International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	MODERN NANOTECHNOLOGY-BASED DRUG DELIVERY SYSTEMS FOR INFLAMMATORY BOWEL DISEASE TREATMENT: A COMPREHENSIVE REVIEW
DOI	https://doi.org/10.31435/ijitss.4(48).2025.4489
RECEIVED	02 October 2025
ACCEPTED	22 December 2025
PUBLISHED	30 December 2025
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

MODERN NANOTECHNOLOGY-BASED DRUG DELIVERY SYSTEMS FOR INFLAMMATORY BOWEL DISEASE TREATMENT: A COMPREHENSIVE REVIEW

Konrad Zieliński *(Corresponding Author, Email: konrad.zielinski222@gmail.com)*
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0005-3652-592X

Stanisław Jurkowski
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0005-9715-8385

Mikołaj Zalewski
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0002-7803-6145

Marianna Rudzińska
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0002-9622-7439

Karolina Ganczar
F. Chopin University Teaching Hospital, Rzeszów, Poland
ORCID ID: 0009-0003-8152-8076

Michał Mazurek
F. Chopin University Teaching Hospital, Rzeszów, Poland
ORCID ID: 0009-0005-7111-2397

Karolina Buć
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0000-8491-7200

Paweł Buć
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0001-1533-6610

Jagoda Józefczyk
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0007-5235-2074

Łukasz Krzystek
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0001-1988-0402

ABSTRACT

Background: Inflammatory bowel disease (IBD), principally comprising ulcerative colitis (UC) and Crohn's disease (CD), represents a growing global health burden characterized by chronic, relapsing inflammation of the gastrointestinal tract. The pathogenesis is multifactorial, involving genetic susceptibility, gut microbiota dysbiosis, and a dysregulated immune response. Current pharmacological strategies, including aminosalicylates, corticosteroids, immunomodulators, and biologics, are effective but often limited by non-specific distribution, low local bioavailability due to rapid gastrointestinal clearance, and severe systemic adverse effects such as immunosuppression and hepatotoxicity. Consequently, there is an urgent clinical need for novel therapeutic approaches that can deliver drugs precisely to the inflamed mucosa while minimizing systemic exposure. Nanotechnology has emerged as a transformative strategy to address these challenges by enabling targeted, controlled, and efficient drug delivery.

Objective: This narrative review aims to provide a comprehensive evaluation of the state-of-the-art nanotechnology-based drug delivery systems (DDSs) for IBD treatment. It critically analyzes specific targeting mechanisms-including passive accumulation via the epithelial enhanced permeability and retention (eEPR) effect, active receptor targeting, and stimuli-responsive release-and assesses the therapeutic efficacy of novel nanocarriers loading a wide range of bioactive agents.

Materials and Methods: A structured narrative review was conducted based on an extensive analysis of scientific literature published between 2015 and 2025. The review included original in vitro and in vivo studies focusing on organic (polymeric, lipid, hydrogel), inorganic (metallic, silica), and biomimetic nanocarriers. Data extraction prioritized physicochemical properties (size, charge), specific targeting ligands (e.g., hyaluronic acid, mannose, folate), and the modulation of key inflammatory pathways (NF-κB, ROS scavenging, cytokine production).

Results: The analysis revealed that nanoparticle-based systems significantly enhance drug accumulation in inflamed colonic tissues compared to free drugs. Passive targeting strategies leveraging the eEPR effect and charge-dependent mucoadhesion demonstrated improved retention times. Active targeting utilizing ligands for CD44 (hyaluronic acid), mannose receptors (CD206), and transferrin receptors facilitated superior cellular uptake by activated macrophages and epithelial cells. Innovative stimuli-responsive formulations, such as pH-sensitive liposomes, ROS-responsive nanozymes (e.g., cerium oxide, manganese-polyphenol), and enzyme-degradable polysaccharide carriers, provided precise release profiles triggered by the pathological microenvironment. These systems effectively restored the intestinal barrier, significantly reduced pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), and mitigated oxidative stress in murine colitis models. Furthermore, natural compounds like curcumin and resveratrol showed dramatically improved bioavailability and therapeutic potential when encapsulated in nanocarriers.

Conclusion: Nanotechnology-based DDSs represent a promising frontier in IBD therapy, offering a paradigm shift from systemic immunosuppression to precision local treatment. By maximizing local drug concentration and minimizing off-target effects, these systems address the fundamental limitations of current pharmacotherapy. While preclinical results are highly encouraging, further research focusing on long-term safety, scalable manufacturing, and rigorous clinical validation is essential to translate these innovations into standard clinical practice.

KEYWORDS

Inflammatory Bowel Disease, Nanotechnology, Targeted Drug Delivery, Nanoparticles, Ulcerative Colitis, Macrophage Polarization, ROS Scavenging, Immune Modulation

CITATION

Konrad Zieliński, Stanisław Jurkowski, Mikołaj Zalewski, Marianna Rudzińska, Karolina Ganczar, Michał Mazurek, Karolina Buć, Paweł Buć, Jagoda Józefczyk, Łukasz Krzystek. (2025) Modern Nanotechnology-Based Drug Delivery Systems for Inflammatory Bowel Disease Treatment: A Comprehensive Review. *International Journal of Innovative Technologies in Social Science*. 4(48). doi: 10.31435/ijitss.4(48).2025.4489

1. Introduction

Inflammatory bowel disease (IBD) represents a group of chronic, immune-mediated disorders of the gastrointestinal (GI) tract, primarily including ulcerative colitis (UC) and Crohn's disease (CD). The pathogenesis of IBD is multifactorial and not yet fully understood, involving complex interactions between genetic susceptibility (e.g., mutations in *NOD2*, *ATG16L1*), environmental factors (diet, smoking), gut microbiota dysbiosis, and a dysregulated mucosal immune response [1]. The global prevalence of IBD is rising, particularly in newly industrialized countries in Asia, Africa, and South America, posing a significant public health burden and economic cost due to the chronic nature of the disease and the need for lifelong treatment [1].

Current pharmacological management aims to induce and maintain clinical and endoscopic remission, prevent complications, and avoid surgical intervention. The standard therapeutic armamentarium includes 5-aminosalicylic acid (5-ASA) compounds, corticosteroids, thiopurine immunomodulators (e.g., azathioprine), and biological agents such as anti-TNF-α antibodies (infliximab, adalimumab) or anti-integrin agents (vedolizumab) [2, 3]. Despite their proven efficacy, these conventional treatments face significant pharmacokinetic and pharmacodynamic challenges. Oral administration often leads to premature drug absorption in the upper GI tract or degradation by gastric acid and digestive enzymes, resulting in sub-therapeutic concentrations at the colonic site of inflammation. Conversely, systemic administration (intravenous or subcutaneous) is associated with widespread biodistribution, leading to severe adverse effects, including opportunistic infections, osteoporosis, bone marrow suppression, and hepatotoxicity [3, 4].

To address these critical limitations, nanotechnology-based drug delivery systems (DDSs) have garnered substantial attention in recent years. Nanoparticles (NPs), typically ranging from 1 to 1000 nm in size, offer unique physicochemical properties that can be tailored for site-specific delivery. In the context of IBD, NPs can be designed to passively accumulate in inflamed tissues via the epithelial enhanced permeability and retention (eEPR) effect or actively target specific immune cells (e.g., macrophages) through receptor-ligand interactions [5, 6]. Furthermore, "smart" nanocarriers can respond to the specific microenvironment of the inflamed gut, such as altered pH, elevated levels of reactive oxygen species (ROS), or the presence of specific bacterial enzymes, to release their payload precisely where it is needed [5].

This narrative review aims to synthesize current evidence regarding the design, mechanisms, and therapeutic efficacy of various nanocarriers for IBD. It covers a broad spectrum of platforms, including polymeric nanoparticles, lipid-based carriers, inorganic nanoparticles, and hydrogel systems, loading a variety of therapeutic agents ranging from natural compounds to potent biologics.

2. MATERIALS AND METHODS

2.1 Search Strategy

This review was conducted following the principles of a structured narrative review. A comprehensive literature search was performed using electronic databases including PubMed, ScienceDirect, and Web of Science. The search strategy employed combinations of keywords and Medical Subject Headings (MeSH) terms such as: "Inflammatory bowel disease", "Nanoparticles", "Drug delivery systems", "Targeted therapy", "Ulcerative colitis", "Crohn's disease", "Macrophage targeting", "Curcumin", "Infliximab", "Selenium nanoparticles", "Nanozymes", and "Hydrogels". The search covered articles published up to the year 2025 to ensure the inclusion of the most recent advancements.

2.2 Eligibility Criteria

To ensure the relevance and quality of the review, the following criteria were applied:

Inclusion Criteria:

- Original research articles, systematic reviews, and meta-analyses investigating nanotechnology-based therapies for IBD (UC or CD).
- Articles describing specific targeting mechanisms, including passive (eEPR), active (ligand-receptor), and stimuli-responsive (pH, ROS, enzymes) strategies.
- Studies evaluating novel nanocarriers for small molecules (e.g., 5-ASA, corticosteroids), biologics (e.g., infliximab, gene therapy), or natural compounds (e.g., curcumin, resveratrol).
- Studies providing mechanistic insights into immune modulation, such as macrophage polarization or ROS scavenging.
- In vitro and in vivo studies published in English.

Exclusion Criteria:

- Studies not related to gastrointestinal inflammation or IBD.
- Articles without full-text availability.
- Non-scientific sources, editorials, and conference abstracts lacking sufficient methodological data.

2.3 Data Extraction

Data were systematically extracted from eligible studies regarding:

- **Nanocarrier characteristics:** Type (polymeric, lipid, inorganic, etc.), size, surface charge (zeta potential), and encapsulation efficiency.
- **Therapeutic agent:** The specific drug or bioactive compound loaded into the carrier.
- **Targeting mechanism:** The specific strategy employed to reach the inflamed tissue (e.g., pH-dependent coating, hyaluronic acid functionalization).
- **Experimental model:** The type of study (cell culture lines like Caco-2, RAW 264.7 or animal models like DSS-induced colitis).
- **Key outcomes:** Effects on mucosal healing, reduction of pro-inflammatory cytokines, histological scores, and barrier integrity restoration.

2.4 Data Synthesis

Due to the heterogeneity of the included studies-which utilized varying nanocarrier types, therapeutic agents, and disease models-a quantitative meta-analysis was not feasible. Instead, a narrative synthesis approach was used. Findings were grouped and analyzed according to the targeting strategy (passive vs. active) and the class of therapeutic agent delivered (natural compounds, biologics, inorganic agents), allowing for a comprehensive overview of the field.

3. RESULTS

3.1 Pathophysiological Barriers and Targeting Opportunities in IBD

The gastrointestinal tract in IBD presents specific physiological alterations that act as barriers to conventional therapy but also offer unique opportunities for targeted nanomedicine [1, 3].

- **Mucus Barrier Alterations:** In healthy states, the mucus layer protects the epithelium. In IBD, this layer can be disrupted or thickened with altered composition (e.g., changes in mucin glycosylation). Nanoparticles must be engineered to penetrate this layer to reach the underlying epithelium and immune cells. Strategies such as PEGylation (coating with polyethylene glycol) create "slippery" particles that can diffuse through the mucus mesh [3, 20].
- **pH Gradient Variations:** The physiological pH of the colon is typically 6.8–7.2. However, in patients with active colitis, the colonic pH can drop significantly to acidic levels (2.3–5.5) due to the production of lactic acid by bacteria and inflammatory processes. This variability necessitates robust pH-responsive systems that can prevent premature release in the stomach and small intestine while ensuring drug release in the inflamed colon [14, 15].
- **Immune Cell Infiltration:** The inflamed mucosa is characterized by massive infiltration of immune cells, particularly neutrophils and macrophages. These cells produce high levels of ROS and pro-inflammatory cytokines (TNF-α, IL-6, IL-1β), sustaining the inflammation. This accumulation provides a cellular target for nanotherapeutics [1, 7].

3.2 Passive and Environmental Targeting Strategies

Epithelial Enhanced Permeability and Retention (eEPR): Analogous to the EPR effect in tumors, the inflamed intestinal mucosa exhibits increased vascular permeability and disruption of the epithelial barrier. This allows nanoparticles to passively accumulate in the interstitial space of inflamed tissues. Studies indicate that particle size is a critical determinant; nanoparticles <200 nm tend to have higher translocation rates into the mucosa, while larger particles (~600 nm) may adhere to the apical surface, providing a local depot effect [3, 5].

Charge-Dependent Targeting: Surface charge significantly influences biodistribution and mucoadhesion. Cationic nanoparticles can adhere to the negatively charged intestinal mucus via electrostatic interactions, prolonging residence time. Conversely, anionic nanoparticles can target positively charged proteins (such as transferrin and bactericidal/permeability-increasing protein) that accumulate specifically at inflammation sites, thereby minimizing non-specific binding to healthy tissue [3, 6].

Stimuli-Responsive Systems:

- **pH-Responsive:** Utilizing the pH differential in the GI tract, polymers like Eudragit® S100 (dissolves at pH > 7.0) or modified chitosan are used to encapsulate drugs. This prevents drug release in the acidic stomach and triggers release in the neutral to slightly alkaline environment of the colon [14, 15].
- **ROS-Responsive:** The inflamed gut generates excessive Reactive Oxygen Species (ROS), leading to oxidative stress. Nanocarriers incorporating ROS-sensitive linkers (e.g., thioketal bonds) or antioxidant materials (e.g., cerium oxide, manganese dioxide) can release drugs specifically at sites of high oxidative stress while simultaneously acting as ROS scavengers [10, 16, 18].
- **Enzyme-Responsive:** Colonic bacteria produce specific enzymes (e.g., azoreductase, polysaccharidases like pectinase) that are distinct from those in the upper GI tract. Polysaccharide-based nanocarriers (e.g., chitosan, alginate, pectin) can be specifically degraded by these enzymes, triggering drug release precisely in the colon [7, 13].

3.3 Active Targeting Strategies

To further enhance specificity and cellular uptake, nanoparticles are functionalized with ligands that bind to receptors overexpressed in IBD tissues.

CD44 Receptor Targeting: The CD44 receptor is highly overexpressed on the surface of activated macrophages and epithelial cells in inflamed tissues. Hyaluronic acid (HA), a natural ligand for CD44, has been extensively used to coat nanoparticles. Studies have shown that HA-functionalized nanoparticles loaded with drugs like magnolol or the anti-inflammatory tripeptide KPV significantly enhance cellular uptake via receptor-mediated endocytosis and improve therapeutic efficacy compared to non-targeted controls [4, 12, 19].

Mannose Receptor (CD206) Targeting: The mannose receptor is abundant on macrophages, particularly those of the M2 phenotype (anti-inflammatory). However, targeting these receptors can also facilitate uptake into M1 (pro-inflammatory) macrophages for reprogramming. Mannose-modified nanocarriers (e.g., mannosylated selenium nanoparticles) have been successfully used to deliver agents that promote macrophage repolarization from the pro-inflammatory M1 to the tissue-repairing M2 phenotype, thereby restoring immune homeostasis [8, 11].

Other Molecular Targets: Other receptors investigated for active targeting include the transferrin receptor (TfR), which is upregulated in inflamed enterocytes, the folate receptor (FR), and peptide transporter 1 (PepT1). Targeting these pathways can facilitate transcytosis across the epithelial barrier [4].

3.4 Therapeutic Applications: Specific Agents and Carriers

Natural Compounds:

- **Curcumin:** Despite its potent anti-inflammatory properties, curcumin suffers from poor aqueous solubility and rapid metabolism. Nanoparticulate formulations (polymeric NPs, micelles, liposomes) significantly improve its stability and bioavailability. Studies confirm that these systems effectively reduce TNF-α, IL-1β, and IL-6 levels, prevent body weight loss, and improve histological scores in DSS-induced colitis models [21, 22].
- **Resveratrol:** Nano-delivery systems for resveratrol have been shown to protect the compound from rapid metabolism and enhance its antioxidant effects in the colon. Resveratrol-loaded nanocarriers effectively downregulate the NF-κB signaling pathway and modulate gut microbiota composition [23].
- **Magnolol:** HA-functionalized magnolol nanoparticles have demonstrated superior capabilities in promoting mucosal healing and inhibiting the TLR4/NF-κB signaling pathway, offering a potent natural alternative to synthetic drugs [19].

Biologics and Immunosuppressants:

- **Oral Infliximab:** Delivering monoclonal antibodies orally is challenging due to gastric degradation. New lipid-polymeric nanocarriers (e.g., PLGA-PEG) encapsulate and protect infliximab, allowing for local release in the colon. These systems have shown enhanced accumulation at the inflamed barrier, accelerating healing and reducing systemic exposure compared to standard intravenous administration [24].
- **Tacrolimus:** Tacrolimus is a potent immunosuppressant with significant nephrotoxicity. pH-responsive polymeric nanoparticles loaded with tacrolimus have effectively reduced systemic toxicity while maintaining high therapeutic drug levels in the colonic tissue [14, 15].

Inorganic and Hybrid Systems:

- **Selenium Nanoparticles (SeNPs):** SeNPs exhibit intrinsic immunomodulatory and antioxidant properties. When functionalized (e.g., with mannose or polysaccharides), they not only scavenge ROS but also actively modulate macrophage polarization (promoting M2 phenotype), offering a dual therapeutic mechanism that addresses both inflammation and oxidative stress [11, 25].
- **Nanozymes:** Novel manganese-polyphenol coordination nanoparticles and copper-tannic acid nanozymes act as mimics of natural antioxidant enzymes like superoxide dismutase (SOD) and catalase (CAT). These nanozymes efficiently eliminate excess ROS, protecting the intestinal barrier from oxidative damage and reducing inflammation [16, 17].
- **Yeast-Inspired Systems:** A novel yeast-cell-wall-encapsulated nanocomposite has demonstrated the ability to survive the harsh GI environment and target macrophages, effectively scavenging ROS and restoring gut immune homeostasis [18].

4. Discussion

The synthesis of recent literature confirms that nanotechnology-based therapies offer significant advantages over conventional IBD treatments. The fundamental shift from systemic immunosuppression to targeted, local treatment represents a major advancement in patient safety and therapeutic efficacy.

Mechanistic Advantages of Nanomedicine: The superiority of nanomedicines lies in their ability to perform multiple functions simultaneously ("theranostics" or multifunctional carriers). Unlike free drugs, nanoparticles can:

1. **Protect the payload:** Prevent degradation of sensitive biologics (antibodies, peptides) and natural compounds in the stomach.
2. **Target specific cells:** Selectively deliver drugs to activated macrophages or epithelial cells via CD44 or mannose receptors, sparing healthy tissue.
3. **Exert intrinsic therapeutic effects:** Inorganic nanoparticles like cerium oxide or selenium act as antioxidants themselves, scavenging ROS and reducing oxidative stress independently of the loaded drug.
4. **Modulate the immune system:** Nanocarriers can actively induce macrophage reprogramming (M1 to M2 transition), addressing the root cause of chronic inflammation [7, 11, 25].

Synergistic Therapies: Combination therapies delivered via nanocarriers are particularly promising. Systems co-delivering antioxidants (like nanozymes or selenium) with anti-inflammatory drugs (like thalidomide, sulfasalazine, or curcumin) show synergistic effects, tackling both oxidative stress and immune dysregulation simultaneously [10, 16]. Furthermore, the integration of natural polymers (chitosan, alginate) and protein-based carriers (albumin, silk fibroin) enhances biocompatibility and biodegradability, which is crucial for chronic therapy [8, 13, 22]. Additionally, the use of hydrogels as platforms for nanoparticle delivery adds an extra layer of control, allowing for prolonged adhesion to the mucosa and sustained drug release over time [9].

Clinical Implications and Future Directions: While most studies are currently preclinical, the data strongly suggest that oral nanomedicines could replace injectable biologics or high-dose systemic steroids in the future management of IBD. This would drastically improve patient compliance and quality of life. The use of "food-derived" or natural materials (anthocyanins, polysaccharides, yeast cell walls) also suggests a path toward safer, more biocompatible formulations that could be used as dietary supplements or medical foods [6, 13, 22].

5. Limitations

Despite the promising results, several limitations must be acknowledged. First, the majority of data comes from murine models (e.g., DSS-induced colitis), which, while useful, do not perfectly mimic the chronic, relapsing, and spontaneous nature of human IBD. Second, the scale-up of manufacturing for complex, multi-functional nanocarriers remains a technical hurdle. Third, the long-term nanotoxicology and potential accumulation of inorganic particles (like gold, silica, or metallic nanozymes) in the body require rigorous safety assessments before clinical trials can proceed. Finally, the heterogeneity of IBD patients means that a "one-size-fits-all" nanocarrier may not be effective for everyone, necessitating personalized approaches based on individual disease biomarkers.

6. Conclusions

The comprehensive analysis of recent literature underscores that nanotechnology represents a pivotal advancement in the management of Inflammatory Bowel Disease. By exploiting the unique pathophysiological alterations characteristic of the inflamed gut-including the epithelial enhanced permeability and retention (eEPR) effect, distinct pH gradients, overproduction of reactive oxygen species (ROS), and overexpression of specific receptors-nanocarriers offer a highly sophisticated approach to drug delivery.

The superiority of nanomedicines over conventional therapies is evident in several key areas. Firstly, they provide enhanced bioavailability and stability for therapeutic agents that are otherwise labile or poorly soluble, such as curcumin, resveratrol, and peptide drugs. Secondly, active targeting strategies utilizing ligands like hyaluronic acid, mannose, and antibodies allow for the selective delivery of drugs to key effector cells, specifically activated macrophages and inflamed epithelial cells. This precise targeting not only maximizes therapeutic efficacy at the site of disease but also drastically reduces the risk of systemic toxicity associated with potent immunosuppressants and corticosteroids.

Furthermore, the emergence of multifunctional and "theranostic" systems marks a significant evolution in the field. Inorganic nanoparticles, such as selenium and cerium oxide nanozymes, do not merely serve as inert vehicles but possess intrinsic antioxidant and immunomodulatory properties. These systems are capable of scavenging excess ROS and reprogramming macrophages from a pro-inflammatory (M1) to an anti-inflammatory (M2) phenotype, thereby addressing the root causes of chronic inflammation and promoting mucosal healing synergistically with the loaded drug.

Despite the robust preclinical evidence supporting the efficacy of these systems in murine models, several hurdles remain before clinical translation can be realized. The complexity of large-scale manufacturing, the need for precise characterization of batch-to-batch variability, and the lack of long-term toxicological data on nanomaterial accumulation in the human body are critical challenges. Moreover, the heterogeneity of IBD patients suggests that a "one-size-fits-all" nanocarrier may not be feasible, highlighting the need for personalized nanomedicine approaches based on individual disease biomarkers.

In summary, nanotechnology holds the potential to revolutionize IBD therapy by providing safer, more effective, and patient-friendly treatment options. Future research efforts must now pivot towards bridging the gap between bench and bedside, with a strong emphasis on regulatory compliance, safety assessments, and the design of clinical trials to validate these promising technologies in human patients.

Disclosure

Author's contributions:

Conceptualization: Konrad Zieliński, Mikołaj Zalewski
Methodology: Karolina Buć, Michał Mazurek
Software: Konrad Zieliński, Jagoda Józefczyk
Check: Paweł Buć, Łukasz Krzystek
Formal Analysis: Karolina Ganczar, Marianna Rudzińska
Investigation: Konrad Zieliński, Mikołaj Zalewski
Resources: Michał Mazurek, Karolina Buć, Jagoda Józefczyk
Data curation: Paweł Buć, Łukasz Krzystek
Writing - Original draft: Karolina Ganczar, Marianna Rudzińska
Writing - Review & editing: Stanisław Jurkowski, Mikołaj Zalewski
Visualization: Stanisław Jurkowski, Michał Mazurek
Supervision: Karolina Buć, Jagoda Józefczyk
Project administration: Paweł Buć, Łukasz Krzystek
All authors have read and agreed with the published version of the manuscript.

Funding Statement: Not applicable.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: Not applicable.

Conflict of Interest Statement: The authors have declared no conflicts of interest.

Declaration of the use of generative AI and AI-assisted technologies in the writing process: In preparing this work, the authors used Google Gemini for the purpose of improving language and readability. After using this tool, the authors have reviewed and edited the content as needed.

REFERENCES

1. Guan Q. (2019). A Comprehensive Review and Update on the Pathogenesis of Inflammatory Bowel Disease. Journal of immunology research, 2019, 7247238. https://doi.org/10.1155/2019/7247238
2. Raine, T., Bonovas, S., Burisch, J., Kucharzik, T., Adamina, M., Annese, V., Bachmann, O., Bettenworth, D., Chaparro, M., Czuber-Dochan, W., Eder, P., Ellul, P., Fidalgo, C., Fiorino, G., Gionchetti, P., Gisbert, J. P., Gordon, H., Hedin, C., Holubar, S., Iacucci, M., … Doherty, G. (2022). ECCO Guidelines on Therapeutics in Ulcerative Colitis: Medical Treatment. Journal of Crohn's & colitis, 16(1), 2–17. https://doi.org/10.1093/ecco-jcc/jjab178
3. Hua, S., Marks, E., Schneider, J. J., & Keely, S. (2015). Advances in oral nano-delivery systems for colon targeted drug delivery in inflammatory bowel disease: selective targeting to diseased versus healthy tissue. Nanomedicine : nanotechnology, biology, and medicine, 11(5), 1117–1132. https://doi.org/10.1016/j.nano.2015.02.018
4. Liu, P., Gao, C., Chen, H., Vong, C. T., Wu, X., Tang, X., Wang, S., & Wang, Y. (2021). Receptor-mediated targeted drug delivery systems for treatment of inflammatory bowel disease: Opportunities and emerging strategies. Acta pharmaceutica Sinica. B, 11(9), 2798–2818. https://doi.org/10.1016/j.apsb.2020.11.003
5. Gao, J., Li, J., Luo, Z., Wang, H., & Ma, Z. (2024). Nanoparticle-Based Drug Delivery Systems for Inflammatory Bowel Disease Treatment. Drug design, development and therapy, 18, 2921–2949. https://doi.org/10.2147/DDDT.S461977
6. Lin, Z., Zhao, Z., Lin, X., Yang, Z., Wang, L., Xi, R., & Long, D. (2025). Advances in oral treatment of inflammatory bowel disease using protein-based nanoparticle drug delivery systems. Drug delivery, 32(1), 2544689. https://doi.org/10.1080/10717544.2025.2544689
7. Cui, M., Zhang, M., & Liu, K. (2021). Colon-targeted drug delivery of polysaccharide-based nanocarriers for synergistic treatment of inflammatory bowel disease: A review. Carbohydrate polymers, 272, 118530. https://doi.org/10.1016/j.carbpol.2021.118530
8. Liu, H., Lv, H., Duan, X., Du, Y., Tang, Y., & Xu, W. (2023). Advancements in Macrophage-Targeted Drug Delivery for Effective Disease Management. International journal of nanomedicine, 18, 6915–6940. https://doi.org/10.2147/IJN.S430877
9. Liu, Y., Huang, J., Li, S., Li, Z., Chen, C., Qu, G., Chen, K., Teng, Y., Ma, R., Wu, X., & Ren, J. (2024). Advancements in hydrogel-based drug delivery systems for the treatment of inflammatory bowel disease: a review. Biomaterials science, 12(4), 837–862. https://doi.org/10.1039/d3bm01645e
10. Wang, D., Jiang, Q., Shen, R. et al. ROS-responsive nanoparticles targeting inflamed colon for synergistic therapy of inflammatory bowel disease via barrier repair and anti-inflammation. Nano Res. 17, 5409–5423 (2024). https://doi.org/10.1007/s12274-024-6435-6
11. Yang, H., Wang, Z., Li, L., Wang, X., Wei, X., Gou, S., Ding, Z., Cai, Z., Ling, Q., Hoffmann, P. R., He, J., Liu, F., & Huang, Z. (2024). Mannose coated selenium nanoparticles normalize intestinal homeostasis in mice and mitigate colitis by inhibiting NF-κB activation and enhancing glutathione peroxidase expression. Journal of nanobiotechnology, 22(1), 613. https://doi.org/10.1186/s12951-024-02861-2
12. Xiao, B., Xu, Z., Viennois, E., Zhang, Y., Zhang, Z., Zhang, M., Han, M. K., Kang, Y., & Merlin, D. (2017). Orally Targeted Delivery of Tripeptide KPV via Hyaluronic Acid-Functionalized Nanoparticles Efficiently Alleviates Ulcerative Colitis. Molecular therapy : the journal of the American Society of Gene Therapy, 25(7), 1628–1640. https://doi.org/10.1016/j.ymthe.2016.11.020
13. Basak, A., Ghosh, S., Ganguly, D., Garain, S., Ghosh, R., Choudhury, A., Deka, H., & Sarmah, J. (2023). Current Trends and Future Perspectives of Natural Polymer Loaded Nanoparticle Based Drug Delivery System for the Management of Inflammatory Bowel Disease. Journal of Applied Pharmaceutical Research, 11(4), 1–9. https://doi.org/10.18231/j.joapr.2023.11.4.1.9
14. Altaf, S., Zeeshan, M., Ali, H., Zeb, A., Afzal, I., Imran, A., Mazhar, D., Khan, S., & Shah, F. A. (2024). pH-Sensitive Tacrolimus loaded nanostructured lipid carriers for the treatment of inflammatory bowel disease. European journal of pharmaceutics and biopharmaceutics : official journal of Arbeitsgemeinschaft fur Pharmazeutische Verfahrenstechnik e.V, 204, 114461. https://doi.org/10.1016/j.ejpb.2024.114461
15. Cai, X., Wang, X., He, M., Wang, Y., Lan, M., Zhao, Y., & Gao, F. (2021). Colon-targeted delivery of tacrolimus using pH-responsive polymeric nanoparticles for murine colitis therapy. International journal of pharmaceutics, 606, 120836. https://doi.org/10.1016/j.ijpharm.2021.120836
16. Yan, J. H., Liang, C. X., Ma, R. R., Li, B. J., Chen, Q. W., Li, W., Zeng, X., & Zhang, X. Z. (2025). Sulfasalazine-Loaded Copper-Tannic Acid Coordination Nanozyme Enables ROS Scavenging and Immunomodulation for Inflammatory Bowel Disease Therapy. Advanced healthcare materials, 14(26), e2403738. https://doi.org/10.1002/adhm.202403738
17. Dong, L., Wang, W., Zheng, H., Sun, Y., & Han, S. (2025). Construction of Mn2+-Polyphenol Nanoparticles and Its Application in the Treatment of Ulcerative Colitis. ACS applied bio materials, 8(5), 4367–4382. https://doi.org/10.1021/acsabm.5c00471

18. Zhang, X., Yang, H., He, Y., Zhang, D., Lu, G., Ren, M., Lyu, Y., Yuan, Z., & He, S. (2025). Yeast-Inspired Orally-Administered Nanocomposite Scavenges Oxidative Stress and Restores Gut Immune Homeostasis for Inflammatory Bowel Disease Treatment. ACS nano, 19(7), 7350–7369. https://doi.org/10.1021/acsnano.4c18099
19. Li, Y., Chen, T., Chen, L., Wu, D., & Hu, J. (2024). Construction of hyaluronic acid-functionalized magnolol nanoparticles for ulcerative colitis treatment. International journal of biological macromolecules, 268(Pt 2), 131920. https://doi.org/10.1016/j.ijbiomac.2024.131920
20. Li, Q., Lin, L., Zhang, C., Zhang, H., Ma, Y., Qian, H., Chen, X. L., & Wang, X. (2024). The progression of inorganic nanoparticles and natural products for inflammatory bowel disease. Journal of nanobiotechnology, 22(1), 17. https://doi.org/10.1186/s12951-023-02246-x
21. Meng, Z. W., Chang, B., & Sang, L. X. (2024). Use of curcumin and its nanopreparations in the treatment of inflammatory bowel disease. World journal of gastroenterology, 30(3), 280–282. https://doi.org/10.3748/wjg.v30.i3.280
22. Zhao X, Su W, Zhang X, Tan M. Visual foodborne nanoparticles for oral site-specific delivery of anthocyanins in the treatment of inflammatory bowel disease. Materials today Nano. 2023;24:100431. https://doi.org/10.1016/j.mtnano.2023.100431
23. Gowd, V., Kanika, Jori, C., Chaudhary, A. A., Rudayni, H. A., Rashid, S., & Khan, R. (2022). Resveratrol and resveratrol nano-delivery systems in the treatment of inflammatory bowel disease. The Journal of nutritional biochemistry, 109, 109101. https://doi.org/10.1016/j.jnutbio.2022.109101
24. Mohan, L. J., Daly, J. S., Ryan, B. M., & Ramtoola, Z. (2023). Oral infliximab nanomedicines for targeted treatment of inflammatory bowel diseases. European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences, 183, 106379. https://doi.org/10.1016/j.ejps.2023.106379
25. Chen, G., Yang, F., Fan, S., Jin, H., Liao, K., Li, X., Liu, G. B., Liang, J., Zhang, J., Xu, J. F., & Pi, J. (2022). Immunomodulatory roles of selenium nanoparticles: Novel arts for potential immunotherapy strategy development. Frontiers in immunology, 13, 956181. https://doi.org/10.3389/fimmu.2022.956181