paper Type: Original Article

Recent Advances in Nanoengineered Coating Technologies for Targeted Drug Delivery in Gastrointestinal Diseases

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Citation:

Received: 28 July 2025 *Revised: 04 November 2025* *Accepted: 27 January 2026*	Cevallos Torres, L. J. (2026). Recent advances in nanoengineered coating technologies for targeted drug delivery in gastrointestinal diseases. *Nano Nexus & Applications, 1*(2), 106-126.

Abstract

Gastrointestinal (GI) diseases remain a major global health concern due to their increasing prevalence and the limitations of conventional oral drug delivery systems. Physiological barriers within the GI tract, including variable pH, digestive enzymes, mucus turnover, epithelial tight junctions, and first-pass metabolism, often compromise drug stability, bioavailability, and site-specific delivery. Nanoengineered coating technologies have emerged as a promising strategy to overcome these challenges by enhancing drug protection, controlled release, targeted delivery, and therapeutic efficacy. This review summarizes recent advances in nanoengineered coatings for GI drug delivery, highlighting the design principles and therapeutic applications of enteric, pH-responsive, enzyme-responsive, mucoadhesive, microbiota-responsive, stimuli-responsive, and hybrid coating systems. In addition, the roles of natural polymers, synthetic polymers, lipid-based materials, and multifunctional nanomaterials in improving oral drug delivery are discussed. Particular emphasis is placed on the application of these coating technologies in the treatment of Inflammatory Bowel Disease (IBD), colorectal cancer, gastric ulcers, *Helicobacter pylori* infection, celiac disease, and other GI disorders. Furthermore, the review discusses the major challenges associated with nanoengineered GI coatings, including biological variability, nanomaterial safety, formulation stability, manufacturing scalability, and regulatory considerations. Overall, nanoengineered coatings represent a versatile and rapidly evolving platform with significant potential to improve targeted GI drug delivery and facilitate the development of safer and more effective oral therapies.

Keywords: Nanoengineered, Nanotechnology, Gastrointestinal, Oral delivery, Drug delivery, Biomaterials, Smart coatings.

1 | Introduction

Gastrointestinal (GI) diseases represent a major global healthcare burden, encompassing a wide spectrum of acute and chronic disorders that affect millions of individuals worldwide [1–3]. These conditions include

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https://doi.org/10.48314/nna.vi.67

Inflammatory Bowel Diseases (IBD), such as Crohn's disease and ulcerative colitis, colorectal cancer, gastric ulcers, Helicobacter pylori-associated infections, celiac disease, Irritable Bowel Syndrome (IBS), and various GI inflammatory disorders. The increasing prevalence of these diseases, coupled with their chronic nature and substantial impact on patients' quality of life, has intensified the demand for more effective and targeted therapeutic strategies. Despite remarkable progress in pharmaceutical sciences, the treatment of GI disorders remains challenging due to the complex physiological and biochemical environment of the GI tract [4–6].

Oral administration remains the most preferred route for drug delivery because of its convenience, high patient compliance, cost-effectiveness, and non-invasive nature. However, the GI tract presents numerous barriers that limit the therapeutic efficacy of orally administered drugs. These barriers include highly variable pH conditions, enzymatic degradation, mucus turnover, rapid GI transit, epithelial tight junctions, and extensive first-pass metabolism [6–11]. Moreover, many therapeutic agents, particularly peptides, proteins, nucleic acids, and poorly water-soluble drugs, exhibit low oral bioavailability due to premature degradation or insufficient absorption. Consequently, conventional oral formulations often fail to achieve adequate drug concentrations at the desired disease site, leading to reduced therapeutic outcomes and increased systemic side effects. To overcome these limitations, considerable attention has been directed toward the development of site-specific drug delivery systems capable of protecting therapeutic agents during GI transit and releasing them selectively at target locations. Among these approaches, coating technologies have emerged as one of the most effective and versatile strategies for enhancing drug stability, improving bioavailability, and achieving controlled or targeted drug release [11–13]. Pharmaceutical coatings can provide physical and chemical protection against harsh gastric conditions, modulate drug release kinetics, prolong residence time, and facilitate site-specific delivery within different regions of the GI tract. Traditional coating systems, particularly enteric coatings, have been extensively utilized to protect acid-labile drugs from gastric degradation and to prevent gastric irritation caused by certain active pharmaceutical ingredients. Enteric polymers such as methacrylic acid copolymers, Cellulose Acetate Phthalate (CAP), Hydroxypropyl Methylcellulose Phthalate (HPMCP), and Polyvinyl Acetate Phthalate (PVAP) have demonstrated significant success in enabling pH-dependent drug release in the small intestine and colon [14]. Nevertheless, conventional coating systems often exhibit limitations related to variability in GI pH, unpredictable transit times, insufficient targeting precision, and incomplete adaptation to disease-specific microenvironments.

Recent advances in materials science, nanotechnology, and biomedical engineering have revolutionized the field of oral drug delivery by introducing nanoengineered coating systems. Nanotechnology has emerged as a transformative platform capable of addressing many of the shortcomings associated with conventional formulations. Nanoengineered coatings incorporate nanoscale materials, functional polymers, nanocomposites, and stimuli-responsive components to create intelligent delivery systems with enhanced targeting capabilities [9]. The integration of nanotechnology into pharmaceutical coating design has enabled the development of multifunctional systems capable of responding to specific physiological triggers, thereby improving therapeutic precision and minimizing off-target effects. Nanoengineered coatings offer several distinct advantages over traditional coating approaches. First, their high surface-area-to-volume ratio enhances interactions with biological tissues and facilitates improved drug absorption. Second, nanoscale modifications can significantly improve the stability of encapsulated therapeutic agents against enzymatic and chemical degradation [12]. Third, nanoengineered systems can be functionalized with targeting ligands, bioadhesive molecules, and environmentally responsive polymers to achieve selective accumulation at diseased sites. Furthermore, nano-coatings can provide precise control over drug release kinetics, enabling sustained, pulsatile, or stimuli-responsive drug delivery profiles tailored to specific therapeutic requirements.

Among the various nanoengineered coating strategies, pH-responsive systems have received substantial attention for GI applications. These coatings exploit physiological pH gradients throughout the GI tract to trigger site-specific drug release. In addition, enzyme-responsive coatings have emerged as promising platforms for colon-targeted drug delivery, utilizing enzymes produced by gut microbiota to initiate coating degradation and drug release. Such systems offer unique opportunities for the treatment of colorectal diseases by ensuring minimal drug release in the upper GI tract while maximizing drug availability in the

colon [2–5]. Another rapidly expanding area involves the development of mucoadhesive nano-coatings designed to prolong GI residence time and enhance local drug concentrations at disease sites. Polymers such as chitosan, alginate, hyaluronic acid, and carbomers have demonstrated remarkable mucoadhesive properties that improve drug retention and absorption across mucosal surfaces. These systems are particularly attractive for the management of IBD and localized GI infections, where prolonged contact with inflamed tissues can significantly improve therapeutic efficacy [11–15].

In recent years, increasing attention has also been devoted to stimuli-responsive and smart coating systems capable of responding to multiple environmental cues. These advanced coatings can be engineered to react to changes in pH, enzyme activity, redox potential, temperature, Reactive Oxygen Species (ROS), inflammatory mediators, and microbial metabolites. Such intelligent systems offer unprecedented opportunities for precision medicine by enabling drug release exclusively within diseased tissues while minimizing exposure to healthy regions. Furthermore, the integration of nanotechnology with responsive materials has facilitated the development of highly sophisticated platforms capable of adapting dynamically to pathological conditions [16]. The gut microbiota has emerged as another important target for advanced coating technologies. Growing evidence suggests that microbial dysbiosis plays a central role in the pathogenesis of numerous GI disorders. Consequently, microbiota-responsive nano-coatings have gained considerable interest as innovative systems capable of exploiting microbial enzymatic activity to achieve highly selective drug release. These approaches represent a promising frontier in GI drug delivery and may contribute significantly to the advancement of personalized medicine [10–13]. Despite the substantial progress achieved in this field, several challenges continue to hinder the clinical translation of nanoengineered coating technologies. Issues related to large-scale manufacturing, formulation reproducibility, long-term stability, regulatory approval, safety assessment, and cost-effectiveness remain significant concerns. Additionally, the complex interactions between nanomaterials, GI physiology, immune responses, and gut microbiota require further investigation to ensure optimal therapeutic performance and patient safety [12–16].

Given the rapid expansion of research in this area and the growing demand for targeted therapies for GI disorders, a comprehensive evaluation of current nanoengineered coating technologies is timely and necessary [14]. As illustrated in *Fig. 1*, nanoengineered coatings provide a multifunctional platform capable of overcoming the major physiological barriers of the GI tract while improving drug stability, controlled release, site-specific delivery, and therapeutic efficacy. This review aims to provide an in-depth overview of the latest advances in nanoengineered coatings for targeted drug delivery in GI diseases. Particular emphasis is placed on the design principles, functional materials, mechanisms of action, and therapeutic applications of pH-responsive, enzyme-responsive, mucoadhesive, microbiota-responsive, and stimuli-responsive coating systems. Furthermore, the current challenges, translational barriers, and future perspectives associated with these emerging technologies are critically discussed to provide insights into their potential role in next-generation GI therapeutics.

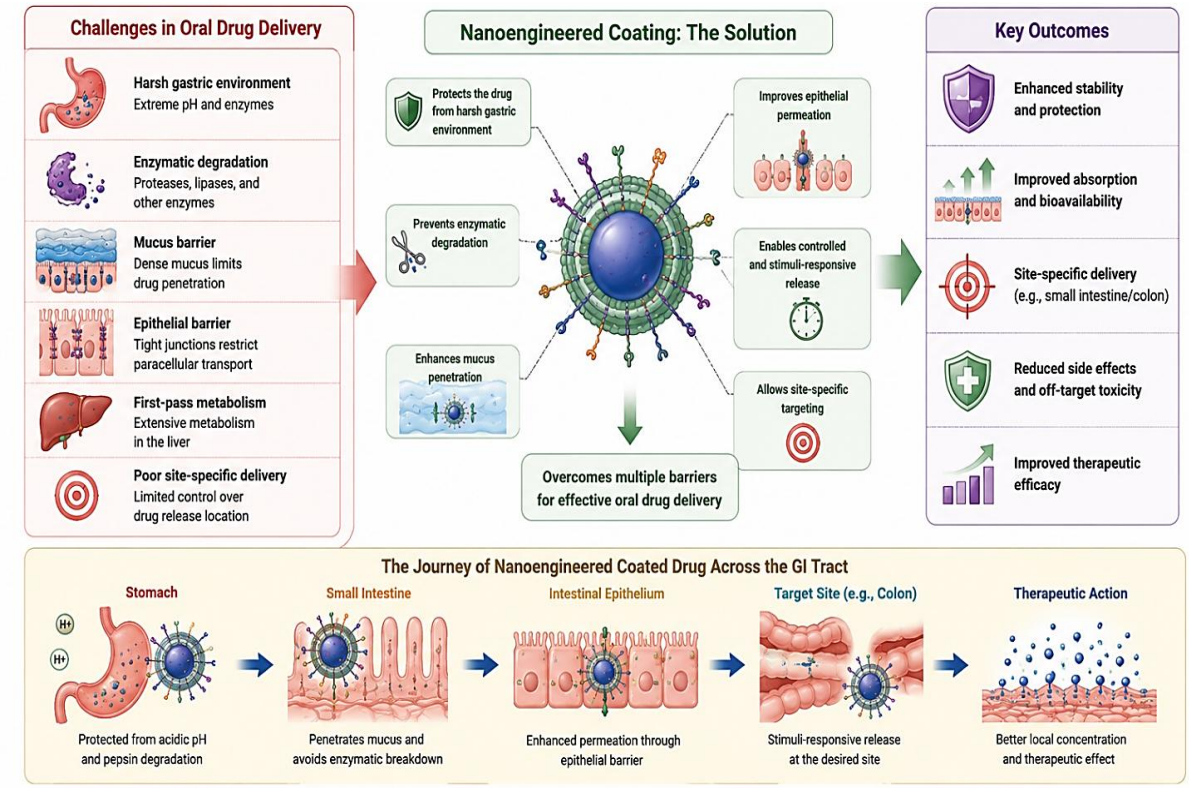

Fig. 1. The role of nanoengineered coatings in overcoming GI barriers for targeted oral drug delivery.

2 | Gastrointestinal Barriers and the Rationale for Nanoengineered Coatings

The GI tract represents one of the most challenging biological environments for drug delivery. Despite being the most convenient and preferred route of administration, oral drug delivery faces numerous physiological, biochemical, and anatomical barriers that significantly affect drug stability, absorption, and therapeutic efficacy. These barriers are particularly problematic for sensitive therapeutic agents such as peptides, proteins, nucleic acids, and poorly soluble drugs. Consequently, the development of advanced delivery systems capable of overcoming these obstacles has become a major focus in pharmaceutical research [12]. As illustrated in *Fig. 2*, nanoengineered coatings provide multifunctional strategies to overcome GI barriers by enhancing drug stability, absorption, and site-specific delivery. In recent years, nanoengineered coating technologies have emerged as promising solutions to address these challenges by enhancing drug protection, targeting efficiency, and controlled release performance.

2.1 | Physiological Barriers in the Gastrointestinal Tract

The human GI tract is characterized by a highly dynamic and complex environment that has evolved to efficiently digest food and prevent the entry of harmful substances. Unfortunately, these protective mechanisms also hinder the successful delivery of therapeutic agents. One of the most significant barriers is the variation in pH throughout the GI tract. The stomach possesses an extremely acidic environment, typically ranging from pH 1 to 3, which can rapidly degrade acid-sensitive drugs. In contrast, the pH gradually increases in the small intestine and reaches near-neutral or slightly alkaline conditions in the colon. Such variations can profoundly influence drug solubility, stability, and release behavior. Another important challenge involves digestive enzymes. Proteolytic enzymes, including pepsin, trypsin, chymotrypsin, and carboxypeptidases, can degrade peptide- and protein-based therapeutics before they reach their intended site

of action. Similarly, lipases and other metabolic enzymes may compromise the integrity of lipid-based formulations and reduce drug availability. The mucus layer covering the GI epithelium serves as an additional protective barrier. This viscoelastic gel layer traps foreign particles and facilitates their removal through continuous mucus turnover. While beneficial for host defense, mucus significantly limits the penetration and retention of many drug delivery systems [10].

Furthermore, epithelial tight junctions restrict the paracellular transport of molecules, particularly hydrophilic macromolecules and nanoparticles. This selective permeability contributes to poor absorption and low bioavailability for many therapeutic agents. In addition, active efflux transporters such as P-glycoprotein can pump absorbed drugs back into the intestinal lumen, further reducing drug uptake [9].

The first-pass hepatic metabolism also presents a major obstacle for orally administered drugs. Following intestinal absorption, many drugs undergo extensive metabolic transformation in the liver before reaching systemic circulation, thereby decreasing their therapeutic effectiveness. Collectively, these physiological barriers create a highly unfavorable environment for efficient oral drug delivery and highlight the need for advanced protective and targeting strategies.

2.2 | Limitations of Conventional Oral Drug Delivery Systems

Conventional oral dosage forms, including tablets, capsules, suspensions, and powders, have long been used for the treatment of GI disorders. However, these formulations often suffer from several intrinsic limitations that compromise therapeutic outcomes. A major concern is premature drug degradation in the acidic gastric environment. Numerous drugs lose their biological activity before reaching the intestine or target disease site. Additionally, conventional formulations frequently exhibit uncontrolled drug release patterns, resulting in fluctuations in plasma drug concentrations and suboptimal therapeutic efficacy. Poor site specificity represents another significant limitation. Most traditional oral formulations distribute drugs throughout the GI tract regardless of the disease location. Consequently, only a fraction of the administered dose reaches the affected tissue, while the remainder may contribute to systemic side effects and toxicity [10–16]. The short residence time of many formulations within the GI tract further limits therapeutic effectiveness. Rapid transit through the stomach and intestines reduces the opportunity for drug absorption and local therapeutic action. This issue is particularly relevant in the treatment of IBD, colorectal cancer, and localized GI infections, where prolonged contact between the drug and diseased tissue is often required. Moreover, conventional formulations generally lack responsiveness to disease-specific microenvironments. They cannot distinguish between healthy and inflamed tissues, nor can they selectively release drugs in response to pathological signals such as inflammation-associated enzymes, altered pH, oxidative stress, or microbial activity. These shortcomings have motivated researchers to develop next-generation delivery systems capable of providing enhanced protection, prolonged retention, targeted delivery, and controlled release [12].

2.3 | The Rationale for Nanoengineered Coatings

Nanoengineered coatings have emerged as one of the most promising approaches for overcoming GI barriers and improving oral drug delivery performance. By integrating nanotechnology with advanced coating materials, these systems offer multifunctional capabilities that extend far beyond the protective functions of conventional coatings. One of the primary advantages of nanoengineered coatings is their ability to protect encapsulated drugs from harsh GI conditions [15–18]. Functional nano-coatings can shield therapeutic agents from acidic degradation, enzymatic attack, and premature release during transit through the upper GI tract. The nanoscale architecture of these coatings provides a significantly increased surface area, promoting enhanced interactions with biological tissues and improving drug absorption. In addition, nano-coatings can be engineered using stimuli-responsive materials that trigger drug release only under specific physiological conditions. Examples include pH-responsive coatings that dissolve in the intestine, enzyme-responsive coatings activated by colonic microbiota, and inflammation-responsive coatings designed to release drugs selectively at diseased sites [16]. Nanoengineered coatings can also improve mucoadhesion and tissue

retention. Surface-functionalized nanoparticles coated with polymers such as chitosan, alginate, and hyaluronic acid exhibit prolonged residence times within the GI tract, thereby enhancing local drug concentrations and therapeutic efficacy. Another important advantage is the potential for active targeting. By incorporating specific ligands, antibodies, peptides, or receptor-binding molecules onto the coating surface, nanocarriers can selectively interact with diseased tissues while minimizing exposure to healthy cells. Such targeting strategies are particularly valuable in colorectal cancer therapy and IBD management. Furthermore, nanoengineered coatings facilitate controlled and sustained drug release, reducing dosing frequency and improving patient compliance. The ability to combine multiple functionalities within a single coating system, including protection, targeting, responsiveness, and controlled release, has positioned nanoengineered coatings at the forefront of modern GI drug delivery research. As a result, these advanced systems are increasingly being investigated as next-generation platforms for the treatment of various GI diseases, including IBD, colorectal cancer, gastric ulcers, Helicobacter pylori infection, and other chronic inflammatory disorders [11].

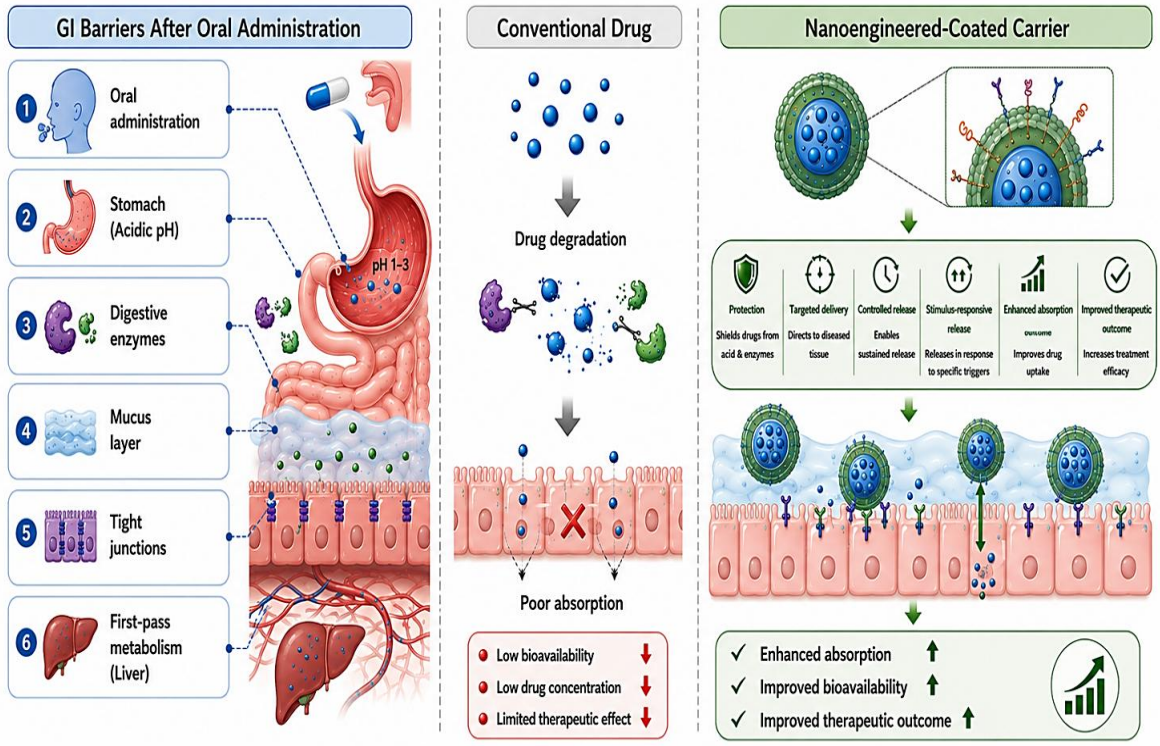

Fig. 2. Gastrointestinal barriers affecting oral drug delivery and the role of nanoengineered coatings in improving drug protection, targeted delivery, controlled release, and therapeutic outcomes.

3 | Classification of Nanoengineered Coatings for Gastrointestinal Drug Delivery

Recent advances in nanotechnology and material science have led to the development of a diverse range of nanoengineered coating systems designed to overcome GI barriers and improve therapeutic outcomes. Unlike conventional pharmaceutical coatings, nanoengineered coatings incorporate nanoscale materials, functional polymers, and responsive components that provide enhanced protection, targeted delivery, controlled release, and site-specific therapeutic action. Based on their mechanism of action and responsiveness to physiological stimuli, nanoengineered coatings can be broadly classified into several categories, including enteric nano-coatings, pH-responsive nano-coatings, enzyme-responsive nano-coatings, mucoadhesive nano-coatings, microbiota-responsive nano-coatings, stimuli-responsive nano-

coatings, and multifunctional hybrid systems [13]. Different nanoengineered coating strategies, their mechanisms, and GI applications are summarized in *Table 1*.

3.1 | Enteric Nano-Coatings

Enteric coatings represent one of the earliest and most widely used coating technologies for oral drug delivery. Their primary function is to protect drugs from the acidic gastric environment and prevent premature drug release in the stomach. Nanoengineered enteric coatings build upon conventional enteric systems by incorporating nanoscale structures and functional materials that improve coating uniformity, drug protection, and release precision. These coatings are typically formulated using pH-sensitive polymers such as CAP, HPMCP, and PVAP. At acidic pH values, these polymers remain intact and insoluble. Upon exposure to the higher pH conditions of the small intestine or colon, the coating dissolves and facilitates drug release. Nanoengineering strategies have enabled the fabrication of thinner, more homogeneous coatings with improved mechanical stability and reduced variability in drug release behavior. Nanocomposite enteric coatings can also enhance the protection of sensitive biomolecules such as peptides and proteins against gastric degradation. Enteric nano-coatings have been extensively investigated for the treatment of IBD, colorectal cancer, and intestinal infections, where protection from gastric conditions is essential for therapeutic success [17–20].

3.2 | pH-Responsive Nano-Coatings

pH-responsive nano-coatings are among the most extensively studied smart coating systems for GI drug delivery. These coatings exploit the natural pH gradient along the GI tract to achieve site-specific drug release. The stomach exhibits highly acidic conditions, whereas the pH gradually increases in the small intestine and colon. pH-responsive polymers undergo structural changes, swelling, erosion, or dissolution when exposed to specific pH environments, thereby triggering drug release at predetermined locations. Common materials include methacrylic acid copolymers, Eudragit derivatives, alginate, chitosan derivatives, poly(acrylic acid), and pH-sensitive hydrogels. The incorporation of nanostructured components further enhances responsiveness, release precision, and targeting capability. These systems are particularly valuable in the management of IBD, where local drug delivery to the distal intestine and colon is often required. In addition, pH-responsive nano-coatings have demonstrated significant potential for colon-targeted chemotherapy in colorectal cancer treatment. Despite their advantages, pH-responsive systems may be affected by interindividual variability in GI pH, disease-related pH alterations, and dietary influences. Consequently, combination strategies integrating multiple targeting mechanisms are increasingly being explored [19].

3.3 | Enzyme-Responsive Nano-Coatings

Enzyme-responsive nano-coatings utilize the enzymatic activity present within specific regions of the GI tract to trigger drug release. These systems are particularly attractive for colon-targeted drug delivery because the colon harbors a diverse microbial population capable of producing a wide variety of degradative enzymes. Polymers such as pectin, guar gum, dextran, chitosan, inulin, and amylose can be selectively degraded by microbial enzymes, including pectinases, dextranases, glycosidases, and azoreductases. Drug release occurs only after enzymatic degradation of the coating matrix, thereby minimizing premature drug leakage in the upper GI tract. Nanoengineering has significantly improved the performance of enzyme-responsive systems through enhanced coating stability, optimized degradation kinetics, and improved drug encapsulation efficiency. Furthermore, nanostructured enzyme-responsive coatings provide higher specificity compared with conventional pH-dependent systems. Applications include the localized treatment of ulcerative colitis, Crohn's disease, colorectal cancer, and microbiota-associated GI disorders [12–15].

3.4 | Mucoadhesive Nano-Coatings

Mucoadhesive nano-coatings are designed to enhance the residence time of drug delivery systems within the GI tract by promoting adhesion to mucus-covered epithelial surfaces. Prolonged retention at the target site increases local drug concentration, improves absorption, and enhances therapeutic efficacy. Several natural and synthetic polymers exhibit strong mucoadhesive properties, including chitosan, sodium alginate, hyaluronic acid, carbopol, polycarbophil, and cellulose derivatives. These materials interact with mucin through hydrogen bonding, electrostatic interactions, hydrophobic forces, and polymer chain interpenetration. At the nanoscale level, surface modification techniques can significantly improve mucoadhesion while maintaining particle stability and controlled drug release characteristics. Mucoadhesive nano-coatings have demonstrated particular promise in IBD therapy, gastric ulcer treatment, and Helicobacter pylori eradication. One of the major advantages of these systems is their ability to overcome rapid GI transit and mucus clearance. However, excessive adhesion may sometimes limit penetration into deeper mucus layers, creating a balance that must be carefully optimized during formulation design [20].

3.5 | Microbiota-Responsive Nano-Coatings

The growing understanding of the gut microbiome has stimulated the development of microbiota-responsive nano-coatings capable of exploiting microbial activity for highly selective drug delivery. These coatings are engineered to respond to microbial enzymes, metabolites, or environmental conditions unique to the intestinal microbiota. Unlike traditional pH-dependent systems, microbiota-responsive coatings provide greater specificity because they rely on biological triggers that are often localized within the colon. Materials commonly employed include polysaccharides such as pectin, dextran, guar gum, chitosan, and inulin, which undergo degradation by microbial enzymes produced by colonic bacteria. The resulting systems allow highly selective drug release at sites where microbial activity is greatest. Microbiota-responsive coatings are increasingly being investigated for the treatment of IBD, colorectal cancer, and microbiome-associated GI disorders. These systems also represent an important step toward personalized medicine, as future formulations may be tailored to individual microbial profiles [12–17].

3.6 | Stimuli-Responsive Nano-Coatings

Stimuli-responsive nano-coatings constitute a rapidly emerging class of intelligent drug delivery systems capable of responding to internal or external physiological signals. These coatings can undergo structural transformations when exposed to specific stimuli, thereby initiating drug release in a controlled manner. Internal stimuli include pH changes, enzymatic activity, oxidative stress, ROS, inflammatory mediators, temperature fluctuations, and redox gradients. External stimuli may involve light, ultrasound, magnetic fields, or electrical signals. In GI diseases, inflammation-responsive nano-coatings have gained particular attention because inflamed tissues often exhibit elevated ROS levels and altered biochemical environments. By exploiting these pathological characteristics, responsive coatings can selectively release therapeutic agents within diseased regions while minimizing systemic exposure. The integration of stimuli-responsive materials with nanotechnology has enabled the development of highly sophisticated delivery platforms that combine targeting, protection, and controlled release functions within a single system [15].

3.7 | Hybrid and Multifunctional Nano-Coatings

Although individual coating strategies have demonstrated significant therapeutic potential, increasing evidence suggests that combining multiple targeting mechanisms can further improve drug delivery performance. Consequently, hybrid and multifunctional nano-coatings have emerged as one of the most promising directions in advanced GI drug delivery research. These systems integrate two or more functionalities within a single coating platform. Examples include pH-responsive and enzyme-responsive coatings, mucoadhesive and microbiota-responsive systems, or inflammation-responsive coatings combined with active targeting ligands. Hybrid coatings offer superior targeting precision, reduced premature drug

release, enhanced retention, and improved therapeutic efficacy. Furthermore, multifunctional systems can compensate for the limitations associated with individual approaches, resulting in more robust and reliable drug delivery performance. Recent developments in nanotechnology, biomaterials engineering, and precision medicine are expected to accelerate the clinical translation of hybrid nano-coating platforms, positioning them as key components of next-generation therapies for GI diseases [16].

Table 1. Classification of nanoengineered coating systems for GI drug delivery, including their triggering mechanisms, representative materials, and therapeutic applications.

Coating Type	Trigger Mechanism	Common Materials	Main GI Applications
Enteric nano-coatings	Intestinal pH	Eudragit, HPMCP, CAP	IBD, Colon cancer
pH-responsive nano-coatings	pH gradient	Eudragit, Alginate	Colon targeting
Enzyme-responsive nano-coatings	Microbial enzymes	Pectin, Dextran, Inulin	Ulcerative colitis
Mucoadhesive nano-coatings	Mucin interaction	Chitosan, HA, Carbopol	Gastric ulcer, H. pylori
Microbiota-responsive nano-coatings	Gut microbiota activity	Pectin, Guar gum	IBD, Colon cancer
Stimuli-responsive nano-coatings	ROS, inflammation, temperature	Smart polymers	Precision therapy
Hybrid nano-coatings	Multiple triggers	Composite systems	Advanced GI targeting

4 | Materials Used in Nanoengineered Gastrointestinal Coatings

The success of nanoengineered coating systems largely depends on the selection of appropriate materials capable of providing protection, targeting, controlled release, biocompatibility, and stability throughout the GI tract. Over the past decade, a wide variety of natural polymers, synthetic polymers, lipids, and hybrid materials have been investigated for the fabrication of advanced GI coating systems. These materials not only determine the physicochemical characteristics of the coating but also influence drug release behavior, tissue interaction, biodegradation, and therapeutic performance [18–21]. An ideal material for GI nano-coatings should possess several essential characteristics, including biocompatibility, biodegradability, non-toxicity, mechanical stability, mucoadhesive potential, responsiveness to physiological stimuli, and scalability for industrial production. Depending on the intended application, different materials may be selected individually or combined to achieve multifunctional coating systems. The major materials employed in nanoengineered GI coatings and their corresponding properties and applications are summarized in *Fig. 3*.

4.1 | Natural Polymers

Natural polymers have gained considerable attention in GI drug delivery owing to their excellent biocompatibility, biodegradability, low toxicity, and abundant availability. In contrast to many synthetic materials, natural polymers often possess intrinsic biological functions, such as mucoadhesion, bioactivity, and responsiveness to physiological or enzymatic stimuli, which can further improve therapeutic performance. These properties make them particularly attractive for the fabrication of nanoengineered coating systems designed to enhance drug stability, prolong GI residence time, and achieve controlled or site-specific drug release [9]. In addition, the chemical versatility of natural polymers allows easy surface modification and functionalization with bioactive molecules, targeting ligands, or other nanomaterials to develop multifunctional drug delivery platforms. Their ability to interact with the mucus layer and intestinal epithelium also contributes to enhanced drug absorption and localized therapeutic effects. Consequently, natural polymers such as chitosan, alginate, pectin, dextran, and inulin have been extensively investigated as coating materials for oral nanocarriers intended for the treatment of various GI diseases [7–11].

4.1.1 | Chitosan

Chitosan is one of the most extensively investigated natural biopolymers for GI drug delivery applications. Derived from the deacetylation of chitin, chitosan exhibits excellent biocompatibility, biodegradability, low

toxicity, and remarkable mucoadhesive properties, making it an ideal material for oral nanoengineered coating systems. The cationic nature of chitosan enables strong electrostatic interactions with negatively charged mucosal surfaces, thereby prolonging GI residence time and enhancing drug absorption. Furthermore, chitosan has been shown to transiently open epithelial tight junctions, facilitating paracellular transport of hydrophilic molecules, peptides, proteins, and other macromolecular therapeutics. Besides its drug delivery functions, chitosan also possesses intrinsic antimicrobial and wound-healing activities, which may further contribute to therapeutic efficacy in GI disorders. Nanoengineered chitosan coatings have been widely investigated for colon-targeted drug delivery, IBD treatment, oral peptide delivery, vaccine delivery, and localized therapy for GI infections owing to their excellent protective and bioadhesive characteristics [15].

4.1.2 | Alginate

Alginate is a naturally occurring anionic polysaccharide extracted primarily from brown seaweed and has become one of the most widely used natural polymers in GI drug delivery. It possesses excellent biocompatibility, biodegradability, and gel-forming ability in the presence of divalent cations such as calcium ions, allowing the formation of stable hydrogel matrices suitable for controlled drug release. Alginate-based nano-coatings effectively protect encapsulated drugs against the acidic gastric environment while enabling pH-responsive drug release in the intestine. Owing to their mild preparation conditions and favorable safety profile, alginate formulations are particularly suitable for the encapsulation of proteins, peptides, probiotics, and other sensitive biological therapeutics. In addition, alginate can be combined with polymers such as chitosan or pectin to develop multifunctional coating systems with enhanced mechanical stability, mucoadhesion, and targeting capability. These systems have demonstrated promising applications in gastric ulcer therapy, probiotic delivery, intestinal-targeted drug delivery, and inflammatory GI diseases [19].

4.1.3 | Pectin

Pectin is a biodegradable plant-derived polysaccharide extensively employed in colon-targeted drug delivery systems because of its selective degradation by pectinolytic enzymes produced by the colonic microbiota. Unlike many conventional polymers, pectin remains relatively stable during passage through the stomach and small intestine, minimizing premature drug release before reaching the colon. This characteristic makes pectin an excellent candidate for enzyme-responsive and microbiota-responsive nanoengineered coating systems. Furthermore, pectin exhibits excellent biocompatibility and can readily form composite materials with chitosan, alginate, and synthetic polymers to improve mechanical strength and drug release behavior. Pectin-coated nanocarriers have demonstrated considerable therapeutic potential for localized treatment of ulcerative colitis, Crohn's disease, colorectal cancer, and other chronic inflammatory disorders affecting the colon [20].

4.1.4 | Dextran and inulin

Dextran and inulin are naturally occurring microbial polysaccharides that have attracted increasing attention as coating materials for colon-specific drug delivery. Both polymers are resistant to digestion in the upper GI tract but undergo selective enzymatic degradation by the intestinal microbiota after reaching the colon, allowing highly localized and controlled drug release. Their excellent biocompatibility and biodegradability make them suitable candidates for developing microbiota-responsive nanoengineered coating systems. In addition, dextran and inulin can be chemically modified or combined with other natural and synthetic polymers to improve coating stability, drug loading efficiency, and targeting performance. Nanoengineered systems utilizing dextran or inulin coatings have shown promising results in IBD therapy, colorectal cancer treatment, probiotic delivery, and microbiome-targeted therapeutic strategies, highlighting their growing importance in precision GI drug delivery [12].

4.2 | Synthetic Polymers

Synthetic polymers have become indispensable components of advanced nanoengineered coating systems owing to their superior control over physicochemical properties, molecular weight distribution, degradation kinetics, mechanical strength, and responsiveness compared with many natural polymers. Their well-defined chemical structures allow precise tailoring of material characteristics, enabling the development of drug delivery systems with predictable performance, controlled drug release, and site-specific targeting. These advantages have made synthetic polymers widely employed in the fabrication of oral nanocarriers for GI applications [13]. Furthermore, synthetic polymers can be chemically modified or combined with natural polymers and lipid-based materials to produce multifunctional coating systems with improved stability, enhanced mucoadhesion, prolonged GI residence time, and stimuli-responsive behavior. Their excellent reproducibility and scalability also facilitate industrial manufacturing and regulatory compliance, making them attractive candidates for pharmaceutical commercialization. Among the most extensively investigated synthetic polymers for GI nano-coatings are Eudragit, poly(lactic-co-glycolic acid) (PLGA), and polyethylene glycol (PEG), each offering unique advantages for targeted oral drug delivery [14–17].

4.2.1 | Eudragit polymers

Eudragit polymers are among the most widely utilized materials in GI coating technology. These methacrylic acid copolymers exhibit pH-dependent solubility profiles that enable site-specific drug release. Different grades of Eudragit dissolve at distinct pH values, allowing precise targeting of the small intestine or colon. Eudragit-based nano-coatings have demonstrated exceptional effectiveness in enteric protection, colon-targeted delivery, and controlled release applications [22].

4.2.2 | Poly(lactic-co-glycolic acid)

PLGA is one of the most extensively studied biodegradable synthetic polymers in pharmaceutical nanotechnology and has been approved by the U.S. Food and Drug Administration (FDA) for a wide range of drug delivery applications. The polymer undergoes hydrolytic degradation into lactic acid and glycolic acid, which are naturally metabolized through normal physiological pathways, contributing to its excellent biocompatibility and safety profile. Owing to its tunable degradation rate, mechanical stability, and versatile formulation characteristics, PLGA has become an ideal material for the fabrication of nanoengineered coating systems. PLGA-based nanocarriers can be functionalized with various coating materials, including chitosan, PEG, alginate, and pH-responsive polymers, to enhance GI stability, prolong drug residence time, and achieve controlled as well as site-specific drug release. In addition, PLGA nanoparticles provide effective protection for encapsulated drugs against acidic gastric conditions and enzymatic degradation, thereby improving oral bioavailability. Due to these favorable properties, PLGA-based delivery systems have been extensively investigated for the oral administration of anticancer agents, anti-inflammatory drugs, peptides, proteins, vaccines, and nucleic acid therapeutics, particularly for the treatment of colorectal cancer, IBD, and other GI disorders [23].

4.2.3 | Polyethylene glycol

PEG is a hydrophilic synthetic polymer widely employed as a surface-modifying material in nanoengineered drug delivery systems. Surface functionalization with PEG, commonly referred to as PEGylation, enhances nanoparticle colloidal stability, minimizes particle aggregation, and reduces nonspecific interactions with biological components. These properties contribute to improved formulation stability during GI transit and prolonged residence time within the intestinal environment. In addition to improving physicochemical stability, PEGylation facilitates mucus permeation by reducing adhesive interactions between nanoparticles and mucin fibers, thereby promoting closer contact with the intestinal epithelium and enhancing drug absorption. PEG-coated nanocarriers can also be combined with targeting ligands or stimuli-responsive polymers to create multifunctional delivery platforms with improved pharmacokinetic behavior and therapeutic efficiency. Consequently, PEG-containing nano-coatings have been widely incorporated into

advanced GI drug delivery systems for the oral administration of small molecules, peptides, proteins, and biologics, where enhanced bioavailability, prolonged circulation, and controlled drug release are required [19].

4.3 | Lipid-Based Materials

Lipid-based materials have emerged as important components of nanoengineered coating systems owing to their excellent biocompatibility, biodegradability, and ability to enhance the solubility and oral bioavailability of poorly water-soluble drugs. These materials provide a protective lipid matrix that shields encapsulated therapeutic agents from the harsh GI environment, including acidic pH, digestive enzymes, and premature degradation. Furthermore, lipid-based nanocarriers can improve drug absorption by promoting close interaction with the intestinal epithelium and facilitating lymphatic uptake, thereby reducing first-pass metabolism. The incorporation of functional coating materials, such as chitosan, alginate, PEG, or Eudragit, further enhances their stability, mucoadhesion, site-specific targeting, and controlled drug release. Consequently, lipid-based nano-coating systems have attracted considerable attention for the oral delivery of small molecules, peptides, proteins, and nucleic acid therapeutics in the management of GI diseases [15].

4.3.1 | Solid lipid nanoparticles

Solid Lipid Nanoparticles (SLNs) are among the earliest lipid-based nanocarriers developed for controlled drug delivery applications. They consist of physiologically compatible solid lipids stabilized by surfactants, forming a stable matrix capable of encapsulating both hydrophilic and lipophilic drugs. The solid lipid core protects encapsulated drugs from chemical and enzymatic degradation during GI transit while enabling sustained and controlled drug release. Surface modification of SLNs with functional polymers, including chitosan, PEG, alginate, and pH-responsive materials, can further improve their mucoadhesive properties, GI residence time, targeting efficiency, and drug absorption. Owing to these advantages, SLNs have been extensively investigated for the oral delivery of anti-inflammatory agents, anticancer drugs, antibiotics, and peptide therapeutics, demonstrating significant potential for improving treatment outcomes in IBD, colorectal cancer, and other GI disorders [16].

4.3.2 | Nanostructured lipid carriers

Nanostructured Lipid Carriers (NLCs) represent the second generation of lipid-based nanocarriers and were developed to overcome the limitations associated with conventional SLNs, particularly their limited drug loading capacity and potential drug expulsion during storage. NLCs are composed of a mixture of solid and liquid lipids, creating a less ordered lipid matrix that accommodates a greater amount of therapeutic agents while improving formulation stability. This unique structural organization minimizes drug leakage and enables sustained drug release, making NLCs highly suitable for oral drug delivery applications. Furthermore, surface functionalization of NLCs with polymers such as chitosan, PEG, alginate, or pH-responsive materials can enhance mucoadhesion, prolong GI residence time, and facilitate site-specific drug delivery. Polymer-coated NLCs have demonstrated promising therapeutic potential in the treatment of colorectal cancer, IBD, and gastric disorders by improving drug bioavailability, reducing systemic toxicity, and increasing local drug concentrations at diseased tissues [14].

4.3.3 | Liposomes and niosomes

Liposomes and niosomes are vesicular nanocarriers capable of encapsulating both hydrophilic and hydrophobic therapeutic agents within their aqueous core and lipid or surfactant bilayer, respectively. Their structural versatility allows the incorporation of a wide range of pharmaceuticals, including small-molecule drugs, peptides, proteins, and nucleic acids. However, conventional liposomes and niosomes often exhibit limited stability in the harsh GI environment due to acidic pH, bile salts, and digestive enzymes. To overcome these limitations, surface coating with functional polymers such as chitosan, PEG, alginate, pectin, or Eudragit has been widely investigated. These coatings improve vesicle stability, enhance mucoadhesion,

reduce premature drug leakage, and provide controlled as well as site-specific drug release. Coated liposomes and niosomes have shown considerable promise for oral peptide delivery, colon-targeted therapy, eradication of Helicobacter pylori, treatment of IBD, and localized chemotherapy for colorectal cancer. Their excellent biocompatibility, high drug-loading versatility, and capacity for multifunctional surface modification make them attractive platforms for next-generation GI drug delivery systems [23].

4.4 | Hybrid and Composite Materials

Recent advances in nanotechnology have promoted the development of hybrid materials that combine the advantages of multiple material classes within a single delivery platform. Hybrid nano-coatings may consist of combinations such as polymer-polymer, polymer-lipid, polymer-inorganic, or lipid-inorganic systems. These multifunctional materials can simultaneously provide protection, targeting, mucoadhesion, responsiveness, and controlled release. Examples include chitosan-coated PLGA nanoparticles, alginate-coated liposomes, Eudragit-coated lipid nanoparticles, and pectin-functionalized nanocomposites. Such systems have demonstrated superior performance compared with single-material formulations and represent a promising direction for future GI drug delivery technologies [24].

4.5 | Emerging Smart Biomaterials for Gastrointestinal Nano-Coatings

The latest generation of GI nano-coatings incorporates smart biomaterials capable of responding dynamically to pathological conditions. These materials can sense environmental triggers such as pH changes, ROS, inflammatory mediators, temperature fluctuations, and microbial metabolites. Smart biomaterials enable highly selective and controlled drug release, reducing systemic exposure and improving therapeutic precision. The integration of these advanced materials with nanotechnology is expected to drive the development of next-generation precision drug delivery systems for GI diseases. The continuous evolution of material science is providing increasingly sophisticated tools for the design of multifunctional nanoengineered coatings. Future innovations will likely focus on combining biocompatibility, targeting capability, stimuli responsiveness, and manufacturability to facilitate clinical translation and personalized treatment strategies [21].

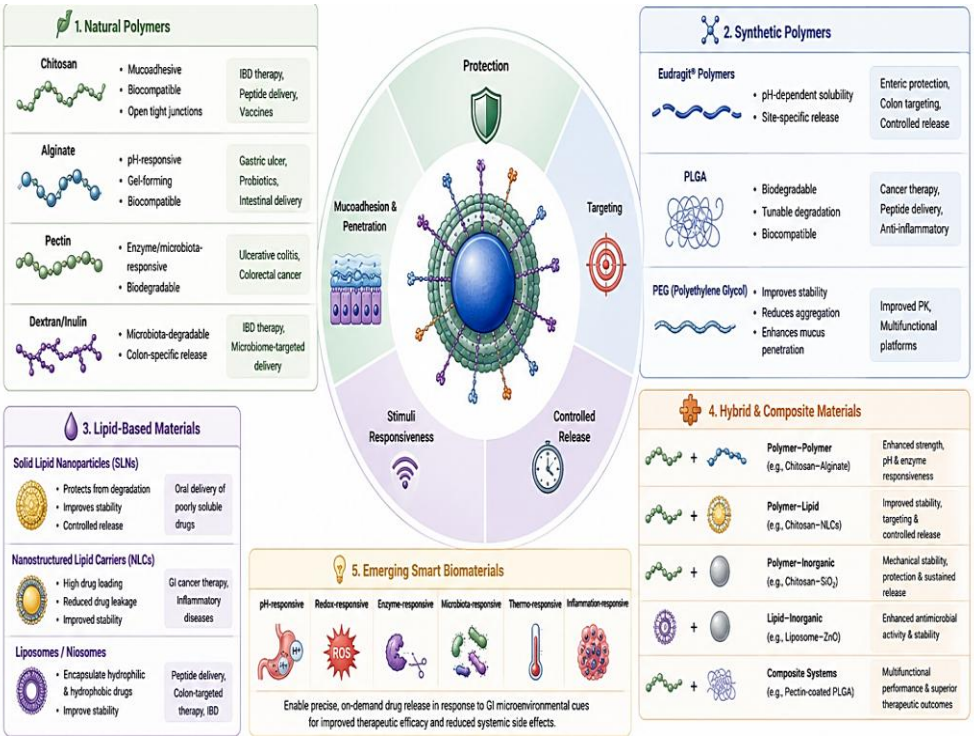

Fig. 3. Materials used in nanoengineered GI coatings.

5 | Applications of Nanoengineered Coatings in Gastrointestinal Diseases

The development of nanoengineered coating technologies has created new opportunities for improving the management of GI diseases by enabling targeted, controlled, and localized drug delivery. Conventional oral therapies often suffer from poor stability, insufficient drug accumulation at disease sites, and systemic adverse effects. Nano-coated delivery systems provide advanced solutions by protecting therapeutic agents during GI transit, enhancing drug retention, improving bioavailability, and enabling disease-specific release. The application of nanoengineered coatings in GI disorders has gained significant attention due to their ability to interact with complex biological environments, including altered pH conditions, inflammatory microenvironments, enzymatic activity, and gut microbiota changes. This section discusses the major applications of nanoengineered coatings in important GI diseases [22].

5.1 | Inflammatory Bowel Disease

IBD, including Crohn's disease and ulcerative colitis, is a chronic inflammatory disorder characterized by persistent inflammation of the GI mucosa. The pathogenesis of IBD involves complex interactions between genetic factors, immune responses, intestinal barrier dysfunction, and microbiota imbalance. Current therapeutic approaches include corticosteroids, immunosuppressive agents, biologics, and anti-inflammatory drugs. However, many conventional treatments are associated with poor site specificity, systemic toxicity, and reduced effectiveness due to inadequate drug concentration at inflamed intestinal regions. Nanoengineered coatings have emerged as promising strategies for improving IBD therapy by enabling selective drug delivery to inflamed intestinal tissues. pH-responsive nano-coatings are widely investigated because they can protect drugs during gastric and small intestinal transit while releasing therapeutic agents in the colon. Materials such as Eudragit S100, Eudragit L100, alginate, and methacrylate-based polymers have been used to develop colon-targeted formulations containing anti-inflammatory drugs. These systems enhance local drug concentration and reduce systemic exposure. In addition, inflammation-responsive nano-coatings have gained increasing interest. Inflamed intestinal tissues exhibit elevated levels of ROS, inflammatory enzymes, and oxidative stress markers. Smart coatings designed to respond to these pathological signals can achieve selective drug release at diseased sites. Mucoadhesive nano-coatings also provide significant advantages in IBD treatment by prolonging contact between the formulation and damaged intestinal mucosa. This prolonged residence time enhances therapeutic efficacy and supports mucosal healing. Nanoengineered coatings represent a powerful approach for improving IBD treatment through localized delivery, reduced side effects, and enhanced therapeutic outcomes [25].

5.2 | Colorectal Cancer

Colorectal cancer is one of the most common GI malignancies and remains a major cause of cancer-related mortality worldwide. Chemotherapeutic agents used in colorectal cancer treatment often exhibit limited therapeutic windows due to systemic toxicity and poor tumor selectivity. Nanoengineered coatings provide new possibilities for improving colorectal cancer therapy by facilitating targeted drug delivery and controlled release within the tumor microenvironment. Colon-targeted nano-coatings can protect anticancer drugs during GI transit and promote drug release specifically in the colon. Enzyme-responsive coatings based on polysaccharides such as dextran, pectin, and guar gum exploit bacterial enzymatic activity in the colon to trigger drug release. Furthermore, nanocarriers coated with targeting ligands can enhance selective interaction with cancer cells. Surface modification using specific molecules may improve tumor accumulation and reduce damage to healthy tissues. Polymer-coated nanoparticles, lipid-based nanocarriers, and hybrid nano-systems have been investigated for delivering chemotherapeutic agents, nucleic acids, and natural anticancer compounds. These systems provide improved drug stability, enhanced cellular uptake, and prolonged therapeutic action. The combination of nano-coatings with stimuli-responsive mechanisms represents a promising strategy for precision colorectal cancer therapy [21–25].

5.3 | Gastric Ulcers and Helicobacter pylori Infection

Gastric ulcers are characterized by damage to the gastric mucosa resulting from an imbalance between protective mechanisms and aggressive factors such as gastric acid, oxidative stress, and bacterial infection. Helicobacter pylori is a major causative agent associated with chronic gastritis, peptic ulcer disease, and increased risk of gastric cancer. Current treatment approaches rely mainly on antibiotic combinations and acid-suppressive agents. However, antibiotic resistance and poor drug retention within the gastric environment remain important challenges. Nanoengineered coatings can improve gastric therapy by enhancing drug stability, prolonging gastric residence time, and increasing local drug concentration. Mucoadhesive nano-coatings based on chitosan, alginate, and related polymers can adhere to gastric mucus, improving retention at the infection site. This prolonged interaction enhances antibacterial activity against H. pylori. Additionally, nanoparticle coatings can improve the delivery of antimicrobial agents by protecting them from premature degradation and increasing penetration into the gastric mucosal layer. These strategies provide promising alternatives for improving eradication efficiency and reducing treatment failure caused by conventional formulations [20–22].

5.4 | Celiac Disease

Celiac disease is an immune-mediated GI disorder triggered by gluten exposure in genetically susceptible individuals. The disease results in chronic inflammation and damage to intestinal villi, leading to impaired nutrient absorption. Although a strict gluten-free diet remains the primary treatment, drug-based approaches are being explored to reduce intestinal inflammation and restore barrier function. Nanoengineered coatings may contribute to future celiac disease therapies by enabling targeted delivery of anti-inflammatory agents, enzymes, and immune-modulating molecules. Mucoadhesive and enzyme-responsive coatings can improve drug localization within affected intestinal regions, while protecting sensitive therapeutic molecules from degradation. Furthermore, nano-coated delivery systems may provide opportunities for controlled release of therapeutic agents aimed at restoring intestinal homeostasis [21].

5.5 | Gastrointestinal Infections

GI infections caused by bacteria, viruses, and parasites remain significant health concerns worldwide. Conventional antimicrobial treatments often face limitations, including poor drug stability, resistance development, and insufficient local drug concentration. Nanoengineered coatings provide several advantages for infection management by improving antimicrobial delivery and enhancing interaction with microbial targets. Polymeric and lipid-based nano-coatings can protect antimicrobial agents from degradation and facilitate prolonged exposure at infection sites. In addition, surface modifications may improve interactions with bacterial biofilms and resistant microbial populations. Chitosan-based nano-coatings have attracted considerable attention due to their intrinsic antimicrobial activity and ability to enhance the effectiveness of encapsulated drugs [23].

5.6 | Irritable Bowel Syndrome and Functional Gastrointestinal Disorders

Functional GI disorders such as IBS involve altered intestinal motility, visceral hypersensitivity, and changes in gut microbiota. Although IBS management remains challenging, nanoengineered coatings may provide new strategies for delivering probiotics, phytochemicals, and bioactive compounds. Microbiota-responsive coatings can selectively interact with intestinal microbial populations, supporting restoration of microbial balance and improving intestinal function. Nano-coated probiotic delivery systems have demonstrated improved stability and survival during GI transit, suggesting potential applications in microbiome-based therapies [19]. The major GI diseases, their associated therapeutic challenges, nanoengineered coating strategies, and corresponding therapeutic benefits are summarized in *Table 2*.

Table 2. Therapeutic applications of nanoengineered coating strategies in major GI diseases.

Disease	Main Challenge	Nano-Coating Strategy	Therapeutic Benefit
IBD	Local inflammation	pH/ROS responsive coatings	Colon targeting
Colorectal cancer	Drug toxicity	Targeted nano-coatings	Tumor-selective delivery
H. pylori infection	Poor gastric retention	Mucoadhesive coatings	Enhanced eradication
Gastric ulcer	Acid degradation	Protective coatings	Mucosal protection
Celiac disease	Barrier dysfunction	Responsive coatings	Local therapy
GI infections	Resistance	Antimicrobial nano-coatings	Improved efficacy
IBS	Microbiota imbalance	Microbiota-responsive systems	Microbiome modulation

6 | Challenges and Translational Barriers of Nanoengineered Gastrointestinal Coatings

Despite remarkable advances in nanoengineered coating technologies for GI drug delivery, several challenges remain before these systems can achieve widespread clinical translation. Although nano-coated delivery platforms have demonstrated promising results in laboratory and preclinical studies, their successful development into clinically approved products requires addressing critical issues related to formulation complexity, biological interactions, safety, manufacturing, and regulatory considerations. Understanding these limitations is essential for guiding future research toward more reliable, reproducible, and clinically applicable nanoengineered coating systems [25].

6.1 | Complexity of Gastrointestinal Physiology and Biological Variability

The GI tract is a highly dynamic biological environment influenced by multiple physiological factors, including pH fluctuations, enzymatic activity, mucus composition, intestinal motility, diet, and microbiota composition. Although nanoengineered coatings are designed to respond to specific GI conditions, significant interindividual variability may affect their performance. For example, variations in intestinal pH between individuals can influence the dissolution behavior of pH-responsive coatings. Similarly, differences in gut microbiota composition may alter the enzymatic degradation of microbiota-responsive materials. Disease conditions can further modify GI physiology. IBD, for instance, may change mucus thickness, intestinal permeability, and microbial populations, potentially affecting the behavior of nano-coated delivery systems. Therefore, future nano-coating platforms must be designed with sufficient adaptability to accommodate physiological variations among patients [21].

6.2 | Nanomaterial Safety and Biocompatibility Concerns

The safety of nanomaterials remains one of the most important considerations in the development of nanoengineered drug delivery systems. Although many commonly used materials, including chitosan, alginate, PLGA, and lipid-based nanoparticles, exhibit favorable biocompatibility profiles, nanoscale properties may introduce unique biological interactions. Particle size, surface charge, morphology, and chemical composition can influence cellular uptake, immune responses, and potential toxicity. Some nanoparticles may interact with intestinal epithelial cells, immune cells, or the gut microbiota in unexpected ways. Long-term exposure to certain nanomaterials may raise concerns regarding accumulation, inflammatory responses, or disruption of intestinal homeostasis. Consequently, a comprehensive toxicological evaluation, including acute and chronic safety studies, is essential before clinical application [26].

6.3 | Challenges in Controlled and Predictable Drug Release

Achieving precise control over drug release remains a major challenge in GI nano-coating design. Although stimuli-responsive coatings provide advanced targeting capabilities, their performance may be affected by variations in physiological conditions. For example, a pH-responsive coating optimized for a specific intestinal region may demonstrate altered release behavior under pathological conditions. Similarly, enzyme-responsive systems depend on biological triggers that may vary between individuals. Excessive dependence on a single stimulus may result in incomplete or premature drug release. To overcome these limitations, future approaches should focus on multifunctional nano-coatings capable of responding to multiple physiological signals simultaneously [12–15].

6.4 | Manufacturing and Scale-Up Challenges

One of the major barriers limiting the clinical translation of nanoengineered coatings is the difficulty of large-scale manufacturing. Laboratory-scale preparation methods often involve complex procedures, specialized equipment, and precise control of formulation parameters. However, industrial production requires scalable, reproducible, and cost-effective manufacturing processes. Variations in particle size distribution, coating thickness, drug loading efficiency, and surface characteristics may significantly influence therapeutic performance. Therefore, developing standardized manufacturing protocols and quality control strategies is essential for successful commercialization [14–16].

6.5 | Stability and Storage Issues

The long-term stability of nanoengineered coating systems remains another important challenge. Nanoparticles may undergo aggregation, structural changes, drug leakage, or degradation during storage. Environmental factors such as temperature, humidity, and light exposure can affect formulation stability. For oral delivery systems, stability during GI transit is equally important. The coating must remain intact during passage through unfavorable environments while maintaining its ability to release the drug at the intended site. Advanced stabilization strategies, including surface modification, lyophilization techniques, and optimized packaging systems, may improve the shelf-life and reliability of nano-coated formulations [17].

6.6 | Regulatory and Clinical Translation Barriers

Regulatory approval represents a significant challenge for nanoengineered drug delivery systems. Compared with conventional formulations, nanotechnology-based products require more extensive evaluation due to their complex physicochemical properties and potential biological interactions. Regulatory agencies require detailed characterization of nanoparticles, including particle size, morphology, surface chemistry, degradation behavior, toxicity profile, and pharmacokinetic performance. Additionally, establishing standardized guidelines for evaluating nano-coated drug delivery systems remains challenging due to the diversity of materials and preparation approaches. Close collaboration between researchers, pharmaceutical industries, and regulatory organizations will be necessary to accelerate clinical translation [14–16].

6.7 | Cost and Patient Accessibility

Although nanoengineered coatings provide advanced therapeutic advantages, their development and production may involve expensive materials and sophisticated technologies. High manufacturing costs may limit accessibility, particularly in developing healthcare systems. Therefore, future research should focus not only on improving therapeutic performance but also on developing economically feasible and scalable formulations. The use of naturally derived polymers, green synthesis approaches, and simplified manufacturing strategies may help reduce production costs [21].

6.8 | Need for Standardized Evaluation Methods

Another major challenge is the lack of standardized evaluation protocols for GI nano-coated systems. Different studies often use diverse experimental models, dissolution conditions, animal models, and characterization techniques, making direct comparison between formulations difficult. Establishing standardized in vitro and in vivo evaluation methods will improve understanding of formulation performance and support regulatory approval [23].

7 | Conclusion

Nanoengineered coating technologies have fundamentally transformed the landscape of GI drug delivery by providing innovative solutions to overcome the complex physiological and biochemical barriers of the GI tract. Unlike conventional oral formulations, which often suffer from premature drug degradation, poor bioavailability, nonspecific distribution, and limited therapeutic efficacy, nanoengineered coatings offer multifunctional capabilities that integrate drug protection, controlled release, site-specific targeting, and enhanced interaction with biological tissues. These advanced coating platforms have significantly expanded the possibilities for precision drug delivery, particularly in the treatment of chronic and localized GI diseases [12–14].

This review highlights the remarkable progress achieved in the design and development of diverse nanoengineered coating systems, including enteric, pH-responsive, enzyme-responsive, mucoadhesive, microbiota-responsive, stimuli-responsive, and multifunctional hybrid coatings. The combination of nanotechnology with advanced biomaterials has enabled the fabrication of intelligent delivery systems capable of responding to disease-specific microenvironments, thereby improving therapeutic efficacy while minimizing systemic toxicity. In addition, the continuous evolution of natural polymers, synthetic polymers, lipid-based materials, and hybrid nanocomposites has considerably broadened the design flexibility and functional performance of GI drug delivery systems. The therapeutic applications of these technologies extend across a broad spectrum of GI disorders, including IBD, colorectal cancer, gastric ulcers, Helicobacter pylori infection, celiac disease, and other inflammatory or microbiota-associated conditions. By improving local drug accumulation, prolonging GI residence time, enhancing epithelial penetration, and enabling controlled drug release, nanoengineered coatings have demonstrated substantial potential to address many of the limitations associated with existing oral therapies. These advances not only improve pharmacological efficacy but also offer opportunities to reduce dosing frequency, minimize adverse effects, and enhance patient adherence [13–16].

Despite these promising developments, several important challenges continue to impede the successful clinical translation of nanoengineered GI coatings. The complexity of GI physiology, interpatient variability, long-term nanomaterial safety, large-scale manufacturing, formulation reproducibility, regulatory standardization, and economic feasibility remain critical issues that require further investigation. Moreover, although numerous experimental studies have demonstrated encouraging preclinical outcomes, the number of clinically validated nano-coated GI drug delivery systems remains relatively limited. Bridging this translational gap will require greater integration of pharmaceutical sciences, biomaterials engineering, nanotechnology, clinical medicine, and regulatory science [15]. Looking forward, future research should move beyond the development of increasingly complex nanocarriers toward the rational design of clinically translatable systems that combine high therapeutic performance with simplicity, reproducibility, scalability, and regulatory compatibility. Emerging approaches such as multifunctional hybrid coatings, biomimetic nanomaterials, microbiota-responsive platforms, artificial intelligence-assisted formulation design, and personalized drug delivery strategies are expected to shape the next generation of GI therapeutics [16]. Furthermore, advances in computational modeling, organ-on-chip technologies, and patient-derived disease models may accelerate formulation optimization and improve the predictive accuracy of preclinical evaluations.

In conclusion, nanoengineered coatings represent one of the most promising frontiers in modern GI drug delivery [21–26]. Their unique ability to integrate multiple therapeutic functions within a single platform provides unprecedented opportunities for targeted, controlled, and patient-centered treatment strategies. Although significant scientific and translational challenges remain, continued interdisciplinary collaboration among researchers, clinicians, material scientists, and the pharmaceutical industry will undoubtedly accelerate the transition of these technologies from laboratory innovation to clinical practice. As the field continues to evolve, nanoengineered coatings are poised to play a pivotal role in the development of safer, more effective, and personalized therapies for GI diseases, ultimately contributing to improved clinical outcomes and a higher quality of life for patients worldwide.

Authors' Contributions

The author solely conducted the research and prepared the manuscript and has approved its final version.

Data Availability

The data are available from the corresponding author upon reasonable request.

Funding

This work was carried out without financial support from any public, commercial, or non-profit organizations.

Conflict of Interest

There are no competing interests to declare.

Consent for Publication

The author confirms consent for the publication of this work.

Ethics Approval and Consent to Participate

This article does not include experiments involving humans or animals.

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